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The synthesis and properties of unsaturated nitro-compounds of the furan series

R A Karakhanov, V I Kelarev, Yu N Polivin

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Abstract. A systematic account is provided of data in the field of the chemistry of unsaturated nitro-compounds of the furan series. The methods of synthesis of nitroalkenes of the furan series and the characteristic features of the structure and reactivity of furylnitroalkenes are examined. The general characteristics and distinctive features of the chemical reactions of furylnitroalkenes are discussed and their applications are noted. The bibliography includes 212 references.

I. Introduction

The chemistry of unsaturated nitro-compounds is a promising and vigorously developing field in modern organic chemistry. This is associated with the progress achieved in the methods of synthesis of such compounds and their high reactivity.[1-6]

During the last decades, investigators have devoted much attention to unsaturated nitro-compounds of the furan series, since they are used as synthons in the synthesis of physiologically active substances, natural products, and various furan derivatives with a functional group in the side chain and also because of their high biological activity.

Considerable data have now accumulated in the literature on the synthesis, chemical reactions, and practical applications of furylnitroalkenes, which are, however, scattered in numerous article and patent sources. Some general information about furylnitroalkenes has been briefly described in monographs.[1,7,8]

In the present review we attempted to give a systematic account and to examine critically the most significant, from our point of view, aspects of the chemistry of furylnitroalkenes: data on modern methods of synthesis, structure, reactivity, and the synthetic possibilities of these furan derivatives as well as their practical applications.

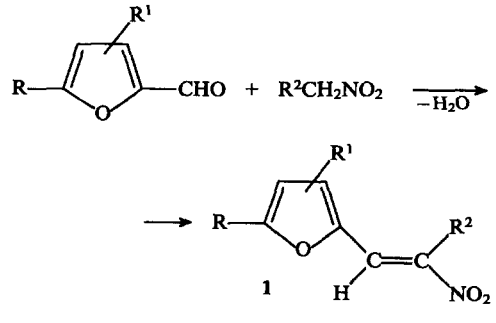
R A Karakhanov, V I Kelarev, Yu N Polivin Gubkin State Academy of Petroleum and Gas, Leninskii prosp. 65, 117917 GSP-1 Moscow, Fax (7-095) 135 8895

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II. Methods of synthesis of furylnitroalkenes

The most thoroughly investigated representatives of unsaturated nitro-compounds in the furan series are conjugated β-(5-R-2-furyl)nitroalkenes. Various methods of synthesis of conjugated heteroarylnitroalkenes have now been developed, among which the most important is the reaction involving the condensation of heteroaromatic aldehydes with primary nitro-compounds in the presence of basic catalysts — solutions of alkalies, alkali metal alkoxides, primary aliphatic amines, ammonium acetate, etc.[1-3]

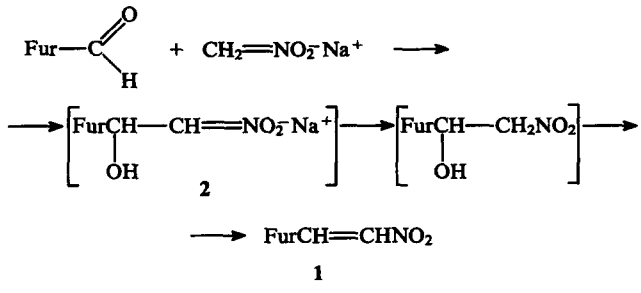
Numerous β-nitroalkenes, formed as a result of the condensation of furfural or ring-substituted furfurals with nitromethane,[9-35] nitroethane,[13,19,23,28,36-45] 1-nitropropane,[37,39,46] 1-nitrobutane,[37] 2-methyl-1-nitropropane,[46] 1-nitropentane,[39] 3-methyl-1-nitrobutane,[46] phenylnitromethane,[36,47-51] chloronitromethane,[12,52] bromonitromethane,[23,47] and nitroacetic acid derivatives — the methyl ester[53] and the nitrile,[54,55] have been described. It is noteworthy that these reactions (with the exception of the condensation involving methyl nitroacetate) take place stereoselectively and lead to the nitroalkenes **1**, having the (*E*)-configuration, which has been confirmed by spectroscopic methods.



R = H, Me, Cl, Br, I, NO_2, $HOCH_2$, MeOOC, CN, Me_2N, morpholino, PhN(Me), aryl, arylthio, $MeSO_2$, $PhSO_2$, $3\text{-}NO_2C_6H_4O$, heteroarylthio; R^1 = H, 4-Cl, 4-Br, 3-I, $3\text{-}NO_2$; R^2 = H, Me Et, Pr^n, Pr^i, Bu^n, Bu^i, Ph, $4\text{-}ClC_6H_4$, Cl, Br, NC, MeOOC, $MeOOCCH_2$.

In the synthesis of β-nitroalkenes of the above type, alkali metal hydroxides or alkoxides as well as primary amines (methylamine, butylamine, 1-aminopentane, etc.) are usually employed as condensing agents. Two main preparative methods of synthesis of β-(5-R-2-furyl)nitroalkenes **1** have been developed accordingly.

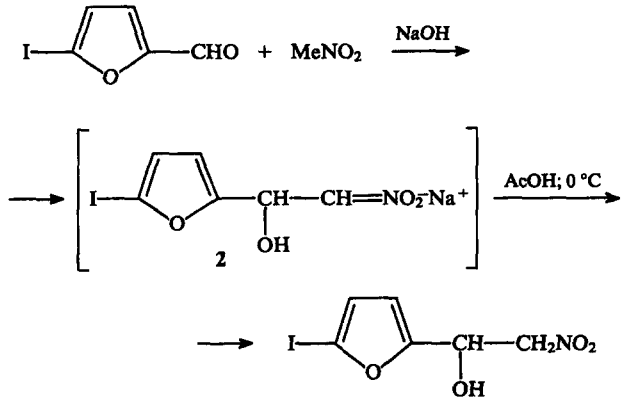
According to the first method, an equimolar mixture of an aldehyde of the furan series and nitromethane in methanol or ethanol is gradually treated, whilst cooling (−15 to −10 °C), with equivalent amounts of an aqueous or alcoholic solution of alkali or a sodium alkoxide solution in the corresponding alcohol. The reaction is accompanied by an appreciable heat change and is completed by the formation of an insoluble salt of the β-nitroalcohol **2**, which is then dissolved by adding water. On subsequent acidification with a dilute solution of an inorganic acid, the β-nitroalkene **1** is isolated in 50%–92% yield (method *A*).[9–23,26–28,30–35,56–58]



Here and henceforth Fur = 2-furyl.

This reaction should be regarded[1,3] as the result of the nucleophilic attack by the nitromethane anion on the electron-deficient carbon atom of the carbonyl group of 5-R-furfural, which leads initially to the aldol condensation product — a salt of the β-nitroalcohol **2**. There are no literature data concerning the mechanism of the dehydration of salts of β-nitroalcohols by inorganic acid solutions.

It has been reported[30] that, when the reaction mixture in the reaction of 5-iodofurfural with nitromethane and NaOH (1 : 1 : 1 molar ratios) is acidified cautiously with acetic acid, it is possible to isolate the unstable 1-(5-iodo-2-furyl)-2-nitroethanol. This finding constitutes confirmation of the formation in the given reaction of the salt **2** as an intermediate.

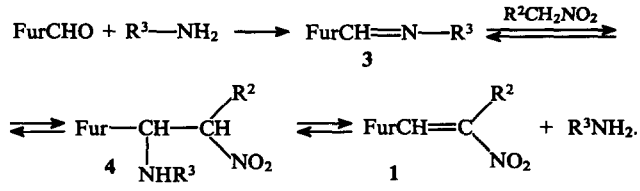


The study[59] of the kinetics of the condensation of furfural with nitromethane in aqueous alcohol in the presence of KOH also confirmed the intermediate formation of the salt **2**. The kinetic curves for the decrease in the furfural concentration are described by the equation for first-order reversible reactions under pseudo-unimolecular conditions with respect to furfural or by the equation for second-order reactions at comparable concentrations of furfural and nitromethane.

The condensation of furfural with nitromethane,[21] in which a solution of $Ca(OH)_2$ is used as condensing agent, is of interest for industrial application. It is noteworthy that alkalies and alkali metal alkoxides proved to be effective condensing agents in the reactions of furfural and its substituted derivatives not only with nitromethane but also with nitroethane,[19,23,28,36,40,41,43] chloronitromethane,[12,52] and bromonitromethane.[23,47] However, in the case of phenylnitromethane, 1-nitropropane, and 1-nitrobutane, the use of alkaline catalysts leads to appreciable charring of the reaction mixture.

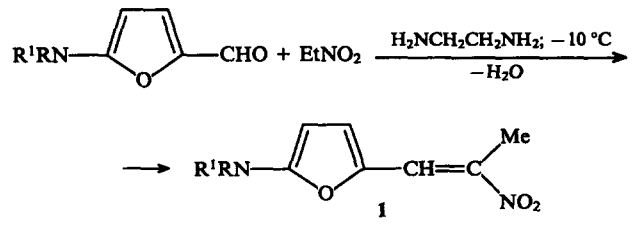
The second method (method *B*) of synthesis of β-(5-R-2-furyl)-nitroalkenes **1** represents a modified Knoevenagel reaction using methylamine, butylamine, 1-aminopentane, ethylenediamine, or piperidine as the catalysts.[13,29,36–38,41,42,44–48] In this method, an equimolar mixture of the furan aldehyde, and nitroalkane in dry ethanol is kept at 20 °C for 3–10 days[47,60] or is refluxed for several hours[13,37,61,62] with 5–10 mol% of a primary amine: under these conditions, the yield of the nitroalkenes **1** is 35–85%.

The mechanism of the catalytic action of primary amines apparently reduces to the formation of the azomethines **3** as intermediates, which react with nitroalkanes to form adducts — unstable β-nitroamines **4**. The latter decompose to the β-nitroalkene **1** and an amine under the influence of the excess nitroalkene:[1,3]



Although a clear cut correlation between the influence of substituents in the furfural ring on the reactivity of the carbonyl group in condensation reactions with nitroalkanes and the yields of β-nitroalkenes **1** are not quoted in the literature, nevertheless certain qualitative features of these reactions can be traced on the basis of the available data. For example, it has been noted[47] that the rate of condensation of 5-R-furfurals with bromonitromethane (method *A*) and phenylnitromethane (method *B*) diminishes in the sequence H > CH_3 > Cl > Br > NO_2 depending on the nature of the substituent R. Thus β-(5-nitro-2-furyl)-α-phenylnitroethylene was obtained in 26% yield only after keeping the reaction mixture at 20 °C for 14 days. On raising the temperature, appreciable charring was observed. The authors[12] were unable to synthesise α-bromo-β-(5-nitro-2-furyl)-nitroethylene by the direct condensation of 5-nitrofurfural with bromonitromethane under the conditions of method *A*; on the other hand, the condensation of 5-nitrofurfural with chloronitromethane and NaOH in aqueous methanol leads to α-chloro-β-(5-nitro-2-furyl)nitroethylene in 41% yield.

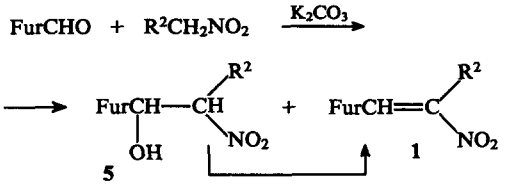
Attempts to obtain β-(5-dimethylamino-2-furyl)nitroethylene by the condensation of 5-dimethylaminofurfural with nitromethane in the presence of alkaline agents proved unsuccessful.[18] However, *N*,*N*-disubstituted 5-aminofurfurals[41,42] react with nitroethane in the presence of catalytic amounts of ethylenediamine at −10 to 0 °C, affording the corresponding β-nitroalkenes **1** in satisfactory yields (50%–80%).



R = R^1 = Me; R = Ph, R^1 = Me; RR^1N = morpholino.

According to patent data,[44] 5-(4-chlorophenyl)-2-(2-nitroprop-1-enyl)furan is formed in 50% yield on refluxing 5-(4-chlorophenyl)furfural in nitroethane in the presence of piperidine.

It has been reported[46] that the condensation of furfural with primary nitroalkanes in ethanol in the presence of K_2CO_3 or $KHCO_3$ results in the formation, together with β-(2-furyl)nitroalkenes **1**, also of the corresponding β-nitroalcohols **5**—the products of aldol condensation, their yield reaching 70%.

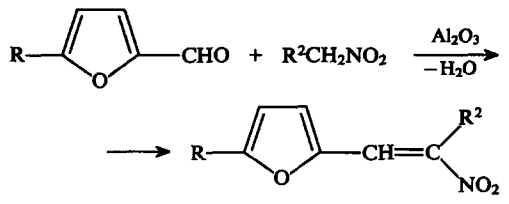


R^2 = H, Me, Et, Pr, Pr^i, Bu^i.

The dehydration of the β-nitroalcohols **5** leads to the β-nitroalkenes **1**; for example,[63] treatment of 1-(2-furyl)-2-nitroethanol **5** (R^2 = H) with dicyclohexylcarbodiimide in the presence of Cu_2Cl_2 in ether (35 °C, 24 h) affords β-(2-furyl)nitroethylene **1** in 66% yield.

Anion-exchange resins have also been used as catalysts in the condensation of furfural with nitromethane.[64,65] β-(2-Furyl)-nitroethylene was synthesised in 38%–46% yield in the presence of the AN-2F anion-exchange resin. The catalytic activities of various anion-exchange resins have been investigated[65] and it has been established that they decrease in the following sequence: EFE-10P > AN-2F > PE-9 > AN-9F. The strongly basic EFE-10P anion-exchange resin, containing quaternary ammonium groups, proved to be the most active catalyst in the above reaction. When this catalyst was used, the yield of β-(2-furyl)nitroethylene was 78%–86% (40 °C, 5 h).

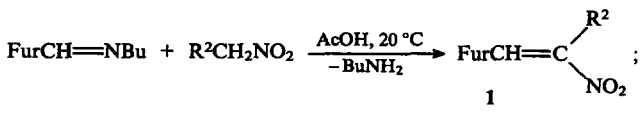
In 1985, Italian workers[39] proposed an effective method of synthesis of β-nitroalkenes of the furan series in 70%–93% yields by condensing equimolar amounts of 5-R-furfurals with nitroalkanes and carboxylic nitroacid esters on the surface of chromatographic Al_2O_3 without a solvent (20 °C, 30–48 h).



R = H, Me; R^2 = Me, Et, Bu^n, $MeOOCCH_2$, $MeOOC(CH_2)_5$, 2-methyl-1,3-dioxolan-2-ylmethyl.

The authors note that this reaction apparently involves the intermediate formation of the corresponding β-nitroalcohols **5**, which are subsequently dehydrated.

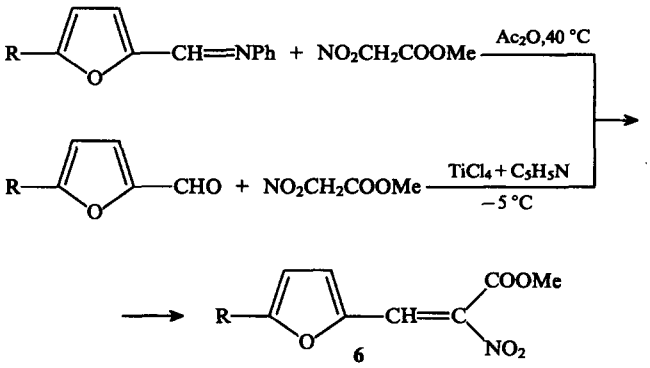
Robertson[49,50] used the condensation of phenyl- or 2-chlorophenyl-nitromethane with *N*-furfurylidenebutylamine in order to synthesise β-(2-furyl)-α-arylnitroethylenes (**1**, R = R^1 = H, R^2 = Ph, 2-ClC_6H_4):



R^2 = Ph, 2-ClC_6H_4.

The reaction was carried out by keeping equimolar amounts of the reactants in glacial acetic acid for several hours at 20 °C.

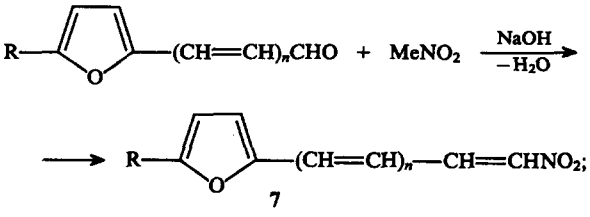
Czechoslovak scientists[53] synthesised the methyl esters of β-(5-R-2-furyl)-α-nitroacrylic acids **6** by condensing methyl nitroacetate with *N*-(5-R-furfurylidene)anilines in acetic anhydride (40–50 °C, 10 h: yield 30%–45%) or with 5-R-furfurals in the presence of $TiCl_4$ and pyridine in CCl_4 (−5 to 0 °C, 24 h; yield 77%–85%). However, the latter method has not come to be widely used for the synthesis of furylnitroalkenes.



R = H, Br, I, Me, MeOOC, NO_2.

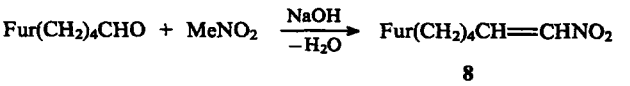
It is noteworthy that the reaction with 5-nitrofurfural takes place stereoselectively[53] to form the (*E*)-isomer of compound **6**. On the other hand, the condensation of other furan aldehydes with nitroacetic acid ester results in the formation of a mixture of (*E*)- and (*Z*)-stereoisomeric nitroalkenes **6** in which the (*Z*)-isomer predominates.

There are isolated literature data[29,66,67] concerning the synthesis of conjugated nitrodienes and nitrotrienes of the furan series **7**. Compounds of this type were synthesised in 70%–75% yield by condensing β-(2-furyl)acroleine or 5-(2-furyl)penta-2,4-dienal with nitromethane in the presence of NaOH (method *A*):

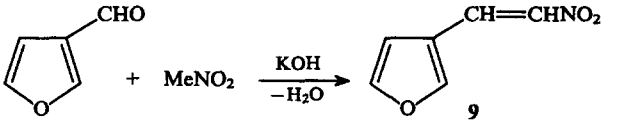


n = 1, 2; R = H, NC.

6-(2-Furyl)-1-nitrohex-1-ene **8** was synthesised in 47% yield by condensing 5-(2-furyl) pentanal with nitromethane and NaOH at 0 °C.[68]



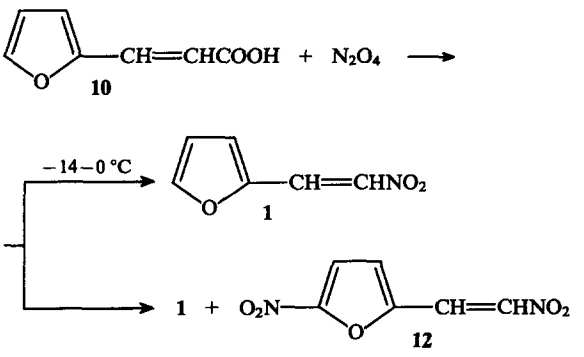
Data concerning the synthesis[69,70] of β-(3-furyl)nitroethylene **9** in 80%–86% yield by the condensation of 3-formylfuran, which is difficult to obtain, with nitromethane in the presence of KOH in methanol appeared in the literature in recent years.



β-Nitroalkenes of the furan series have been obtained using as the starting compounds β-(2-furyl)acrylic acids, which are formed in a high yield on condensation of furfural or substituted furfurals with malonic acid in the presence of piperidine.[7,71]

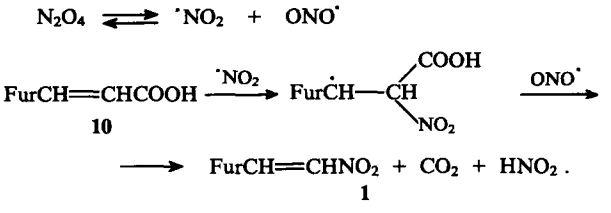
The nitration of (*E*)-β-(2-furyl)acrylic acid **10** with concentrated nitric acid in acetic anhydride has been described.[8,72–76] (*E*)-β-(5-Nitro-2-furyl)acrylic acid **11** was isolated as the main reaction product in all the investigations. It has been established[77] that (*E*)-β-(2-furyl)nitroethylene (**1**, R = R^1 = R^2 = H) and (*E*)-β-(5-nitro-2-furyl)nitroethylene **12** are formed under these

conditions as side products. The last two substances have also been obtained by passing nitrogen dioxide through a solution of the acid **10** in benzene, acetic acid, or acetic anhydride.[78]



When the acid **10** is nitrated with an equimolecular amount of nitrogen tetroxide in ether[79] at −12 to −14 °C or in benzene and acetic acid[78] at 0 °C, the nitro-group enters preferentially the side chain and the main reaction product is β-(2-furyl)nitroethylene **1** (yield 16%–18%).

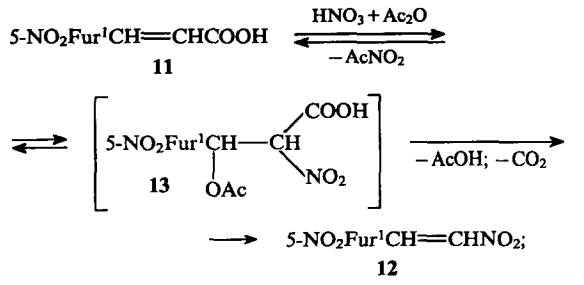
At a higher temperature, the ring is also nitrated;[78] the reaction products contain up to 15% of the β-nitroalkene **12**. According to Sitkin and Klimenko,[79] the synthesis of β-nitroethylene **1** from the acid **10** proceeds at reduced temperatures by a radical mechanism, which can be represented schematically as follows:



Together with the nitroalkene **1**, oxalic acid, formed as a result of the partial oxidation of the nitroalkene **1**, was isolated in the above reaction as a side product; the reaction was accompanied also by the formation of tarry products.

When the acid **10** is acted upon by a large excess of N_2O_4 at −10 °C, products of nitration in the furan ring are obtained[79] — β-(5-nitro-2-furyl)acrylic acid **11** (51.5%) and insignificant amounts of the β-nitroalkene **12**.

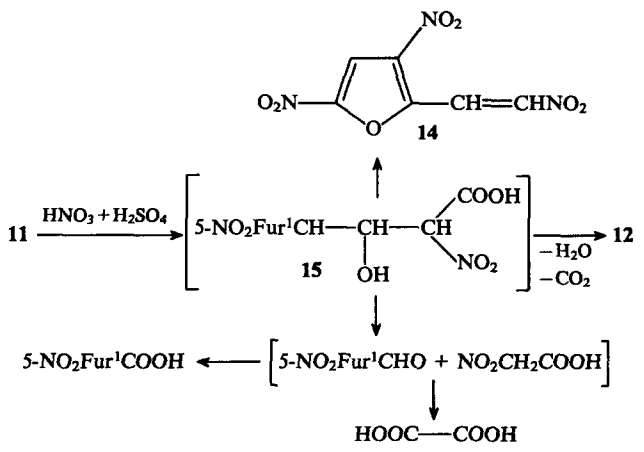
When the acid **11** is nitrated with fuming HNO_3 in acetic anhydride[80] (−20 °C; or 20 °C, 4 h), the nitroalkene **12** is formed in 15% yield:



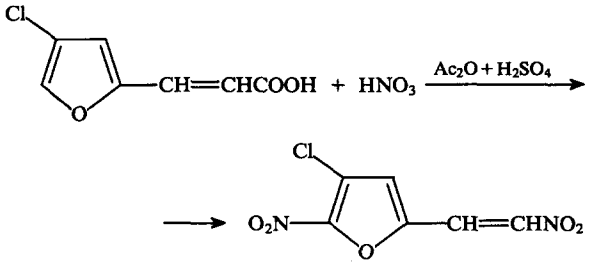
here and henceforth 5-NO_2Fur^1 = 5-nitro-2-furyl.

The unstable adduct **13** — the product of the addition of acetyl nitrate, formed in the mixture of acetic anhydride and fuming HNO_3, is an intermediate in this reaction.

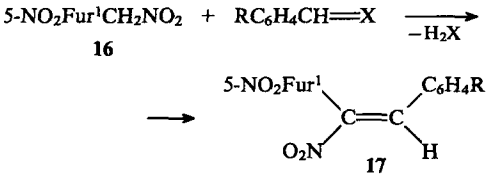
The authors established that the β-nitroalkene **12** is formed in 77% yield when the acid **11** is refluxed with 10% HNO_3; 5-nitrofurfural and 5-nitrofuran-2-carboxylic acid were isolated as side products under these conditions. Treatment of the acid **11** with the nitrating mixture comprising fuming nitric acid and concentrated sulphuric acid[80] at 5 °C affords 13% of β-(3,5-dinitro-2-furyl)nitroethylene **14** together with the β-nitroalkene **12**. The intermediate under these conditions is the unstable adduct **15** — the product of the addition of the elements of HNO_3 to the double bond; 5-nitrofuran-2-carboxylic acid and oxalic acid are formed as side products.



When β-(4-chloro-2-furyl)acrylic acid is nitrated with fuming HNO_3 in acetic anhydride (molar ratios 1 : 4 : 10) in the presence of catalytic amounts of H_2SO_4 at −10 to −5 °C, β-(4-chloro-5-nitro-2-furyl)nitroethylene is obtained in 70% yield.[23]



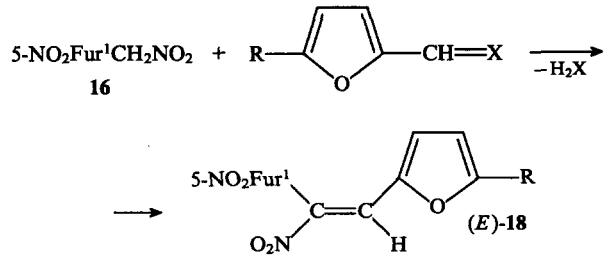
Condensation of 2-nitromethyl-5-nitrofuran **16** with aromatic aldehydes, ammonium acetate, and acetic acid in benzene (refluxing for 3–5 h) or with *N*-benzylidenebutylamines in acetic acid at 20 °C leads to α-nitro-α-(5-nitro-2-furyl)-β-arylethylene **17** having the (*E*)-configuration.[81–83]



X = O, NBu; R = H, 4-Me, 4-MeO, 2-MeO, 4-Me_2N, 2-F, 4-Cl, 4-NC, 2-NO_2, 4-NO_2, 4-AcNH.

The authors note that the first method makes it possible to obtain the β-nitroalkenes **17** in a satisfactory yield (25%–30%) only from benzaldehydes containing electron-donating substituents. The α-nitroalkenes **17** are synthesised by the second method from benzaldehydes with electron-accepting groups (yield 41%–84%).

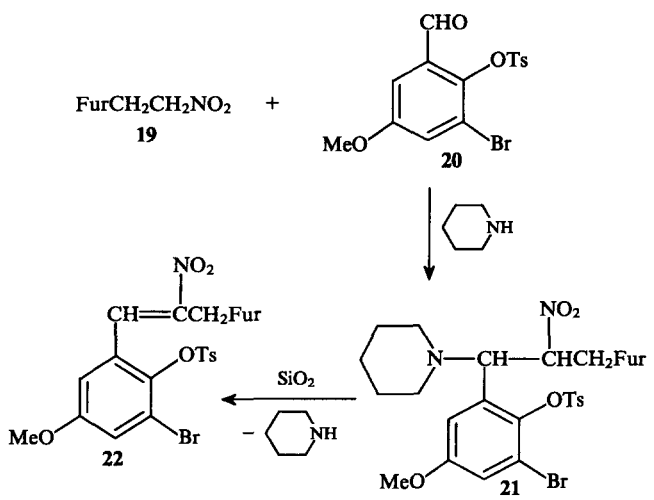
(*E*)-α-nitro-α-(5-nitro-2-furyl)-β-(5-R-2-furyl)ethylenes **18** were obtained in 28%–91% yield under analogous conditions from the nitromethyl derivative **16** and the 5-substituted furfurals or *N*-(5-R-furfurylidene)butylamines.[84]



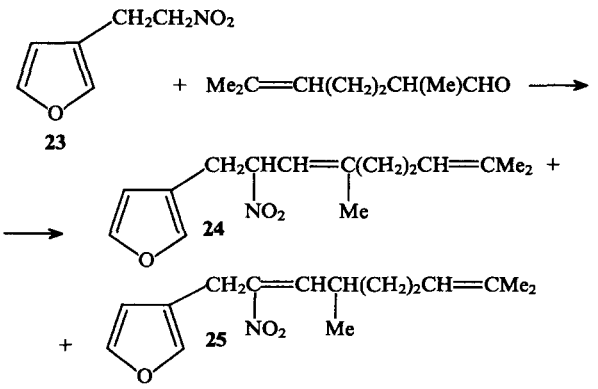
X = O, NBu; R = H, Me, Br, I, Ph, 4-ClC_6H_4, 2-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4, 4-$NO_2C_6H_4$.

However, the condensation of compound **16** with 5-nitrofurfural or with *N*-(5-nitrofurfurylidene)butylamine results in the formation of a 1:2 mixture of (*E*)- and (*Z*)-α,β-di(5-nitro-2-furyl)nitroethylene (**18**, R = NO_2) in 48% yield.

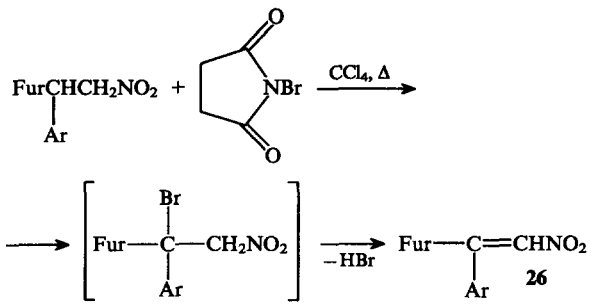
The condensation of 2-(2-furyl)-1-nitroethane **19** with a derivative of salicylaldehyde **20** in the presence of piperidine under the conditions of the Knoevenagel reaction[85] leads to the β-nitroamine **21** (yield 65%), the deamination of which on the surface of silica gel affords the nitroalkene **22** in 65% yield.



2-(3-Furyl)-1-nitroethane **23** reacts with 2,6-dimethylhept-5-enal in the presence of *N*,*N*-dimethylethylenediamine in toluene (refluxing for 2 h) to form a mixture of the allylic nitro-compound **24** (yield 46%) and the conjugated nitroalkene **25** (yield 25%).[70] On refluxing with triethylamine in benzene, the latter isomerises quantitatively to the nitroalkene **24**, which is a key compound in the synthesis of the pheromone dendrolasin.

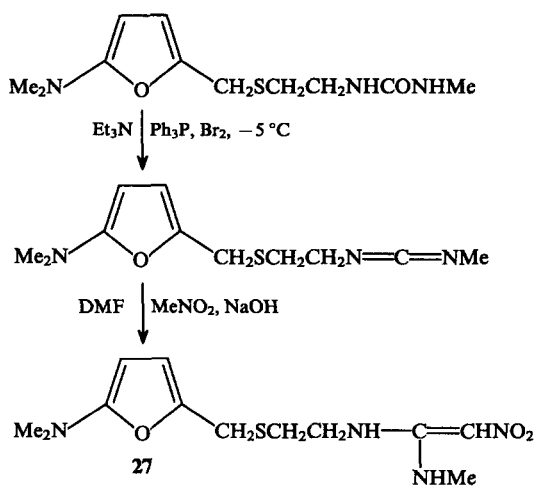


The bromination of 1-aryl-1-(2-furyl)nitroethanes by treatment with *N*-bromosuccinimide in CCl_4 (refluxing for 1 h) results in the formation of β-aryl-β-(2-furyl)nitroethylenes **26** in the form of a mixture of the (*E*)- and (*Z*)-isomers in 40%–43% yield.[86]



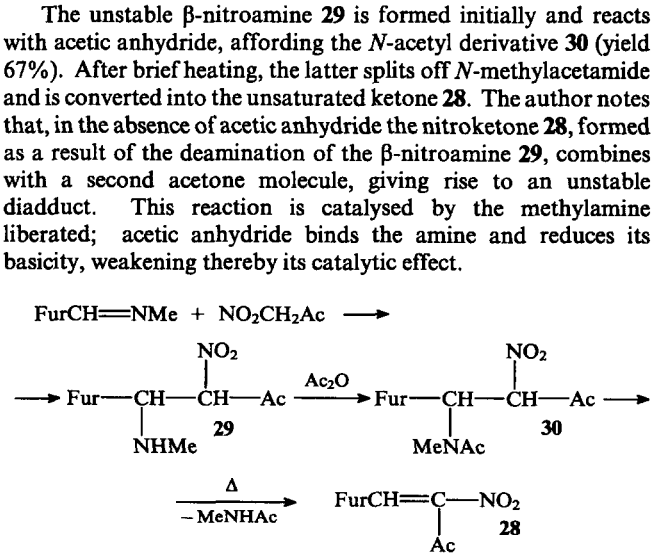
Ar = Ph, 3,4-$(OCH_2O)C_6H_3$.

An effective method of synthesis of the ulcerostatic preparation ranitidine **27**, which is nitrovinyl derivative of the furan series, in accordance with the scheme shown below has been reported.[87]



There exist also isolated data concerning the synthesis of unsaturated nitroketones of the furan series. By condensing furfurylidenemethylamine with nitroacetone in the presence of acetic anhydride, Dornow[88] synthesised 4-(2-furyl)-3-nitrobut-3-en-2-one **28** in 17% yield.

The unstable β-nitroamine **29** is formed initially and reacts with acetic anhydride, affording the *N*-acetyl derivative **30** (yield 67%). After brief heating, the latter splits off *N*-methylacetamide and is converted into the unsaturated ketone **28**. The author notes that, in the absence of acetic anhydride the nitroketone **28**, formed as a result of the deamination of the β-nitroamine **29**, combines with a second acetone molecule, giving rise to an unstable diadduct. This reaction is catalysed by the methylamine liberated; acetic anhydride binds the amine and reduces its basicity, weakening thereby its catalytic effect.



In 1969 German scientists[89] synthesised an unsaturated nitroketone of another type — 1-(2-furyl)-4-nitrobut-2-en-1-one **31**, which is an interesting and promising synthon for the preparation of various furan derivatives with functional groups in the side chain. Compound **31** is formed in 80% yield on reaction of

equimolar amounts of 2-acetylfuran and 2-dimethylamino-1-nitroethylene in the presence of potassium ethoxide (60–70 °C) with subsequent hydrolysis (20 °C) of the intermediate potassium salt **32**.

$$\text{FurAc} + \text{Me}_2\text{NCH}=\text{CHNO}_2 \xrightarrow[-\text{Me}_2\text{NH}]{\text{EtOK}-\text{EtOH}} \text{FurCOCH}=\text{CH}-\text{CHNOO}^-\text{K}^+ \xrightarrow{\text{HOH}} \underset{\mathbf{31}}{\text{FurCOCH}=\text{CHCH}_2\text{NO}_2}$$

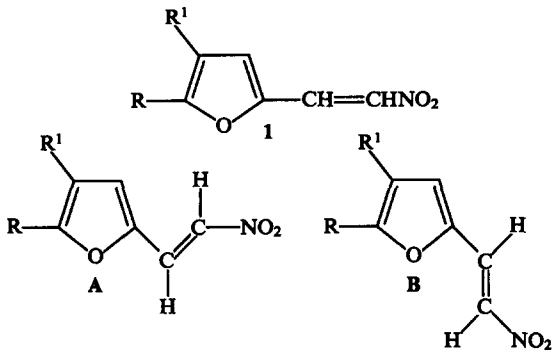
The authors note that this nitroketone is highly reactive and enters into many reactions characteristic of α,β-unsaturated ketones and primary nitrocompounds.

III. Structure and reactivity of furylnitroalkenes

1. The dipole moments of furylnitroalkenes

Important information about the steric structure and reactivity of β-(5-R-2-furyl)nitroalkenes has been obtained by studying their dipole moments.[1,62,90–94] The low aromaticity of furan[95,96] makes it possible to expect a strong π-interaction in the chain between the double bond of the vinyl fragment and the NO_2 group with participation of the furan ring and its substituents in the 5-position.

β-(5-R-4R¹-2-Furyl)nitroethylenes **1** are regarded[49,91] as planar *trans*-isomers which can exist in two forms — *trans*-(*S*)-*trans* (form *A*) and *cis*-(*S*)-*trans* (form *B*), depending on the positions of the double bonds of the furan and the vinyl group relative to the C(2)–C_β bond.



R = H, Me, Cl, Br, I, NO_2; R¹ = H; R = Br, I; R¹ = Br.

The low aromaticity of the system makes the *trans*-(*S*)-*trans* structure, i.e. structure *A*, energetically more favourable.[41,91] The observed discrepancies between the experimental and calculated dipole moments ($\Delta\mu = \mu_{exp} - \mu_{calc}$) are then attributed to the interaction moment (μ_{int}) arising as a result of the π-conjugation in the molecule.

By analogy with 5-halofurfurals,[93] negative values of μ_{int} should be expected for β-(5-halo-2-furyl)nitroethylenes (**1**; R = Cl, Br, I; R¹ = H, Br) as a consequence of the $-J$ effect of these substituents. However, a higher value of μ_{exp} compared with μ_{calc} is observed for all the compounds of this series (Table 1). This is apparently caused by the stronger electron-accepting properties of the β-nitrovinyl group compared with the aldehyde group.[3,41,94] The electronic interaction of the halogen with the furan ring in the given compound should therefore be expressed by the $+M$ effect. Hence it is of interest to note that an increase in μ_{int} is observed for β-nitroalkenes **1** in the following sequence of substituents 5-R: I < Br < Cl (0.13, 0.30, and 0.76 D).

Table 1. The dipole moments of (*E*)-β-(5R-4R¹-2-furyl)-α-R²-nitroethylenes.[41,90–92,97]

R	R¹	R²	Dipole moments/D		
			μ_{exp}	μ_{calc}	μ_{int}
H	H	H	4.94	4.81	0.13
Me	H	H	4.76	5.31	0.45
Cl	H	H	4.97	4.21	0.76
Br	H	H	4.65	4.35	0.30
I	H	H	4.81	4.68	0.13
NO_2	H	H	4.15	3.56	0.59
Br	Br	H	3.70	3.03	0.67
I	Br	H	3.52	3.39	0.13
H	H	Me	4.87	5.07	−0.20
Me	H	Me	5.46	5.31	0.15
Cl	H	Me	4.35	4.31	0.04
Br	H	Me	4.24	4.35	−0.11
I	H	Me	4.38	4.68	−0.30
NO_2	H	Me	4.05	3.56	0.49
Morpholino	H	Me	5.66	–	–
MeNPh	H	Me	6.97	6.27	0.70
Me_2N	H	Me	6.62	6.28	0.34
Br	Br	Me	3.23	3.03	0.20
I	Br	Me	3.40	3.39	0.01
H	H	Ph	5.17	5.07	0.10
Me	H	Ph	5.66	5.31	0.35
Cl	H	Ph	4.59	4.21	0.35
Br	H	Ph	4.22	4.35	−0.13
I	H	Ph	4.45	4.68	−0.23
NO_2	H	Ph	3.88	3.56	0.32
Br	Br	Ph	3.41	3.03	0.38
I	Br	Ph	3.29	3.39	−0.10
H	H	Br	4.71	4.70	0.01
Me	H	Br	5.49	4.99	0.50
Cl	H	Br	4.40	4.22	0.18
Br	H	Br	4.44	4.31	0.13
I	H	Br	4.30	4.46	−0.16
NO_2	H	Br	3.77	4.54	−0.77
Br	Br	Br	3.41	3.50	−0.09
I	Br	Br	3.71	3.59	0.12
H	H	Cl	4.80	4.71	0.09
Br	H	Cl	4.32	4.30	0.02
NO_2	H	Cl	3.67	4.52	−0.85

The experimental dipole moments of β-(5-R-4-R¹-2-furyl)-α-methylnitroethylenes **33** are lower by 0.2–0.6 D than the corresponding values for β-(5-R-4-R¹-2-furyl)nitroethylenes **1** (Table 1).[41,92]

The dipole moment probably changes as a result of the breakdown of the planar configuration due to steric hindrance between the methyl group, the nitro-group, and the oxygen of the furan ring. Rotation about the C_α–N and C(2)–C_β bonds weakens the π-interaction involving the electrons of the substituents in the 5-position in the vinyl group and of the NO_2 group, which decreases the dipole moment. The angle of rotation can then be estimated approximately from the formula

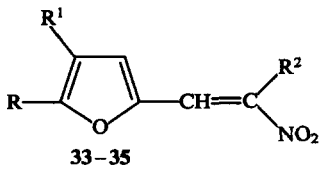
$$\mu = \mu_{int} \cos^2\theta ,$$

where $\Delta\mu = \mu_{exp} - \mu_{calc}$ for the β-nitroalkene **33**, and θ is the effective angle of rotation.

The angle θ is approximately 60° for β-(5-methyl-2-furyl)-α-methylnitroethylene (**33**, R = Me, R¹ = H, R² = Me), where appreciable changes in the dipole moment of the C(5)–Me bond due to the breakdown of conjugation do not occur because the methyl group has weak electron-donating properties.[41]

The introduction of the phenyl group in the α-position should induce an even greater breakdown of the planar configuration via the rotation of the C_α–N and C(2)–C_β bonds. However, the values of μ_{exp} for β-(5-R-4-R¹-2-furyl)-α-phenylnitroethylenes **34**

occupy an intermediate position between those for the nitroethylenes **1** and the α-methylnitroethylenes **33**. This is apparently caused by the simultaneous rotation of the phenyl group, which creates conditions for the minimum deviation of the principal fragment of the molecule from the planar structure.[91]



33–35

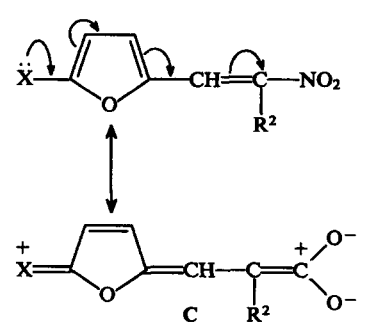
R = H, Me, Cl, Br, I, NO_2, Me_2N, morpholino, PhNMe; R^1 = H;
R = Br, I; R^1 = Br;
33: R^2 = Me; **34**: R^2 = Ph; **35**: R^2 = Cl, Br.

It has been suggested[41] that the $+M$ effect of the halogens predominates in the β-(5-halo-2-furyl)nitroethylenes **1** owing to the strong electron-accepting properties of the nitrovinyl fragment and the planar configuration of these molecules. On the other hand, the decrease in the degree of conjugation in the non-coplanar molecules of β-(5-halo-2-furyl)-α-R^2-nitroethylenes (**33**, **34**; R^2 = Me, Ph) promotes the appearance of the usual electron-accepting properties of the halogen in the 5-position. The latter follows from the appreciably smaller (R = Cl) and even negative (R = Br, I) values of μ_{int}. Evidently this is associated with the fact that the interaction of the electron-accepting nitrovinyl group with the substituent in the furan ring weakens when the planar conformation of the molecules breaks down.[91]

On the other hand, more favourable conditions for the planar molecular structure arise for β-(5-R-4-R^1-2-furyl)-α-halonitroethylenes (**35**; R^2 = Cl, Br).[91] High values of μ_{int}, characteristic of planar-(5,R-4-R^1-2-furyl)nitroethylenes **1**, are typical for these compounds. The high degree of conjugation in these compounds can be accounted for by the operation of two factors: the smaller bulk of the halogens compared with the methyl and phenyl groups and the greater electronegativity of the α-halo-α-nitrovinyl fragment.

2. Electronic absorption spectra of furylnitroalkenes

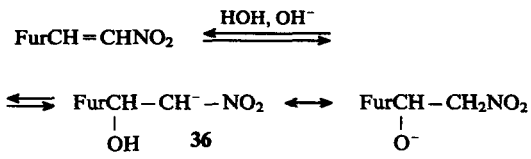
There are three absorption bands in the UV spectra of β-(5-R-4-R^1-2-furyl)-α-R^2-nitroalkenes **1** and **33–35** in the ranges 205–245, 234–282, and 322–428 nm. The first two bands can be assigned to the $\pi-\pi^*$ and $n-\pi^*$ electronic transitions in the furan, the aryl substituents, and the vinyl group.[18,98] The most intense band in the spectra of the given compounds (322–428 nm; the *K* band) refers to the $\pi-\pi^*$ transition throughout the conjugated polyene system and yields important information about the planarity of the system.[1,18,91,98,99] The observed bathochromic shift compared with 2-vinylfuran (261 nm) is associated with the appearance of the dipolar structure **C** as a consequence of direct polar conjugation:



C

We may note that the corresponding absorption band of β-nitrostyrene (309 nm)[1] lies below that of β-(2-furyl)nitroethylene **1** (346 nm) as a consequence of the stronger electron-donating properties of the furyl group.[95]

It has been reported[59,100] that, when the UV spectrum of the β-nitroethylene **1** is recorded in aqueous ethanol at pH 11.5–12.6, the absorption band at λ_{max} = 346 nm vanishes and a band appears at λ_{max} = 252–255 nm. This finding can be accounted for by the appearance of the stable mesomeric ion **36**.



The extinction coefficient ε for this nitroalkene (ε = 24 516) is approximately three times greater than for *cis*-β-(2-furyl)acrylic acid (ε = 9780), which is also evidence in support of the *trans*-conformation of furylnitroethylenes.[100]

In the UV spectra of β-(2-furyl)-α-R^2-nitroethylenes, and absorption *K* band undergoes a bathochromic shift as R^2 is varied in the sequence H (346) < Me (348) < Ph (353) < Cl (358) < Br (365) < CN (371 nm).[18,47,55,59,91,100] The appreciable bathochromic shift and the hyperchromic effect for β-(2-furyl)-α-nitroacrylonitrile (λ_{max} = 371 nm; ε = 21 500) compared with β-(2-furyl)nitroethylene indicates an increased contribution of the dipolar structure **C** to the ground state of the molecule.[55]

A bathochromic shift of the absorption *K* band is observed in the spectra of β-(5-R-2-furyl)nitroethylenes **1**. It increases in the following sequence of substituents R: H (346) < NO_2 (350) < Cl (358) < Br (355) < I (357) < Me (367) < PhS (370) < NMe_2 (428 nm).[18,55,59,80,91,100] The relatively small shift of the absorption maximum for R = NO_2 is associated with the non-coplanarity of this substituent relative to the nitrovinyl fragment.[91] The UV spectrum of β-(3,5-dinitro-2-furyl)nitroethylene **14** exhibits a hypsochromic shift of the *K* band (λ_{max} = 340 nm) as a consequence of the decrease in the mobility of the π-electron system induced by the introduction of the second nitro-group into the furan ring.[80]

The appreciable bathochromic shift of the *K* band in the spectra of β-(5-dimethylamino-2-furyl)-R^2-nitroethylenes (R^2 = H, λ_{max} = 428 nm; R^2 = Me, λ_{max} = 480 nm) can be explained by the possibility of direct polar conjugation in the molecules of these compounds and by the approach to a planar structure.[91]

The absorption maxima of the *K* band in the spectra of different β-(5-halo-2-furyl)-α-R^2-nitroethylenes can be arranged in the following sequence based on increasing wavelengths as a function of the substituents R^2;[18,47,91] Cl < Br < I. This is characteristic also of 4-halonitrobenzenes.[101] This sequence is the reverse of that observed for the changes in the dipole moment μ_{int} in terms of the same substituents, which can be explained by the greater $+M$ effect of the chlorine atom compared with bromine and iodine. The decrease in the C(5)–halogen bond polarity,§ which depends on this factor, is particularly appreciable for chloro-derivatives in view of the insignificant contribution of the π-interaction with the unoccupied *d* orbitals of the halogen atom. The latter feature is most favourable for halogens with a large radius.[102] It is essential to note that both the $+M$ and $-M$ effects of the halogens lead simultaneously to the stabilisation of the ground and excited states, which in fact accounts for the observed order of the bathochromic shifts for the group of furylnitroalkenes examined.

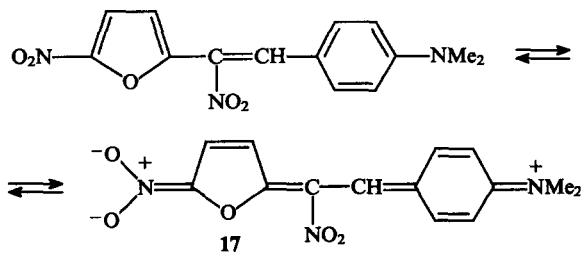
§The decrease in the C(5)–halogen polarity leads to an increase in the resulting molecular dipole moment.[41,91]

As the conjugation chain increases, the UV spectra of nitropolyenes of the furan series Fur(CH=CH)$_n$NO$_2$ **7** exhibit a bathochromic shift of the absorption *K* band (n = 0, λ_{max} = 310; n = 1, λ_{max} = 346; n = 2, λ_{max} = 380; n = 3, λ_{max} = 410 nm) and an increase in its intensity.[67,103]

R^2	λ_{max}/nm		
	Cl	Br	I
H	352	355	357
Me	353	355	362
Ph	360	363	369
Br	369	375	367

The electronic absorption spectra of α-nitro-α-(5-nitro-2-furyl)-β-(R-phenyl)ethylenes **17** contain two absorption bands in the range 216–275 and 298–318 nm,[81,82] which can be assigned to the electronic transitions in furan[104] and benzene.[99] Apart from the above absorption bands, compounds of this type, containing electron-donating groups in the aryl fragment, have yet another absorption band in the long-wavelength region (R = 4-MeO, λ_{max} = 363; R = 2-MeO, λ_{max} = 362; R = 4-NMe$_2$, λ_{max} = 370; R = 4-AcNH, λ_{max} = 460 nm).[81,82] This can be explained by the appearance of the corresponding quinnoid structure.

In the spectra of other α-nitroalkenes **17** (R = 2-F, 4-Cl, 4-NC, 4-NO$_2$, 2-NO$_2$), there is no absorption in this region, which is an indication of the incomplete coplanarity of the above compounds. Conjugation can also be prevented by the partial displacement of the 5-nitrofuryl and aryl fragments from the plane of the double bond induced by the bulky α-nitro-group.[81]



17

The UV spectra of (*E*)-α-nitro-α-(5-nitro-2-furyl)-β-(5-R-2-furyl)ethylenes **18** contain two absorption bands in the ranges 295–345 and 357–440 nm (*K* band).[84] It is noteworthy that, for example, the molecules of α-(5-nitro-2-furyl)-β-phenylethylene and α-(5-nitro-2-furyl)-β-(phenyl-2-furo)ethylene are planar systems and contain in the UV spectra an intense *K* band in the visible region. On the other hand, in the spectra of their α-nitro-analogues, this band has undergone a hypsochromic shift by 15–20 nm, which indicates the non-planarity of the molecules of these compounds.

The hypsochromic shift of the *K* band and the hyperchromic shift in the UV spectrum of (*E*)-α,β-di(5-nitro-2-furyl)ethylene (λ_{max} = 372 nm, lgε = 4.15) relative to the (*Z*)-isomer (λ_{max} = 392 nm, lgε = 4.18)[84] are noteworthy. This is apparently associated with the fact that the steric strain involving the substituents at the double bond in the (*E*)-isomer is greater than that in the (*Z*)-isomer and hence in the former case the system deviates more appreciably from planarity.

An appreciable hypsochromic shift of the *K* band is observed also in the spectra of the methyl esters of (*Z*)-β-(5-R-2-furyl)-α-nitroacrylic acids **6** (R = H, λ_{max} = 313; R = Br, λ_{max} = 321; R = I, λ_{max} = 333; R = Me, λ_{max} = 325; R = MeOOC, λ_{max} = 320 nm).[53]

3. IR spectra of furylnitroalkenes

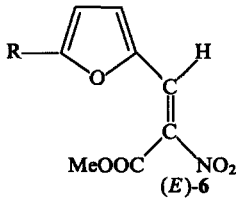
In the IR spectra of furylnitroalkenes there are intense absorption bands in the range 1610–1660 cm^{-1}, which are characteristic of conjugated double bonds in the *trans*-isomers of ethylene compounds.[105] The absorption band at 1660–1670 cm^{-1} is associated with the stretching vibrations of the C–C bonds of the furan ring,[100,104] which is typical for furan derivatives with unsaturated substituents in the 2-position. Absorption maxima in the range 1510–1550 and at 1340 cm^{-1} correspond[105,106] to the asymmetric and symmetric stretching vibrations of the NO$_2$ group.

The IR spectroscopic data confirm the features of the variation of the configurations of β-(5-R-4R^1-2-furyl)-α-R^2-nitroethylenes (**1**, **33**, **34**; R^2 = H, Me, Ph). The most planar molecules (**1**, R^2 = H) are characterised by a low-frequency $\nu_{C=C}$ absorption (1635–1642 cm^{-1}).[91,100] The deviation from the planar configuration on passing from R^2 = Ph (**34**) and specially to R^2 = Me (**33**) increases the $\nu_{C=C}$ absorption frequency (1640–1655 and 1653–1663 cm^{-1}) respectively.

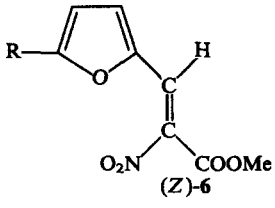
It was noted above that more favourable conditions for a planar molecular structure are created in β-(5-R-4-R′-2-furyl)-α-halonitroethylenes **35**. The high degree of conjugation in these compounds is reflected also in the $\nu_{C=C}$ frequency (1610–1628 cm^{-1}), which is reduced compared with compounds **1**, **33**, and **34**.[47,91]

The appreciable decrease in the $\nu_{C=C}$ absorption frequency in the spectra of N-substituted β-(5-amino-2-furyl)-α-methylnitroethylenes (**33**, R = Me$_2$N, PhNMe, morpholino) (1638–1645 cm^{-1}) compared with the remaining compounds of the same series (R = H, Me, Cl, Br, NO$_2$; 1653–1632 cm^{-1}) is noteworthy.[91] This can be explained by the direct polar conjugation in the β-(5-amino-2-furyl)-α-nitroethylene molecules and their approach to a planar structure.

The (*E*)- and (*Z*)-isomers of the methyl esters of β-(5-R-2-furyl)-α-nitroacrylic acids **6** differ in the absorption frequencies ν_{as} and ν_s of the α-nitro-group. The absorption bands due to these vibrations in the spectra of the (*E*)-isomers are at higher frequencies (1540–1542 and 1321–1330 cm^{-1}) than the analogous bands in the structure of the (*Z*)-isomers (1549–1552 and 1373–1375 cm^{-1}).[53]



(*E*)-**6**

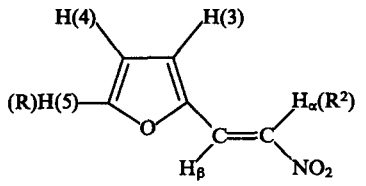


(*Z*)-**6**

The vibrations of the C=C valence bonds in the IR spectra of α-nitro-α-(5-nitro-2-furyl)-β-arylethylenes **17** are represented by moderately intense absorption bands in the range 1654–1670 cm^{-1}.[81,82] The introduction of electron-donating substituents (Me, MeO, NMe$_2$) into the benzene ring induces a bathochromic shift of the bands; electron-accepting substituents (NO$_2$, CN) induce the opposite shift. In the region of the symmetrical stretching vibrations of the NO$_2$ group in the spectra of these compounds, two absorption bands are observed at 1310–1340 and 1350–1360 cm^{-1}. The band at the higher frequency corresponds to the vibrations of the nitro-group in the furan ring.[81]

In the spectra of α-nitro-α-(5-nitro-2-furyl)-β-(5-R-2-furyl)-ethylenes **18**, absorption maxima in the range 1640–1655 cm^{-1} (R = H, Me, Br, I, NO$_2$) or in the range 1650–1662 cm^{-1} (R = aryl) refer to the C=C bond stretching vibrations.[84] The asymmetric stretching vibrations of the NO$_2$ group are represented by absorption bands at 1540–1560 cm^{-1}, while the

Table 2. ^{1}H NMR spectroscopic data for β-(5-R-2-furyl)-α-R^2-nitroethylenes



R	R^2	δ (ppm)					SSCC/Hz				Solvent	Ref.
		H(3)	H(4)	H(5)	H_α	H_β	J_{34}	J_{35}	J_{45}	$J_{\alpha\beta}$		
H	H	7.15	6.67	7.80	7.57	7.90	3.55	0.72	1.83	13.30	Acetone-d_6	8, 108, 109
H	H	6.81	6.53	7.25	7.66	7.37	3.48	0.72	1.82	13.26	CS_2	8, 109
H	H	7.00	6.65	7.70	7.53[a]	7.81[b]	3.60	–	1.80	13.00	CCl_4	110
H	H	6.03	6.05	7.01	7.04	7.55	3.40	–	1.80	13.50	C_6D_6	110
H	H	6.89	6.56	–	7.53	7.70	3.53	–	–	13.10	$CDCl_3$	18
H	E	6.90	6.67	7.56	–	7.80	–	–	–	–	$CDCl_3$	39
H	B	6.93	6.70	7.60	–	7.90	–	–	–	–	$CDCl_3$	39
NO_2	H	5.33	6.21	–	6.78	6.72	4.03	–	–	13.10	$CDCl_3$	18
NO_2[b]	H	–	8.25	–	8.20	8.46	–	–	–	14.00	Acetone-d_6	80
Br	H	6.51	6.83	–	7.66	7.50	3.51	–	–	13.10	$CDCl_3$	18
PhS	H	6.50	6.74	–	7.51	7.29	3.50	–	–	13.10	$CDCl_3$	18
$PhSO_2$	H	6.89	7.24	–	7.66	7.55	3.47	–	–	13.80	$CDCl_3$	18
3-$NO_2C_6H_4$	H	6.25	7.53	–	7.95	7.80	3.80	–	–	13.40	$CDCl_3$	18
Me_2N	H	7.16	7.38	–	8.15	8.07	3.79	–	–	13.50	$CDCl_3$	18

[a] Calculated from Pasqual's equation:[111] δ_{H_α} = 7.65 ppm; δ_{H_β} = 8.10 ppm.
[b] β=(3,5-Dinitro-2-furyl)nitroethylene.

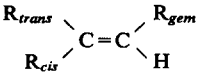
symmetric vibrations are represented by two bands at 1315–1340 cm^{-1} (the α-nitro-group) and 1355–1365 cm^{-1} (the nitro-group in the furan ring).

4. ^{1}H NMR spectra of furylnitroalkenes

The ^{1}H NMR spectra of β-(5-R-2-furyl)-α-R^2-nitroethylenes **1** and **33–35** contain the resonance bands of three or two protons of the furan ring in the form of doublets with chemical shifts and spin–spin coupling constants usual for these compounds.[104,107,108] Table 2 lists the chemical shifts of the most characteristic protons in the ^{1}H NMR spectra of certain furylnitroalkenes. Depending on the nature of the substituents R in the furan ring and of the solvent, the signals due to the protons of the furan ring are observed in the ranges 5.33–7.16 ppm for H(3), 6.05–7.53 ppm for H(4), and 7.01–7.80 ppm for H(5).

The protons attached to the double bond in β-(5-R-2-furyl)-nitroethylenes **1** give rise to doublet signals in the ranges 6.78–8.20 ppm (H_α) and 6.72–8.46 ppm (H_β) with spin–spin coupling constants of 13.0–14.0 Hz, which is characteristic of protons in the *trans*-position at the double bond.[105] Thus the spin–spin coupling constants ($^3J_{\alpha\beta}$) of the protons in the nitrovinyl group constitute yet another confirmation of the (*E*)-configuration of nitroethylenes of the given type.

It has been shown[110] that the chemical shifts of the vinyl protons in the spectra of β-(2-furyl)nitroethylene **1** are satisfactorily correlated with the values calculated from Pasqual's equation[111] taking into account the additive increments for different protons:

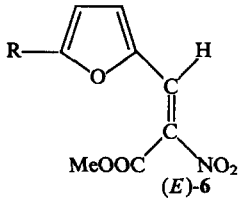


$$\delta_H = 5.25 + \Sigma z_i$$

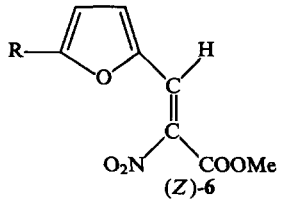
$z_i^{gem} = 2.00$; $z_i^{trans} = 0.46$; $z_i^{cis} = 1.67$.

Kovac and coworkers[53] noted that the (*E*)- and (*Z*)-isomers of the methyl esters of β-(5-R-2-furyl)-α-nitroacrylic acids **6** may be identified from the difference between the chemical shifts of the β-proton and the protons of the methoxy-group. The signal of the H_β vinyl proton in the spectra of the (*E*)-isomers is located downfield relative to the spectra of the (*Z*)-isomers (Table 3). Thus an appreciable shift of the signal due to this proton is induced by the greater magnetic anisotropy of the nitro-group compared with the carbonyl group. The H_β chemical shifts of the (*E*)- and (*Z*)-isomers of these nitroalkenes have also been calculated from Pasqual's equation using the additive increments:[112] δ_{H_β} is 8.75 ppm for the (*E*)-isomer and 8.10 ppm

Table 3. ^{1}H NMR spectroscopic data[53] for the (*E*)- and (*Z*)-isomeric methyl esters of β-(5-R-2-furyl)-α-nitroacrylic acids **6**.



(*E*)-**6**



(*Z*)-**6**

R	Isomer	δ_{H_β}[a] (ppm)	$\Delta\delta_{H_\beta}$ (ppm)	δ_{MeO} (ppm)	$\Delta\delta_{MeO}$ (ppm)
H	*Z*	7.25	0.50	3.81	0.06
	E	7.75		3.87	
Br	*Z*	7.20	0.55	3.81	0.09
	E	7.75		3.90	
I	*Z*	7.20	0.50	3.81	0.14
	E	7.70		3.95	
Me	*Z*	7.22	0.53	3.80	0.10
	E	7.75		3.90	
MeOOC	*Z*	7.37	0.40	3.86	0.14
	E	7.77		4.00	
NO_2	*Z*	7.28	0.49	3.86	0.15
	E	7.77		4.01	

[a] Calculated values: δ_{H_β} = 8.10 ppm for the (*Z*)-isomer; δ_{H_β} = 8.75 ppm for the (*E*)-isomer.

for the (*Z*)-isomer. The experimental and calculated H_β chemical shifts differ by approximately 1 ppm, which is an indication of the deviation of the system from planarity.

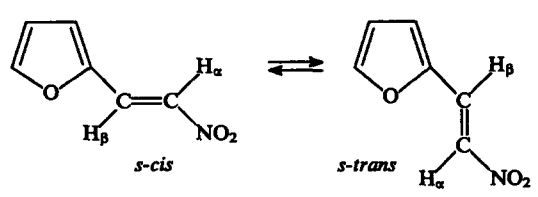
In the ^1H NMR spectra of the (*E*)-α-nitro-α-(5-nitro-2-furyl)-β-(R-phenyl) ethylenes **17**, the resonance signal of the vinyl proton is observed in the range 8.45–8.81 ppm,[81] which agrees well with the calculated value for the (*E*)-isomer (8.23 ppm). The signals due to the protons of the furan fragments are manifested as doublets at 6.77–7.17 ppm [H(3) and 7.36–7.80 ppm [H(4)] with $J_{3,4}$ = 3.7–3.9 Hz, which is characteristic of 2-substituted 5-nitrofurans.[8] The authors note that the substituent in the phenyl group hardly affects the signal of the vinyl proton. This may be due to the non-planarity of the given systems, where there is no mesomeric influence of the substituents.

The absence of an effect by the substituent R in the furan fragment on the chemical shift of the vinyl proton is also characteristic of (*E*)-α-nitro-α-(5-nitro-2-furyl)-β-(5-R-2-furyl)-ethylenes **18**. The chemical shift is observed in the range 8.44–8.53 ppm.[84] In the case of the (*E*)- and (*Z*)-isomers of α, β-di-(5-nitro-2-furyl)nitroethylene, the chemical shift of the above proton agrees well with the calculated data: 8.58 ppm for the (*E*)-isomer of compound **18** (calculated value 8.23 ppm) and 7.31 ppm for the (*Z*)-isomer (calculated value 7.45 ppm).

It is known[8,113] that the constants for the long-range (across five bonds) spin–spin coupling (^5J) between the β-proton in the side chain and the protons in the heterocyclic ring are highly stereospecific and are used to determine the most preferred configurations of the substituents in the side chain. Table 4 lists the experimental long-range spin–spin coupling constants for β-(2-furyl)nitroethylene as well as their values calculated using different methods of the molecular orbital theory.[114]

The results of the calculations of the populations of the conformational states and of the barriers to internal rotation by the molecular orbital method both at the level of the non-empirical (*ab initio*) and semiempirical (INDO2-MO-FRT, CNDO/2, etc.) approximations and the high stereospecificity show that the *s-trans*-conformer of β-(2-furyl)nitroethylene predominates in polar and non-polar salts. The value of $^6J_{\beta5}$ indicates the existence of an associative bond between H_α and H_β across the heteroatom.[109]

Table 4. The long-range spin–spin coupling constants for the ^1H NMR spectrum of β-(2-furyl)nitroethylene.[109,114]



SSCC	Experimental values for *s-trans*/Hz		Calculated values/Hz			
	CS_2	acetone-d_6	*s-trans* [a]	*s-cis* [a]	*s-trans* [b]	*s-cis* [b]
$^4J_{\alpha3}$	−0.42	−0.40	−1.01	−0.94	−1.23	−0.16
$^5J_{\alpha4}$	0.22	0.29	0.14	0.93	0.04	0.49
$^5J_{\alpha5}$	0.54	0.53	0.67	−0.22	0.56	0.09
$^5J_{\beta3}$	0.58	0.58	0.62	0.41	–	–
$^6J_{\beta4}$	0.06	0.03	−0.22	−0.10	–	–
$^6J_{\beta5}$	0.50	0.48	0.40	0.51	–	–

[a] The INDO-MO-FRT method.
[b] The CNDO-2 method.

The authors[114] concluded that the constant ^5J, incorporating $^5J_{\alpha5}$ and $^5J_{\alpha4}$, is highly stereospecific from the comparison of the experimental spin–spin coupling constants and the values predicted by calculation using the method of finite perturbations. The above constant reflects the transmission of the spin–spin coupling via the σ-electronic mechanism.

5. Quantum-chemical calculations for furylnitroalkene molecules and their reactivity

It was noted above that, among the possible planar structures of the series of β-(R-2-furyl)nitroalkenes **1**, two sterically unhindered forms can be realised: *trans-s-trans* (form **A**) and *cis-s-trans* (form **B**).[41,91]

The planar structures **A** and **B** should be energetically more favourable compared with the analogous structures of the furan aldehydes and ketones owing to the presence in them of a strong intramolecular π–π conjugation between the furan ring and the nitrovinyl fragment, demonstrated by the method of dipole moments and UV spectroscopic data.

Quantum-chemical calculation (EHM method) of the energies of the conformers **A** and **B** of β-(2-furyl)nitroethylene showed that the energy difference between the two planar conformers is comparatively small (ΔE = 0.143 kcal mol^{-1}) and the extent to which the non-planar form with a perpendicular disposition of the molecular fragments (O–C–C–H_β dihedral angle of 90°, *s*-90-conformer[114]) is unfavourable on energy grounds is much greater (E^* ≃ 10 kcal mol^{-1}).[97] The high degree of equalisation of the π-bonds C(2) ⋯ C_β ⋯ C_α ⋯ N in the planar structures of β-(2-furyl)nitroethylene is also consistent with this finding. Thus an appreciable energy barrier to rotation indicates a high stability of the above conformers and a low probability of their spontaneous interconversion.[97,114]

Certain β-(5-R-2-furyl)-α-R^2-nitroethylenes (**1** and **6**; R = H, NO_2; R^2 = H, MeOOC) have been characterised[115] by the Hückel molecular orbital method from the standpoint of their π-electronic structure. The quantum-chemical data obtained by the above investigators were compared with the physical properties (geometry and IR, UV, and ^1H and ^{13}C NMR spectra).

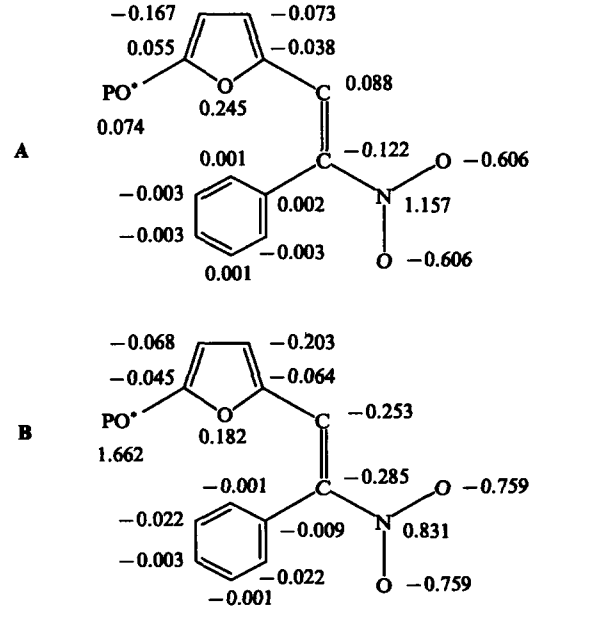


Figure 1. Distribution of the π-electron density of β-(5-chloro-2-furyl)-phenylnitroethylene **34** in the static (**A**) and transition (**B**) states: PO*—pseudo-orbital.

In order to consider the reactivity of furylnitroalkenes relative to nucleophiles, the π-electronic structures and the energies of the molecules in the static and transition (ST) states were calculated by the Hückel molecular orbital method for β-(5-chloro-2-furyl)-α-R^2-nitroethylenes (**1**, **33**, and **34**; R^2 = H, Me, Ph) (Fig. 1).[91,116] It was assumed that in the transition state the nucleophile and the chlorine atom being substituted can be represented in terms of a pseudo-orbital (PO) whose parameters have been published.[116-118]

The data on the distribution of π-electron density in the molecule of β-(5-chloro-2-furyl)-α-phenylnitroethylene **34** in the static and transition states show that nucleophilic substitution of the chlorine atom in the transition state is accompanied by a shift of π-electron density to the NO_2 group, while the phenyl group hardly participates in the electron shifts.[91] As a result of such displacement of π-electron density, the transition state energy is lowered i.e. the nitro group activates the nucleophilic substitution reactions.

Table 5 presents certain reactivity indices for β-(5-chloro-2-furyl)-α-R^2-nitroethylenes. The difference between the π-electron energies of the molecule in the static and transition states in units of the resonance integral $\beta(\Delta E^{\pi/\beta})$ is the π-electronic component of the activation energy and characterises the capacity for the nucleophilic substitution of the chlorine atom.[117] The π-electron density q^7 in the static approximation characterises the capacity for addition to multiple bonds.

The π-electron density at the C_β atom decreases in the sequence H > Ph > M, so that an increase in the capacity of the double bond to combine with nucleophiles in the same sequence should be expected.[91]

It is noteworthy that the above calculated quantities refer to hypothetical planar molecular models. If, on the other hand, account is taken of the breakdown of the planar configuration in compounds **33** (R^2 = Me) and **34** (R^2 = Ph) and of the associated decrease in the delocalisation of the π-electron cloud, then the differences in the capacity for nucleophilic addition in the sequence of R^2 substituents H > Ph > Me should be even more appreciable.

The quantity $\Delta E^{\pi/\beta}$ changes little as a function of the substituent R^2 and such variation is different for the variants of the parameters of the NO_2 group being compared.[117] It has therefore been suggested[91] that the interaction of the substituent R^2 with the NO_2 group alters the degree of its conjugation with the multiple bond and controls the rate of nucleophilic substitution of the chlorine atom. As a result of the electronic effects associated with the nature of the substituent R^2 and the change in configuration, the polarity of the C(5)–Cl bond (and hence also the rate of the nucleophilic substitution of the chlorine atom) diminishes after the introduction of the substituent R^2 in the following sequence: Me > Ph > H > Cl > Br.

Thus, comparison of the effects of the substituent R^2 on the behaviour in relation to nucleophiles permits the following conclusions.

1. β-(5-Halo-2-furyl)-α-methylnitroethylenes (**33**, R^2 = Me) exhibit the greatest tendency to undergo halogen substitution reactions.

Table 5. The reactivity indices for β-(5-chloro-2-furyl)-α-R^2-nitroethylenes.[91,117]

Variant	Index	R^2		
		H	Me	Ph
1	$\Delta E^{\pi/\beta}$	2.861	2.893 [a]	2.834
	q^7	0.092	0.080 [a]	0.088
2	$\Delta E^{\pi/\beta}$	1.952	1.946	1.958
	q^7	0.192	0.128	0.172

[a] Estimated by the perturbation theory method.[116]

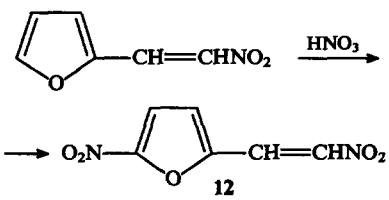
2. Addition reactions are more characteristic of β-(5-halo-2-furyl)nitroethylenes (**1**, R^2 = H) and β(5-halo-2-furyl)-α-halonitroethylenes (**35**; R^2 = Cl, Br).

According to patent data,[119] the interaction of β-(5-halo-2-furyl)-α-R^2-nitroethylenes **1** and **33**–**35** with morpholine leads to the polymerisation of the nitroalkenes when R^2 = H (**1**) and to the substitution of the halogen by morpholine R^2 = Me (**33**); for R^2 = Ph (**34**), products of the substitution and addition of the amine to the double bond were detected in the reaction mixture.

IV. Chemical properties

1. Substitution reactions in the furan ring

The most thoroughly investigated reaction of this type is the nitration of β-(2-furyl)nitroethylene **1** which leads to β-(5-nitro-2-furyl)nitroethylene **12**.



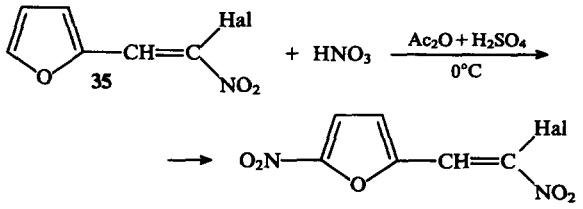
12

Nazarova[12] carried out the nitration with a tenfold excess of fuming HNO_3 in acetic anhydride at −5 to 0 °C and obtained compound **12** in 60.5% yield. Sasaki[72] used a fivefold excess of concentrated HNO_3 in acetic anhydride for nitration, whereupon the yield of the nitroalkene **12** did not exceed 35%.

The study of the nitration of β-(2-furyl)nitroethylene is of definite theoretical interest from the standpoint of the development of the theory of the nitration of furans. It is known[8] that the first elementary step in the nitration of acidophobic furans is the formation of oxonium compounds, which then either rearrange to 2,5-dihydrofuran derivatives or decompose with the opening of the furan ring to butane-1,4-diol derivatives, which char rapidly.

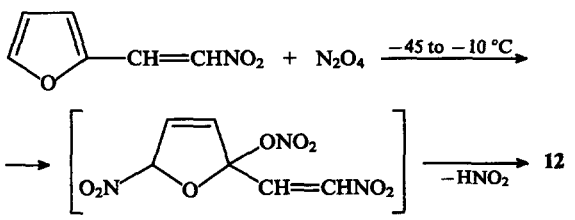
In the nitration of β-(2-furyl)nitroethylene **1**, this reaction pathway is excluded as a consequence of the influence of the electron-accepting NO_2 group, which lowers the tendency of the furan oxygen to be protonated and hence stabilises the entire furan system. Hillers and Nerklava[120] established that the nitration of compound **1** can be most usefully carried out with fuming HNO_3 in acetic anhydride (molar ratios $1:HNO_3:Ac_2O$ = 1:4:10) in the presence of catalytic amounts of H_2SO_4 at −10 to −5 °C; under these conditions, the yield of the nitroalkene **12** is 70%–80%. The authors showed that in this instance the true nitrating agent is the nitronium ion formed in HNO_3 solutions in acetic anhydride, particularly in the presence of H_2SO_4.

Nitration of β-(2-furyl)-α-halonitroethylenes (**35**; R^2 = Cl, Br) under similar conditions results in the formation of β-(5-nitro-2-furyl)-α-halonitroethylenes in 85%–88% yield.[47,52,91]

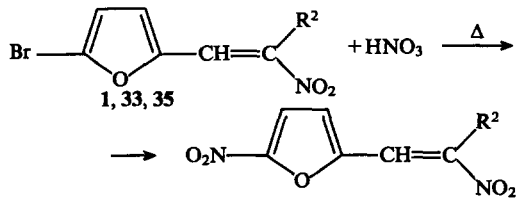


Hal = Cl, Br.

It has been shown[121] that the nitroalkene **12** is formed in 57% yield on treatment of β-(2-furyl)nitroethylene with a 50-fold excess of nitrogen tetroxide at low temperatures in ether.

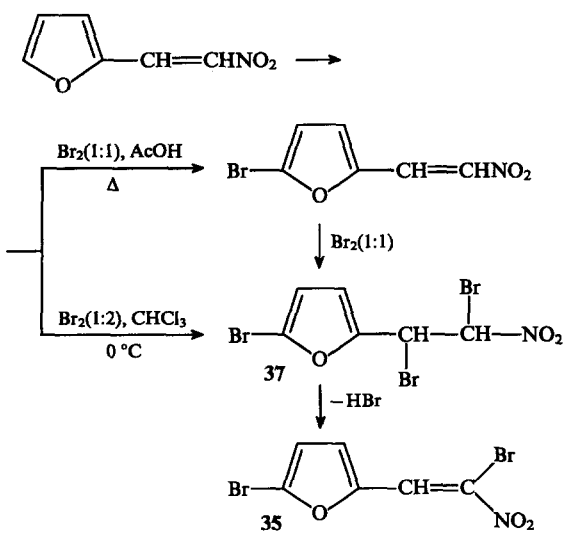


When β-(5-bromo-2-furyl)-α-R^2-nitroethylenes (**1**, **33**, and **35**) are heated with dilute HNO_3, the bromine atoms in the furan ring are substituted with formation of the corresponding 5-nitro-derivatives.[12,41,43,47,52,91] It is noteworthy that 5-bromofurfural does not afford 5-nitrofurfural under these conditions.



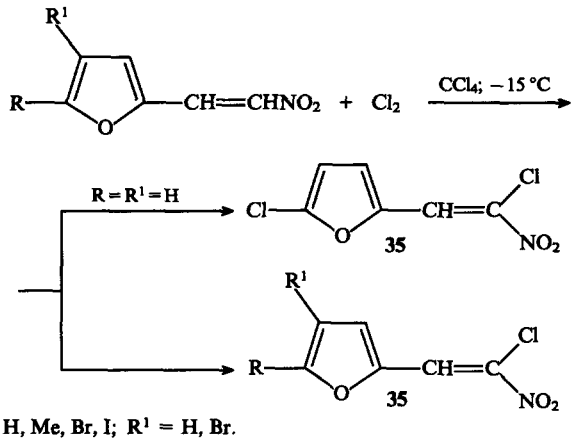
R^2 = H, Me, Cl. Br.

When β-(2-furyl)nitroethylene **1** is refluxed with an equimolar amount of bromine in acetic acid, β-(5-bromo-2-furyl)nitro-ethylene (**2**, R = Br) is formed.[12] Under similar conditions, β-(5-bromo-2-furyl)-α-chloronitroethylene (**35**; R = Br, R^2 = Cl) is obtained from β-(2-furyl)-α-chloronitroethylene. On the other hand, the bromination of compound **1** (molar ratio **1** : Br_2 = 1 : 2) in chloroform in the cold or bromination of β-(5-bromo-2-furyl)nitroethylene affords the unstable tribromo-derivative **37**, which decomposes on storage and distillation. Its dehydrobrom-ination with an aqueous solution of alkali at 20 °C leads to the synthesis of β-(5-bromo-2-furyl)-α-bromonitroethylene (**35**; R = R^2 = Br) in 64% yield.[52]



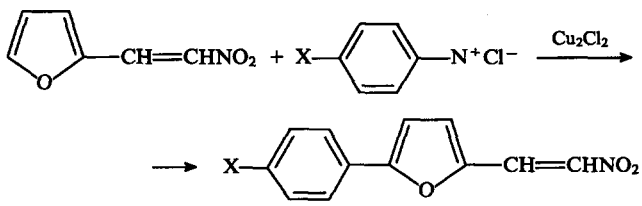
According to patent data,[122] chlorination of the nitroalkene **1** in chloroform or CCl_4 at −15 °C results in the simultaneous substitution of the hydrogen atoms in the 5-position in the furan ring and in the α-position in the vinyl fragment with formation of β-(5-chloro-2-furyl)-α-chloronitroethylene **35**. Chlorination of other β-(5-R-4-R^1-2-furyl)nitroethylenes under analogous conditions leads to the corresponding α-chloronitroalkenes **35** in 61% – 96% yield.

Oleinik and coworkers[98,123,124] reported for the first time the synthesis of (*E*)-β-(5-aryl-2-furyl)nitroethylenes (**1**; R = aryl) in 40% yield by arylating under the conditions of the Meerwein reaction (aqueous acetone, 40 °C) β-(2-furyl)nitroethylene with diazonium salts (molar ratio 1 : 1) containing electron-accepting substituents in the benzene ring.



R = H, Me, Br, I; R^1 = H, Br.

The authors' EPR spectroscopic study of the intermediates in the Meerwein arylation reaction permitted the conclusion that the given process has a radical mechanism.[124]



X = Cl, Br, NO_2.

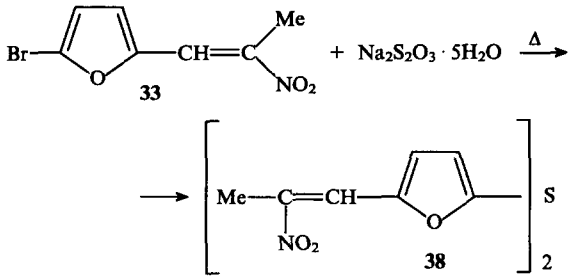
The influence of certain factors on the reactivity of β-(5-halo-2-furyl)-α-R^2-nitroethylenes relative to nucleophiles was examined in Section III.

It is known[93] that mainly the $-J$ effect of the halogens is manifested in 5-halofurfurals, as a result of which the C(5) atom of the furan ring acquires a positive charge, which increases in the sequence I < Br < Cl. The mobility of the halogens relative to the nucleophiles increases in the same sequence. On the other hand, in the case of β-(5-halo-2-furyl)nitroalkene the $n-\pi$ interaction with the furan nucleus is a $+M$ effect, which should diminish the positive charge on the C(5) atom and hinder substitution by nucleophiles compared with halofurfurals. The latter is manifested particularly strongly for β-(5-chloro-2-furyl)-α-R^2-nitroethylenes (**1**, **33**, and **35**; R^2 = H, Me, Ph, Cl, Br), which is indicated by the maximum value of μ_{int} in this instance (Table 1).

It has been shown[43,45] that when β-(5-halo-2-furyl)-α-methyl-nitroethylenes **33** are acted upon by nucleophiles (secondary amines, $Na_2S_2O_3$), the halogen in the 5-position in the furan ring is substituted, whereas in the case of β-(5-halo-2-furyl)nitro-ethylenes **1**, polymerisation or addition to the double bond takes place. These findings can be accounted for as follows. The direct polar conjugation in the planar structure of compound **1** (R^2 = H) leads to the appearance of a high positive charge on the β-atom of the vinyl fragment. The $+M$ interaction of the halogens in the 5-position with the furan ring in these compounds lowers simultaneously the effective positive charge on the C(5) atom of the furan. On the other hand, the introduction of the methyl group in the 5-position disturbs the planar configuration of the molecule and lowers the degree of conjugation, and hence promotes an increase in the positive charge on the C(5) atom of the furan ($-J$ effect of the halogen) and nucleophilic substitution.

The interaction of β-(5-bromo-2-furyl)-α-methylnitroethylene **33** with sodium thiosulphate in aqueous alcohol (refluxing for 2 h) leads to bis[5-(β-nitroprophenyl)-2-furyl] sulphide **38**.[43]

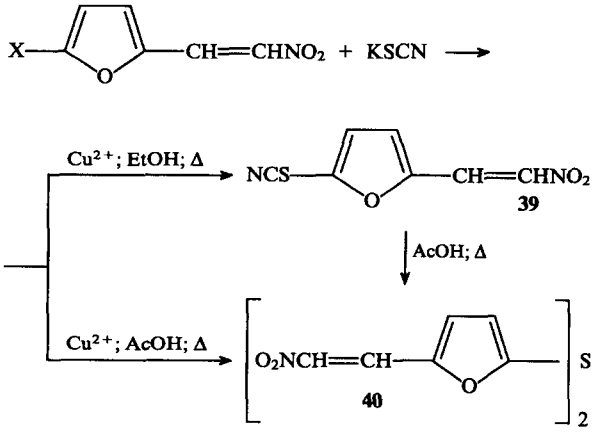
It is noteworthy that β-(2-furyl)-α-methylnitroethylene does not combine with sodium thiosulphate at the double bond, the methyl group apparently reducing the reactivity of the latter.[43]



On the other hand, Nazarova and coworkers[125,126] established that, on treatment with potassium thiocyanate or sodium sulphide, β-(5-halo-2-furyl)nitroethylenes form the products of the substitution of the halogen in the furan ring, i.e. in the reaction with the above reagents they behave similarly to the nitroalkenes **33**.

The reaction involving the exchange of bromine for the thiocyanato-group in the nitroalkenes **1** occurs only after prolonged refluxing of the reactants in anhydrous solvents (acetone, methanol, ethanol) in the presence of copper or cobalt salts. Under these conditions, β-(5-thiocyanato-2-furyl)nitroethylene **39** is formed in 78%–85% yield. This compound is more stable than 5-thiocyanatofurfural.[125]

The interaction of compound **1** with potassium or barium thiocyanate in acetic acid in the presence of copper or cobalt salts leads to the sulphide **40**, which is also formed on hydrolysis of the thiocyanate **39** in acetic acid.[126] The reaction of β-(5-halo-2-furyl)-α-R^2-nitroethylenes (compounds **1** and **33**; R^2 = H, Me) with sodium sulphide affords Na derivatives of β-(5-mercapto-2-furyl)-α-R^2-nitroethylenes **41**, whose treatment with formic acid gives rise to the corresponding mercaptans **42**. The sulphides **40** (R^2 = H, Me) are synthesised by the reaction of the Na derivatives **41** with β-(5-halo-2-furyl)nitroethylenes **1** and **33**.[126]

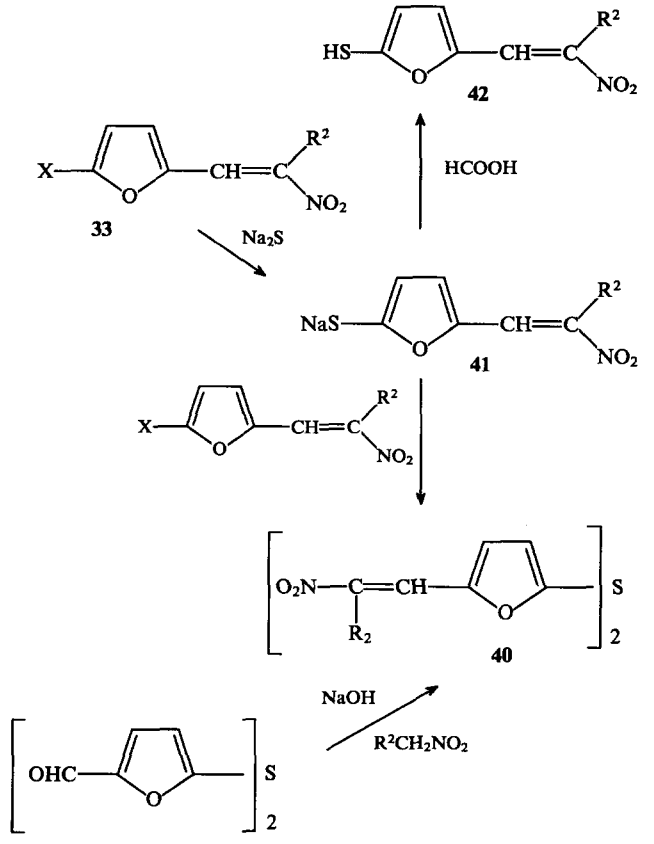


X = Cl, Br, I.

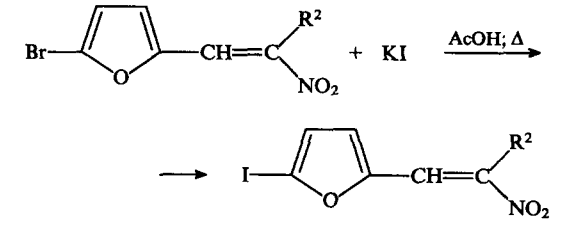
The structures of the sulphides **38** and **40** were confirmed also by unambiguous synthesis — the condensation of bis(5-formyl-2-furyl) sulphide with nitromethane or nitroethane in the presence of alkali.

A preparative method of synthesis of β-(5-iodo-2-furyl)-α-R^2-nitroethylenes (**1**, **33**, and **35**; R^2 = H, Me, Cl, Br) involves the nucleophilic substitution of bromine atoms in the corresponding 5-bromo derivatives.[12,30,43,47] The reaction involving the exchange of bromine for iodine occurs when the substrates are refluxed with potassium iodide in acetic acid for several hours; the target 5-iodo-derivatives are then formed in 50%–82% yield.

We may note that the chlorine or bromine atoms in the β-(5-nitro-2-furyl)-α-halonitroethylenes do not exchange for iodine under analogous conditions.[30]



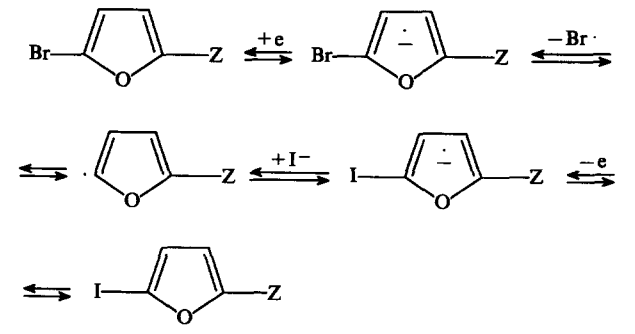
X = Br, I; R^2 = H, Me.



R^2 = H, Me, Cl, Br.

The kinetics of the exchange of bromine for iodine in β-(5-bromo-2-furyl)-nitroethylene have been investigated.[127] It was established that the reaction is reversible and is inhibited by oxidants (atmospheric oxygen, aromatic nitro-compounds, Schiff bases). The authors proposed a cryptoreductive reaction mechanism, which can operate in accordance with two schemes. According to Scheme 1, which includes the reversible electron transfer from the reducing supporting electrolyte generated by

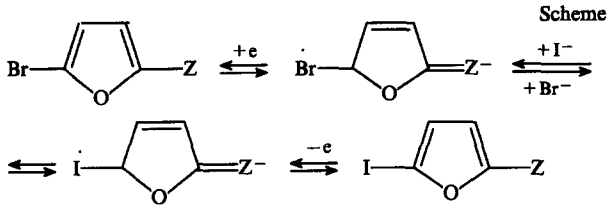
Scheme 1



Z = CH=CHNO$_2$.

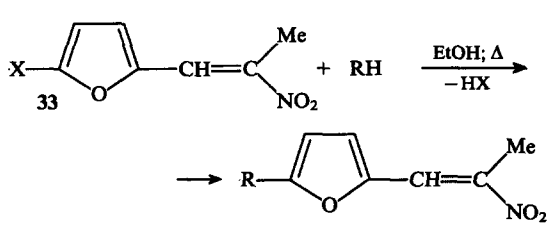
iodide anions to the halofuran molecule, the intermediate formation of a radical-anion with subsequent elimination from the latter of a bromide ion is postulated. The resulting furyl radical reacts with one of the halide ions of the reaction mixture with formation of either the initial or final products. On the other hand, one can assume that the furyl radical is not formed in this reaction as a kinetically independent species: without emerging from the reaction 'cage', it interacts with a second anion, which is also incorporated in the activated complex. In the limiting case, there is a possibility in this instance of a synchronous reaction involving the mutual exchange of the halogens in the radical-anions (illustrated in Scheme 2 in mesomeric form with separation of the radical and ionic fragments)—in terms of Bunnett's terminology,[128] this mechanism can be designated as $S_{RN}2$.

Scheme 2



It is noteworthy that, in terms of the decreasing rate of exchange of bromine for iodine, the substituents Z can be arranged in the following sequence: CH=CHCOPh > CHO > Ac > $CH=CHNO_2$, which is inconsistent with the activating strength of the above groups in reactions proceeding via the classical multistage mechanism of the 'addition–elimination' type.[127] The latter is characteristic, for example, of the reactions of 2-substituted 5-halofurans with secondary amines.[129]

Certain features of the interaction of furylnitroalkenes with secondary amines were noted in Section III. Nazarova and coworkers[45,119] established that the nucleophilic substitution of a halogen by secondary amine residues takes place most smoothly with β-(5-halo-2-furyl)-α-methylnitroethylenes **33**.

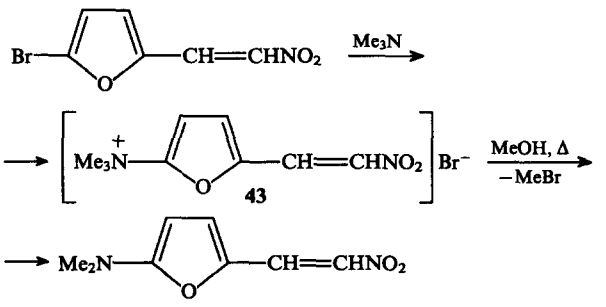


X = Br, I; R = morpholino, PhNMe.

The structure of the substitution products was confirmed by unambiguous synthesis from the corresponding N-substituted 5-aminofurfurals. The authors note that, when piperidine, diethylamine, or dimethylamine is introduced into the reaction, the double bond is also subjected to nucleophilic attack. The reaction of β-(5-bromo-2-furyl)nitroethylene with secondary amines proceeds very vigorously and leads to the products of the polymerisation of the initial alkene.

As a result of the study of the kinetics of the interaction of β-(5-halo-2-furyl)nitroethylenes **1** with secondary amines (dimethylamine, piperidine, and morpholine), Novikov and coworkers[130] showed that the halogen exchange reaction takes place against the background of the reversible interaction of the amine with the nitrovinyl group. The latter reaction is then 'asymmetric' as regards mechanism—the addition process takes place as a base-catalysed multistage reaction, while elimination is a synchronous unimolecular process.

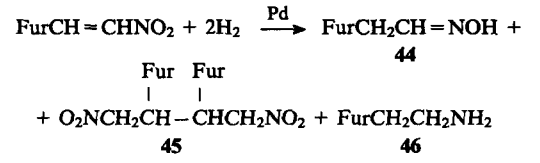
The interaction of the bromo-derivative **1** with trimethylamine in benzene affords the quaternary ammonium salt **43** in quantitative yield. On refluxing in methanol, the salt is converted into β-(5-dimethylamino-2-furyl)nitroethylene in 51% yield.[13]



2. Reduction of furylnitroalkenes

Depending on the chosen reduction method, the nature of the reductant, and the process conditions, the reduction of unsaturated nitro-compounds results in the formation of different classes of organic compounds.[1-3] From this standpoint, furylnitroethylenes are not an exception among other nitroalkenes.

Freidlin and coworkers[31] investigated the hydrogenation of β-(2-furyl)nitroethylene in the presence of palladium black in different solvents at atmospheric pressure and 25 °C. The reaction is zero order with respect to the nitroalkene and the rate of absorption of hydrogen remains constant up to the complete conversion of the initial compound. The main reaction products are furylacetaldehyde oxime **44** and a hydrodimer—2,3-di(2-furyl)-1,4-dinitrobutane **45**. 1-Amino-2-(2-furyl)ethane **46** is formed in very small amounts.



In the hydrogenation of compound **1** in a 1 : 1 ethanol–acetic acid mixture, the yield of the oxime **44** reaches 97%. When the hydrogenation is carried out in ethanol or dioxan, the yield of the oxime **44** reaches 25%–54% together with the hydrodimer **45**; the dimerisation reaction is suppressed in the presence of weak organic acids (HCOOH, CH_3COOH). We may note that under comparable conditions the nitroalkene **1** is hydrogenated at approximately the same rate as β-nitrostyrene; the rate of hydrogenation of the thiophene analogue—β(2-thienyl)nitroethylene—is appreciably lower.[131]

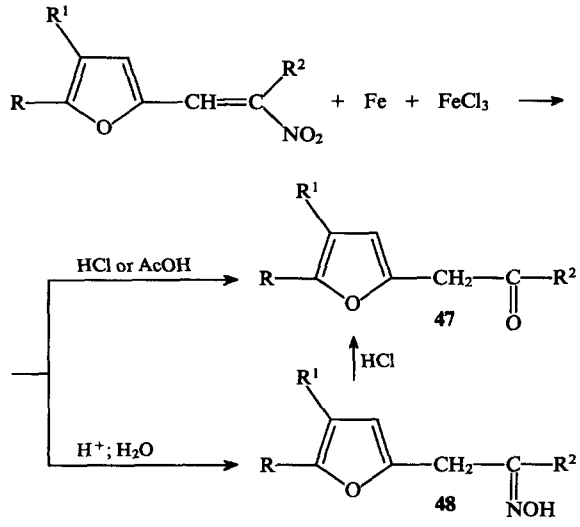
The reduction of β-(2-furyl)nitroethylene **1** with zinc dust in acetic acid results in the formation of the oxime **44** in 60%–70% yield.[16,57]

The reduction of β-(5-R-4R^1-2-furyl)-α-R^2-nitroethylenes with iron filings and $FeCl_3$ in hydrochloric acid (85–95 °C, 5–6 h)[37,48,132,133] or in acetic acid (80–100 °C, 1.5 h)[44] leads to ketones of the furan series with the carbonyl group in the 2-position in the side chain (compounds **47**) or to their oximes **48**, which are difficult to obtain by other methods.

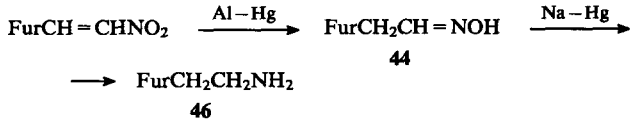
It has been established that an increase in the excess of acid promotes the formation of the ketones **47**, whose yield is usually 35%–70%, while a decrease in its amount raises the yield of the ketoximes **48**.

It has been recommended[132] that β-(4-methyl-2-furyl)-α-methylnitroethylene be reduced with an Fe + $FeCl_3$ mixture in 30% HCl, this being followed by treatment of the reaction product with a solution of $TiCl_3$ and ammonium acetate in water.

Japanese workers[14] synthesised 1-amino-2-(2-furyl)ethane **46** by the stepwise reduction of β-(2-furyl)nitroethylene with aluminium amalgam in ether and then with sodium amalgam in an ethanol–acetic acid mixture.

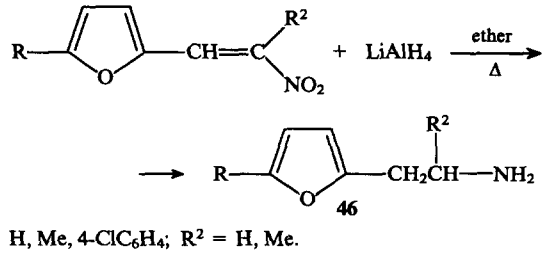


R = H, Me, 4-ClC$_6$H$_4$; R^1 = H, Me; R^2 = Me, Et, Pr, Ph.



The C=C bond, which is inert to the action of lithium tetrahydroaluminate, is readily reduced when it is conjugated with electron-accepting groups.[134] Lithium tetrahydroaluminate has therefore been used successfully for the reduction of a wide variety of nitroalkenes.[1] The structure of the reaction product depends to a large extent on the reduction conditions, primarily on temperature.

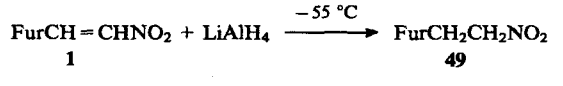
For example, in the reduction of furylnitroalkenes in boiling ether (molar ratio nitroalkene : $LiAlH_4$ = 1 : 2) the reaction is completed by the formation of the corresponding furylethylamines **46** in 52% – 65% yield.[13,25,38,98,135]



R = H, Me, 4-ClC$_6$H$_4$; R^2 = H, Me.

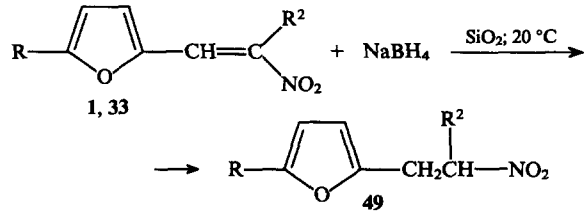
It is noteworthy that this method is the most effective procedure for the synthesis of 2-amino-1-(5-R-2-furyl)propanes (**46**; R = H, Me; R^2 = Me)—non-toxic analogues of the familiar preparation amphetamine.[38]

The reduction of β-(2-furyl)nitroethylene with 0.5 equiv. of $LiAlH_4$ at a low temperature (−55 to −60 °C) does not involve the nitro-group and only the double bond is reduced, the process being completed by the formation of 2-(2-furyl)-1-nitroethane **49**. However, the reaction is accompanied by appreciable charring and the yield[136] of the nitroalkene **49** does not exceed 16%.



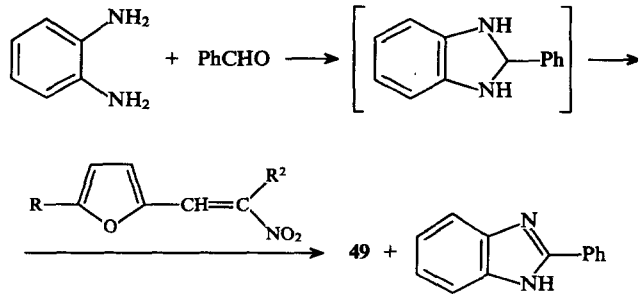
When the nitroalkene **1** is reduced with trimethoxyhydroborate and sodium tetrahydroborate in ether (−40 °C, molar ratios 1 : 1 : 3) or with lithium tetrahydroborate in ether (−73 °C, molar ratio 1 : 0.5),[136] the yield of the nitroalkane **49** can be raised to 28% – 31%.

According to Bogacheva,[137] on reduction of furylnitroalkenes **1** and **33** with sodium tetrahydroborate (molar ratio 1 : 4) in the presence of silica gel in a chloroform – 2-propanol mixture (20 °C, 2 – 4 h), the corresponding 1-nitro-1-R^2-2-(5-R-2-furyl)ethanes **49** can be obtained in 33% – 43% yield.

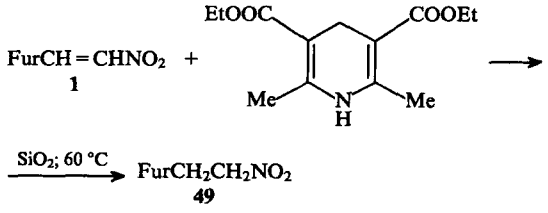


R = H, Me, NO_2; R^2 = H, Me.

2-Phenylbenzimidazoline, generated *in situ* from *o*-phenylenediamine and benzaldehyde, has been used as the selective reductant for the double bond in the furylnitroalkenes **1** and **33**.[137,138] This method affords the nitroalkanes **49** in 45% – 65% yield when nitroalkenes react with *o*-phenylenediamine and benzaldehyde (molar ratios 1.0 : 1.2 : 1.2) in 1-butanol at 20 °C.

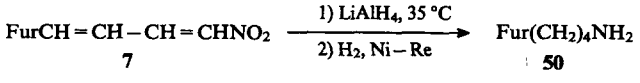


Japanese workers[139,140] proposed an effective method for the selective reduction of the double bond in conjugated nitroalkenes by reaction with the diethyl ester of 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylic acid (Hantzch's ester) in the presence of silica gel. When β-(2-furyl)nitroalkene is reduced with this reagent in benzene (60 °C, 20 h), the yield of the nitroalkane **49** reaches 93%. The authors note that the reduction does not occur in the absence of silica gel.



The reduction of β-(3-furyl)nitroethylene **9** by this method leads to a 94% yield of 2-(3-furyl)-1-nitroethane,[70] which is a key compound in the synthesis of various limonoid structures[69] and the pheromone dendrolasin.[70]

The reduction of 1-(2-furyl)-4-nitrobutadiene **7** with an excess of lithium tetrahydroaluminate in boiling ether affords, instead of the expected 4-amino-1-(2-furyl)butane **50**, a mixture of four unidentified incomplete reduction products.[141] Without additional purification, this mixture was subjected to catalytic hydrogenation over Raney nickel (methanol, 20 °C, initial hydrogen pressure 120 atm); under these conditions, the amine **50** is formed in 61% yield.



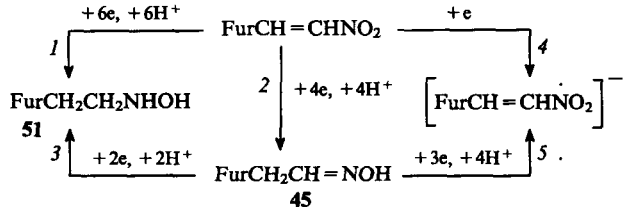
The authors note that the catalytic hydrogenation of the nitrodiene **7** with the aim of obtaining compound **50** in one stage leads to tarry products even under mild conditions.

The reduction of the potassium salt of the aci-form of 1-(2-furyl)-4-nitrobut-2-en-1-one **32** with sodium tetrahydroborate in water at 20 °C results in the formation[89] of the unstable sodium salt of 1-(2-furyl)-4-nitrobut-2-en-1-ol, which is converted into the nitrodiene **7** in 56% yield after acidification.

$$\text{FurCOCH=CHCH=NOO}^-\text{K}^+ \xrightarrow[H_2O]{NaBH_4} \text{FurCHCH=CHCH=NOO}^-\text{Na}^+ \xrightarrow{H^+} \underset{\text{OH}}{\text{FurCHCH=CHCH=NOO}^-\text{Na}^+} \longrightarrow \underset{\mathbf{7}}{\text{FurCH=CHCH=CHNO}_2}$$

Takamoto[142] obtained 1-amino-2-(2-furyl)ethane **46** from β-(2-furyl)nitroethylene (yield 91%) by electrochemical reduction using amalgamated nickel as the cathode and a lead plate as the anode (the catholyte was an ethanol–acetic acid mixture and the anolyte was dilute H_2SO_4). The electrolysis was carried out at 30–35 °C at a current of 4–45 A.

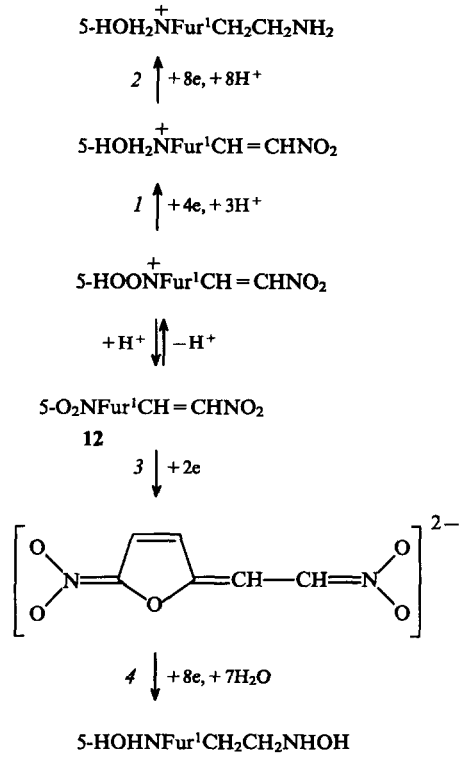
Reikhman et al.[143] investigated the mechanism of the polarographic reduction of β-(2-furyl)nitroethylene as a function of the mixture composition as well as the protolytic reactions of the compound. On the basis of the polarographic data recorded in aqueous alcoholic Britton–Robinson buffer solutions in the pH range from 2–12 in the presence of 0.1 M LiCl as the supporting electrolyte, the authors proposed the following mechanism of the polarographic reduction of this nitroalkene:



In acid solutions with a low ethanol content, 6-electron reduction to the substituted hydroxylamine **51** (reaction *1*) takes place. In neutral media, there is 4-electron reduction (reaction *2*) to the oxime **45** and the subsequent stage involving the addition of two further electrons (reaction *3*) is displaced towards negative potentials (−0.85 to −1.30 V) and is manifested by separate wave B, the half-wave potential $E_{1/2}$ of which corresponds to the electrochemical reduction potentials of oximes.[8,144,145]

In an alkaline medium, the 4-electron process *2* is split into 1-electron (reaction *4*) and 3-electron (reaction *5*) stages. The waves become clearly separated at pH > 10, where a dimunition of all the waves is observed. The latter is apparently due to the fact that the anionic form of compound **1** is polarographically inactive. in solutions with a high alcohol content at pH < 7, the reduction takes place in two stages (reactions *2* and *3*). In alkaline media and in DMF, distinct processes *4* and *5* take place.

In the electrochemical reduction of β-(5-nitro-2-furyl)-nitroethylene **12**, two reaction centres are reduced simultaneously.[8,145,146] In aqueous and 10% aqueous alcoholic Britton–Robinson buffer solutions in an acid medium (pH ⩽ 3) at potentials in the range 0 to −0.1 V, the 4-electron reduction of the nitro-group, characteristic of derivatives of 5-nitrofuran takes place (stage *1*). At more negative potentials (−0.3 to −0.7 V) the subsequent 8-electron wave, corresponding to the electrochemical reduction of the nitro-group conjugated with a double bond (stage *2*), takes place.



In more alkaline media (pH > 6), the primary step in the electrochemical reduction of this compound is the direct addition of two electrons (stage *3*) to the entire system of conjugated π-bonds of the molecule and is followed at potentials of −1.45 V by the 8-electron process *4* involving the electrochemical reduction of the dianion formed. This somewhat unusual mechanism of the electrochemical reduction is supported by the presence on the polarogram of a distinct 2-electron wave, by the independence of its $E_{1/2}$ of the pH, and also by the similarity to the mechanism of the chemical reduction of *p*-dinitrobenzene.[146]

At pH 9, the polarogram shows a sharp decrease in the height of all the waves. Spectrophotometric studies indicate the occurrence in these solutions of irreversible chemical reactions, whose products are polarographically inactive.[146]

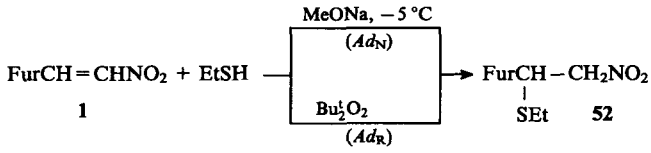
It has been shown[147] that β-aryl-α-(5-nitro-2-furyl)-α-nitroethylenes **34** are reduced at a mercury dropping electrode with two or three one-electron waves ($E^1_{1/2} = -0.6$ V, $E^2_{1/2} = 1.25$ V, and $E^3_{1/2} = -1.4$ V relative to 1 M LiCl at a calomel electrode). Unstable radicals with a lifetime of several seconds and with the unpaired electron centred on the nitro-group (according to EPR data) arise under these conditions.

3. Reactions involving addition to the double bond

It was noted in Section III that the tendency of furylnitroalkenes to undergo nucleophilic addition at the activated double bond depends primarily on the structure of the nitroalkenyl fragment.

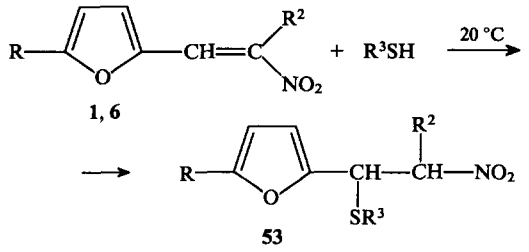
In considering reactions of this type, account must be taken not only of the appreciable polarity and ready polarisability of the activated double bond but also of the high probability of the delocalisation of the negative charge in the transition state. These factors determine the exceptionally high reactivity of furylnitroalkenes with respect to nucleophiles such as amines, alcohols, phenols, and mercaptans. As a result of the addition of these reagents, with formation of C–S, C–O, and C–N bonds, a wide variety of β-substituted nitroalkyl derivatives of the furan series may be synthesised. However, one should note that in the majority of cases the adducts formed are (in contrast to the analogous adducts in the series of aliphatic, acyclic, and aromatic nitroalkenes[1–3]) thermodynamically unstable, decomposing fairly rapidly and charring.

Ethanethiol adds to the double bond of β-(2-furyl)nitroalkene via both nucleophilic and radical mechanisms[148] with formation of the stable 2-ethylthio-2-(2-furyl)-1-nitroethane **52**.



The nucleophilic addition was carried out in the presence of an equimolar amount of sodium methoxide in methanol at −5 to 0 °C, while the radical addition was carried out by heating the reactants in the presence of *tert*-butoxide in sealed tubes, the yield of the adduct being appreciably higher in the latter case (~85%).

In a series of investigations by Czechoslovak workers[149-155] undertaken to investigate the mechanism of the biological activity of furylnitroalkenes **1** and **6** and to establish the structure–reactivity correlation for these compounds, a study was made of the interaction with various mercaptans in methanol at 20 °C, which leads to 1-R²-2-(R³-thio)-2-(5-R-2-furyl)-1-nitroethanes **53**.



R = H, Me, Br, I, MeOOC, NO_2; R^2 = H, MeOOC; R^3 = $PhCH_2$, $HOOCCH_2$, $HOCH_2CH_2$, $H_2NCH_2CH_2$.

The authors explain the cytotoxic and antimicrobial activities of the vinylfuran derivatives by the action of these biocides on the main processes of the energy metabolism of the cell, primarily on glycolysis. The basis of this interaction is the inhibition of certain enzymes — hexokinase, phosphofructokinase, and glycerol-3-phosphate dehydrogenase. These enzymes are deactivated as a result of the direct chemical modification of their catalytically active HS groups. The capacity of the furylnitroalkenes to undergo the nucleophilic addition of mercapto-derivatives constitutes an index of their antimicrobial and cytotoxic additivities.[156]

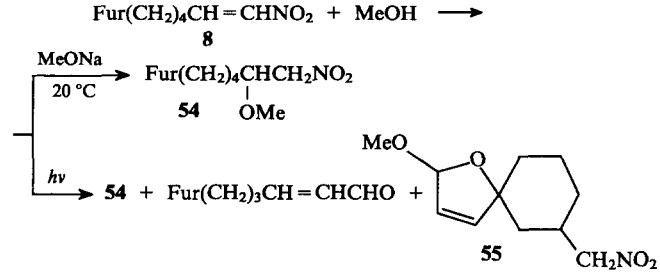
Kinetic study of the reactions of furylnitroethylenes with thiols showed that these reactions proceed via a nucleophilic addition mechanism and that the attack of the mercapto-anion is directed to the electron-deficient carbon atom of the double bond. It has been established that in an aqueous buffer system (pH 4.9) the reactions have second-order rate constants; the activity of furylnitroalkenes increases with enhancement of the electron accepting character of the substituent both in the 5-position in the furan ring and in the α-position in the nitrovinyl fragment. Using the Hammett constants, it has been established that this rule is quantitative. for example, in a study[151] of the reaction of the methyl esters of β-(5-R-2-furyl)-α-nitroacrylic acids **6** with mercaptoacetic acid (25 °C, aqueous Clark buffer, pH 4.9), it was found that $\lg K = 1.134\sigma_r + 7.125$ (correlation coefficient $r = 0.971$, $n = 6$).

Depending on the nature of the substituents R and R^2, furyl-nitroethylenes can be arranged in the following sequence in terms of the decrease in their reactivity in reactions with mercaptans:[151-153] NO_2, COOMe > COOMe, COOMe > I, COOMe > Br, COOMe > H, COOMe > Me, COOMe > NO_2, H > H, H.

The reactivity of mercaptans in the reactions with furylnitro-ethylenes increases with increase in their basicity. For example, the following sequence has been established for the reactions of mercaptans with β-(5-nitro-2-furyl)nitroethylene (25 °C, pH 4.4) in terms of the variation of the reactivity of the mercaptans:[153] $HSCH_2COOH$ (pK_a = 10.22) ≫ $HSCH_2CH_2OH$ (pK_a = 9.72) > $PhCH_2SH$ (pK_a = 9.43) > glutathione (pK_a = 8.56) > $HSCH_2CH_2NH_2$ (pK_a = 8.35) > $HSCH_2CH\cdot(NH_2)COOH$ (pK_a = 8.15).

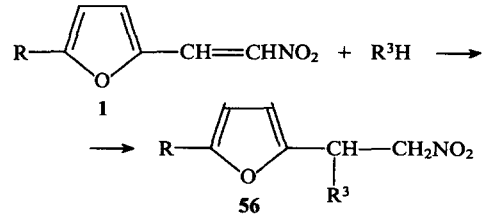
However, one should note that in the above investigations the authors carried out only kinetic measurements (mainly spectrophotometrically) and did not isolate or identify the adduct **53** formed.

The addition of methanol to the double bond of 6-(2-furyl)-1-nitrohex-1-ene **8** at 20 °C in the presence of calytic amounts of sodium methoxide has been reported.[68] Under these conditions, the yield of the methoxy-derivative **54** was 47%. The authors note that, when a solution of compound **8** in methanol is irradiated with UV light (450 W high-pressure Hg lamp argon-filled), 6-(2-furyl)hex-2-enal and 2-methoxy-6-nitromethyl-1-oxaspiro-[4.5]dec-3-ene **55** are formed together with the methoxy-derivative **54**.



As a result of the nucleophilic addition of amines to the double bond of β-(5-R-2-furyl)nitroethylenes **1**, the β-nitroamines **56** are formed.[18,155,157]

The interaction of β-(5-bromo-2-furyl)- and β-(5-nitro-2-furyl)-nitroethylenes with pyrrolidine and morpholine in ethanol, acetone, DMF, or DMSO leads even at 20 °C to appreciable charring and the formation of unstable adducts. Stable adducts could be obtained[18] only in the reaction of β-(2-furyl)- and β-(5-phenylthio-2-furyl)-nitroethylenes with 4-phenylpiperazine, whereupon the corresponding β-nitroamines **56** (R = H, PhS; R^3 = 4-phenylpiperazino) were isolated in 80%–90% yield.



R = H, Br, NO_2, PhS, $PhSO_2$, 4-$MeC_6H_4SO_2$; R^3 = pyrrolidino, piperidino, morpholino, 4-phenylpiperazine, BuNH, PhNH, $HOOCCH_2NH$

The study of the kinetics of the reaction of β-(2-furyl)nitro-ethylene with secondary amines showed that the reaction is second-order with respect to the substrate and first-order with respect to the nucleophile.[18,157] The rate of reaction at 25–45 °C increases with increase in the nucleophilicity of the reagents: pyrrolidine > piperidine > morpholine. A high rate constant for the reaction of the nitroalkene **1** with pyrrolidine is observed in non-polar solvents, diminishing with increasing solvent polarity in the sequence heptane > toluene > diethyl ether > DMSO > methanol.[18,157]

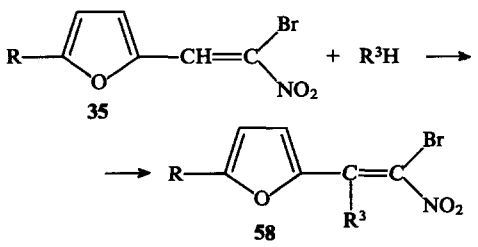
In terms of its influence on the rate of addition of secondary amines to the nitroalkenes **1** (MeOH, 25 °C), the substituents R can be arranged in the following sequence: $PhSO_2$ > 4-$MeC_6H_4SO_2$ > PhS ≃ Br > H, i.e. strongly electron-accepting groups induce an increase in the rate of reaction.[18,157]

The kinetics of the interaction of the methyl esters of β-(5-R-2-furyl)-α-nitroacrylic acid esters **6** and β-(5-nitro-2-furyl)nitroethylene with butylamine aniline, and certain aminoacids have been investigated[155,156] and it has been shown that in the case of amines the second-order rate constant is appreciably lower than in the case of mercaptans.

The interaction of the nitroalkene **1** with an equimolar amount of hydroxylamine in methanol leads[158] to the stable 2-hydroxyamino-2-(2-furyl)-1-nitroethane **57** in 80% yield.

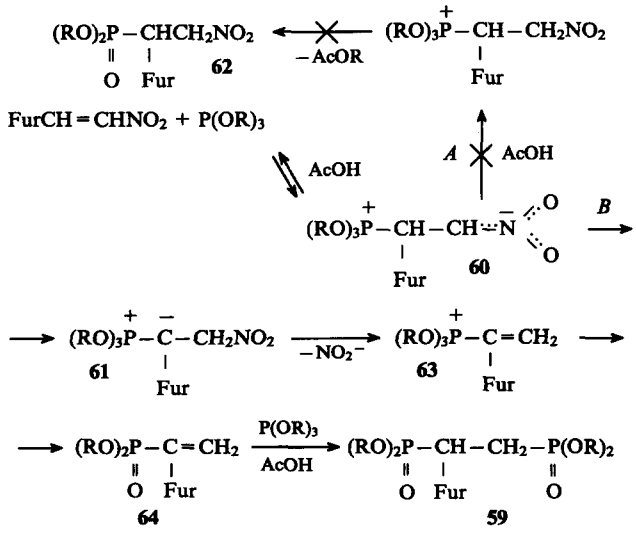
$$\underset{\mathbf{1}}{FurCH{=}CHNO_2} + NH_2OH \longrightarrow \underset{\mathbf{57}}{FurCH(NHOH)-CH_2NO_2}$$

It has been reported[159] that α-bromo-β-(5-R-2-furyl)nitroethylenes **35** react with alcohols and secondary amines via an addition–elimination type of mechanism with formation of β,β-disubstituted nitroethylenes **58**.



Conjugated nitroalkenes can react with trivalent phosphorus acid esters in different ways depending on the nature of the nitroalkene, the groups surrounding the phosphorus atom, and the medium.[160,161]

It has been established that the interaction of β-(2-furyl)nitroethylene with trialkyl phosphites in acetic acid at 40 °C proceeds less vigorously than the reaction with β-nitrostyrene; under these conditions, 4 moles of the phosphite are consumed per mole of the alkene. As a result of the reaction, it was possible to isolate[162,163] 1,2-bis(dialkylphosphinyl)-1-(2-furyl)ethanes **59**. According to the proposed reaction mechanism,[163] the adduct formed initially as a result of addition to the double bond (the betaine **60**) can be either protonated in acetic acid (pathway *A*) or can be converted into the phosphinilide **61** as a result of the migration of the proton from the α- to the β-carbon atom (pathway *B*).



R = Me, Et

The dialkyl esters of 1-(2-furyl)-2-nitroethylphosphonic acid **62**, which should form as a result of the protonation of the intermediate betaine **60**, were not detected in the reaction mixture. This shows that the rate of migration of the protons from the C_α to the C_β atom in the adduct **60** appreciably exceeds the rate of its protonation even in a solvent such as acetic acid.

The phosphinilide **61** is stabilised as a result of the elimination of the nitrite anion with formation of the cation **63**, which is subsequently converted into 1-(dialkoxyphosphinyl)1-(2-furyl)-ethylene **64** in conformity with the second stage of the Arbuzov reaction. However, the latter could not be detected in the reaction mixture, owing to the high rate of addition of trialkyl phosphite to it, which leads to the final product **59**.

According to patent data,[164] the reaction of the nitroalkene **1** with diphenyl(trimethylsilyl)phosphine oxide leads to the corresponding β-nitroethylphosphine oxide **65**, in 80% yield.

$$\underset{\mathbf{1}}{FurCH{=}CHNO_2} + Ph_2P(O)SiMe_3 \longrightarrow \underset{\mathbf{65}}{Ph_2P(O)-CH(Fur)-CH_2NO_2}$$

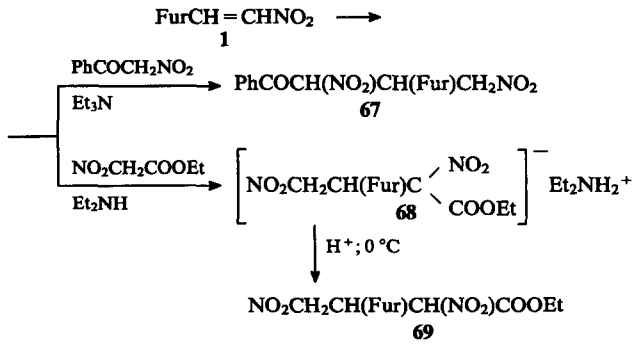
Reactions involving addition to nitroalkenes of the furan series with formation of new C–C bonds are of considerable theoretical and practical interest. Furylnitroalkenes enter fairly readily into the Michael reaction with a wide variety of CH acids, forming stable β-substituted β-furylnitroalkenes. For example, the interaction of β-(2-furyl)nitroethylene **1** with compounds containing activated methyl groups (2,4,6-trinitrotoluene, 9-methylacridine, and the quinaldine and 2-methylbenzothiazole methiodides) in benzene (20–80 °C, 1–2 h) in the presence of triethylamine, leads to the formation of the monoadducts-[3-R^3-2-(2-furyl)-1-nitropropanes] **66** in 63%–84% yield.[165]

$$\underset{\mathbf{1}}{FurCH{=}CHNO_2} + R^3Me \xrightarrow{Et_3N} \underset{\mathbf{66}}{R^3-CH_2-CH(Fur)-CH_2NO}$$

R^3 = 2,4,6-$(NO_2)_3C_6H_2$, 9-acridinyl, 1-methyl-2-quinolinylinium iodide, 3-methyl-2-benzothiazolylinium iodode.

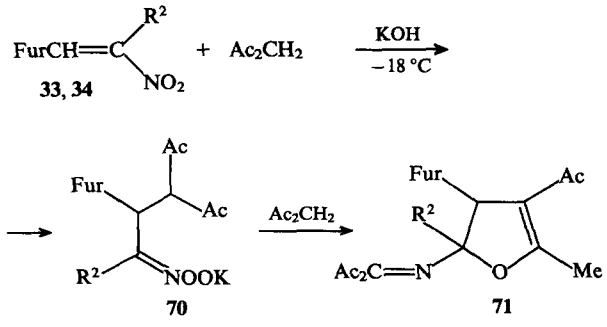
The reaction of the nitroalkene **1** with benzoylnitromethane in the presence of catalytic amounts of triethylamine in benzene (80 °C, 5–10 min) leads to the α,γ-dinitroketone **67** in 50%–54% yield.[166]

The interaction of β-(2-furyl)nitroethylene **1** with ethyl nitroacetate takes place only in the presence of equimolar amounts of diethylamine and leads to the formation of the diethylammonium salt **68**, whose acidification at 0 °C affords ethyl 3-(2-furyl)-2,4-dinitrobutanoate **69** in 25% yield.



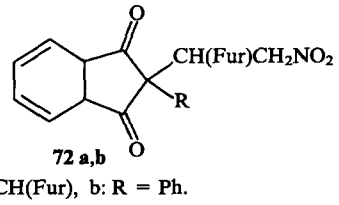
German workers[168,169] reported the reactions of β-(2-furyl)-α-R^2-nitroethylenes (**33** and **34**; R_2 = Me, Ph) with acetylacetone. The interaction of these reagents in aqueous methanol at −18 °C in the presence of equimolar amounts of alkali leads to the salts of 5-acinitro-5-R^2-3-acetyl-4-(2-furyl)pentan-2-ones **70** in 80%–88% yield.[168]

When the reaction is carried out in an excess of the β-diketone,[169] 3-acetyl-5-(diacetylmethylene)amino-4-(2-furyl)-2-methyl-5-R^2-4,5-dihydrofurans **71** are formed in low yields.



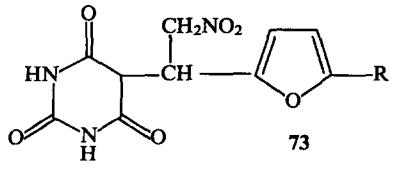
R^2 = Me, Ph.

The interaction of β-(2-furyl)nitroethylene with indan-1,3-dione and 2-phenylindan-1,3-dione (phenylin) in benzene (20 °C) in the presence of triethylamine led to the synthesis of the corresponding diadducts **72a** or the monoadducts **72b** in 50%–56% yield.[170]



72 a,b

a: R = $NO_2CH_2CH(Fur)$, b: R = Ph.



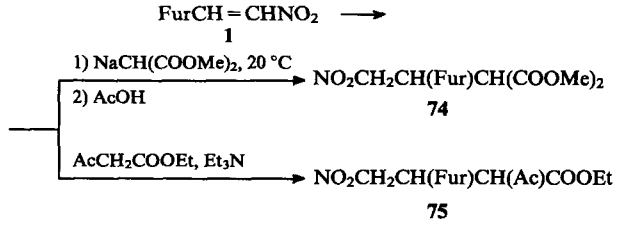
73

R = H, Me, NO_2.

When equimolar amounts of β-(5-R-2-furyl)nitroethylenes and barbituric acid are refluxed in aqueous ethanol, the monoadducts **73** are obtained in 73%–90% yield.[171] The authors note that the reaction of furylnitroethylenes with barbituric acid proceeds under more severe conditions than the reaction with β-nitrostyrene,[1] which is due to the more pronounced electron-donating influence of the furyl fragment compared with the phenyl group. The reactions could not be carried out at room temperature both in the presence and absence of a basic catalyst. On heating in the presence of alkaline catalysts (i.e. catalysts typical for the Michael reaction), partial or even complete charring takes place.

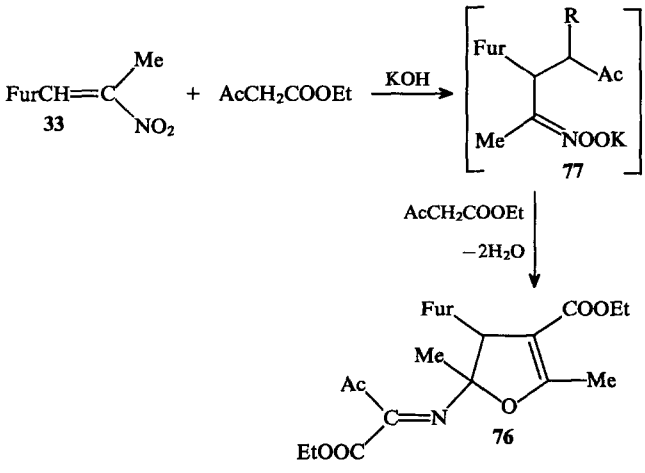
The reaction of sodiomalonic ester with β-(2-furyl)nitroethylene **1** and subsequent treatment with acetic acid lead to an 87% yield of the ester of 3-(2-furyl)-2-methoxycarbonyl-4-nitrobutanoic acid **74**—a valuable intermediate for the synthesis of furyl-containing γ-aminoacids and pyrrolidinones.[172,173]

The mode of interaction of acetoacetic ester with furylnitroalkenes depends primarily on the structure of the latter. For example, the ester of 2-acetyl-3-(2-furyl)-4-nitrobutanoic acid **75** was obtained in 60%–82% yield by the reaction of acetoacetic ester with β-(2-furyl)nitroethylene in the presence of triethylamine (benzene, 20 °C, 48–144 h).[174,175]



On the other hand, the interaction of acetoacetic ester with β-(2-furyl)-α-methylnitroethylene **33** and KOH (in molar proportions of 3 : 1 : 1) in ether led to the isolation of the ester of 5-[acetyl(ethoxycarbonyl)methyleneamino]-4-(2-furyl)-2,5-dimethyl-4,5-dihydrofuran-3-carboxylic acid **76** in 26% yield.[176] The authors believe that the potassium salt **77** of the aci-form of the 1 : 1 adduct is an intermediate in this reaction. It reacts subsequently with a second molecule of acetoacetic ester to form the dihydrofuran **76**.

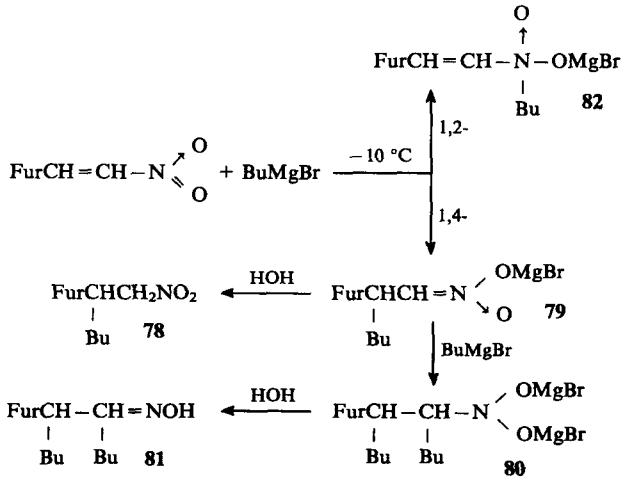
It is noteworthy that there are still no literature data concerning the involvement of furylnitroalkenes in the Michael reaction with reactive CH acids such as nitro- and *gem*-dinitroalkanes, trinitromethane, benzyl cyanide, cyanoacetic ester, dimedone, cyclopentane-1,3-dione, etc.



Unsaturated nitro-compounds are capable of reacting with organometallic compounds, forming nitroalkanes derived from isonitroso-compounds, oximes, and hydroxylamine.[1-3] However, there is only one communication in the literature[177] about the reaction of β-(2-furyl)nitroethylene with butylmagnesium bromide, which leads to 2-(2-furyl)-1-nitrohexane **78** in 33% yield.

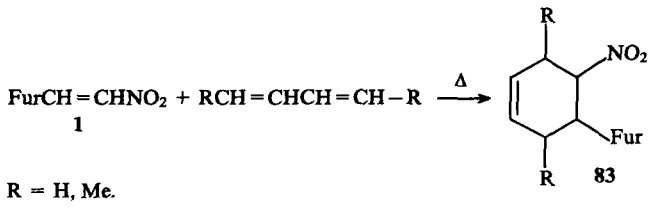
The 1,4-addition of the Grignard reagent to the conjugated system of the nitroalkene **1** affords predominantly complex **79**, whose hydrolysis leads to the nitroalkene **78**. However, by virtue of the presence of the $-C=N \rightarrow O$ system in complex **79**, it becomes possible to add a second molecule of the Grignard complex and to form complex **80**, which is converted into the oxime **81** on hydrolysis. The Grignard reagent adds partly to the 1,2-positions with formation of complex **82**, whose hydrolysis leads to a *N,N*-disubstituted hydroxylamine.

The authors note that, in order to suppress the nitroalkene polymerisation side reaction, it is useful to carry out the process at 10 °C with an excess of the Grignard reagent.



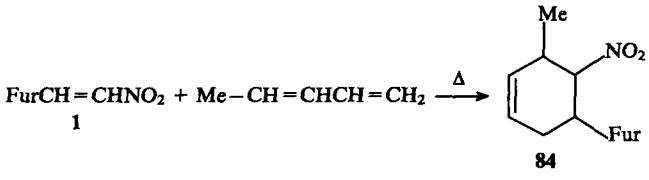
4. The cycloaddition reaction

According to the data of Kataev and Matveeva,[178] heating (150 °C, 10–16 h) of β-(2-furyl)nitroethylene **1** with butadiene and hexa-2,4-diene (molar ratio 1 : 3) in the presence of hydroquinone in a sealed tube affords a 45% yield of 5-(2-furyl)-4-nitrocyclohexenes **83**. The authors note that the reaction is accompanied by appreciable charring.

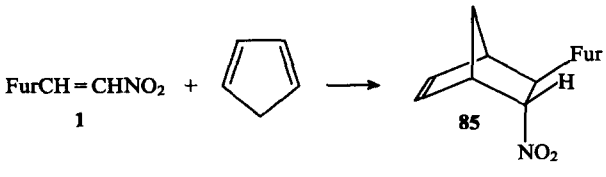


R = H, Me.

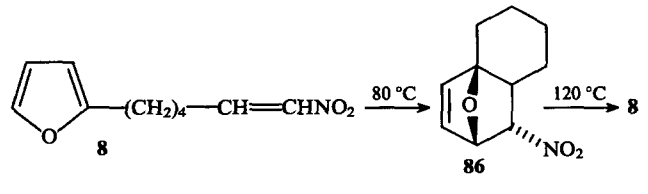
The study of the cycloaddition of the nitroalkene **1** to penta-2,4-diene showed that the reaction proceeds regioselectively with formation of only one regioisomer[178] — 5-(2-furyl)-3-methyl-4-nitrocyclohexene **84** in 55% yield.



endo-3-(2-Furyl)-2-nitrobicyclo[2.2.1]hept-5-ene **85** can be obtained in 78% yield by the reaction of the nitroalkene **1** with an equimolar amount of cyclopentadiene.[179] The stereochemistry of the process and the relative reactivity of the nitroalkene **1** with respect to cyclopentadiene are correlated with quantum-chemical CNDO/2 calculations.

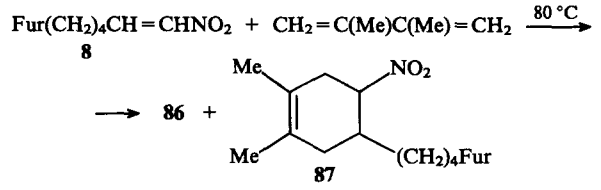


When 6-(2-furyl)-1-nitrohex-1-ene **8** is refluxed in benzene with catalytic amounts of pyridine, an intramolecular Diels–Alder reaction takes place with formation of the tricyclic adduct **86** in 52% yield.[68] On heating to 120 °C, the latter is reconverted into the initial compound **8**:



Prolonged (182 h) heating of the nitroalkene **8** with 2,3-dimethylbutadiene (molar ratio 1 : 10) in benzene produces a mixture containing 13.4% of the cyclic adduct **86**, 42.8% of 5-[4-(2-furyl)butyl]-1,2-dimethyl-*p*-nitrocyclohexene **87**, and 22% of compound **8**. Compound **8** is apparently formed as a result of the retroreaction of the adduct **86**.

Heating on compound **86** with 2,3-dimethylbutadiene (molar ratio 1 : 20) in benzene (80 °C, 251 h) affords a mixture containing 36.7% of compound **8**, 25.9% of compound **86**, and 30.8% of cyclohexene **87**.[68]



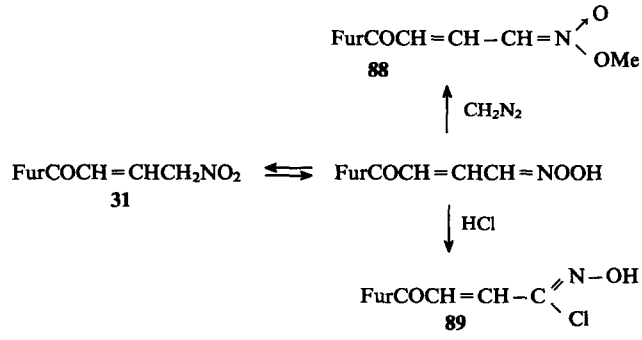
5. Other reactions of furylnitroalkenes

When β-(2-furyl)nitroethylene **1** is heated with concentrated hydrochloric acid, the furan ring is cleaved with formation of 6-nitro-4-oxocaproic acid.[180]

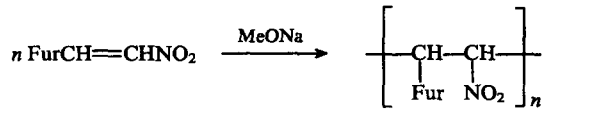


Methylation of 1-(2-furyl)-4-nitrobut-2-en-1-one **31** with diazomethane affords a 50% yield of the *o*-methyl ester of the acinitro-form **90**.[89]

Treatment of a solution of the nitroketone **31** in dioxane with concentrated hydrochloric acid gives rise to the chloride of the corresponding hydroxamic acid **89** in 45% yield.[89]



Studies on the polymerisation of β-(2-furyl)nitroethylene in the presence of anionic initiators (sodium methoxide, sodium ethoxide, etc.) have been reported.[180–182] The reactions were carried out in the temperature range −15 to 20 °C in different solvents — toluene, THF, and DMF. In the presence of cationic and radical initiators, the polymerisation of β-(2-furyl)nitroethylene was not observed.

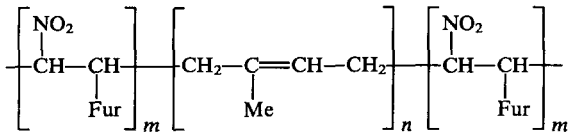


It has been shown that, with increase in the solvating capacity and polarity of the solvent, the yield of the polymer increases.[181] For example, when the polymerisation is carried out in toluene (0 °C, 150 min) the yield of the polymer is 15%, while in THF and in DMF the yields are 68% and 55% respectively. The polymer formed under these conditions is of the rigid-chain type and has no glass point in the range 20–250 °C.

The rate of polymerisation of β-(2-furyl)nitroethylene increases with increase in temperature and initiator and monomer concentrations; the molecular weight of the polymer rises as the temperature and initiator concentration are reduced and the monomer concentration is increased.[181] The study of the kinetics of the polymerisation reaction showed that the activation energy for the process in THF at temperatures in the range −15 to 20 °C is 2.8 kcal mol^{-1}.

It has been established[181-183] that the rate of anionic polymerisation of nitroalkenes increases in the sequence $FurCH=CHNO_2 < PhCH=CHNO_2 < MeCH=CHNO_2$. As the electron-accepting properties of the substituent in the nitroalkene molecule of the type $R-CH=CHNO_2$ are enhanced (Me < Ph < 2-furyl), the electron density at the double bond increases, which induces a decrease in the reactivity of the nitroalkenes in anionic polymerisation reactions.

Copolymerisation of β-(2-furyl)nitroethylene with isoprene resulted in the synthesis of block-copolymers of the B–A–B type.[183-185]



$m = 5-65$, $n = 400-3200$.

Under static conditions, the copolymers can be synthesised only in the presence of cationic initiators, for example dilithiopolyisoprene or dipotassiopolyisoprene. The reaction was carried out in benzene at temperatures in the range 10–70 °C and the block-copolymers were then obtained in 35%–65% yield. The composition of the copolymers included up to 30 mol% of the nitroalkene.

It has been established[185] that the statistical copolymerisation of isoprene with furylnitroethylene can be achieved also in the presence of $SnCl_4$ in solution in chloroform at temperatures in the range −50 to 50 °C.

It has been noted[181] that 1-(2-furyl)-4-nitrobuta-1,3-diene (**7**, $n = 1$) does not exhibit a tendency to undergo anionic polymerisation owing to the influence of steric effects. In the presence of sodium methoxide, 1-(2-furyl)-6-nitrohexa-1,3,5-triene (**7**, $n = 2$) gives rise to a dimer in yields up to 12%.

V. Practical applications of furylnitroalkenes

Unsaturated nitro-compounds of the furan series are used widely in organic synthesis as starting materials and intermediates of the preparation of various functional derivatives of the furan series, which are difficult to obtain by other methods, and also for the synthesis of biologically active substances and natural products.

Furylnitroalkenes are also of significant interest because of their high physiological activity. For example, β-(5-nitro-2-furyl)-nitroethylenes **12**, used in medical practice under the name nitrofurylene, effectively suppresses the growth of pathogenic fungi.[186,187] In this respect, its activity corresponds to the activity of the most active of the known antifungal antibiotics — nystatin, griseofulvin, etc. Clinical experience gained using this preparation indicates the virtual absence of resistance of the microflora to it and its satisfactory transferability.[188]

β-(5-Chloro-2-furyl)-α-R^2-nitroethylenes (**1** and **33**; R^2 = H, Me) exhibit a powerful lachrymatory activity.[28] This ability diminishes for substituents[23] R in the 5-position in the furan ring in the following sequence: Cl > Br > I > Me > H. The introduction of the nitro- or thiocyanate group in the 5-position weakens the irritant activity and enhances the bacteriostatic properties. For example,[47,125] β-(5-thiocyanato-2-furyl)nitroethylene **39** is capable of arresting the growth of the Siberian ulcer bacillus and of the staphylococcus at dilutions of 1 : 10000.

The introduction of the methyl group in the side chain is not reflected significantly in the nature of the physiological activity,[65] while the presence of a chlorine atom at the double bond of the side chain greatly enhances the bactericidal properties and leads to the appearance of new valuable qualities. For example, α-chloro-β-(5-nitro-2-furyl)nitroethylene **35** exhibits the capacity to inhibit the growth of the blue rot bacillus, but it is fairly toxic.[47]

β-[5-(4-R-phenyl)-2-furyl]-α-R^2-nitroethylenes (R = Cl, NO_2; R^2 = H, Me) have been patented as substances with bactericidal activity.[35]

The antibacterial activity of the methyl esters of β-(5-R-2-furyl)-α-nitroacrylic acids **6** has been reported.[53] The authors note that the 5-nitrofuryl derivative exhibits the highest activity among compounds of this type.

Czechoslovak workers[189-199] carried out a systematic study of the pharmacological activity of substituted vinylfurans, including furylnitroethylenes. It was established that furylnitroalkenes possess antimicrobial,[189-191] cytotoxic,[193] chemotherapeutic,[194,195] carcinogenic,[196-198] and in certain cases mutagenic activities. It was shown that the antimicrobial and cytotoxic activities are associated with the reactivity of the furylnitroalkenes in relation to nucleophiles — mainly low-molecular-weight thiols.[196] The mutagenic activity is associated with the presence of the nitro-group in the 5-position in the furan ring.[191,192,196] Together with the reactivity of furylnitroalkenes, their lipophilic-hydrophilic properties are very important physicochemical parameters which determine the intensity of the biological activity.[189] Attempts to establish quantitative structure–activity correlations in the series of furylnitroalkenes have been reported.[190,191,193,197]

It is noteworthy that β-(5-methanesulphonyl-2-furyl)-nitroethylene exhibits a high antimicrobial activity,[33] while β-(5-cyano-2-furyl)nitroethylene and 4-(5-cyano-2-furyl)-1-nitrobuta-1,3-diene possess only a slight activity.[29]

It has been established that furylnitroalkenes inhibit the activity of alcohol dehydrogenase[195,200-202] and xenobiotic receptors[198] and the fermentation of HS-enzymes[196,200] and are also effective antagonists of histamine.[203]

Furylnitroalkenes exhibit an appreciable fungicidal activity.[31,35,47,204,205] Hillers et al.[206] established that the nitrofurylene **12** is an effective fungicidal preparation. After the introduction of nitrofurylene as an additive to cotton, acetate, or polyester fibres, materials with fungicidal properties are obtained.[207] β-(5-Iodo-2-furyl)nitroethylene[208] and β-(5-aryl-2-furyl)nitroethylenes[209] also exhibit an appreciable fungicidal activity.

β-(2-Furyl)-α-methylnitroethylene **33** has been patented as an effective insecticide.[17] Furylnitroalkenes of different structure have been tested also as repellents.[210,211] It was established that they are excellent agents against rodents. According to patent data,[212] β-(2-furyl)-α-R^2-nitroethylenes (R^2 = alkyl, Ph) can be used as effective nematocides.

Copolymers of isoprene with β-(2-furyl)nitroethylene can be used as multifunctional additives to motor oils, thermoplastic elastomers, emulsifiers in hydrophobic emulsions for drilling in petroleum and gas deposits, and also as components of inhibited thin-film coatings.[181,183-185]

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