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DIENE SYNTHESIS WITH DIENOPHILES CONTAINING HETERO-ATOMS

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I. INTRODUCTION

Diene synthesis consists in the addition of a double or triple bond in a compound termed the dienophile to conjugated dienes having a *cis* arrangement of their double bonds, addition occurring at the 1,4 positions to form a six-membered ring[1-8].

The dieneophiles used comprise compounds containing an ethylenic and acetylenic bond, azo-compounds, nitroso--compounds, *N*-sulphinylamines and *N*-sulphinylamides, carbonyl and thiocarbonyl compounds, nitriles, azomethines, imidoyl chlorides, and quaternary immonium salts.

Study of the reactions of 1,3-dienes with dienophiles of different structures has shown that conjugation of the double or triple bond of the dienophile with electron-acceptor groups enhances, while conjugation of the multiple bond of the dienophile with electron-donor substituents diminishes the reactivity of the dienophile. On the other hand, electron-donor substituents enhance, while electron-acceptor substituents diminish the reactivity of the diene. Consequently dienophiles are electrophilic, and dienes nucleophilic, reagents[2,5-11].

The cause of the enhanced reactivity of dienophiles in which multiple bonds are conjugated with electron-acceptor groups is not the displacement of electrons in the same direction in the dienophile molecules, but a decrease in electron density on their multiple bonds. Investigations have shown that the reactivity of dienes and dienophiles depends also on their geometrical configuration[2,7-9,11,12].

The stereochemical and structural orientation of diene synthesis is of great interest[2,5,8,12]. It has been established that the position of the substituents with respect to the ring in the Diels–Alder adducts is the same as it had

been relative to the double bond in the dienophile. Hence *cis* addition takes place with respect to the dienophile. This also occurs with respect to the diene, as is indicated by the cyclic structure of the adducts. Finally, reaction can take place sterically in two ways, substituents in the dienophile being located in the adduct either on the same side as the cyclic double bond (*endo* position) or on the opposite side from the double bond (*exo* position). The *endo* adducts are usually formed.

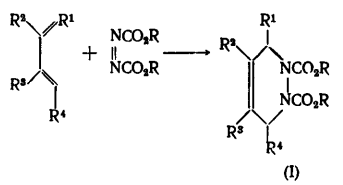
Structural isomers can be formed when 1- and 2-substituted dienes condense with unsymmetrical dienophiles. A vast amount of information has accumulated on the structural orientation of diene synthesis. Experiments have shown that it is affected by steric and polarisation factors. In several cases, however, it has been found that these factors do not determine the reaction sequence [2,7,12,13].

The steric and structural direction of diene condensations is obviously governed by the geometrical configuration of the transition state. However, there is at present no generally accepted view of the mechanism of diene synthesis, and its steric and structural orientation have not yet received a satisfactory theoretical explanation [7,12-18].

The present paper deals with diene syntheses involving dienophiles containing hetero-atoms. The literature published up to 1st March 1964 has been covered.

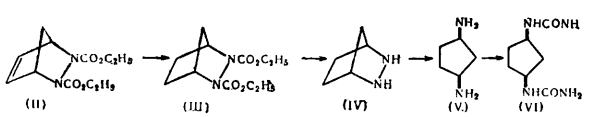
II. DIENE SYNTHESIS WITH AZO-COMPOUNDS

In 1925 Diels found [19,20] that azodicarboxylic esters† add on to conjugated dienes at the 1,4 positions to form dialkyl 1,2,3,6-tetrahydropyridazine-1,2-dicarboxylates (I):



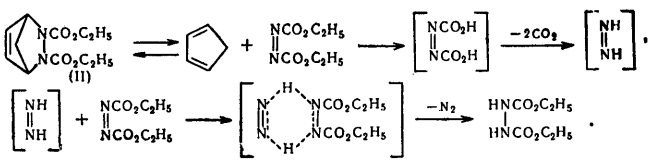
(I)

Diels obtained the adduct (II) by the interaction of diethyl azodicarboxylate with cyclopentadiene. The reaction took place in ethereal solution and was accompanied by the evolution of much heat, the adduct being obtained in high yields (90–95%). Diels established the structure of the adduct (II) by reducing it catalytically to the dihydro--derivative (III), saponification of which with alcoholic alkali gave the hydrazo-compound (IV). This was reduced with tin and hydrochloric acid to cyclopentane-*cis*-1,3-diamine (V), which was identified by conversion into the *cis*-1,3-diureido-derivative (VI), obtained by an alternative synthesis from cyclopentane-*cis*-1,3-dicarboxylic anhydride *via* the dimethyl ester, the dihydrazide, the diazide of the acid, the diurethane, and the diamine.

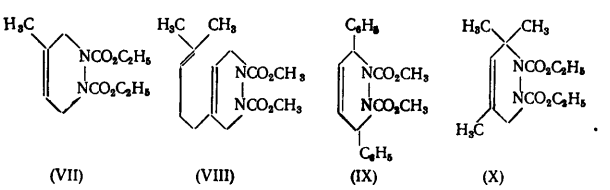


(II) (III) (IV) (V) (VI)

Stille has recently found [23] that hydrolysis of the adduct (II) with 10% hydrochloric acid yields hydrazodicarboxylic ester, the reaction probably involving the stages — (1) breakdown of the adduct into its original components, (2) partial hydrolysis of the azodicarboxylic ester to the acid, (3) decarboxylation of this acid to form reactive diimide, and (4) reduction by the diimide of the unhydrolysed portion of the azodicarboxylic ester, by a cyclic mechanism, to give the hydrazodicarboxylic ester:

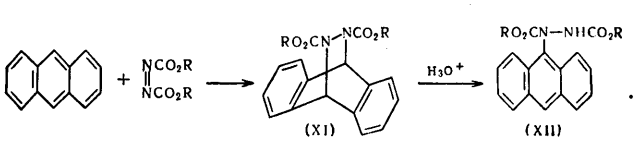


Diels obtained the adduct (VII) by reaction of diethyl azodicarboxylate with isoprene; the adducts (VIII) and (IX) were formed on reaction of dimethyl azodicarboxylate with myrcene [7-methyl-3-methyleneocta-1,6-diene] and with *trans*-1,*trans*-4-diphenylbutadiene. Diels assigned the structure of a 1,4 adduct (X) to the product obtained from diethyl azodicarboxylate and 2,4-dimethylpentadiene.



(VII) (VIII) (IX) (X)

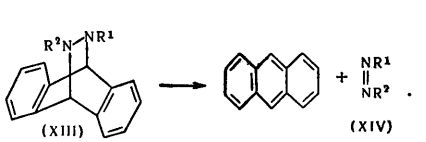
In 1938 Diels showed [24] azodicarboxylic esters react with anthracene in boiling toluene to form adducts (XI). In acid medium these adducts undergo isomerisation to form products, the structure of which was established by Alder [25] in 1954 as (XII).



(XI) (XII)

(*a*) R=CH_3; (*b*) R=C_2H_5.

In 1962 Corey and Mock found [26] that hydrolysis of the adduct (XI*b*) with alcoholic alkali at 25° yields 9,10-hydrazo-9,10-dihydroanthracene (XIII*a*), which on being heated dissociates into anthracene and diimide (XIV*a*). The compound (XIII*a*) has been used for the stereospecific reduction of double bonds. Thus deuteration of maleic and fumaric acids by means of the (XIII*a*)–deuterium oxide–dioxan system at 85° gave respectively *meso*- and (±)-2,3-dideuterosuccinic acid, in conformity with results of the diimide reduction of double bonds with other reducing systems [27-29].



(XIII) (XIV)

(*a*) $R^1=R^2=H$; (*b*) $R^1=H$, $R^2=CO_2C_2H_5$; (*c*) $R^1=CN$, $R^2=CO_2C_2H_5$.

In 1963 Harley-Mason reported [30] that on alkaline saponification of the adduct (XI*b*) the monodecarboxylated compound (XIII*b*) was formed as well as hydrazodihydroanthracene (XIII*a*). With cyanogen bromide, (XIII*b*) gave the

† For the *cis-trans* configuration of azodicarboxylic esters, see Refs. 21 and 22.

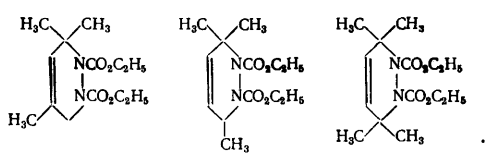
N-cyano-derivative (XIII*c*), which on being heated in a vacuum decomposed into anthracene and the cyano-ester (XIV*c*). This last compound proved to be an extremely reactive dienophile, adding on readily to anthracene to form the adduct (XIII*c*), and reacting with 1,4-diphenylbutadiene with the evolution of heat.

The reaction of azodicarboxylic esters with 1,3-dienes, discovered by Diels and leading to the formation of "diene" adducts (I), has been investigated by several workers. Adducts have been obtained from azodicarboxylic esters with butadiene[25,31-37], isoprene[32,33,35], pentadiene[32,33,35], 2,3-dimethylbutadiene[32,33,35,38], hexa-2,4-diene[32,33,35,39], 2-methylpentadiene[31], 3-methylpentadiene[35], 1-methoxybutadiene[40], 2-chlorobutadiene[40], cyclopentadiene[31,34,41-44], cyclohexadiene[39,45,46], 1,1′-bi(cyclopentenyl)[35], 1,1′-bi(cyclohexenyl)[47], 1-arylbutadienes[33,48-50], 1-phenylpentadiene[33,51], 1,4-diphenylbutadiene[25,31,33,49,51,52], anthracene[31], 2-chloroanthracene[53], ethyl sorbate[38], furan[34,54], 2-methylfuran[54], furfurylidene diacetate[25], 2,3-benzacridine[55], 5,6-dimethylenebicyclo[2,2,1]hept-2-ene[47], bicyclo[4,2,0]octa-2,4-diene[56], and 1-8-octamethylbicyclo[4,2,0]octa-2,4,7-triene.[57,58]

Rodgman and Wright[41] made a kinetic study of the reaction between azodicarboxylic esters and cyclopentadiene, and found it to be of the second order overall and the first order with respect to each reactant.

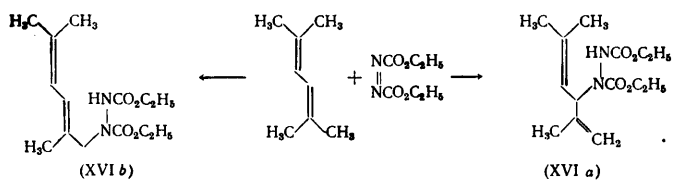
It has recently been found that, if the 1,4 positions in dienes are strongly substituted, reaction with azodicarboxylic ester takes place by a mechanism not of diene synthesis but of substitutive addition.

In 1957 Levina and her collaborators[35] obtained addition products from azodicarboxylic ester with 2,4-dimethylpentadiene, 2-methylhexa-2,4-diene, and 2,5-dimethylhexa-2,4-diene, and ascribed to them the formulae (X), (XV*a*), and (XV*b*).



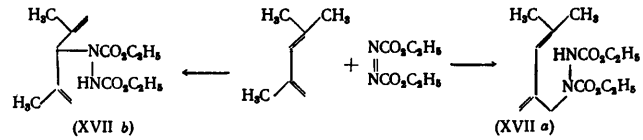
(X) (XV*a*) (XV*b*)

It was later found[59] that the reaction of these dienes with azodicarboxylic ester involves substitutive addition with the formation of monosubstituted derivatives of hydrazodicarboxylic ester. In 1962 Gillis and Beck[38] established that interaction between azodicarboxylic ester and 2,5-dimethylhexa-2,4-diene involves 85% of indirect substitutive addition with formation of the adduct (XVI*a*) and 15% of direct substitutive addition with formation of the adduct (XVI*b*):



(XVI *b*) (XVI *a*)

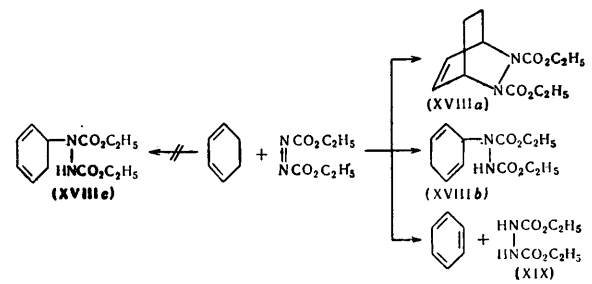
It was further shown[47] that azodicarboxylic ester adds on to 2,4-dimethylpentadiene by indirect substitutive addition to form isomeric adducts (XVII*a*) and (XVII*b*) in the proportions 4 : 1:



(XVII *b*) (XVII *a*)

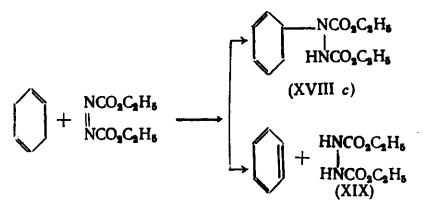
It has recently been found that cyclohexadiene and cycloheptatriene undergo substitutive addition with azodicarboxylic ester.

As early as 1935 Pirsch[45] described the synthesis of the adduct (XVIII*a*) from cyclohexadiene and azodicarboxylic ester. In 1962 Cohen[39] repeated this synthesis, and found that the product of the reaction comprised a mixture of the 1,4 adduct (XVIII*a*), a product of direct substitutive addition (XVIII*c*), and hydrazodicarboxylic ester. A little later it was found[38,60] that these reactants undergo indirect substitutive addition to form the adduct (XVIII*b*). Detailed investigation of the products has shown[46] that the reaction involves 80% of indirect substitutive addition to form (XVIII*b*), 5–15% of diene synthesis yielding (XVIII*a*), and 15–5% of oxidation–reduction with the formation of benzene and hydrazodicarboxylic ester (XIX):



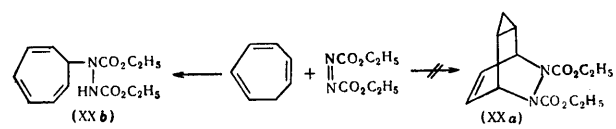
(XVIII *c*) (XVIII *a*) (XVIII *b*) (XIX)

It has been found that cyclohexa-1,4-diene, too, reacts with azodicarboxylic ester in two ways, to form the adduct (XVIII*c*), and benzene and hydrazodicarboxylic ester (XIX)[46,60]:



(XVIII *c*) (XIX)

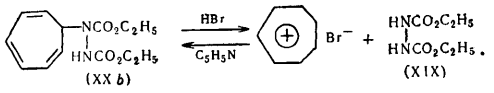
In 1961 Cinnamon and Weiss[61] investigated the reaction between azodicarboxylic ester and cycloheptatriene. This hydrocarbon does not usually react with dienophiles as such, but first passes into bicyclo[4,1,0]hepta-2,4-diene by an intramolecular Diels–Alder reaction[62-66]. It was therefore expected that an addition product of azodicarboxylic ester and bicycloheptadiene (XX*a*) would be formed. Examination of the ultraviolet and infrared spectra of the adduct, however, showed it to be a 7-substituted cycloheptatriene (XX*b*)‡:



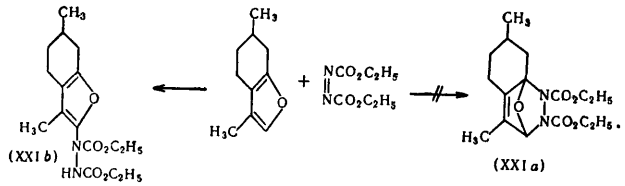
(XX *b*) (XX *a*)

‡ Schenck[67] has found that the adduct (XX*b*) is also formed by the photochemical condensation of cycloheptatriene with azodicarboxylic ester.

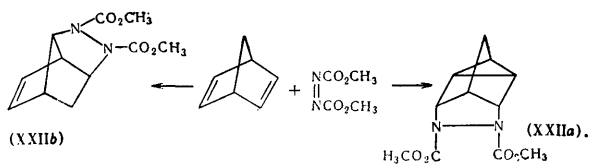
The action of hydrogen bromide on an ethereal solution of the adduct (XX*b*) gave tropylium bromide and hydrazodicarboxylic ester (XIX); these products interact in the presence of pyridine to yield the adduct (XX*b*) again:



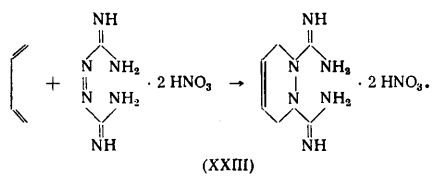
In 1960 Häring[68] and Treibs[69] obtained from methofuran and azodicarboxylic ester an adduct for which the structural formulae (XXI*a*) and (XXI*b*) were possible. Examination of its ultraviolet and infrared spectra showed[69] that its structure was represented by (XXI*b*):



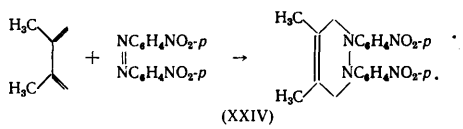
In 1962 Cristol[70] found that dimethyl azodicarboxylate reacts at 150–160° with bicyclo[2,2,1]hepta-2,5-diene to form two crystalline 1 : 1 adducts melting at 60° and 110°. The latter product was regarded as a 2,6 adduct (XXII*a*) on the basis of an examination of the infrared and nuclear magnetic resonance spectra, from study of the chemical properties, and by analogy with addition products of other dienophiles with this hydrocarbon[71–74]. The isomeric adduct of m.p. 60° probably has the structure (XXII*b*). Bicycloheptadiene yields two 1 : 1 adducts with diethyl azodicarboxylate, too[70,75].



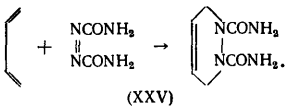
In 1952 MacKenzie *et al.*[31] reported that azodicarboxamidinium dinitrate reacts with butadiene in the presence of pyridine to form the adduct (XXIII):



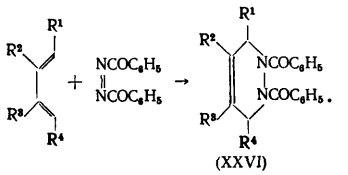
In 1953 Baranger[32] found that *pp'*-dinitroazobenzene reacts at 150–160° with 2,3-dimethylbutadiene to form a 1,4 adduct (XXIV):



Hunter[76] discovered that butadiene reacts with azodicarboxamide at 100° to form the adduct (XXV):



In 1959 Levina and her coworkers[77] showed that dibenzoyldiimide (azodibenzoyl) reacts at room temperature with 1,3-dienes to form 1,2-dibenzoyl-1,2,3,6-tetrahydropyridazines (XXVI):



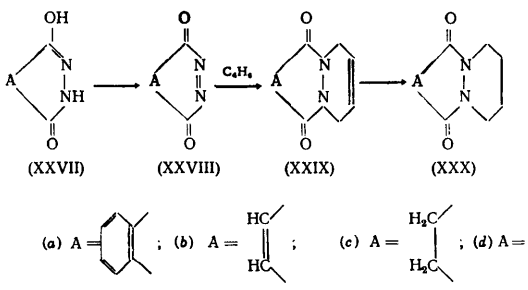
These workers subsequently established[78] that other diaroyldiimides (di-*p*-toluoyldiimide, di-*p*-anisoyldiimide, and *p*-anisoyl-*p'*-nitrobenzoyldiimide) react with 1,3-dienes to form 1,4 adducts.

2,4-Dimethylpentadiene undergoes substitutive addition with dibenzoyldiimide[78].

The reaction of diaroyldiimides with cyclopentadiene is of the second order overall, being of the first order with respect to each of the reactants[79].

During recent years it has been shown that cyclic diacyldiimides possess very high dienophilic activity.

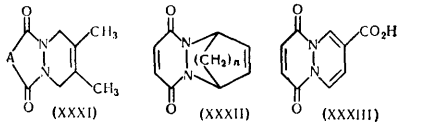
In 1960 Clement[80] found that oxidation of phthalohydrazide (XXVII*a*) with lead tetraacetate yields the extremely unstable 1,4-dihydro-1,4-dioxophthalazine (XXVIII*a*). When oxidation was carried out in acetonitrile at 0°, a green solution of the dione was obtained, from which was isolated a colourless amorphous substance which proved to be a polymer of the dione. On addition of butadiene to the green solution, the colour immediately disappeared, and a Diels–Alder adduct (XXIX*a*) was formed. When oxidation of phthalohydrazide was carried out at 0° in the presence of butadiene, a 90% yield of (XXIX*a*) was obtained. The structure of this adduct was established by catalytic reduction to the dihydro-derivative (XXX*a*), and by alkaline hydrolysis to phthalic acid and 1,2,3,6-tetrahydropyridazine. Finally, the adduct was synthesised by condensing phthalic anhydride with 1,2,3,6-tetrahydropyridazine.



In 1962 Clement[81] found that oxidation of maleohydrazide (XXVII*b*) and succinohydrazide (XXVII*c*) with lead tetraacetate in the presence of butadiene yields the respective adducts (XXIX*b*) and (XXIX*c*), catalytic reduction of both

of which gave the known 1,2-succinyl-1,2-diazacyclohexane (XXX*c*). The adduct (XXIX*b*) was synthesised by condensing 1,2,3,6-tetrahydropyridazine with maleic anhydride.

Kealy[82] suggested a convenient method for preparing the cyclic diacyldiimides (XXVIII*a–c*) by oxidising the potassium or sodium salts of the corresponding cyclic hydrazides at -77°. He found that the cyclic diacyldiimides, which he proposed to call diazaquinones, reacted rapidly in acetone solution at -77° with 1,3-dienes. Under these conditions 1,4-dihydro-1,4-dioxophthalazine (XXVIII*a*) reacts with butadiene and 2,3-dimethylbutadiene to form the adducts (XXIX*a*) and (XXXI*a*). Reaction of 3,6-dihydro-3,6-dioxopyridazine (XXVIII*b*) with butadiene, 2,3-dimethylbutadiene, cyclopentadiene, cyclohexadiene, and coumalic [6-oxopyran-3-carboxylic] acid yielded respectively the adducts (XXIX*b*), (XXXI*b*), (XXXII*a*), (XXXII*b*), and (XXXIII). 4,5-Difluoro-3,6-dihydro-3,6-dioxopyridazine (XXVIII*d*) and 2,3-dimethylbutadiene gave the adduct (XXXI*c*).

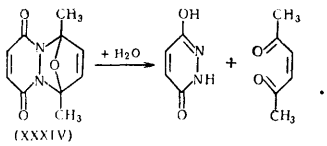


(XXXI) (XXXII) (XXXIII)

for (XXXI) (*a*) A = ; (*b*) A = ; (*c*) A = .

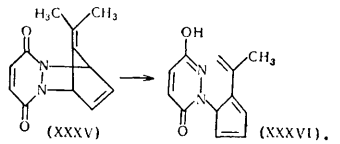
for (XXXII) *a*, *n* = 1; *n* = 2.

Furan and 2,5-dimethylfuran reacted readily with 3,6-dihydro-3,6-dioxopyridazine (XXVIII*b*), but the diene adducts could not be isolated. That produced from furan decomposed during isolation, while the adduct from 2,5-dimethylfuran (XXXIV) underwent hydrolysis on isolation, with the formation of maleichydrazide and hex-3-ene-2,5-dione:



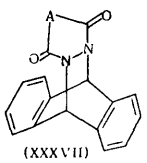
(XXXIV)

From (XXVIII*b*) and $\alpha\alpha$-dimethylfulvene a crystalline adduct (XXXV) was obtained, which gradually underwent rearrangement in the solid state, probably into the monosubstituted hydrazide (XXXVI):



(XXXV) (XXXVI).

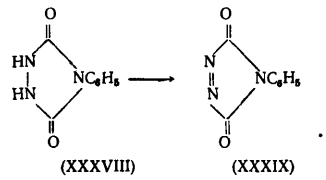
By oxidising the cyclic hydrazides (XXVII*a–c*) with lead tetraacetate in the presence of anthracene, Clement[81] obtained the Diels–Alder adducts (XXXVII*a–c*):



(XXXVII)

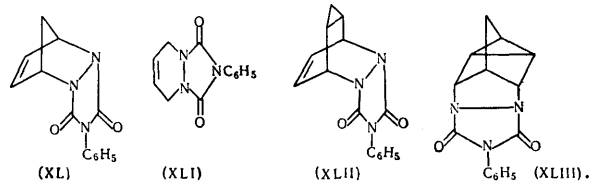
(*a*) A = ; (*b*) A = ; (*c*) A = .

In 1962 Cookson *et al.*[83] found that 3,5-dioxo-4-phenyl-1,2,4-triazolidine (XXXVIII) was oxidised by t-butyl hypochlorite in acetone medium at -78° to 3,5-dioxo-4-phenyl-1,2,4-triazoline (XXXIX):



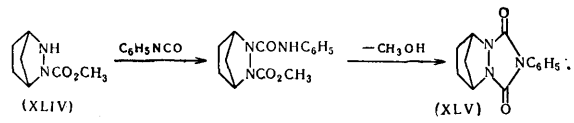
(XXXVIII) (XXXIX)

In acetone solution (XXXIX) reacts instantaneously with cyclopentadiene at -78°, and with butadiene and cycloheptatriene at -50°, to give high yields of the diene adducts (XL)–(XLII). With bicyclo[2,2,1]hepta-2,5-diene it gave a 1 : 1 adduct, which was assigned the 2,6-adduct structure (XLIII) on the basis of the infrared spectrum and by analogy with addition products of other dienophiles with bicycloheptadiene[71–74].



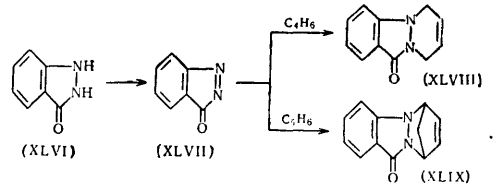
(XL) (XLI) (XLII) (XLIII).

The structure of the adduct (XL) was established by catalytic reduction to the dihydro-derivative (XLV), which was synthesised by the following reactions from the ester (XLIV), which had been obtained previously by Diels[19]:



(XLIV) (XLV)

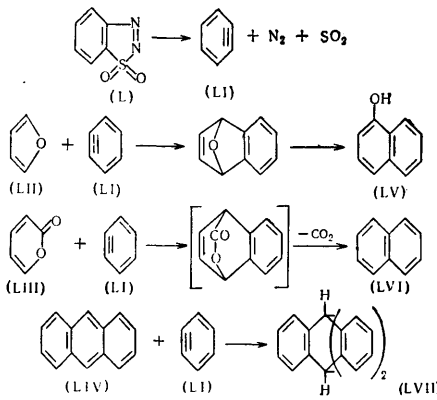
Ullman and Bartkus[84] oxidised 2,3-dihydro-3-oxoindazole (XLVI) in acetonitrile at -10° with lead tetraacetate to a green solution of the 3-oxoindazole (XLVII). On addition of butadiene or cyclopentadiene the colour of the solution at once disappeared, with formation of the Diels–Alder adducts (XLVIII) and (XLIX):



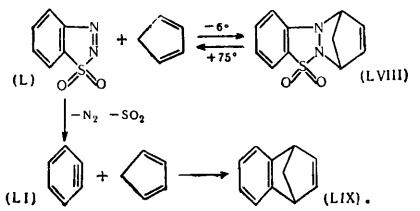
(XLVI) (XLVII) (XLVIII) (XLIX)

Wittig[85–88] diazotised sodium *o*-aminobenzenesulphinate at -15° and obtained the cyclic azo-sulphone (L) as yellow crystals which decomposed explosively at 60°. In solution (L) decomposes rapidly even at 10° to form dehydrobenzene [cyclohexadienyne] (LI), nitrogen, and sulphur dioxide. Decomposition of the azo-sulphone (L) in the presence of furan (LII), 2-pyrone (LIII), and anthracene

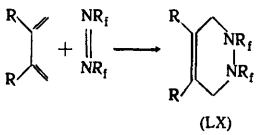
(LIV) gave respectively 1-naphthol (LV), naphthalene (LVI), and triptycene (LVII):



The azo-sulphone (L) reacts with acetonitrile medium at -6° with cyclopentadiene to form the Diels–Alder adduct (LVIII), which at 75° breaks down into the original components. When (LVIII) was decomposed in cyclopentadiene medium, the Diels–Alder condensation product (LIX) of dehydrobenzene (LI) and cyclopentadiene was obtained, and was identified as its adduct with phenyl azide.



In 1962 Chambers[89] observed that fluorinated azoalkanes react at elevated temperatures with 1,3-dienes to form the 1,2-bisfluoroalkyl-1,2,3,6-tetrahydropyridazines. Addition products were obtained from hexafluoroazomethane with butadiene and 2,3-dimethylbutadiene (LX*a*) and (LX*b*), from perfluoroazobutane and butadiene (LX*c*), and from 5*H*, 5′*H*-eicosafluoroazopentane and butadiene (LX*d*):



(*a*) R=H, $R_f=CF_3$; (*b*) R=CH_3, $R_f=CF_3$; (*c*) R=H, $R_f=C_4F_9$;

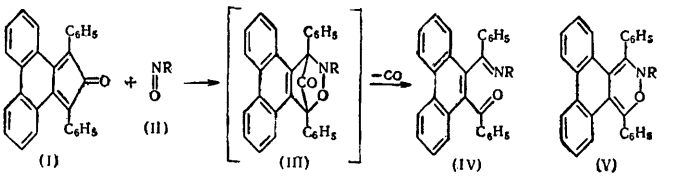
(*d*) R=H, $R_f=H(CF_2)_5$.

Examination of the infrared and nuclear magnetic resonance spectra of the addition products showed them to be Diels–Alder adducts (LX*a–d*). The ability of fluorinated azoalkanes to undergo diene condensation is explained by the electrophilic properties of fluoroalkyl groups, which cause a diminution in the electron density on the azo-group.

III. DIENE SYNTHESIS WITH NITROSO-COMPOUNDS§

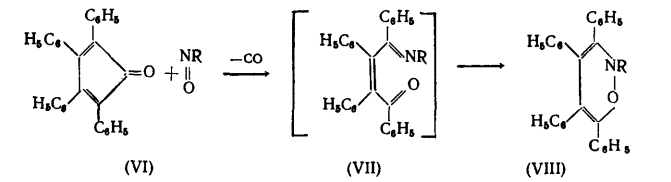
1. Reaction of Aromatic Nitroso-Compounds with Cyclones and 1,3-Diphenylisobenzofuran

During 1939–1940 Dilthey[90,91] studied the reaction of aromatic nitroso-compounds with cyclones. He found that phencyclone (I) and *NN*-dimethyl-*p*-nitrosoaniline (II*a*) interact in pyridine at room temperature to form the anil of 9,10-dibenzoylphenanthrene (IV*a*) and carbon monoxide. An unstable Diels–Alder adduct containing an *endo*-carbonyl bridge (III*a*) is probably first formed in this reaction, and decomposes under the experimental conditions into carbon monoxide and the anil (IV*a*). On treatment with acids, (IV*a*) rearranges into a 1,2-oxazine derivative (V*a*). Reaction of phencyclone (I) with nitrosobenzene (II*b*) gave the anil (IV*b*).



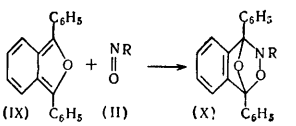
(*a*) R=$C_6H_4N(CH_3)_2$-*p*; (*b*) R=C_6H_5.

NN-Dimethyl-*p*-nitrosoaniline reacted with tetracyclone (VI) only on heating, and in this case the intermediate anil (VII) could not be detected. The product of the reaction was the 1,2-oxazine derivative (VII)¶.



R=$C_6H_4N(CH_3)_2$-*p*.

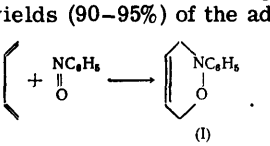
In 1949 Mustafa[94] reported that 1,3-diphenylisobenzofuran (IX) reacts in the presence of piperidine with *NN*-dimethyl-*p*-nitrosoaniline (II*a*) and nitrosobenzene (II*b*) to form the adducts (X*a*) and (X*b*), which at 270° decompose to regenerate the original 1,3-diphenylisobenzofuran:



(*a*) R=$C_6H_4N(CH_3)_2$-*p*; (*b*) R=C_6H_5.

2. Addition of Aromatic Nitroso-Compounds to 1,3-Dienes

In 1945 Khruleva[95] observed that nitrosobenzene reacts with butadiene to form a crystalline compound melting at 50°. In 1948 Arbuzov[96–98] established that the reaction is one of diene synthesis with the formation of 3,6-dihydro-2-phenyl-1,2-oxazine (I). The reaction goes smoothly at 0°, giving high yields (90–95%) of the adduct.



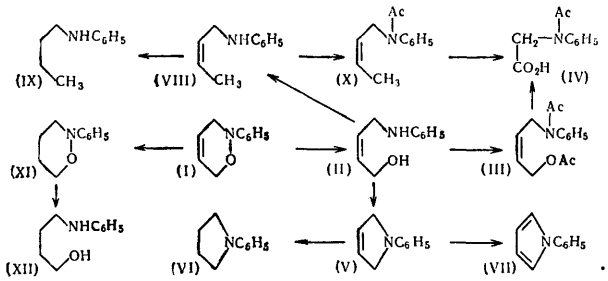
The structure of (I) was established by reducing the adduct with zinc and acetic acid to give the amino-alcohol

§ For the structure and properties of *C*-nitroso-compounds see Refs. 92 and 93.

¶ *Note added in proof*. Rigaudy[196] has recently established that this reaction product is an unsaturated γ-lactam, 1-*p*-dimethylaminophenyl-5-oxo-2,3,4,4-tetraphenyl-Δ^2-pyrroline.

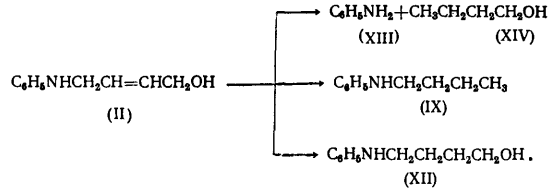
(II), which was converted into the diacetyl derivative (III), oxidation of this compound with potassium permanganate giving *N*-acetyl-*N*-phenylglycine (IV). Examination of the Raman spectrum of solutions of the adduct (I) in acetone or alcohol revealed the frequency of an isolated C=C bond[99].

The structure of the addition product of nitrosobenzene and butadiene was investigated also by Wichterle [100], but he reached the erroneous conclusion that it was 3,4-epoxy-1--phenylpyrrolidine.



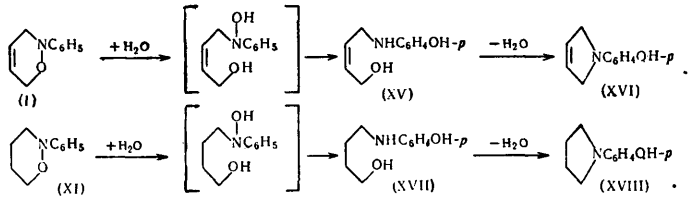
Interesting results were obtained from a study of the chemical transformations of the adduct (I). [101-103] On being heated with acids, the amino-alcohol (II) underwent cyclisation to 1-phenyl-Δ^3-pyrroline (V) catalytic reduction of which yielded 1-phenylpyrrolidine (VI). Oxidation of (V) with potassium permanganate gave 1-phenylpyrrole (VII). Reduction of (I) with sodium and alcohol resulted in *N*-but--2′-enylaniline (VIII), and catalytic reduction of this compound gave *N*-butylaniline (IX). Oxidation of the acetyl derivative (X) of (VIII) with potassium permanganate yielded *N*-acetyl-*N*-phenylglycine (IV). Catalytic reduction of the adduct (I) produced tetrahydro-2-phenyl-1,2--oxazine (XI), which was reduced with zinc and acetic acid to 4-anilinobutan-1-ol (XII).

Catalytic hydrogenation of the amino-alcohol (II) gave aniline (XIII), butan-1-ol (XIV), *N*-butylaniline (IX), and 4-anilinobutan-1-ol (XII). The main products of the reaction were aniline and butanol, whose formation is explained by initial hydrogenolysis of (II) to aniline and but-2-en-1-ol, the latter then being reduced to butanol. *N*-Butylaniline is probably formed by reduction of (II) to *N*-but-2′-enylaniline with subsequent reduction of the latter to *N*-butylaniline.

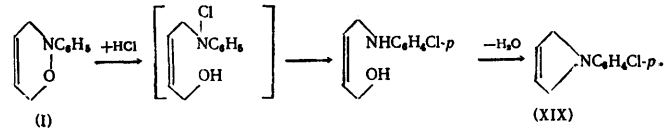


Wichterle [104] studied the reduction of the adduct (I) and of its dihydro-derivative (XI) with organomagnesium compounds. With ethylmagnesium bromide and some other organomagnesium compounds the adduct (I) gave 4-anilino-but-2-en-1-ol (II); 4-anilinobutan-1-ol (XII) was obtained from the dihydro-derivative (XI) and ethylmagnesium bromide.

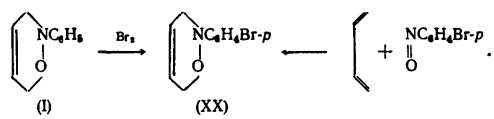
Later Wichterle [105] found that (I) and (XI) are hydrolysed by dilute phosphoric acid to the amino-alcohols (XV) and (XVII). More concentrated phosphoric acid results in cyclisation of these latter compounds to the amines (XVI) and (XVIII).



Kojima [106] showed that reaction of the adduct (I) with concentrated hydrochloric acid yields 1-*p*-chlorophenyl--Δ^3-pyrroline (XIX):



Kresze [107] found that bromination of the adduct (I) gave the hydrobromide of 2-*p*-bromophenyl-3,6-dihydro-1,2-oxazine. The base (XX) isolated from this hydrobromide was identical with the adduct prepared from butadiene and *p*-bromonitrosobenzene.

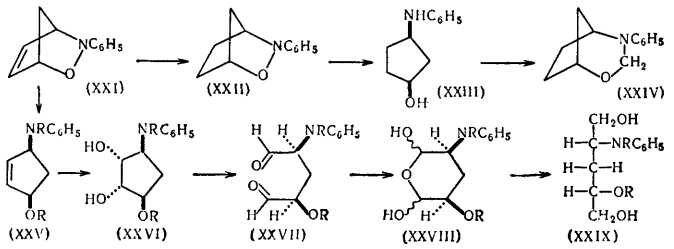


Arbuzov [108-111] investigated the reaction of butadiene with *o*-, *m*-, and *p*-nitrosotoluenes, and found from the structure of the adducts that in all cases the reaction was one of diene synthesis.

It was subsequently found that other 1,3-dienes, as well as butadiene, react with aromatic nitroso-compounds to form 2-aryl-3,6-dihydro-1,2-oxazines. Diels–Alder adducts have been obtained from aromatic nitroso-compounds and isoprene [112,113], pentadiene [94,114], 2,3-dimethylbutadiene [115-120], hexa-2,4-diene [108], cyclopentadiene [121-126], 5-methoxymethylcyclopentadiene [126], cyclopentadien-1--ylmethyl acetate [126], cyclohexadiene [123-125], cycloheptatriene [122,125], cyclooctadiene [125,127], 1,1′-bi(cyclohexenyl) [115], 1-arylbutadienes [115,125,128,129], 1,4-diphenylbutadiene [128], 2-chlorobutadiene [130,131], 2-methoxybutadiene [112], and ethyl sorbate [123].

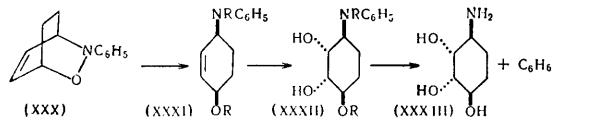
Thus by the action of nitrosobenzene on cyclopentadiene at 0° Kresze [121-124] obtained the unstable 1,4 adduct (XXI), from which an adduct with phenyl azide was obtained. Catalytic reduction of (XXI) at -5° yielded the dihydro--derivative (XXII) and *cis*-3-anilinocyclopentanol (XXIII). Condensation of the latter with formaldehyde resulted in a tetrahydro-1,3-oxazine derivative (XXIV). Reduction of (XXI) with zinc and acetic acid gave *cis*-4-anilinocyclopent-2-enol (XXV*a*), which was converted into the diacetyl derivative (XXV*b*). On oxidation of the latter with potassium permanganate, the 1,4-diacetyl derivative of 4-anilinocyclopentane-1,2,3-triol (XXVI*b*) was obtained, and this was further oxidised with lead tetraacetate to the diacetyl derivative of *erythro*-2-anilino-4-hydroxyglutaraldehyde (XXVII*b*), which was isolated as the internal hemiacetal of the monohydrate [tetrahydro-2,6-dihydroxypyran] (XXVIII*b*).

On reduction of this compound with sodium tetrahydroborate a 2,4-diacetyl derivative of 2-anilino-2,3-dideoxyerythritol [*sic*. 2-acetanilido-4-*O*-acetyl-2,3-dideoxyarabitol ? (Ed. of Translation)] (**XXIX***b*) was formed.



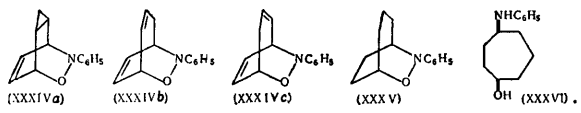
(*a*) R=H; (*b*) R=Ac.

By condensing nitrosobenzene with cyclohexadiene Arbuzov and Mastryukova [132] obtained the diene adduct (**XXX**), which was reduced to *cis*-4-anilinocyclohex-2-enol (**XXXI***a*), and the latter converted into the diacetyl derivative (**XXXI***b*). By oxidising (**XXXI***b*) with potassium permanganate Kresze [123,124] obtained a 1,4-diacetyl derivative of 4-anilinocyclohexane-1,2,3-triol (**XXXII***b*), which was saponified to the triol itself (**XXXII***a*). Catalytic hydrogenolysis of the triol gave 4-aminocyclohexane-1,2,3-triol (**XXXIII**).



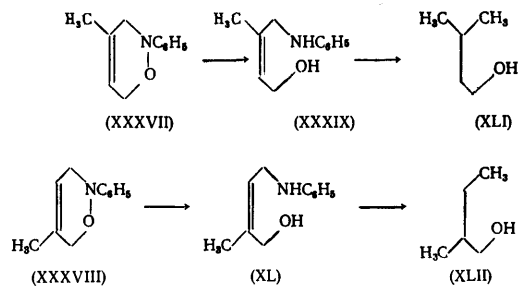
(*a*) R=H; (*b*) R=Ac.

An adduct for which the structural formulae (**XXXIV***a–c*) were possible was obtained by Kresze [122] by the reaction of nitrosobenzene with cycloheptatriene. Structure (**XXXIV***a*) was possible if the cycloheptatriene underwent isomerisation into norcaradiene (see p. 409). Examination of the nuclear magnetic resonance spectrum of the adduct and study of the chemical changes which it underwent eliminated the structure (**XXXIV***a*) and were consistent with the other two structures. Catalytic reduction of the adduct resulted in the tetrahydro-derivative (**XXXV**), which gave *cis*-4-anilinocycloheptanol (**XXXVI**) on reduction with zinc and acetic acid.

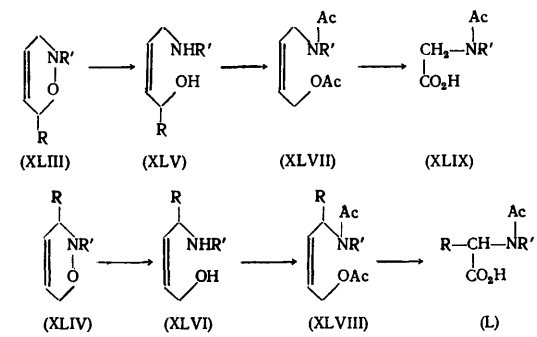


Arbuzov and his coworkers [112,114] investigated the structure of the addition products formed by nitrosobenzene with isoprene and with *trans*-pentadiene. When unsymmetrical dienophiles add on to 1- and 2-substituted 1,3-dienes, the order of addition usually agrees well with the direction of polarisation in both dienophile and diene. In several reactions with 1-substituted dienes, however, the results were inconsistent with the view that polarisation factors determine the structural orientation of diene synthesis [7,12].

It was expected that reaction of nitrosobenzene with isoprene would give the isomer (**XXXVII**) either alone or mixed with a smaller quantity of the isomer (**XXXVIII**). The structure of the adduct was established by reducing it with zinc and acetic acid, when these isomers should give the amino-alcohols (**XXXIX**) and (**XL**), and the latter on catalytic reduction should yield 3-methylbutanol (**XLI**) and 2-methylbutanol (**XLII**). In fact the amino-alcohol obtained by reduction of the adduct yielded only 3-methylbutanol (**XLI**) on catalytic hydrogenation, and hence the adduct has the structure (**XXXVII**).



Reaction of *trans*-pentadiene with nitrosobenzene could yield the isomers (**XLIII***a*) and (**XLIV***a*), reduction of which with zinc and acetic acid would give the amino-alcohols (**XLV***a*) and (**XLVI***a*), which could be converted into diacetyl derivatives (**XLVII***a*) and (**XLVIII***a*); these on oxidation with potassium permanganate should produce *N*-acetyl-*N*-phenylglycine (**XLIX***a*) and *N*-acetyl-*N*-phenylalanine (**L***a*). In fact, on application of the above series of reactions to the adduct, the amino-acids (**XLIX***a*) and (**L***a*) were isolated from the oxidation products in the proportions 1 : 3. It was thus established that the adduct consisted of a mixture of the isomers (**XLIII***a*) and (**XLIV***a*) with the latter predominating. Hence the polarisation factor does not determine the order of addition of nitrosobenzene to *trans*-pentadiene.



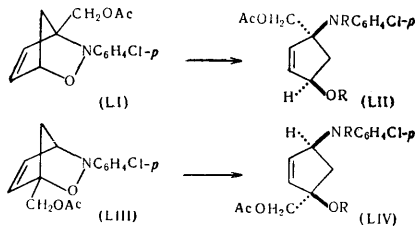
(*a*) R = CH_3, R′ = C_6H_5; (*b*) R = C_6H_5, R′ = C_6H_4Cl-*p*.

Kresze [129] investigated the structure of the addition product of *p*-chloronitrosobenzene and *trans*-1-phenylbutadiene by the method employed by Arbuzov for the adduct of nitrosobenzene and *trans*-pentadiene. The adducts (**XLIII***b*) and (**XLIV***b*) should yield the amino-acids (**XLIX***b*) and (**L***b*) respectively. In fact, on reduction of the adduct to the amino-alcohol, conversion to the diacetyl derivative, and oxidation, only the amino-acid (**XLIX***b*) was isolated from the products. Hence the adduct has the structure (**XLIII***b*). The nuclear magnetic resonance spectrum of the adduct confirmed the structure established by chemical means.

Kresze [129] also prepared addition products formed by *p*-chloronitrosobenzene with *trans*-1-phenylbutadienes containing methoxyl, methyl, chlorine, and a nitro-group as *para* substituent. The nuclear magnetic resonance spectra of these adducts fully corresponded with that of (**XLIII***b*),

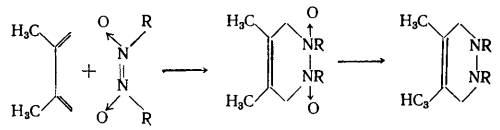
and consequently they are all 6-aryl-2-*p*-chlorophenyl--3,6-dihydro-1,2-oxazines. Thus the order of addition in the reaction of *p*-chloronitrosobenzene with *trans*-1-arylbutadienes is determined by the steric factor, not by the polarisation factor: a 1-aryl group in the diene occupies in the adduct a "*meta*" position with respect to the *p*'-chlorophenyl group.

Kresze [126] also studied the structure of the adduct from cyclopentadien-1-ylmethyl acetate and *p*-chloronitrosobenzene, which could have the structures (LI) and (LIII). Reduction of these with zinc and acetic acid should yield the compound (LII*a*) and (LIV*a*), from which the triacetyl derivatives (LII*b*) and (LIV*b*) would be formed on acetylation. Comparison of the nuclear magnetic resonance spectrum of the triacetyl derivative obtained with that of the diacetyl derivative (XXV*b*) prepared from the addition product of nitrosobenzene and cyclopentadiene showed that the proton spectrum of the former lacked a signal from the proton of a CH group linked to a nitrogen atom and to a C=C bond. Hence the triacetyl derivative had the structure (LII*b*), the adduct being (LI).



(*a*) R = H; (*b*) R = Ac.

In 1963 Hamer [120] reported that *m*- and *p*-nitronitrosobenzenes react with 2,3-dimethylbutadiene at 0° to form the normal 1 : 1 adducts and also the 2 : 1 adducts (LVI*a*) and (LVI*b*), the latter resulting from diene condensation of 2,3-dimethylbutadiene with the dimeric nitroso-compounds (LV*a*) and (LV*b*). The structure of the 2 : 1 adduct (LVI*b*) was established by reducing it with phosphorus trichloride to 1,2,3,6-tetrahydro-4,5-dimethyl-1,2-di-*p*--nitrophenylpyridazine (LVII*b*), which had been obtained in 1953 by Baranger [32] by the diene condensation of 2,3-dimethylbutadiene with *pp*'-dinitroazobenzene (see p. 410).



(*a*) R = $C_6H_4NO_2$-*m*; (*b*) R = $C_6H_4NO_2$-*p*.

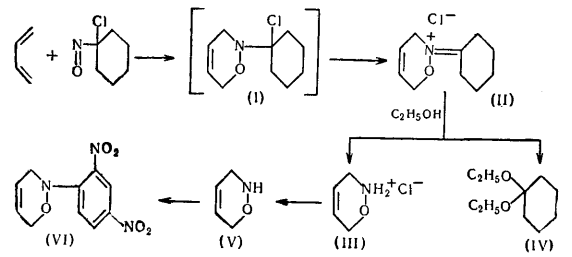
Kinetic investigation of the reaction of aromatic nitroso--compounds with 2,3-dimethylbutadiene has shown it to be of the first order with respect to each of the reactants [127].

3. Reaction of Acyclic and Alicyclic Nitroso-Compounds with 1,3-Dienes

In 1947 Wichterle [100] found that butadiene reacts in the presence of alcohol with 2-chloro-2-nitrosopropane or 1-chloro-1-nitrosocyclohexane to form a crystalline substance having the composition C_4H_8ONCl. By treating this substance with alkali he obtained a liquid C_4H_7ON, which he assumed to be 3,4-epoxypyrrolidine, while the crystalline compound was supposedly the hydrochloride of this base.

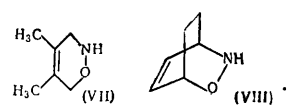
It was to be assumed that the reaction of butadiene with 1-chloro-1-nitrosocyclohexane would be one of diene synthesis, but the adduct (I) obviously underwent immediate rearrangement to the quaternary immonium salt (II), which then suffered alcoholysis to 3,6-dihydro-1,2-oxazinium chloride (III) and 1,1-diethoxycyclohexane (IV).

In order to test this hypothesis, Arbuzov and his coworkers [98,133,134] treated chloronitrosocyclohexane with butadiene in the presence of alcohol in benzene solution, and isolated the hydrochloride (III) and the ketal (IV) from the reaction mixture. If reaction was carried out at -18° in the absence of alcohol, the immonium salt (II) was obtained; this resinified rapidly on warming up to room temperature. If, however, the immonium salt was treated with alcohol cooled to -20°, the hydrochloride (III) was formed. Thus the reaction could be broken down into two stages — (1) formation of the extremely unstable immonium salt (II), and (2) alcoholysis of this salt to give the hydrochloride (III) and the ketal (IV).

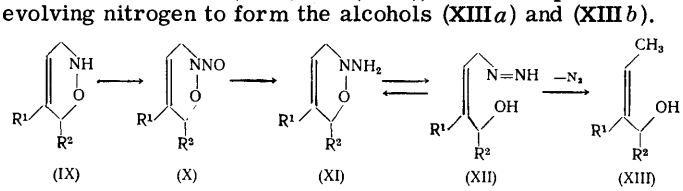


From the hydrochloride (III) was isolated the base (V), whose Raman spectrum contained the frequency of an isolated C=C bond [99]. Arylation of the base (V) with 1-chloro--2,4-dinitrobenzene gave the 2,4-dinitrophenyl derivative (VI) [133].

The action of 2,3-dimethylbutadiene and of cyclohexadiene on 1-chloro-1-nitrosocyclohexane in the presence of alcohol gave the hydrochlorides of the corresponding bases, from which the free bases (VII) and (VIII) were isolated [133].

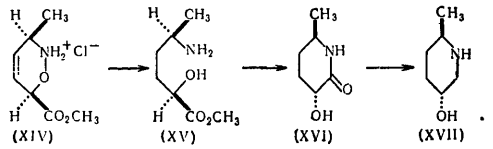


In 1950 Wichterle [135] investigated several chemical reactions of 3,6-dihydro-1,2-oxazine (V). In 1951, he showed [128] that 1-phenylbutadiene and 2-chlorobutadiene react in the presence of alcohol with 1-chloro-1-nitrosocyclohexane to form the hydrochlorides of two bases, from which the bases themselves (IX*a*) and (IX*b*) were isolated. Treatment of these bases with nitrous acid gave the *N*-nitroso-derivatives (X*a*) and (X*b*), reduction of which with zinc and acetic acid or with lithium tetrahydroaluminate yielded respectively 1-phenylbut-2-en-1-ol (XIII*a*) and 2-chlorobut-2-en-1-ol (XIII*b*). He explained the mechanism of these transformations by initial reduction of the *N*-nitroso-derivatives (X*a*) and (X*b*) to hydrazine derivatives (XI*a*) and (XI*b*), which passed into the tautomeric diimide derivatives (XII*a*) and (XII*b*), these compounds evolving nitrogen to form the alcohols (XIII*a*) and (XIII*b*).



(*a*) R^1=H, R^2=C_6H_5; (*b*) R^1=Cl, R^2=H.

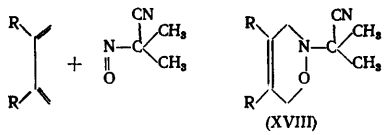
In 1963 Belleau [136] observed that 1-chloro-1-nitrosocyclohexane reacts in the presence of alcohol with methyl *trans*-*trans*-sorbate to form *cis*-3,5-dihydro-6-methoxycarbonyl-3-methyl-1,2-oxazinium chloride (XIV). The structure and the configuration of (XIV) were established by catalytic reduction to methyl *erythro*-5-amino-2-hydroxyhexanoate (XV), which on being heated to 100° gave the lactam (XVI), reduced with lithium tetrahydroaluminate to 3-hydroxy-6-methylpiperidine (XVII). This last compound was shown by its nuclear magnetic resonance spectrum to have the *trans* configuration. Consequently the ester (XV) had the *erythro* configuration, and the hydrochloride (XIV) the *cis* structure.



(XIV) (XV) (XVI) (XVII)

The hydrochloride (XIV) was used for the stereospecific synthesis of two 5-amino-5,6-dideoxy-(±)-hexanose acids.

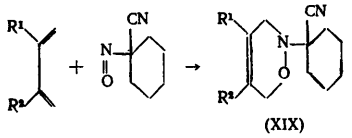
In 1957 Wichterle [137,138] showed that α-methyl-α-nitrosopropionitrile and 1-nitrosocyclohexyl cyanide react at room temperature with butadiene and 2,3-dimethylbutadiene to form the Diels–Alder adducts (XVIII*a*), (XVIII*b*), (XIX*a*), and (XIX*b*). The structure of (XVIII*a*) and (XIX*a*) was demonstrated by synthesis by Strecker's method from 3,6-dihydro-1,2-oxazine (V), a ketone (acetone or cyclohexanone), and hydrogen cyanide.



(XVIII)

(*a*) R=H; (*b*) R=CH_3.

On condensing 1-nitrosocyclohexyl cyanide with 2-chlorobutadiene, Wichterle obtained an adduct (XIX*c*) whose structure was established by synthesis from 5-chloro-3,6-dihydro-1,2-oxazine (IX*b*), cyclohexanone, and hydrogen cyanide.

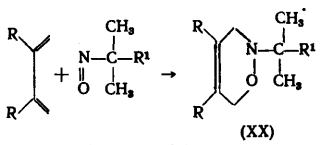


(XIX)

(*a*) $R^1=R^2=H$; (*b*) $R^1=R^2=CH_3$; (*c*) $R^1=H$, $R^2=Cl$.

According to Wichterle's results, 2-methyl-2-nitrosopropane does not react with 2,3-dimethylbutadiene. The enhanced reactivity of *gem*-chloro- and *gem*-cyano--nitroso-compounds is explained by the electron-acceptor properties of chlorine and the nitrile group, which diminished the electron density on the nitroso-group.

In 1963 Klamann [139] reported that aliphatic α-nitroso--ketones and α-nitroso-carboxylic esters, as also nitroso--alkanes containing aromatic substituents, react with 1,3-dienes to form 3,6-dihydro-1,2-oxazines (XX):



(XX)

R=H, CH_3; $R^1=COCH_3$, $CO_2C_2H_5$, C_6H_5.

Trichloronitrosomethane reacts with 1,3-dienes in the presence of alcohols to form 3,6-dihydro-1,2-oxazines and orthocarbonic esters. Aliphatic *gem*-nitro-nitroso-compounds also react with 1,3-dienes in the presence of alcohols, forming 3,6-dihydro-2-nitroso-1,2-oxazines and ketals [139].

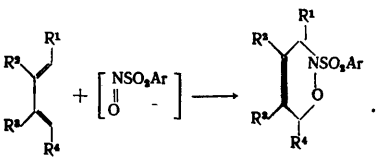
4. Reaction of 1,3-Dienes with Nitrosyl Arenesulphinates

In 1961 Kresze [140] found that aromatic sulphinic acids react with alkyl nitrites in inert solvents to form *NN*-diarenesulphonylhydroxylamines. He regarded the reaction as occurring in two stages, with the intermediate formation of nitrosyl arenesulphinate:

$$ArSO_2H+RONO \rightarrow [ArSO_2NO] + ROH,$$

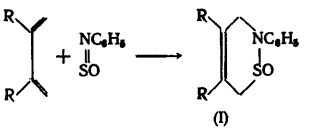
$$ArSO_2H + [ArSO_2NO] \rightarrow (ArSO_2)_2NOH.$$

To confirm this hypothesis, he carried out the reaction of aromatic sulphinic acids with ethyl nitrite in the presence of 1,3-dienes (butadiene, 2,3-dimethylbutadiene, 2-chlorobutadiene), and obtained 2-arenesulphonyl-3,6-dihydro--1,2-oxazines:



IV. DIENE SYNTHESIS WITH *N*-SULPHINYLAMINES AND *N*-SULPHINYLAMIDES

In 1953 Wichterle [141,142] showed that *N*-sulphinylaniline undergoes diene synthesis on being heated with butadiene and 2,3-dimethylbutadiene, with the formation of 3,6-dihydro-1-oxo-2-phenyl-1,2-thiazines (I*a*) and (I*b*):

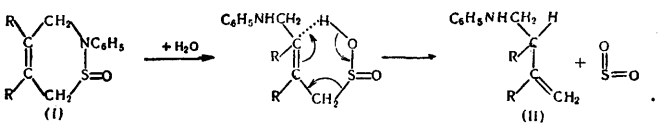


(I)

(*a*) R=H; (*b*) R=CH_3.

Other aromatic *N*-sulphinylamines have been subjected to diene synthesis. Aliphatic *N*-sulphinylamines do not react with 1,3-dienes.

The structure of the adducts (I*a*) and (I*b*) was investigated by acid hydrolysis, when the N–S bond underwent hydrolytic cleavage, sulphur dioxide was split off, and migration of the double bond occurred to give the amines (II*a*) and (II*b*). Wichterle showed that this change takes place by a cyclic mechanism.

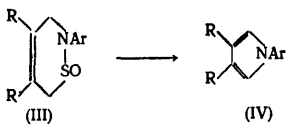


(I) (II)

(*a*) R=H; (*b*) R=CH_3.

When the adducts (III) were heated with alcoholic sodium ethoxide or caustic potash, good yields of 1-arylpyrroles

(IV) were obtained [143,144]. The mechanism of this reaction has not been elucidated.

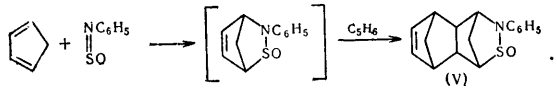


(III) (IV)

R=H, CH_3.

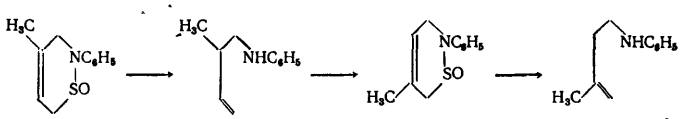
In 1962 Kataev [145] obtained addition products formed by *N*-sulphinylaniline with butadiene, isoprene, pentadiene, cyclopentadiene, and 1-*p*-nitrophenylbutadiene. Examination of the infrared spectra of *N*-sulphinylaniline and of its addition product with butadiene, as well as study of the nuclear magnetic resonance spectrum of its addition product with isoprene, confirmed the structures, established by Wichterle by chemical means, of the adducts of 1,3-dienes with *N*-sulphinylanilines.

In the reaction of *N*-sulphinylaniline with cyclopentadiene a 1:2 adduct (V) was obtained:



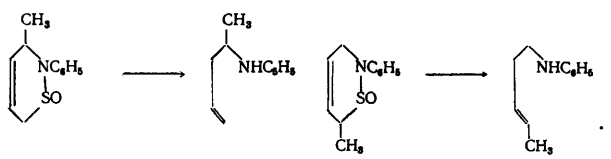
(V)

Kataev investigated the structure of the addition products formed with isoprene and pentadiene. The isoprene adduct could have the formulae (VI*a*) and (VI*b*), giving on acid hydrolysis (VII*a*) and (VII*b*). The infrared spectrum of the product showed the presence of a CH_2:CH group and the absence of CH_2:C(CH_3). Hence the adduct has the structure (VI*a*).



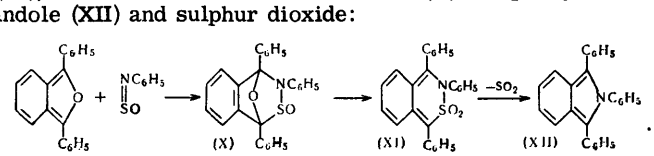
(VI*a*) (VII*a*) (VI*b*) (VII*b*)

With pentadiene the adduct could be (VIII*a*) and (VIII*b*), giving on acid hydrolysis the amines (IX*a*) and (IX*b*). The infrared spectrum of the hydrolysis product showed the presence of CH_2:CH and *trans*-CH:CH groups. Hence the Diels–Alder adduct is a mixture of the isomers (VIII*a*) and (VIII*b*).



(VIII*a*) (IX*a*) (VIII*b*) (IX*b*)

In 1963 Cava [146] discovered that *N*-sulphinylaniline reacts at elevated temperature with 1,3-diphenylisobenzofuran to form 1,2,3-triphenylisoindole (XII). He suggests a mechanism involving initial formation of the Diels–Alder adduct (X), which rearranges to the *o*-quinonoid δ-sultam (XI), and the latter breaks down into 1,2,3-triphenylisoindole (XII) and sulphur dioxide:



(X) (XI) (XII)

In 1962 Kirsanov and his coworkers [147,148] found that *N*-sulphinylarenesulphonamides react at room temperature with butadiene and 2,3-dimethylbutadiene to form 2-arenesulphonyl-3,6-dihydro-1-oxo-1,2-thiazines (XIII*a*) and (XIII*b*):



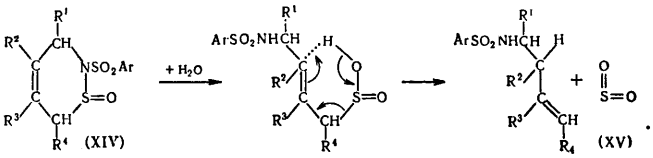
(XIII)

(*a*) R=H; (*b*) R=CH_3.

N-Sulphinylarenesulphonamides take part considerably more readily in diene synthesis than do the structurally similar *N*-sulphinylanilines. The explanation is that replacement of the aryl group of the latter by the more strongly electron-accepting arenesulphonyl group results in a greater decrease in electron density on the sulphinyl group.

Kresze [149,150] obtained addition products from *N*-sulphinylarenesulphonamides with butadiene, 2,3-dimethylbutadiene, 2-chlorobutadiene, cyclohexadiene, 2-chlorocyclohexadiene, 1-*p*-nitrophenylbutadiene, and ethyl sorbate.

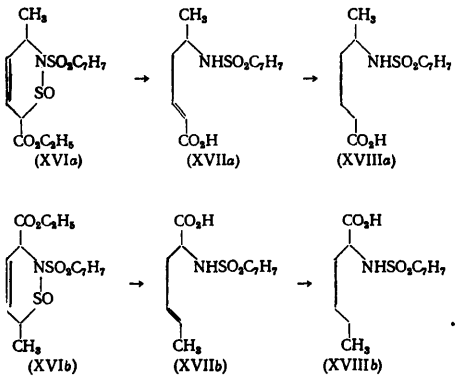
Studies of the chemical properties of the adducts made by Kresze and by Kirsanov showed them to differ in many respects from the properties of 2-aryl-3,6-dihydro-1-oxo-1,2-thiazines. In both acid and alkaline hydrolysis of the adducts (XIV) the ring underwent hydrolytic cleavage at the N–S bond, sulphur dioxide was eliminated, and sulphonamides (XV) were formed with migration of the double bond:



(XIV) (XV)

In no case could pyrrole derivatives be isolated from the products of alkaline hydrolysis of the adducts.

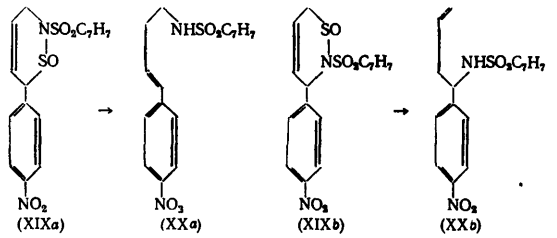
In order to ascertain the order in which *N*-sulphinylarenesulphonamides add on to unsymmetrical dienes, Kresze [149] investigated the structure of the addition products formed by *N*-sulphinyltoluene-*p*-sulphonamide with ethyl sorbate and with 1-*p*-nitrophenylbutadiene. The adduct obtained with ethyl sorbate could have the structure (XVI*a*) or (XVI*b*), which on hydrolysis would give an *N*-toluene-*p*-sulphonyl derivative of an unsaturated amino-acid (XVII*a*) or (XVII*b*), and this could be reduced to the corresponding derivative (XVIII*a*) or (XVIII*b*) of aminohexanoic acid. Examination of the product showed it to have the structure (XVIII*a*), and hence the adduct was (XVI*a*).



(XVI*a*) (XVII*a*) (XVIII*a*)

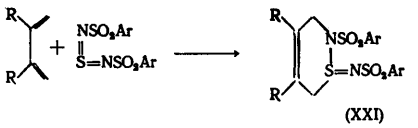
(XVI*b*) (XVII*b*) (XVIII*b*)

1-*p*-Nitrophenylbutadiene could give the adducts (XIX*a*) and (XIX*b*), which on hydrolysis should form the sulphonamides (XX*a*) and (XX*b*). The infrared spectrum of the hydrolysis product showed the absence of a $CH_2:CH$ group and the presence of a *trans*-CH:CH group, while the ultraviolet spectrum showed a *p*-nitrostyrene residue to be present. Hence the adduct has the structure (XIX*a*).



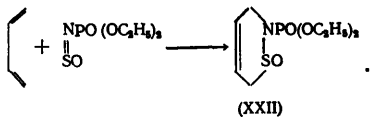
Kresze considers that in both the cases investigated the order of addition is determined mainly by the steric factor: a bulky substituent present in position 1 in the diene is oriented "*meta*" to the arenesulphonyl group in the adduct.

In 1962 Kirsanov [151] observed that sulphur di-*N*-arenesulphonylimides react readily with butadiene and 2,3-dimethylbutadiene to form 2-arenesulphonyl-1-arenesulphonylimino-3,6-dihydro-1,2-thiazines (XXI*a*) and (XXI*b*):



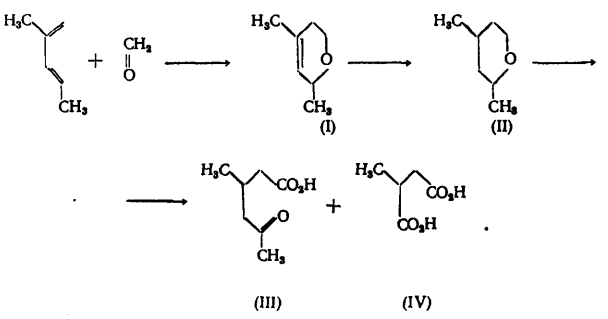
(*a*) R=H; (*b*) $R=CH_3$.

In 1963 Wieczorkowski [152] reported that diethyl *N*-sulphinylphosphoramidate reacts with butadiene to form 2-diethoxyphosphinyl-3,6-dihydro-1-oxo-1,2-thiazine (XXII):

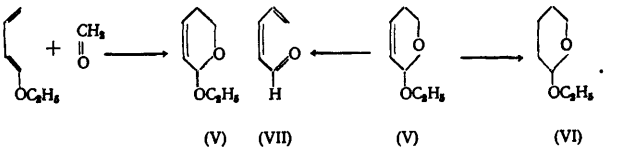


V. DIENE SYNTHESIS WITH CARBONYL AND THIOCARBONYL COMPOUNDS

In 1949 Gresham and Steadman [153] showed that 2-methylpentadiene reacts at 185° with paraformaldehyde to produce Δ^3-dihydro-2,4-dimethylpyran (I). Catalytic reduction of the adduct gave tetrahydro-2,4-dimethylpyran (II), oxidation of which with chromic acid mixture yielded 3-methyl-5-oxohexanoic acid (III) and methylsuccinic acid (IV).

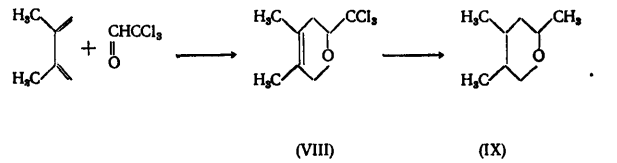


In 1959 Kubler [154,155] treated 1-ethoxybutadiene with paraformaldehyde at 180°, and obtained 2-ethoxy-Δ^3-dihydropyran (V), which was converted by catalytic reduction into 2-ethoxytetrahydropyran (VI) and by acid hydrolysis into pentadienal (VII).

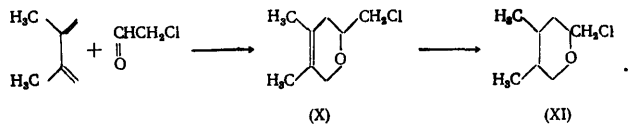


Diene adducts were obtained also from paraformaldehyde with 1-methoxybutadiene, 1-2′-methoxyethoxybutadiene, 1-2′-ethylhexyloxybutadiene, 1-methoxyhexadiene, and 2-ethyl-1-methoxybutadiene.

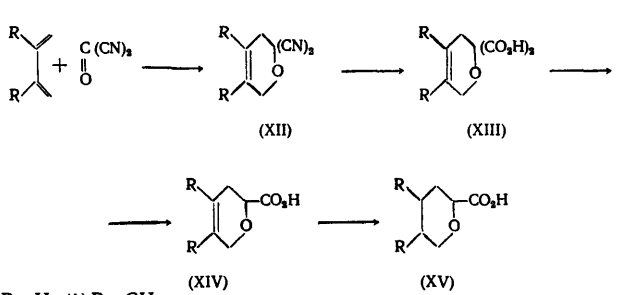
In 1954 Dale and Sisty [156] obtained the diene adduct (VIII) by heating chloral with 2,3-dimethylbutadiene at 150°. Catalytic reduction of the adduct gave a tetrahydropyran derivative (IX).



Isoprene and pentadiene also reacted at 150° with chloral to form diene adducts. Later these workers showed [157] that chloroacetaldehyde reacted at 100° with 2,3-dimethylbutadiene to form the adduct (X), which was catalytically reduced to the tetrahydropyran derivative (XI):

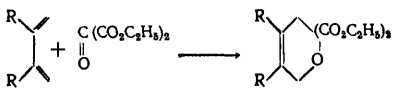


In 1957 Achmatowicz [158-160] investigated the reaction of carbonyl cyanide [mesoxalonitrile] with butadiene and 2,3-dimethylbutadiene. In both cases diene condensation occurred even at room temperature to give the adducts (XII*a*) and (XII*b*). The structure of (XII*a*) was established by alkaline hydrolysis to the dicarboxylic acid (XIII*a*), which was readily decarboxylated to the monocarboxylic acid (XIV*a*), catalytic hydrogenation of which gave the known tetrahydropyran-2-carboxylic acid (XV*a*). In a similar manner the acid (XV*b*) was obtained from the adduct (XII*b*).



(*a*) R=H; (*b*) $R=CH_3$.

Achmatowicz established [158-160] that diethyl mesoxalate condenses with butadiene at 135° and with 2,3-dimethylbutadiene at 70° to give the adducts (XVI*a*) and (XVI*b*):

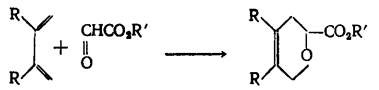


(XVI)

(*a*) R=H; (*b*) R=CH_3.

He also obtained adducts from diethyl mesoxalate with isoprene, pentadiene, hexa-2,4-diene, cyclohexadiene, and ethyl sorbate [160].

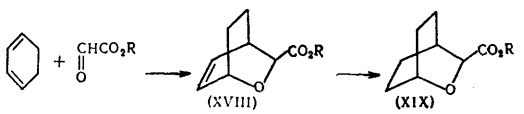
In 1962 Arbuzov *et al.* [161] showed that butadiene and 2,3-dimethylbutadiene react at 120–130° with ethyl glyoxylate, n-butyl glyoxylate, or their hemiacetals to form the Diels–Alder adducts (XVII*a*) and (XVII*b*):



(XVII)

(*a*) R=H, R′=C_2H_5, n-C_4H_9; (*b*) R=CH_3, R′=C_2H_5, n-C_4H_9.

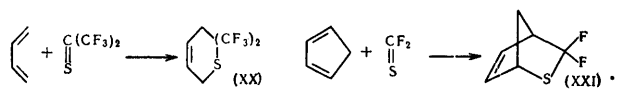
Cyclohexadiene with n-butyl glyoxylate gave the adduct (XVIII), which was reduced to the tetrahydropyran derivative (XIX):



(XVIII) (XIX)

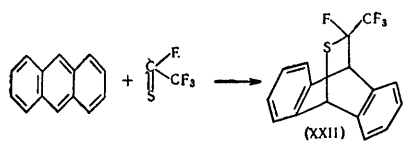
R= n-C_4H_9.

In 1961 Middleton *et al.* [162] discovered that several thiocarbonyl compounds readily undergo diene synthesis. Hexafluorothioacetone reacts instantaneously with butadiene at -78° to give the theoretical yield of the adduct (XX). Thiocarbonyl fluoride reacts rapidly at -20° with cyclopentadiene to form the adduct (XXI).



(XX) (XXI).

Trifluorothioacetyl fluoride reacts at room temperature with anthracene, the adduct being (XXII):



(XXII).

VI. DIENE SYNTHESIS WITH NITRILES

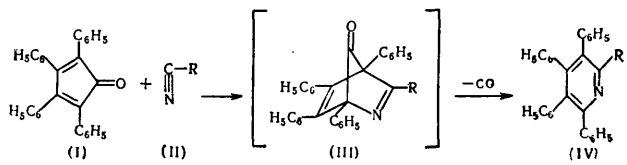
1. Reaction of Aromatic Nitriles with Cyclones

In 1935 Dilthey [163] found that tetracyclone (I) reacts with benzonitrile (II*a*) at 275–300° to form pentaphenylpyridine (IV*a*). An unstable Diels–Alder adduct containing an *endo*-carbonyl bridge (III*a*) is probably formed initially, and breaks down under the experimental conditions into carbon monoxide and (IV*a*).

In 1952 Polaczkowa and Woliński [164] showed that tetracyclone (I) condenses at 230–280° with *p*-tolunitrile (II*b*), *p*-methoxybenzonitrile (II*c*), and *p*-bromobenzonitrile (II*d*) to form the corresponding pentaarylpyridines (IV*b*–*d*).

In 1960 Jaworski [165] established that tetracyclone (I) reacts at 215° with 2-, 3-, and 4-cyanopyridines (II*e*–*g*) with the formation of 3,4,5,6-tetraphenyl-2,2′(3′ and 4′)-bipyridyls (IV*e*–*g*).

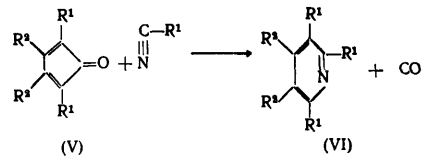
Polaczkowa *et al.* [166] condensed tetracyclone (I) with benzoyl cyanide (II*h*) and with *p*-methoxybenzoyl cyanide (II*i*) at 235°, and obtained the tetraphenylpyridine derivatives (IV*h*) and (IV*i*).



(I) (II) (III) (IV)

R = (*a*) phenyl, (*b*) *p*-tolyl, (*c*) *p*-methoxyphenyl, (*d*) *p*-bromophenyl, (*e*) pyrid-2-yl, (*f*) pyrid-3-yl, (*g*) pyrid-4-yl, (*h*) benzoyl, (*i*) *p*-methoxybenzoyl.

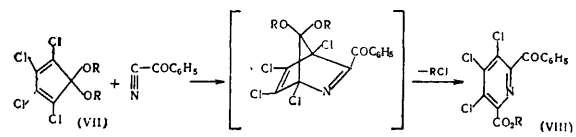
Madroñero Peláez [167] found that heating anisylcyclone (V) with benzonitrile gives the pentaarylpyridine (VI) and carbon monoxide:



(V) (VI)

R^1=phenyl; R^2=*p*-anisyl.

In 1960 Jaworski and Polaczkowa [168] reported that heating the 5,5-dialkoxytetrachlorocyclopentadienes (VII*a*) and (VII*b*) with benzoyl cyanide gives the 6-benzoyl-3,4,5-trichloropyridine-1-carboxylic esters (VIII*a*) and (VIII*b*)†:



(VII) (VIII)

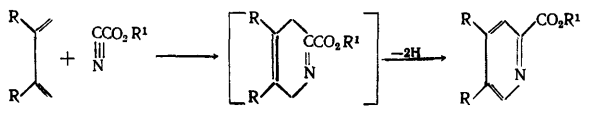
(*a*) R=CH_3; (*b*) R=C_2H_5.

Jaworski [170,171] investigated the kinetics of the reaction of tetracyclone with 2-cyanopyridine, *o*-chlorobenzonitrile, and benzonitrile, and found it to be overall of the second order.

† It has recently been found [169] that the ketal (VII*a*) condenses with dimethyl acetylenedicarboxylate to form trimethyl hemimellitate and methyl chloride.

2. Reaction of Nitriles with 1,3-Dienes

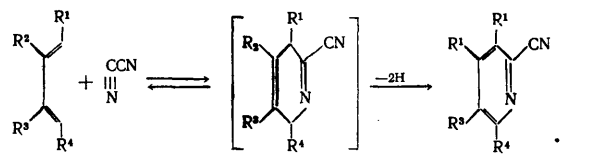
In 1943 Alder [172] reported that butadiene and 2,3-dimethylbutadiene undergo diene synthesis with cyanoformic esters to give the 2,5-dihydropyridine derivatives (I*a*) and (I*b*), which under the experimental conditions are dehydrogenated to the pyridine derivatives (II*a*) and (II*b*):



(I) (II)

(*a*) R=H; (*b*) R=CH_3.

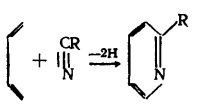
During 1947–1949 Janz [173-178] published a series of papers in which he showed that cyanogen reacts in the vapour phase at 400–600° with 1,3-dienes (butadiene, isoprene, 2-methylpentadiene, and 2-chlorobutadiene) with the formation of 2-cyanopyridines. In this reaction unstable Diels–Alder adducts, 2-cyano-3,6-dihydropyridines (III), are probably formed initially, and break down under the conditions of the experiment into hydrogen and 2-cyanopyridines (IV):



(III) (IV)

Condensation of cyanogen with butadiene at 480°, for example, gave an 18% yield of 2-cyanopyridine (V*a*). [178] 2,2′-Bipyridyl, a condensation product of 2-cyanopyridine with butadiene, was also isolated from the reaction mixture. A kinetic investigation of the reaction between cyanogen and butadiene showed it to be overall of the second order, and of the first order with respect to each of the reactants [179].

Janz [177] found that butadiene reacts at 400–600° with hydrogen cyanide, acetonitrile, and benzonitrile to form respectively pyridine (V*b*), 2-methylpyridine (V*c*), and 2-phenylpyridine (V*d*). Marvel [180] obtained 2-ethylpyridine (V*e*) by the condensation of butadiene with propionitrile at 600°.



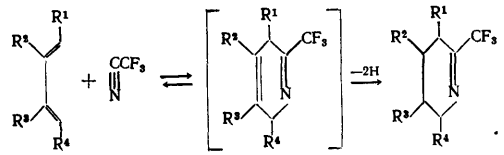
(V)

(*a*) R=CN; (*b*) R=H; (*c*) R=CH_3; (*d*) R=C_6H_5; (*e*) R=C_2H_5; (*f*) R=C_2H_3.

Janz and his coworkers [181-188] found that the condensation of 1,3-dienes with nitriles is catalysed by metal oxides. Reaction of butadiene with cyanogen, hydrogen cyanide, acetonitrile, benzonitrile, propionitrile, and acrylonitrile at 400° in the presence of chromic oxide or activated aluminium oxide gave respectively the pyridines (V*a–f*).

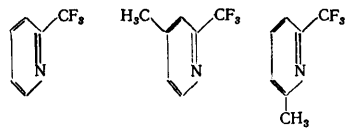
Catalytic condensation of acetonitrile and benzonitrile with isoprene, pentadiene, 2-methylpentadiene, and 2,3-dimethylpentadiene at 400° in the presence of activated aluminium oxide gave the corresponding pyridine derivatives.

It was found in 1956 [189,190] that trifluoroacetonitrile reacts in the gas phase with 1,3-dienes to form 2-trifluoromethylpyridines (VI):



(VI)

Condensation of trifluoroacetonitrile with butadiene, isoprene, and pentadiene at 400° gave high yields of 2-trifluoromethylpyridine (VII), 4-methyl-2-trifluoromethylpyridine (VIII), and 2-methyl-6-trifluoromethylpyridine (IX) respectively.



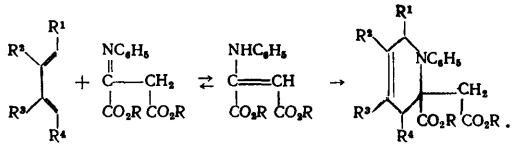
(VII) (VIII) (IX)

Kinetic investigation of the reaction between butadiene and trifluoroacetonitrile showed it to be overall of the second order, and of the first order with respect to each reactant [191].

The high reactivity of trifluoroacetonitrile in diene synthesis is explained by the strong electrophilic properties of the trifluoromethyl group, which results in a decrease in the electron density on the nitrile group.

VII. DIENE SYNTHESIS WITH AZOMETHINES

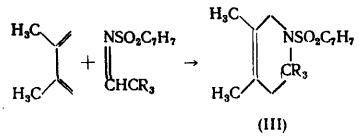
In 1943 Alder [172] reported that the anil of oxaloacetic ester (I*a*), a tautomer of anilinomaleic ester (I*b*), enters into diene synthesis with 1,3-dienes to give 1,2,3,6-tetrahydropyridine derivatives (II):



(I*a*) (I*b*) (II)

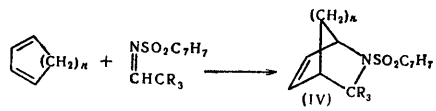
In 1964 Kresze [192] showed that the *N*-toluene-*p*-sulphonylimines of chloral and fluoral react in boiling benzene with 1,3-dienes to form 1,4 adducts which are 1,2,3,6-tetrahydropyridine derivatives. High (93–96%) yields were obtained of the addition products (III*a*) and (III*b*) formed by *N*-trichloroethylidene- and *N*-trifluoroethylidene-toluene-*p*-sulphonamides with 2,3-dimethylbutadiene, the addition

product (IV*a*) of the former sulphonamide with cyclopentadiene, and the addition product (IV*b*) of the latter sulphonamide with cyclohexadiene.



(III)

(*a*) R = Cl; (*b*) R = F.



(IV)

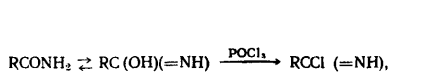
(*a*) *n* = 1, R = Cl; (*b*) *n* = 2, R = F.

Examination of the infrared spectra of the addition products showed them to be 1,4 adducts. The addition product (IV*a*) gave an adduct with phenyl azide.

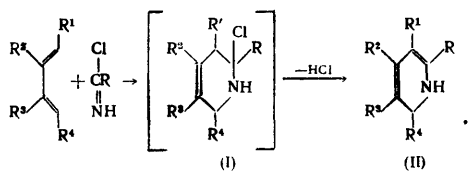
The ability of the *N*-arenesulphonylimines of chloral and fluoral to take part in diene synthesis is explained by the strong electrophilic properties of arenesulphonyl and trihalogenomethyl groups, which result in a decrease in electron density on the azomethine group.

VIII. DIENE SYNTHESIS WITH IMIDOYL CHLORIDES

In 1958 Lora-Tamayo [193,194] found that 1,3-dienes react with alkanoamides or aldoximes in the presence of phosphoryl chloride to give 1,2-dihydropyridine derivatives. Reaction was carried out either in nitrobenzene at 170–180° or in benzene or toluene at 120–130°. It was suggested that the amides or aldoximes were first converted by the phosphoryl chloride into imidoyl chlorides:

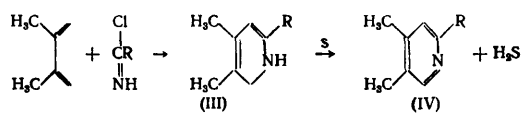


The imidoyl chlorides then underwent diene synthesis with the 1,3-dienes to form adducts (I), which decomposed under the experimental conditions into hydrogen chloride and 1,2-dihydropyridines (II):



(I) (II)

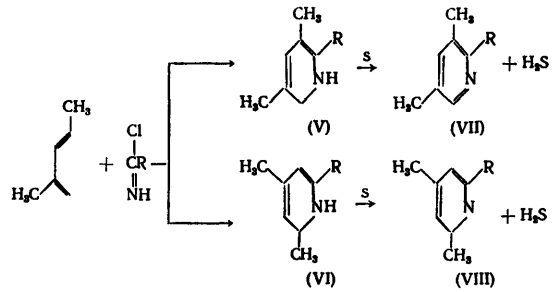
By this method the 1,2-dihydropyridine derivatives (III*a–c*) were obtained from 2,3-dimethylbutadiene with formamide, acetamide (or acetaldoxime), and benzamide (or benzaldoxime):



(III) (IV)

(*a*) R = H; (*b*) R = CH_3, (*c*) R = C_6H_5.

From 2-methylpentadiene with formamide and acetamide were obtained mixtures respectively of the isomers (V*a*) and (VI*a*) and of (V*b*) and (VI*b*):



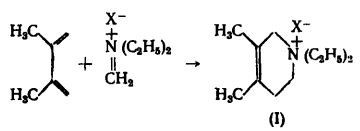
(V) (VII) (VI) (VIII)

(*a*) R = H; (*b*) R = CH_3.

Heating the dihydropyridines (III*a*), (III*b*), (V*a*), and (VI*a*) with sulphur yielded the pyridines (IV*a*), (IV*b*), (VII*a*), and (VIII*a*).

IX. DIENE SYNTHESIS WITH QUATERNARY IMMONIUM SALTS

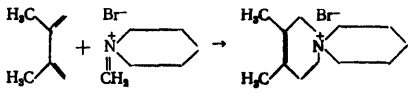
In 1963 Böhme [195] established that 2,3-dimethylbutadiene reacts in dichloromethane with quaternary immonium salts by a mechanism of diene synthesis to form quaternary 1,2,3,6-tetrahydropyridinium salts. Methylenediethylammonium chloride and bromide react with 2,3-dimethylbutadiene at room temperature to give the adducts (I*a*) and (I*b*):



(I)

(*a*) X = Cl; (*b*) X = Br.

N-Methylenepiperidinium bromide condenses with 2,3-dimethylbutadiene at 40° to form the adduct (II):



(II)

1. J.A.Norton, Chem.Rev., 31, 319 (1942).
2. K.Alder and M.Schumacher, Fortschr.Chem.org.Naturstoffe, 10, 1 (1953).
3. W.E.Hahn, Wiadomosci Chemiszne, 9, 616 (1955).
4. S.B.Needelman and M.C.Chang Kuo, Chem.Rev., 62, 405 (1962).
5. E.Müller, "Neuere Methoden der Organischen Chemie" (Translated into Russian), Inostr.Lit., Moscow, 1960, p.387.
6. C.K.Ingold, "Structure and Mechanism in Organic Chemistry" (Translated into Russian), Inostr.Lit., Moscow, 1959, p.568.
7. A.S.Onishchenko, "Dienovyi Sintez" (Diene Synthesis), Izd. Akad.Nauk SSSR, Moscow, 1963.
8. J.G.Martin and R.K.Hill, Chem.Rev., 61, 537 (1961).
9. J.Sauer, Angew.Chem., 73, 545 (1961).
10. J.Sauer, D.Lang, and A.Mielert, Angew.Chem., 74, 352 (1962).

11. J.Sauer, H.Wiest, and A.Mielert, Naturforsch., 17b, 203 (1962).
12. Yu.A.Titov, Uspekhi Khim., 31, 529 (1962) [Russ.Chem. Rev., 267 (1962)].
13. V.Georgian and J.Leppe, J.Org.Chem., 29, 40 (1964).
14. Ya.K.Syrkin and I.I.Moiseev, Uspekhi Khim., 27, 1321 (1958).
15. M.J.S.Dewar, Tetrahedron Letters, 16 (1959).
16. R.B.Woodward and T.J.Katz, Tetrahedron Letters, 19 (1959).
17. R.B.Woodward and T.J.Katz, Tetrahedron, 5, 70 (1959).
18. J.A.Berson and A.Remanick, J.Amer.Chem.Soc., 83, 4947 (1961).
19. O.Diels, J.H.Blom, and W.Koll, Annalen, 443, 242 (1925).
20. O.Diels and K.Alder, Annalen, 450, 237 (1926).
21. C.G.Le Fèvre, R.J.W.Le Fèvre, and W.T.Oh, Austral.J. Chem., 10, 218 (1957).
22. R.J.W.Le Fèvre, W.T.Oh, I.H.Reece, R.Roper, and R.L.Werner, Austral.J.Chem., 11, 92 (1958).
23. J.K.Stille and T.Anyos, J.Org.Chem., 27, 3552 (1962).
24. O.Diels, S.Schmidt, and W.Witte, Ber., 71, 1186 (1938).
25. K.Alder and H.Nikles, Annalen, 585, 81 (1954).
26. E.J.Corey and W.L.Mock, J.Amer.Chem.Soc., 84, 685 (1962).
27. E.J.Corey, D.J.Pasto, and W.L.Mock, J.Amer.Chem.Soc., 83, 2957 (1961).
28. S.Hünig, H.Müller, and W.Theier, Tetrahedron Letters, 353 (1961).
29. F.Aylword and M.Sawistowska, Chem.and Ind., 484 (1962).
30. J.Harley-Mason and J.C.W.Tims, Proc.Chem.Soc., 345 (1963).
31. C.J.MacKenzie, A.Rodgman, and C.F.Wright, J.Org.Chem., 17, 1666 (1952).
32. P.Baranger, J.Levisalles, and M.Vuidert, Compt.rend., 236, 1365 (1953).
33. P.Baranger and J.Levisalles, Bull.Soc.chim.France, 704 (1957).
34. J.C.Kuderna, J.W.Smis, J.F.Wikstrom, and S.B.Solway, J.Amer.Chem.Soc., 81, 382 (1959).
35. V.R.Skvarchenko, M.G.Kuz'min, and R.Ya.Levina, Vestnik Moskov.Univ., Khim., No.3, 169 (1957).
36. W.Vetsch, Thesis, Federal Polytechnic, Zürich, 1960.
37. J.Büchi, W.Vetsch, and P.Fabiani, Helv.Chim.Acta, 45, 37 (1962).
38. B.T.Gillis and P.E.Beck, J.Org.Chem., 27, 1947 (1962).
39. S.G.Cohen and R.Zand, J.Amer.Chem.Soc., 84, 586 (1962).
40. H.R.Snyder and J.C.Michels, J.Org.Chem., 28, 1144 (1963).
41. A.Rodgman and G.F.Wright, J.Org.Chem., 18, 465 (1953).
42. J.G.Kuderna, U.S.P. 2802012.
43. R.Criegee and A.Rimmelsin, Chem.Ber., 90, 414 (1957).
44. S.G.Cohen, R.Zand, and C.Steel, J.Amer.Chem.Soc., 83, 2895 (1961).
45. J.Pirsch and J.Jörgel, Ber., 68, 1324 (1935).
46. B.Franzus, J.Org.Chem., 28, 2954 (1963).
47. B.T.Gillis and P.E.Beck, J.Org.Chem., 28, 3177 (1963).
48. R.Ya.Levina, M.G.Kuz'min, and Yu.S.Shabarov, Vestnik Moskov.Univ., Khim., No.1, 170 (1957).
49. R.Ya.Levina, Yu.S.Shabarov, M.G.Kuz'min, N.N.Vasil'ev, and E.G.Treshchova, Dokl.Akad.Nauk SSSR, 121, 303 (1958).
50. Yu.S.Shabarov, R.Ya.Levina, N.I.Vasil'ev, and N.A.Vasilenko, Zhur.Obshch.Khim., 31, 378 (1961).
51. J.Levisalles and P.Baranger, Compt.rend., 238, 592 (1954).
52. S.G.Cohen, S.Hsiao, E.Saklad, and C.H.Wang, J.Amer. Chem.Soc., 79, 4400 (1957).
53. C.W.Huffman, Canad.J.Chem., 41, 1018 (1963).
54. Yu.K.Yur'ev and N.S.Zefirov, Zhur.Obshch.Khim., 29, 2954 (1959).
55. R.M.Acheson and C.W.Jefford, J.Chem.Soc., 2776 (1956).
56. W.Sanne and O.Schlichting, Angew.Chem., 75, 156 (1963).
57. R.Criegee, Angew.Chem., 74, 703 (1962).
58. R.Criegee, W.-D.Wirth, W.Engel, and H.A.Brune, Chem. Ber., 96, 2230 (1963).
59. R.Ya.Levina, Yu.S.Shabarov, and M.G.Kuz'min, Dokl. Akad.Nauk SSSR, 131, 1080 (1960).
60. B.Franzus and J.H.Surridge, J.Org.Chem., 27, 1951 (1962).
61. J.M.Cinnamon and K.Weiss, J.Org.Chem., 26, 2644 (1961).
62. K.Alder and G.Jacobs, Chem.Ber., 86, 1528 (1953).
63. K.Alder, K.Kaiser, and M.Schumacher, Annalen, 602, 80 (1957).
64. K.Alder, H.Jungen, and K.Rust, Annalen, 602, 94 (1957).
65. W.E.Doering, G.Laber, R.Vonderwahl, N.F.Chamberlain, and R.B.Williams, J.Amer.Chem.Soc., 78, 5448 (1956).
66. E.M.Mil'vitskaya and A.F.Plate, Zhur.Obshch.Khim., 32, 2566 (1962).
67. G.O.Schenck, E.K.von Gustorf, B.Kim, G.von Bünau, and G.Pfundt, Angew.Chem., 74, 510 (1962).
68. M.Häring, Helv.Chim.Acta, 43, 556 (1960).
69. W.Treibs, Annalen, 630, 120 (1960).
70. S.J.Cristol, E.L.Allred, and D.L.Wetzel, J.Org.Chem., 27, 4058 (1962).
71. E.F.Ullman, Chem.and Ind., 1173 (1958).
72. A.T.Blomquist and Y.C.Meinwald, J.Amer.Chem.Soc., 81, 667 (1959).
73. H.K.Hall, J.Org.Chem., 25, 42 (1960).
74. C.G.Krespan, B.C.McKusick, and T.L.Cairns, J.Amer. Chem.Soc., 83, 3428 (1961).
75. R.M.Moriarty, J.Org.Chem., 28, 2385 (1963).
76. W.T.Hunter, U.S.P. 2813867 (1957).
77. Yu.S.Shabarov, N.I.Vasil'ev, and R.Ya.Levina, Dokl.Akad. Nauk SSSR, 129, 600 (1959).
78. Yu.S.Shabarov, N.I.Vasil'ev, I.S.Levina, and R.Ya.Levina, Zhur.Obshch.Khim., 32, 2806 (1962).
79. N.I.Vasil'ev, I.S.Levina, Yu.S.Shabarov, and R.Ya.Levina, Zhur.Obshch.Khim., 33, 734 (1963).
80. R.A.Clement, J.Org.Chem., 25, 1724 (1960).
81. R.A.Clement, J.Org.Chem., 27, 1115 (1962).
82. T.J.Kealy, J.Amer.Chem.Soc., 84, 966 (1962).
83. R.C.Cookson, S.S.H.Giliani, and I.D.R.Stevens, Tetrahedron Letters, 615 (1962).
84. E.F.Ullman and E.A.Bartkus, Chem.and Ind., 93 (1962).
85. G.Wittig and R.W.Hoffmann, Angew.Chem., 73, 435 (1961).
86. G.Wittig, Angew.Chem., 74, 479 (1962).
87. G.Wittig and R.W.Hoffmann, Chem.Ber., 95, 2718 (1962).
88. G.Wittig, Pure Appl.Chem., 7, 173 (1963).
89. W.J.Chambers, C.W.Tullock, and D.D.Coffman, J.Amer. Chem.Soc., 84, 2337 (1962).
90. W.Dilthey and H.Passing, J.prakt.Chem., 153, 35 (1939).
91. W.Dilthey, C.Hurting, and H.Passing, J.prakt.Chem., 156, 27 (1940).
92. B.G.Gowenlock and W.Lüttke, Quart.Rev., 12, 321 (1958).
93. J.W.Linnett and R.M.Rosenberg, Tetrahedron, 20, 53 (1964).
94. A.Mustafa, J.Chem.Soc., 256 (1949).
95. V.I.Khruleva, "Izuchenie Reaktsii mezhdu Divinilom i Nitrobenzolom" (Reaction between Butadiene and Nitrosobenzene), Diploma Thesis, Moscow State University, 1945.
96. Yu.A.Arbuzov, Dokl.Akad.Nauk SSSR, 60, 993 (1948).
97. Yu.A.Arbuzov, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 344 (1952).
98. Yu.A.Arbuzov, Doctoral Thesis, Institute of Organic Chemistry, USSR Academy of Sciences, 1953.

99. A.I.Finkel'shtein, Yu.A.Arbuzov, and P.P.Shorygin, Zhur. Fiz.Khim., 24, 802 (1950).
100. O.Wichterle, Coll.Czech.Chem.Comm., 12, 292 (1947).
101. Yu.A.Arbuzov, Dokl.Akad.Nauk SSSR, 63, 531 (1948).
102. Yu.A.Arbuzov, Dokl.Akad.Nauk SSSR, 76, 681 (1951).
103. Yu.A.Arbuzov, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 547 (1952).
104. O.Wichterle and J.Vogel, Coll.Czech.Chem.Comm., 14, 209 (1949).
105. O.Wichterle and M.Vavruška, Chem.Listy, 46, 237 (1952).
106. S.Kojima, J.Chem.Soc.Japan, Ind.Chem.Sect., 62, 1260 (1959).
107. G.Kresze, G.Schulz, and H.Zimmer, Tetrahedron, 18, 675 (1962).
108. Yu.A.Arbuzov and N.F.Fedyukina, Dokl.Akad.Nauk SSSR, 60, 1173 (1948).
109. Yu.A.Arbuzov, Dokl.Akad.Nauk SSSR, 78, 59 (1951).
110. Yu.A.Arbuzov, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 459 (1951).
111. Yu.A.Arbuzov, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 658 (1952).
112. Yu.A.Arbuzov and L.K.Lysanchuk, Dokl.Akad.Nauk SSSR, 145, 319 (1962); 148, 246 (1963).
113. S.Kojima, J.Chem.Soc.Japan, Ind.Chem.Sect., 57, 819 (1954).
114. Yu.A.Arbuzov and T.A.Pisha, Dokl.Akad.Nauk SSSR, 116, 71 (1957).
115. Yu.A.Arbuzov, N.F.Fedyukina, V.V.Shavyrina, and R.I.Shepeleva, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 566 (1952).
116. S.Kojima, J.Chem.Soc.Japan, Ind.Chem.Sect., 57, 371 (1954); 58, 540 (1955).
117. S.Kojima, J.Chem.Soc.Japan, Ind.Chem.Sect., 59, 951 (1956).
118. R.Lukeš and J.Trojánek, Chem.Listy, 50, 1617 (1956).
119. J.Hamer and R.E.Bernard, Rec.Trav.chim., 81, 734 (1962).
120. J.Hamer and R.E.Bernard, J.Org.Chem., 28, 1405 (1963).
121. G.Kresze and G.Schulz, Angew.Chem., 72, 576 (1960).
122. G.Kresze and G.Schulz, Tetrahedron, 12, 7 (1961).
123. G.Kresze, G.Schulz, and J.Firl, Angew.Chem., 75, 375 (1963).
124. G.Kresze and G.Schulz, Chem.Ber., 96, 2165 (1963).
125. C.E.Griffin, N.F.Hepfinger, and B.L.Shapiro, J.Amer. Chem.Soc., 85, 2683 (1963).
126. G.Kresze, G.Schulz, and H.Walz, Annalen, 666, 45 (1963).
127. J.Hamer, M.Ahmad, and R.E.Holliday, J.Org.Chem., 28, 2034 (1963).
128. O.Wichterle and S.Švastal, Coll.Czech.Chem.Comm., 16, 33 (1951).
129. G.Kresze and J.Firl, Tetrahedron, 19, 1329 (1963).
130. O.Wichterle and M.Kolínský, Chem.Listy, 47, 1787 (1953).
131. O.Wichterle and M.Kolínský, Coll.Czech.Chem.Comm., 19, 493 (1954).
132. Yu.A.Arbuzov and T.A.Mastryukova, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 655 (1952).
133. Yu.A.Arbuzov and A.Markovskaya, Izv.Akad.Nauk SSSR, Otd.Khim.Nauk, 363 (1952).
134. Yu.A.Arbuzov and A.A.Onishchenko, Dokl.Akad.Nauk SSSR, 146, 1075 (1962).
135. O.Wichterle and J.Novak, Coll.Czech.Chem.Comm., 15, 309 (1950).
136. B.Belleau and Y.-K.Au-Young, J.Amer.Chem.Soc., 85, 64 (1963).
137. O.Wichterle and V.Gregor, Chem.Listy, 51, 605 (1957).
138. O.Wichterle and V.Gregor, Coll.Czech.Chem.Comm., 24, 1158 (1959).
139. D.Klamann, P.Weyerstahl, and M.Fligge, Angew.Chem., 75, 1120 (1963).
140. G.Kresze and W.Kort, Chem.Ber., 94, 2624 (1961).
141. O.Wichterle and J.Roček, Chem.Listy, 47, 1768 (1953).
142. O.Wichterle and J.Roček, Coll.Czech.Chem.Comm., 19, 282 (1954).
143. J.Roček, Chem.Listy, 47, 1781 (1953).
144. J.Roček, Coll.Czech.Chem.Comm., 19, 275 (1954).
145. E.G.Kataev and V.V.Plemenkov, Zhur.Obshch.Khim., 32, 3817 (1962).
146. M.P.Cava and R.H.Schlessinger, J.Org.Chem., 28, 2464 (1963).
147. E.S.Levchenko and A.V.Kirsanov, Zhur.Obshch.Khim., 32, 161 (1962).
148. E.S.Levchenko, Ya.G.Bal'on, and A.V.Kirsanov, Zhur. Obshch.Khim., 33, 1579 (1963).
149. G.Kresze, A.Maschke, R.Albrecht, K.Bederke, H.P.Patzschke, H.Smalla, and A.Trede, Angew.Chem., 74, 135 (1962).
150. G.Kresze and A.Maschke, German P. 1117566 (1962).
151. E.S.Levchenko and A.V.Kirsanov, Zhur.Obshch.Khim., 32, 2256 (1962).
152. J.Wieczorkowski, Chem.and Ind., 825 (1963).
153. T.L.Gresham and T.R.Steadman, J.Amer.Chem.Soc., 71, 737 (1949).
154. D.G.Kubler, U.S.P. 2905699 (1959).
155. D.G.Kubler, J.Org.Chem., 27, 1435 (1962).
156. W.J.Dale and A.J.Sisty, J.Amer.Chem.Soc., 76, 81 (1954).
157. W.J.Dale and A.J.Sisty, J.Org.Chem., 22, 449 (1957).
158. O.Achmatowicz and A.Zamojski, Croat.Chem.Acta, 29, 269 (1957).
159. O.Achmatowicz and A.Zamojski, Bull.Acad.polon.Sci., Ser.Sci.chim., geol., geog., Cl.III, 5, 927 (1957).
160. O.Achmatowicz and A.Zamojski, Roczniki Chem., 35, 799, 1251 (1961).
161. Yu.A.Arbuzov, E.M.Klimov, and E.I.Klimova, Dokl.Akad. Nauk SSSR, 142, 341 (1962).
162. W.J.Middleton, E.G.Howard, and W.H.Sharkey, J.Amer. Chem.Soc., 83, 2589 (1961).
163. W.Dilthey, W.Schommer, W.Höschen, and H.Dierichs, Ber., 68, 1159 (1935).
164. W.Polaczkowa and J.Woliński, Roczniki Chem., 26, 407 (1952).
165. T.Jaworski, Roczniki Chem., 34, 899 (1960).
166. W.Polaczkowa, T.Jaworski, and J.Woliński, Roczniki Chem., 27, 468 (1953).
167. R.Madroñero Peláez, Rev.real.acad.cienc.exact., fis.y nat.Madrid, 47, 107 (1953); Chem.Abs., 49, 3206 (1955).
168. T.Jaworski and W.Polaczkowa, Roczniki Chem., 34, 887 (1960).
169. J.Diekamnn, J.Org.Chem., 28, 2881 (1963).
170. T.Jaworski, Bull.Acad.polon.Sci., Ser.Sci.chim., geol., geog., 8, 551 (1960).
171. T.Jaworski, Roczniki Chem., 35, 1309 (1961).
172. K.Alder, "Die Methode der Diensynthese", in "Neuere Methoden der präparativen organischen Chemie", Vol.1, Verlag Chemie, Berlin, 1943, p.355.
173. G.J.Janz, R.G.Ascah, and A.G.Keenan, Canad.J.Res., 25B, 272 (1947).
174. G.J.Janz and A.G.Keenan, Canad.J.Res., 25B, 283 (1947).
175. G.J.Janz, Canad.J.Res., 25B, 331 (1947).
176. G.J.Janz and P.J.Hawkins, Nature, 162, 28 (1948).
177. P.J.Hawkins and G.J.Janz, J.Chem.Soc., 1479 (1949).
178. J.M.Robinson and G.J.Janz, U.S.P. 2494204 (1950).
179. P.J.Hawkins and G.J.Janz, J.Amer.Chem.Soc., 74, 1790 (1952).
180. C.S.Marvel and J.C.H.Hwa, J.Org.Chem., 15, 525 (1950).
181. P.J.Hawkins and G.J.Janz, J.Chem.Soc., 1485 (1949).
182. G.J.Janz, W.J.G.McCulloch, and E.F.Timpane, Ind.Eng. Chem., 45, 1343 (1953).

183. G.J.Janz and R.E.Myers, J.Amer.Chem.Soc., 75, 1910 (1953).
184. G.J.Janz and N.E.Duncan, Nature, 171, 933 (1953).
185. G.J.Janz and N.E.Duncan, J.Amer.Chem.Soc., 75, 5389 (1953).
186. G.J.Janz and S.C.Wait, J.Amer.Chem.Soc., 76, 6377 (1954).
187. G.J.Janz and W.J.H.McCulloch, J.Amer.Chem.Soc., 77, 3014 (1955).
188. G.J.Janz and W.J.H.McCulloch, J.Amer.Chem.Soc., 77, 3143 (1955).
189. J.M.S.Jarvie, W.E.Fitzgerald, and G.J.Janz, J.Amer.Chem.Soc., 78, 978 (1956).
190. G.J.Janz and M.A.DeCrescente, J.Org.Chem., 23, 765 (1958).
191. J.M.S.Jarvie and G.J.Janz, J.Phys.Chem., 60, 1430 (1956).
192. G.Kresze and R.Albrecht, Chem.Ber., 97, 490 (1964).
193. M.Lora-Tamayo, G.Garcia-Muñoz, and R.Madroñero, Bull.Soc.chim.France, 1331 (1958).
194. M.Lora-Tamayo and R.Madroñero, Rev.real.acad.cienc. exacts fiz.y.nat.Madrid, 53, 527 (1959); Chem.Abs., 54, 22 644 (1960).
195. H.Böhme, K.Hartke, and A.Müller, Chem.Ber., 96, 607 (1963).
196. J.Rigaudy, G.Cauquis, and J.Baranne-Lafont, Tetrahedron Letters, 1569 (1964).

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PROGRESS IN THE CHEMISTRY OF THE AMINODEOXY-SUGARS

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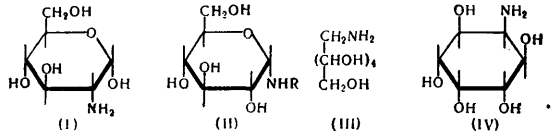
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I. INTRODUCTION

Aminodeoxy-sugars or glycosamines (I) [subsequently abbreviated to AS in the Russian text; this nomenclature has not been retained here (Ed. of Translation)] are carbohydrates containing amino-groups in place of alcoholic hydroxyl groups, and differ from *N*-glycosides (glycosylamines) (II), in the molecules of which the amino-group takes the place of a hemiacetal hydroxyl. A characteristic difference between aminodeoxy-sugars and *N*-glycosides is generally the stability of the carbon–nitrogen bond in the former and the lability of this bond in the latter[1-3]. Aminodeoxy-sugars are sometimes called "amino-sugars", but this term is not sufficiently unambiguous.

Compounds genetically related to the aminodeoxy--sugars are their reduction products — acyclic polyhydric alcohols containing amino-groups — the aminodeoxy-sugar alcohols† (III). Finally, compounds similar to the aminodeoxy-sugars and aminodeoxy-sugar alcohols are the aminodeoxy-derivatives of cyclic alcohols, *i.e.* polyhydroxycyclohexanes, called inosamines[5,6] (IV):



For a long time only two aminodeoxy-sugars — both of natural origin — were known: 2-amino-2-deoxy-D-glucose (glucosamine, 1878) and 2-amino-2-deoxy-D-galactose (galactosamine, 1914), whose configuration was established only in 1937–1939 [7] and 1945 [8] respectively. Individual synthetic aminodeoxy-sugars and aminodeoxy--sugar alcohols were prepared by Fischer and coworkers[9,10], Freudenberg, Helferich, Ohle, and others. Particular interest in aminodeoxy-sugars was aroused by the discovery of 2-deoxy-2-(*N*-methylamino)-L-glucose in the products arising from the extensive degradation of the antibiotic streptomycin[11]; later, other amino-sugars were found in a number of antibiotics. Individual inosamines were also found as components of antibiotics[5]. At the same time increasing attention was drawn to the discovery of aminodeoxy-sugars in biologically important polysaccharides and proteins. In this connection a large number of papers have been published in the last 15 years on the improvement of old methods and the development of new methods for the synthesis of aminodeoxy-sugars and aminodeoxy-sugar alcohols and the study of their properties, and also on the determination of the structure of a number of aminodeoxy-sugars of natural origin.

The importance of aminodeoxy-sugars at the present time is due to the fact that they are present in important macromolecular substances which are found in living organisms and in a number of cases exhibit biological activity; they also take part in the exchange of matter. They

† Aminodeoxy-sugar alcohols with an amino-group on a primary carbon atom are usually called glycamines[1]; it has been suggested[4] that this term be used for aminodeoxy-sugar alcohols in general.