Chemistry of Furazans Fused to Five-Membered Rings

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Contents

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1. Introduction

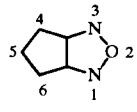
The first preparation of a furazan (1,2,5-oxadiazole) fused to a five membered carbocyclic ring was published 90 years ago [1]. A furazan fused to a five membered heterocycle was first described five years later in 1908 [2]. However, the difficulty in preparing such compounds was a major obstacle to a complete and thorough investigation of these interesting structures. New synthetic routes were described in the 1970's and the chemistry of these compounds has since developed considerably.

Annelation in 5/5-bicyclic systems suggests the presence of strain energy in the molecules. Various structural features induce added distortions. Destabilization of the distorted aromatic oxadiazole results not only from bond stretching, angular distortion, torsional effects, and nonbonded interactions, but also from decreased resonance stabilization. Strain energy is manifested in a tendency to difficulty of formation or the instability of these compounds.

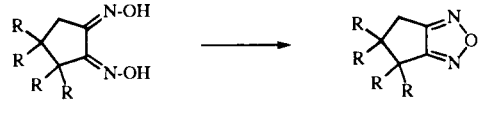
There are a number of five membered ring condensed furazans reported throughout the literature. Although some topics in this review have been incorporated into several earlier reviews [3-11] on furazan derivatives and an extensive monograph [12] concerning the chemistry of furazan *N*-oxides (furoxans), there has not been a comprehensive account devoted entirely to furazans condensed with five-membered rings.

The present review covers the synthesis and chemical behaviour of these derivatives up to January 1994.

2. Cyclopentafurazans.



This ring system has also been referred to as cyclopent[1,2,5]oxadiazole and as trimethylenefurazan. *N*-oxides of this system have also been called cyclopentafuroxan and trimethylenefuroxan. The preparation of this ring system involves the use of cyclopentane intermediates. The first compound in this furazan series was mentioned in the literature in 1928. Ingold and Shoppee [13] claimed to have synthesized **1a** by heating the dioxime **2a** with concentrated aqueous ammonia in a closed tube at 160-170°C for 5 hours.

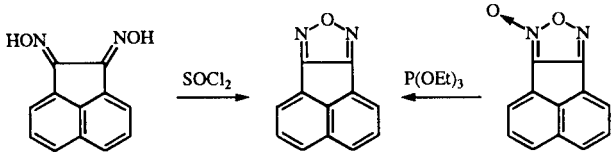


2a,b **1a,b**

a (R = CH_3), **b** (R = H)

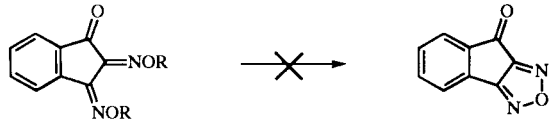
Later, however, this report was considered incorrect [14,16]. More than 30 years later the parent compound, 5,6-dihydro-4-cyclopenta[*c*]furazan (**1b**), was obtained by Tokura and co-workers [15] from the reaction of dioxime

2b with thionyl chloride in liquid sulfur dioxide at room temperature in 98% yield. A convenient modification of this procedure was used for dehydration of the dioxime **3** with thionyl chloride in methylene chloride [16]. The product **4** (55%) was indefinitely stable at room temperature, but slowly transformed to the nitrile oxide **23** on heating. The transformation was followed by ir spectrometry at 72°C in toluene [16].



3 **4** **5**

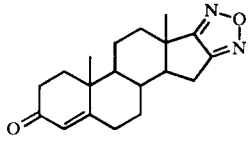
Treatment of both **6a** and its diacyl derivative **6b** with alkali or aqueous ammonia failed to give tricycle **7** [17].



6a,b **7**

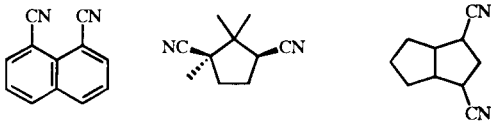
a (R = H), **b** (R = Ac)

Furazans may be prepared from furoxans, especially when the latter are more accessible. Trialkyl phosphites were used as reducing agents in this case [7,8,12b]. The reaction of furoxan **5** with an excess of triethyl phosphite yielded **4** at temperatures where **4** was stable [16]. However, the yield was low (10%). Treatment of the steroid [16,17-*c*]furoxans (*e.g.* **36**, *vide infra*) with triethyl phosphite at 170-180°C under an atmosphere of nitrogen (at elevated pressure) for 5 hours yielded steroidal-[16,17-*c*]furazans (*e.g.* **8**) [18].



8

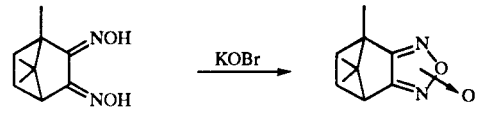
In contrast, on refluxing **5**, **11a**, and **13** with trimethyl phosphite (111°C, atmospheric air) for 3-4 hours, the corresponding dicarbonitriles **9a** (82%), **9b** (88%), and **9c** (50%) were formed as a result of deoxygenation and two-bond cleavages, not furazans [14,19].



9a **9b** **9c**

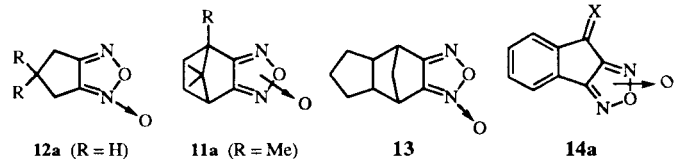
A nitrile was not formed on phosphite reduction of **12b** under similar conditions. The fate of this furoxan was not determined [14]. The reduction of **5** and **13** was studied kinetically [14].

Contrary to furazans of the cyclopentane series, their *N*-oxides, furoxans, have been described more thoroughly. In 1903 Forster [1] reported that dioxime **10a** reacted with an excess of alkaline potassium hypobromite to give 96% yield of furoxan **11a**.

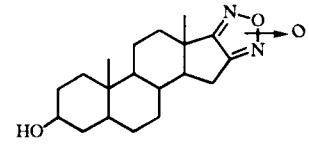


10a **11a**

Oxidative cyclization of dioximes by hypochlorites and hypobromites, usually at about 0°C, was also used to synthesize the corresponding furoxans **5** [20,21], **11a** [22,23], **11b** [14], **12a** [14,21,24], **12b** [14], **13** [14], **14a** (X = H_2) [14], **15** [18], **16a** [18,25], **16b** [18], **17** [18,25] and **18** [26].



12a (R = H)
12b (R = Me)
11a (R = Me)
11b (R = Br)
13
14a



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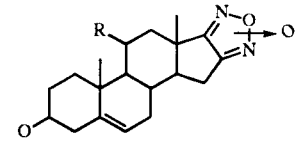
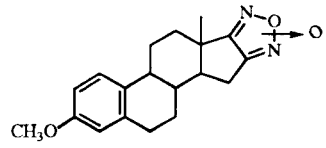


16a (R = H), **16b** (R = OH)



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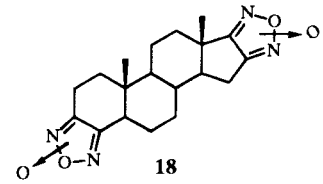
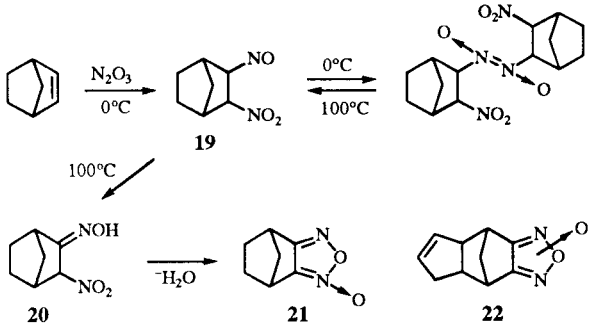


18

Other oxidizing agents were also used to convert dioximes to furoxans. Thus, treatment of the 16,17-dioximino steroid in the androstene series with sodium nitrite in diluted acetic acid at 20°C gave an isomeric mixture of [16,17-*c*]furoxan derivatives **16a** [18]. Lead tetraacetate (LTA) in acetic acid at 70°C for 1 hour oxidized **3** to **5** (95%) [27]. Electrochemical oxidation of **3** to **5** (48%) has also been described [28]. A report of the synthesis of **5** upon treatment of **3** with amyl nitrite is not convincing

[29]. Treatment of dioxime **6a** with nitrogen dioxide in ether solution afforded a resin; no furoxan derivative **14b** (X = O) could be detected [17].

The strained furoxans may be synthesized from readily available appropriate cycloalkenes by treatment with nitrogen trioxide followed by thermal isomerization of the resulting nitronitroso-adducts (*e.g.* **19**) to the nitro-oximes (*e.g.* **20**). Subsequent dehydration at room temperature using sulfur trioxide-DMF or chlorosulfonic acid-DMF yields furoxans as shown below [21,30-37].

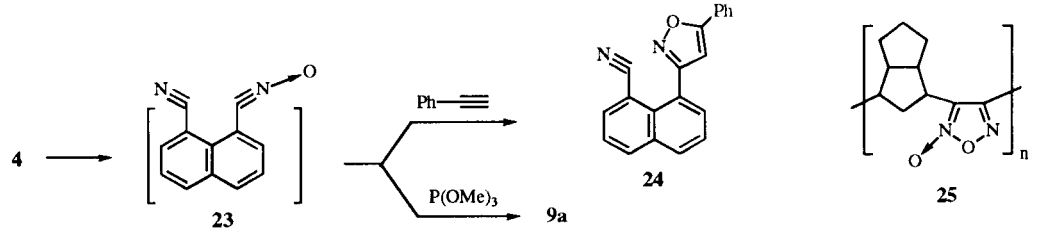


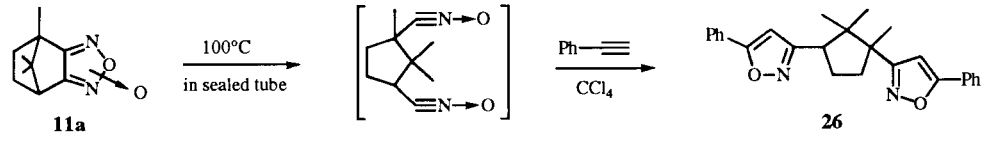
This technique yielded the furoxan **21** in 72% yield. Compounds **12a** (20%) [21,30,33], and **22** (62%) [21,30-37] were obtained in a similar fashion.

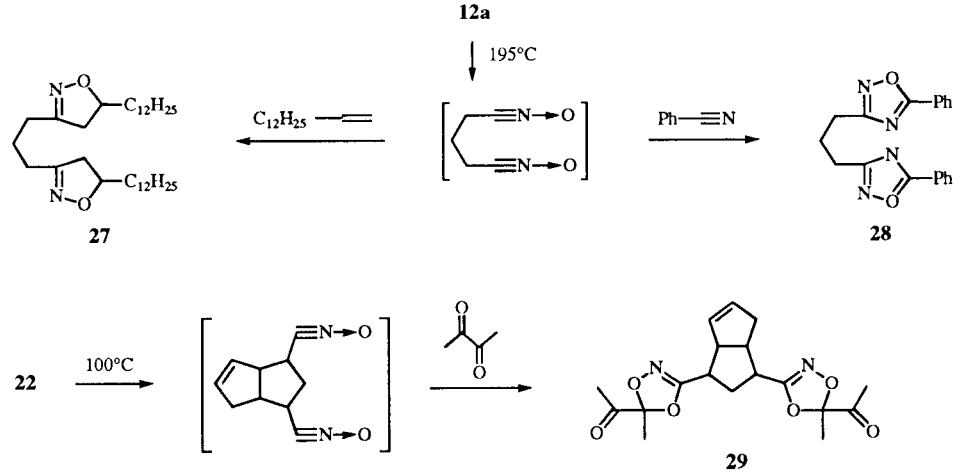
The furazan **4** on heating with phenylacetylene to 125-130°C in xylene gave the adduct **24** (55%), and with trimethyl phosphite at 80°C formed the dinitrile **9a** (95%) [16].

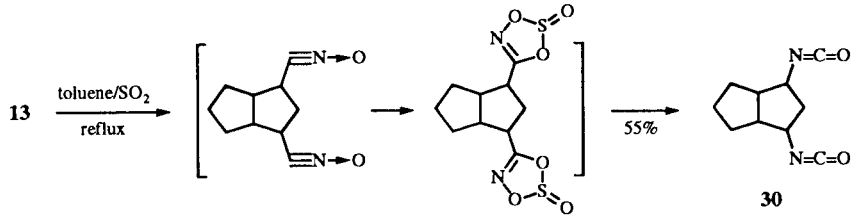
The thermolysis of furoxans of the cyclopentane series results in fragmentation of the oxadiazole ring to bis(nitrile oxides), which form unstrained polymeric furoxans (*e.g.* **25**) [38,39]. In the presence of suitable dipolarophiles the nitrile oxides can be trapped as 1,3-dipolar cycloadducts. Thus, when furoxans **11a**, **12a**, **13**, **21** or **22** were heated at 100-195°C with an excess of olefins [21,24,37], acetylenes [14,21,34,37], nitriles [21,24] or α-dicarbonyl compounds [32], 2:1 adducts (*e.g.* **26**, **27**, **28**, **29**) were formed in moderate to high yields; no adducts could be isolated from **12b** [14] and **5** [14,16].

When thermolysis of furoxans **11**, **13**, **21** and **22** was carried out at 60-100°C in the presence of sulphur dioxide, the isolated products were diisocyanates (*e.g.* **30**)







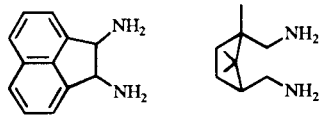


31 30

[31,35,38,39]. This suggests the bis-1,3,2,4-dioxathiazol-2-ones (*e.g.* **31**) as a likely intermediate.

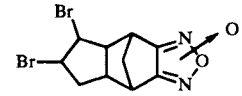
Conversely, unstrained furoxans undergo cycloreversion to nitrile oxides at 200-250°C, and the rearrangement of the nitrile oxide to isocyanate is rapid. In this case the presence of sulphur dioxide was of no value. When **22** is heated at reflux in toluene or *o*-dichlorbenzene in the presence of methanol or aniline, the isocyanate can be trapped as a urethane and urea derivatives, respectively [21,31,32].

Zinc in acetic acid reduced furoxan **11a** to the corresponding dioxime **10a** [1,40]. The furoxan **5** was reduced to dioxime **3** by hydroxylamine [20]. In an ether solution, lithium aluminium hydride reduced the furoxan **5** to the diamine **32** [41]. Under similar conditions, furoxan **11a** was subjected to vigorous reduction with opening of both furoxan and cyclopentane rings to give diamine **33** [41].



32 33

Reactions proceeding with retention of oxadiazole ring have also been described. Thus, treatment with bromine converts **22** to dibromo compound **34** [31].

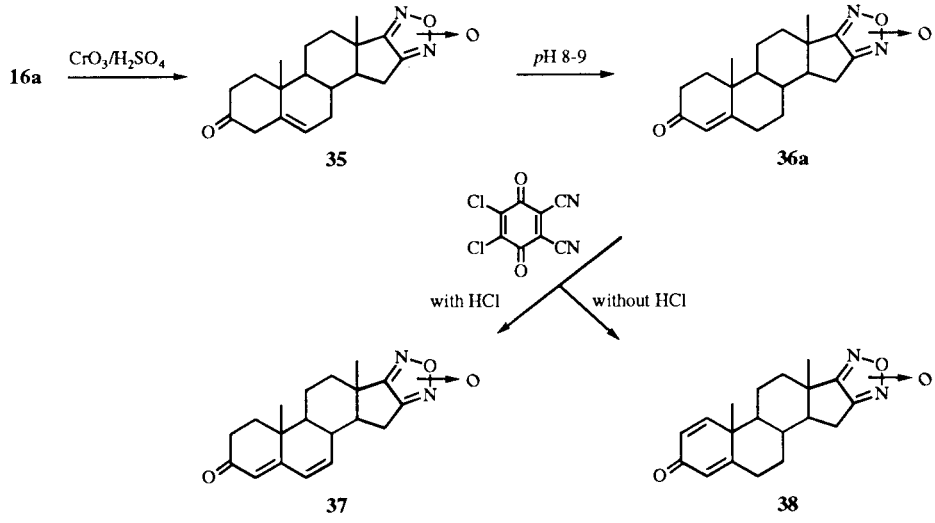


34

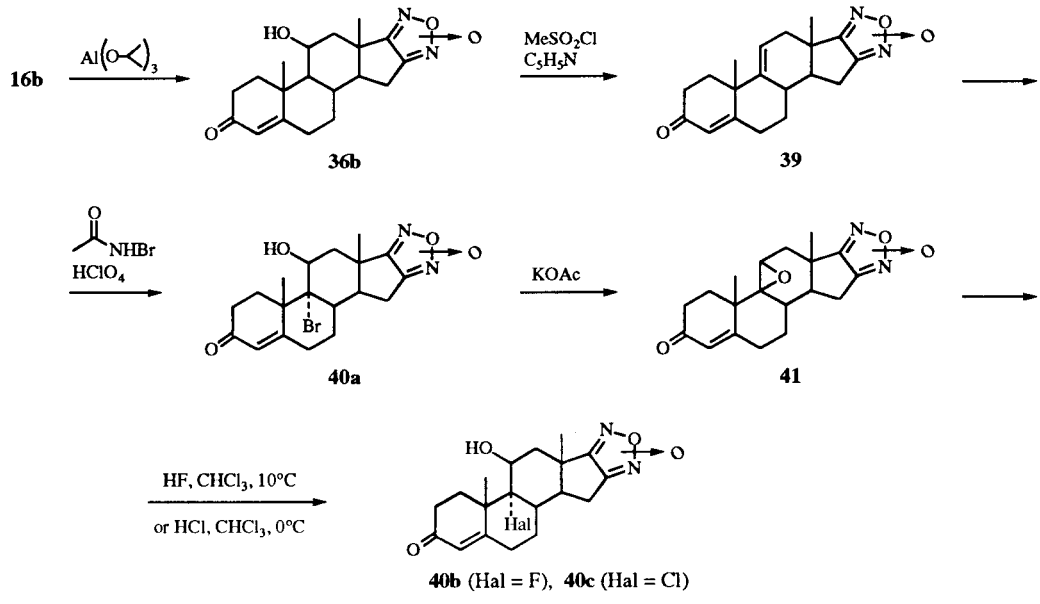
Several modifications of the steroidal furazans were described [18,25]. Hydroxy compound **16** was oxidized with Jones' reagent to the 3-keto analog **35**. The latter was isomerized directly by heating on a steam bath with sodium hydroxide in methanol at *p*H 8-9 to afford the 3-keto-4-androsteno[16,17-*c*]furoxan **36** [18,25]. Treatment of **36a** in dioxane with dichlorodicyanobenzoquinone in the presence of anhydrous hydrogen chloride yielded the diene **37**. In the absence of hydrogen chloride the product was diene **38** [18].

The diene **39** was also synthesized in two steps. Treatment of **39** with *N*-bromoacetamide and perchloric acid in aqueous dioxane yields the bromohydrin **40a**. The dehydrobromination of **40a** with potassium acetate in acetone gave the oxirane **41**. Addition of anhydrous hydrogen fluoride or hydrogen chloride to **41** produced the corresponding halogenohydrins **40b,c** [18].

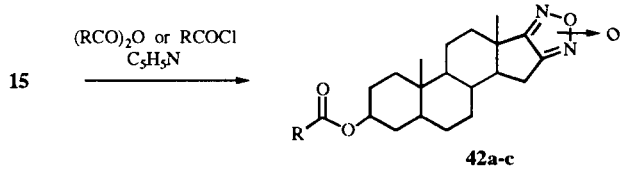
Treatment of the hydroxy compound **15** with organic acid anhydrides or halides gave the corresponding esters **42a-c** [18].



35 36a 37 38



40b (Hal = F), **40c** (Hal = Cl)



42a-c

a (R = CH_3), **b** (R = C_2H_5), **c** (R = Ph)

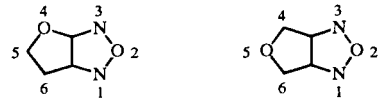
The ^1H nmr spectra of **4** [16], **11b** [14], **12a** [24], **12b** [14], **18** [26] and ^{13}C nmr spectra of **11a** [36], **12a** [24], **13** [36], **21** [36], and **22** [36] have been reported. An X-ray structural analysis of *N*-oxides, **5** [42], **12a** [24], **13** [36] and **22** [36], has been performed. These investigations have shown notable distortions of bond lengths as well as angle strain. Especially important is a considerable lengthening of the O-N(O) bond in the furoxan subunit. This suggests an incipient weakening of this bond which would explain the facile opening of the furoxan ring to give bis(nitrile oxides). The internal molecular strain is also manifested by a tendency of **5** [14], **11a** [14], **12a** [24] and **22** [21,33,36,37] to decompose explosively when heated to 80-150°C without solvent on a scale of about 1 g.

Several patents have been published concerning the utilization of furazan *N*-oxides0 of cyclopentanes as agents for producing cross-linked polymers [21,30]. Very little is known about the biological properties of derivatives of cyclopentafurazan. A variety of furazans and furoxans of the steroid series were described as potential estrogenic and anabolic/androgenic agents [18], or vasodilators [26].

3. Furazans Fused to 5-Membered Heterocycles with One Heteroatom.

Furofurazans.

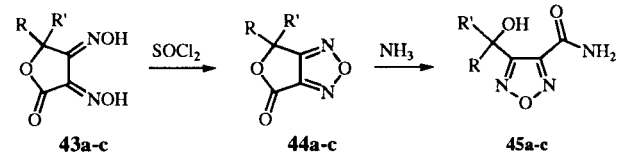
Two furofurazan ring systems, **I** and **II**, are theoretically possible. Only derivatives of type **II** are known.



I **II**

Furo[3,4-*c*]furazans **II**

There is only one published report dealing with the chemistry of this ring system. Referred to as 4-oxo-4,6-dihydrofuro[3,4-*c*]furazan, compounds **44a-c** were prepared in high yields by Pollet and Gelin [43] from the dioxime **43a-c** by treatment with thionyl chloride in dioxane.



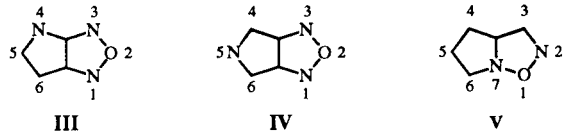
43a-c **44a-c** **45a-c**

a (R = R' = H), **b** (R = H, R' = CH_3), **c** (R = R' = CH_3)

Aminolysis of **44a-c** resulted in lactone ring cleavage and afforded **45a-c** in quantitative yield. The ^1H nmr spectra of **44a-c** have been reported.

Pyrrolofurazans.

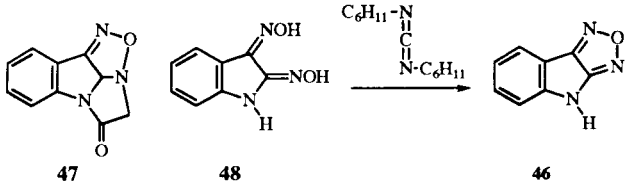
Of the three theoretically possible parent pyrrolofurazan skeletons, types III-V, only IV and V have been reported.



III IV V

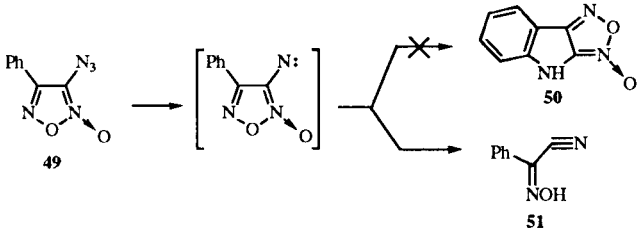
Pyrrolo[2,3-*c*]furazans **III**

This system is known solely in the form of the benzo annelated derivative, indolofurazan **46**. The first report of the preparation of compound **47** [44], involving **46** as a subunit, was disproved [45]. The tricycle **46** was synthesized by dehydration of **48** with dicyclohexylcarbodiimide in 1987 [46].



47 **48** **46**

Irradiation of azide **49** did not result in the formation of *N*-oxide **50**; the product of the reaction was **51** [47].

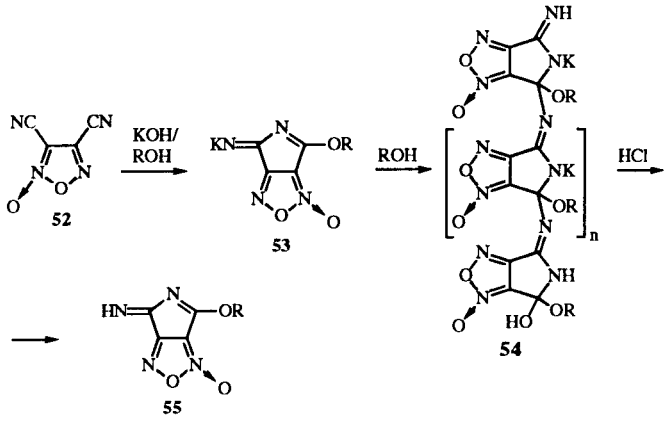


49 **50** **51**

Pyrrolo[3,4-*c*]furazans **IV**

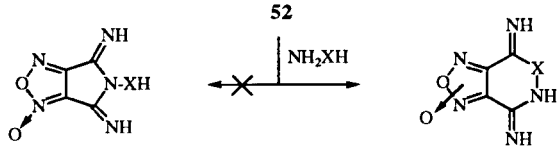
This ring system has also been referred to as pyrrolo-[3,4-*c*]-1,2,5-oxadiazole. 1(3)-Oxides of this bicycle have been called pyrrolo[3,4-*c*]furoxans. 1(3)-Oxides of reduced derivatives were named as pyrrolidino[3,4-*c*]-furoxans. The preparation of this ring system involved the use of both furazan and pyrrole precursors. Only one example of a synthesis starting from furazan *N*-oxide derivatives was reported. Investigation of the reactivity of 3,4-dicyanofuroxan (**52**) resulted in a wide variety of polyfunctional compounds, including the first derivatives of type **IV**. Thus, treatment of **52** with alkali in alcohol solution produced **53**. Heating this in alcohol gave the oligomer **54**. Acidification of **54** with acid yielded **55** [48].

Heating any of these compounds with copper or other transition metal salts afforded colored compounds, probably phtalocyanine analogs [48].

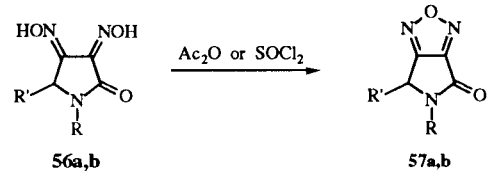


52 **53** **54** **55**

Reaction of **52** with H_2NXH (X = O, NH) did not afford pyrrole ring closure [49].



More common derivatives of this ring system were synthesized from pyrrole precursors by formation of the furazan ring. Treatment of dioximes **56a,b** with acetic anhydride or thionyl chloride in dioxane gave furazans **57a,b** in 69-92% yield [50].

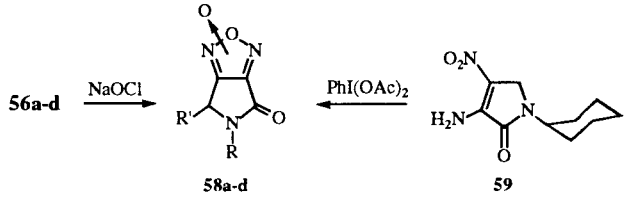


56a,b **57a,b**

a (R = CH_2Ph, R' = H), **b** (R = cyclohexyl, R' = H)

Under similar conditions **56c** yields the corresponding diacetate dioxime, not furazan **57c**.

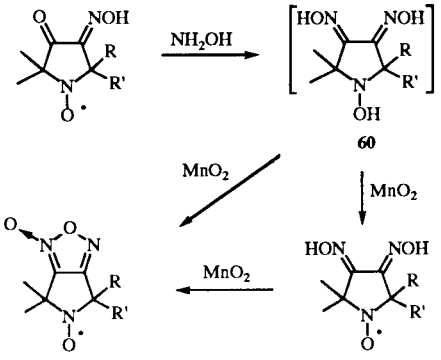
Oxidation of **56a-e** with sodium hypochlorite affords the corresponding furoxans **58a-e** [50,51] in 19-81% yields. Treatment of nitroamino compound **59** with phenyliodo diacetate (PIA) in benzene also gives the furoxan **58b** in 91% yield [51].



56a-d **58a-d** **59**

c (R = Ph, R' = H), **d** (R = CH_3, R' =Ph)

Unusually stable nitroxides **62a-d** were synthesized in about 20% yield by oxidation of dioximes **60** with manganese dioxide in ethyl acetate or chloroform [52,53].

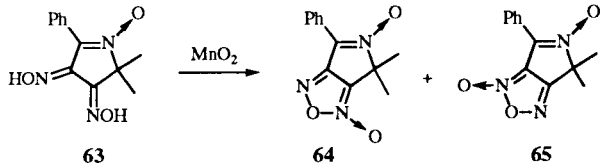


62 **61**

a (R = R' = CH_3), **b** (R = CH_3, R' = Ph), **c** (R = CH_3, 2-pyridyl), **d** (R = R' = Ph)

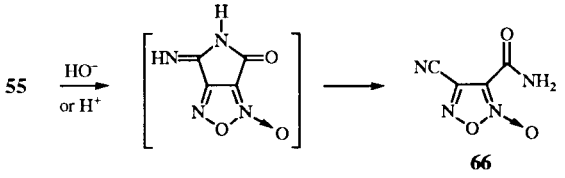
A two-step reaction, *via* nitroxide **61**, afforded an increased yield of **62** up to 90%.

Compound **63** when oxidized with manganese dioxide in ethanol at room temperature formed a mixture of isomeric furoxans **64** and **65** (in a 10:1 ratio) in overall yield of about 90% [54].



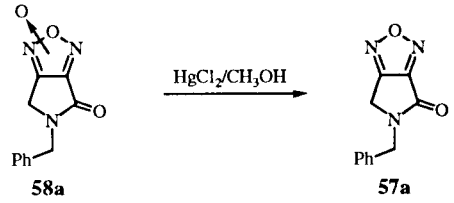
63 **64** **65**

Data on the reactivity of this ring system is limited. Thus, treatment of **55** with both alkali or acid gave an 80% yield of the amide **66**, *via* hydrolytic cleavage of pyrrole ring [48].



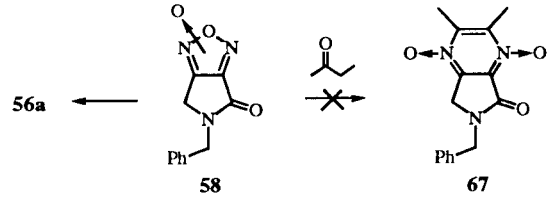
66

Reduction of furoxan **58a** to furazan **57a** (88% yield) using an unusual reagent such as mercury bichloride in aqueous methanol has been reported [50].



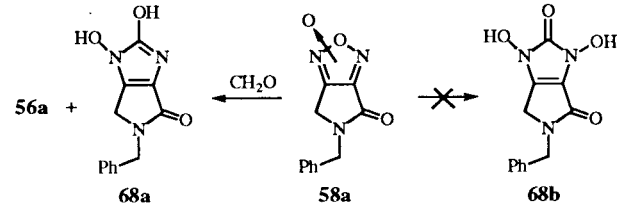
58a **57a**

In contrast to benzofuroxans [55], reaction of **58a** with butan-2-one in methanol in the presence of a base at 40°C afforded the dioxime **56a** (yield >50%), not **67** [50].



58 **67**

Treatment with formalin in aqueous methanol at 40°C in the presence of alkali transformed the furoxan moiety of **58a** to yield **68a** in 11% yield. Another major product also was **56a** [50]. Derivative **68b** which could be expected in these conditions analogously with transformation of benzofuroxans [108], was not found.



68a **58a** **68b**

The ^1H nmr spectra of **57a,b** [50], **58a-d** [50], **64**, **65** [54] and ^{13}C nmr spectra of **58a,b** [51], **64** and **65** [54] have been reported.

Compounds **58a-d**, like furoxans of the cyclopentane series, may be used for the modification of unsaturated polymers, especially the cross-linking, curing or vulcanization of such materials (*e.g.* styrene butadiene rubbers) [51].

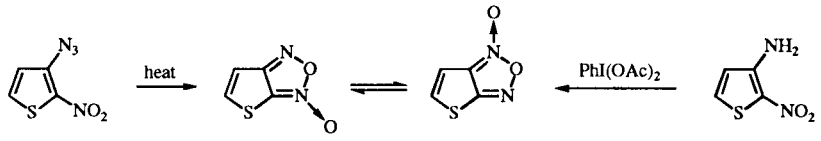
Thienofurazans.

Both possible types of the bicycle, **VI** and **VII**, are known.

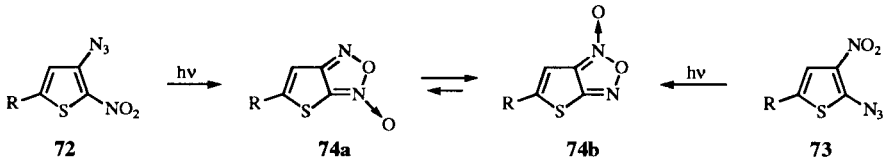
VI **VII**

Thieno[2,3-*c*]furazans **VI**

This ring system has also been referred to as thieno-[2,3-*c*][1,2,5]oxadiazole. The *N*-oxide has also been called thieno[2,3-*c*]furoxan. Only *N*-oxides of the system are known. Boulton and Middleton [56] first reported a synthesis from the thiophene precursors. Thermolysis of nitroazide **69** in acetic acid gave the furoxan **70** in 47%



69 70a 70b 71



72 74a 74b 73

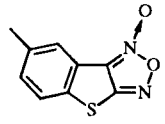
R = CO_2CH_3

yield. Oxidative cyclocondensation of nitroamine **71** with PIA led to **70** in yield 26%.

Investigation of solvent effects on the thermolysis of **69** show that the reaction in benzene gave **70** in approximately quantitative yield [57]. Smaller yields in high boiling solvents are probably a result of the instability of **70**. The compound exists mainly in the form of isomer **70b** [56-58].

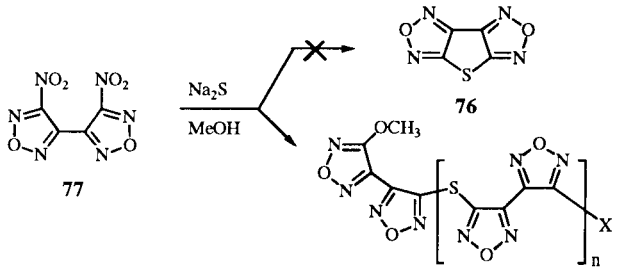
Irradiation of both nitroazide **72** and **73** affords a mixture of furoxans **74a** and **74b**; the latter isomer predominates [59].

The distant position of the *N*-oxide oxygen atom relative to the sulphur atom of the ring in compound **75**, as well as the angle strain of the system were indicated by X-ray analysis [60].



75

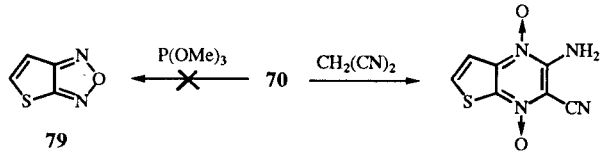
An attempt to synthesize tricyclic system **76** from **77** by treatment with sodium sulfide in methanol failed. Linear products **78** were obtained [61].



77 **76**

78 (X = NO_2, OMe; n = 1,2,3)

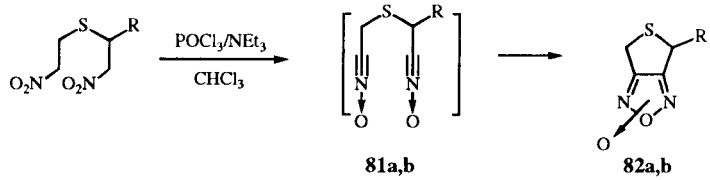
Reduction of **70** with trimethyl phosphite afforded a complicated mixture from which the corresponding furazan **79** failed to be isolated [56]. Condensation of **64** with malononitrile afforded di-*N,N'*-oxide **80** (15%) [50].



79 **70** **80**

Thieno[3,4-*c*]furazan **VII**

Two research groups reported synthesis of these types of compounds in 1977. Thus, Marx *et al* [62-64] obtained derivatives **82a,b** in low yields by intramolecular cyclization of prepared *in situ* bis(nitrile oxides) **81a,b**.



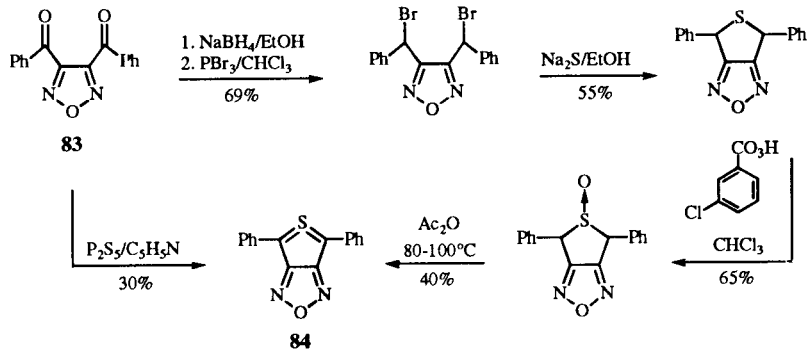
81a,b **82a,b**

a (R = H), **b** (R = $CH_2CH_2CH_2CH_2COOCH_3$)

Optimizing the yield of **82b** increased it to 81%. It is a precursor in biotin preparation.

Tsude *et al* [65] synthesized derivatives of this system starting from a furazan precursor *via* thiophene ring formation. Two routes of transformation of 3,4-dibenzoylfurazan (**83**) into the nonclassical 10-electron heterocycle **84** were examined as outlined in scheme below.

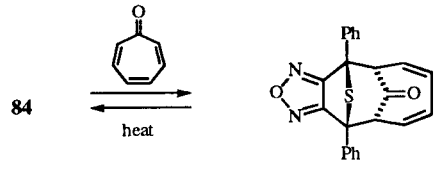
The high reactivity of **84** stimulated work on its reaction with unsaturated compounds. A mixture of equimolar amounts of **84** and dimethyl fumarate or maleate in benzene at reflux under nitrogen for 8 hours gave 1:1 cycloadducts **85** or **86** in 15 and 4% yields, respectively. A major amount of **84** was recovered. Compound **84**



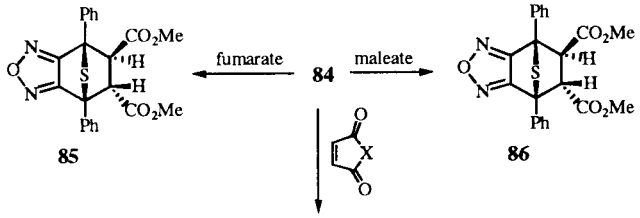
83 84

afforded a mixture of *exo*, **87a-f** (31-51%), and *endo* adducts, **88a-f** (25-38%), in the reaction with maleimides and maleic anhydride under the same conditions [65,66].

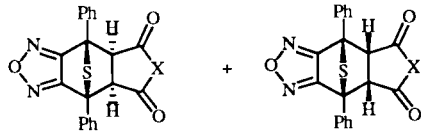
When **84** was allowed to react with norbornene in refluxing benzene, four stereoisomeric 1:2 adducts, **91,** were obtained in an overall yield of about 50% [67]. The



84 92



85 84 86

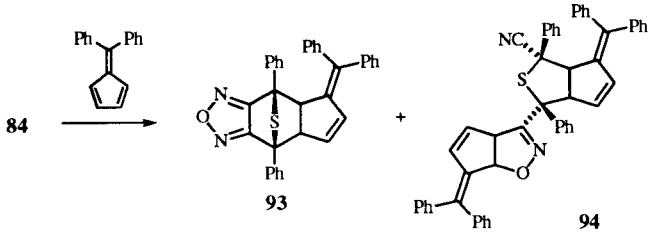


87a-f 88a-f

a (X = NPh), **b** (X = $NC_6H_4NO_2$-*p*), **c** (X = C_6H_4OMe-*p*), **d** (X = NMe), **e** (X = NH), **f** (X = O)

and the tropone were formed in 48 and 44% yields respectively, along with recovery of **92** (48%).

When compound **84** and 6,6-diphenylfulvene react in refluxing benzene for 12 hours under nitrogen, a mixture of the 1:1 adduct, **93** (52%), and 1:2 adduct, **94** (11%) are obtained [68].



84 93 94

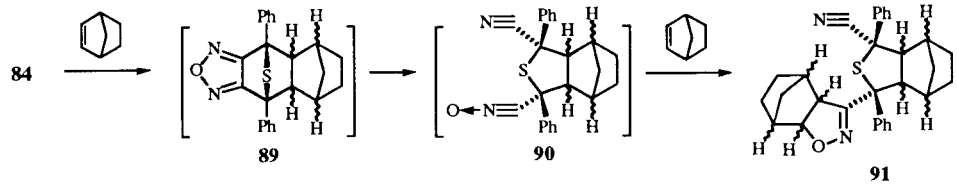
reaction proceeded *via* initial formation of both strained *endo-exo* and *exo-exo* cycloadducts **89**. Subsequent ring cleavage of the furazan ring in **89** generated the nitrile oxide intermediate **90,** capable of undergoing cycloaddition with norbornene to afford the adducts **91**.

The reaction of **84** with 2,4,6-cycloheptatrienone in benzene for 48 hours gave the 1:1 adduct **92** in 30% yield [68].

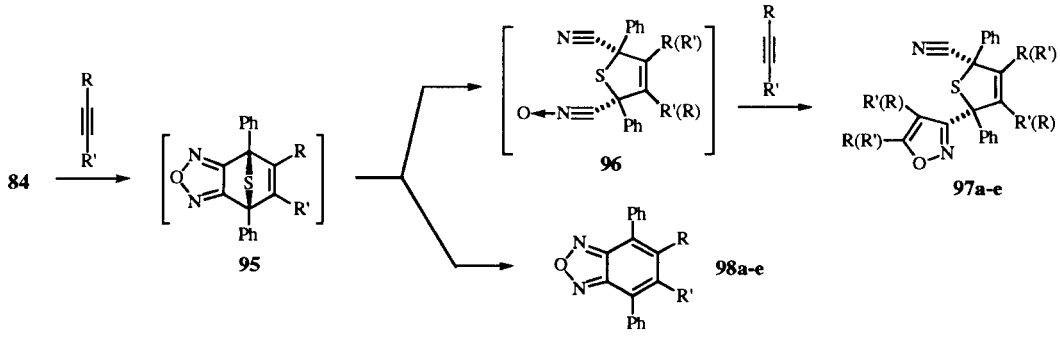
It was also found that **92** underwent a retro-cycloaddition reaction upon refluxing in benzene for 48 hours; **84**

Acetylenes, like norbornene, formed two 1:2 adducts **97a-e**, accompanied by benzofurazans **98a-e**, when refluxed in benzene [69]. The formation of **97a-e** was a result of furazan ring cleavage of the initial 1:1 adduct **95** to yield the nitrile oxide intermediate **96** which is capable of undergoing cycloaddition with acetylenes. Desulfurization of **95** led to the formation of **98a-e**.

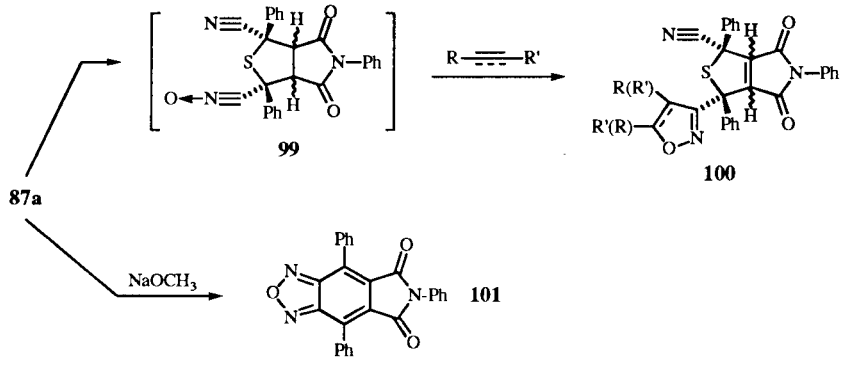
Thermolysis of **87a** or **88a** caused furazan ring opening and afforded nitrile oxide **99.** This was detected as a dipo-



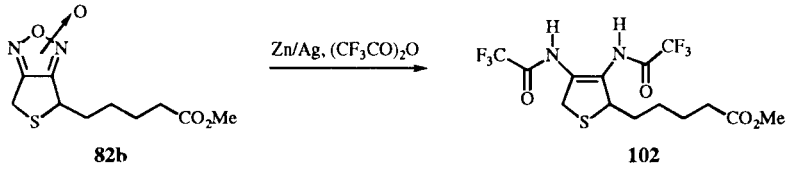
84 89 90 91



a (R = R' = CO_2Me), **b** (R = R' = COPh), **c** (R = H, R' = CO_2Me), **d** (R = H, R' = Ph), **e** (R = Ph, R' = CO_2Me)



lar cycloaddition adduct like **100** [70, 71]. A similar transformation took place upon thermolysis of **87b-e** and **93** with olefins and acetylenes [66]. The desulfurization product, **101**, was formed (81%) *via* thiophene ring opening in the reaction between **87a** and sodium methoxide in methanol [65].



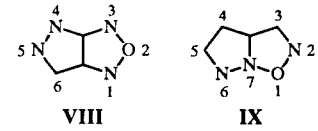
Reaction of **82b** with Zn/Ag in glyme and trifluoroacetic anhydride afforded a diamine *via* reduction of the furoxan ring; the isolated product was diacetamide **102** [62-64].

The ^1H nmr spectra of **70** [56,57], **74** [59], **82b** [62], **85-88** [65], **92** and **93** [68] have been reported. Investigation of the rearrangement of **70a** ⇔ **70b** showed the existence of an anomalously low activation energy, as a result of bond angle strain [56].

4. Furazans Fused to 5-Membered Heterocycles with Two Heteroatoms.

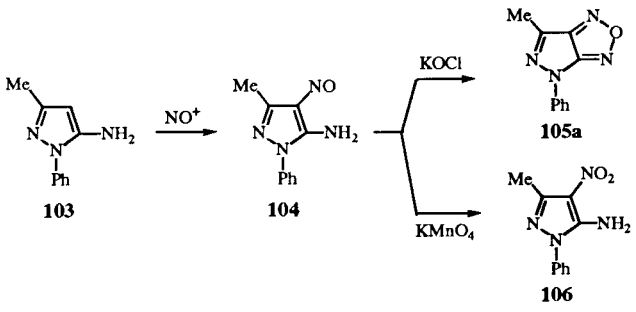
Pyrazolofurazans.

There are two possible types of this ring system, **VIII** and **IX**. Derivatives only of the first one are known.



Pyrazolo[3,4-*c*]furazans **VIII**

This ring system has also been referred to as 1,2,5-oxadiazolo[3,4-*d*]pyrazole and pyrazolo[3,4-*c*][1,2,5]oxadiazole. This was the first bicyclic system in which furazan ring was condensed to a heterocycle. Thus, in 1908 Mohr [2] reported that nitrosation of aminopyrazole **103** afforded



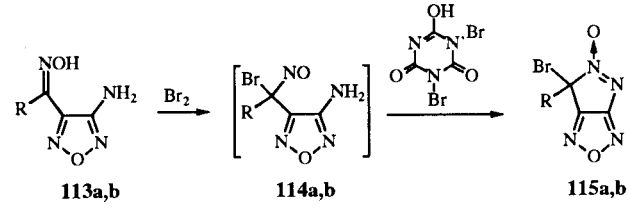
aminonitroso derivative **104**, which after oxidative condensation with potassium hypochlorite in alkali solution gave **105a** in a quantitative yield. The use of potassium permaganate as an oxidizing agent yielded **106** not **105a**.

Analogously, the structure **108** was assigned to the product synthesized from arylaminopyrazole **107** [72]. However, this structure has not been verified.

studied earlier [74-78]. However, true structure of the substances had not been established at that time.

Formation of **105a** (6%) from **112** and iron pentacarbonyl under reflux in THF was unexpected [79].

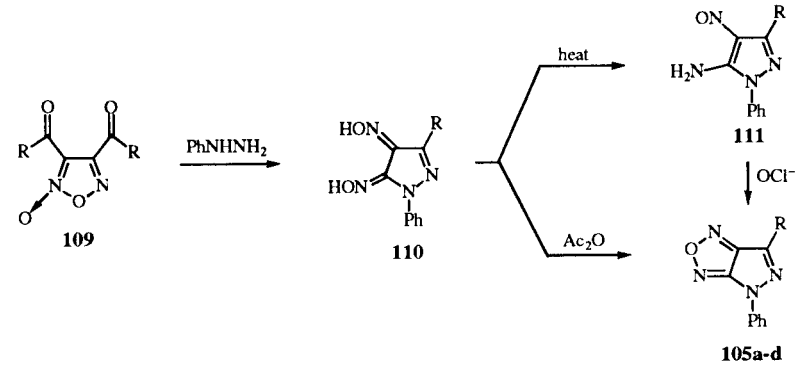
This compound may also be synthesized starting from a furazan precursor. Thus, treatment of the oximes **113a,b** with bromine in the presence of a base in an inert solvent yields nitrosobromide **114a,b**, which reacted with dibromoisocyanurate (DBI) to form the *N*-oxide **115a,b** (47-84%) [80]. Reaction of **113a** with DBI also afforded **115a** in decreased yield (5-8%).



a (R = CH_3), **b** (R = Cl)

The oxime **113a** was treated with PIA to produce the unstable derivative **116** in 11% yield [81].

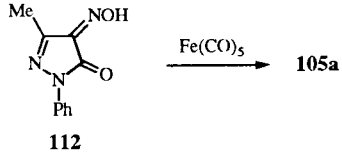
Nitric acid in concentrated sulfuric acid at 20°C for 0.3 hours converted **105a** to the 2,4-dinitro derivative **117** (80%); similar treatment at 80°C converted both **105a** and **117** to the 2,4,6-trinitro derivative **118** (33 and 75%, respectively) [82].

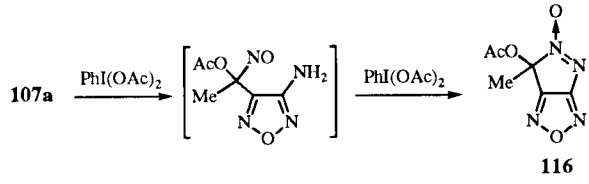


a (R = CH_3), **b** (R = Ph), **c** (R = $C(CH_3)_2CO_2CH_3$), **d** (R = $C(CH_3)_2CO_2H$)

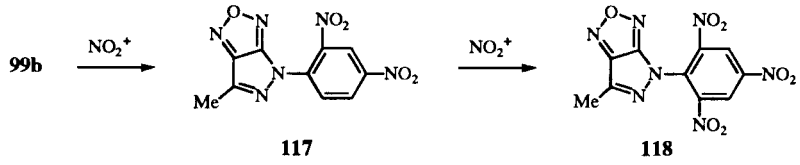
The treatment of diacylfuroxans **109** with phenyl hydrazine yielded glyoximes **110**, which were transformed into **105a-d** by two routes [73].

It should be noted that the reaction of **109** with phenyl hydrazine and the reactivity of the products had been





The ^1H, ^{13}C and ^{14}N nmr spectra of **115a,b** [80], **117** and **118** [82] have been reported. An X-ray structural

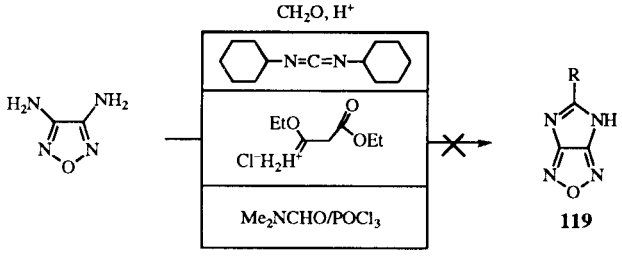


117 118

analysis of **117** [82] has revealed considerable distortions of bond lengths and angles.

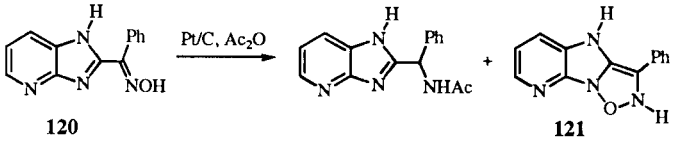
Other Heterocycles.

Attempts to synthesize imidazo[4,5-*c*]furazan **119** were undertaken by a number of research groups. However, none of the pathways shown below were successful [83-89].



119

The structure of **121** [90] which includes the imidazo[1,2-*b*]furazan subunit, assigned to one of the products of hydrogenation over platinum on charcoal of oxime **120** seemed less probable.

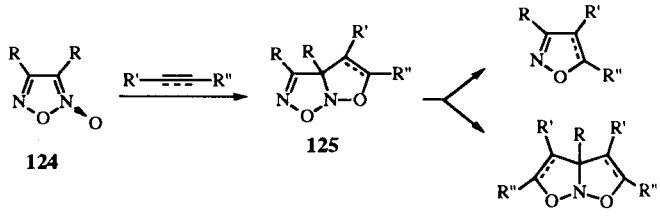


120 121

Treatment of **122a,b** with both alkali [91] and thionyl chloride [92] gives furazan ring closure. Concurrently isoxazole ring cleavages; derivatives of the isoxazolo-[4,5-*c*]furazan **123a,b** are not formed.

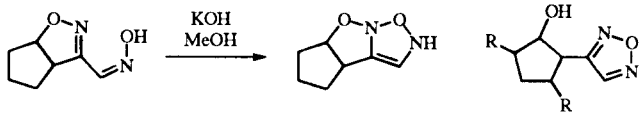
Derivatives of isoxazolo[2,3-*b*]furazan **125** were suggested as intermediates in the reaction of disubstituted furoxans **124** with olefins and acetylenes [93-98].

Further still, one of the articles reported the isolation of stable derivatives of the isoxazolo[2,3-*b*]furazan, *e.g.* **126** [99].



124 125

However, a product from this type of reaction was shown later to be a non condensed furazan, *e.g.* **127** [100].

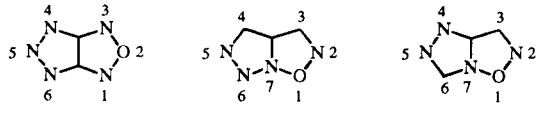


126 127

5. Furazans Fused to 5-Membered Heterocycles with Three Heteroatoms.

Triazolofurazans.

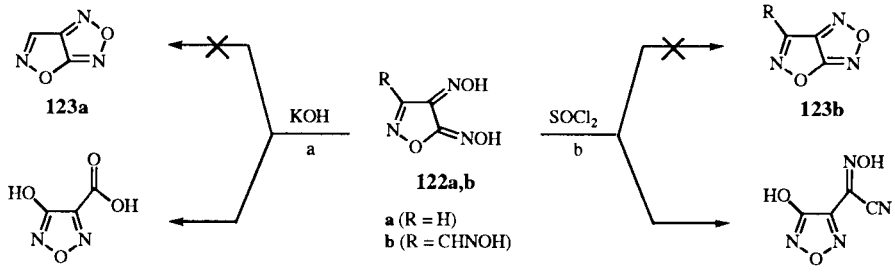
Of the three theoretically possible parent triazolofurazans, skeleton type **X-XII**, only derivatives of **X** have been synthesized.



X XI XII

[1,2,3]Triazolo[4,5-*c*]furazans **X**

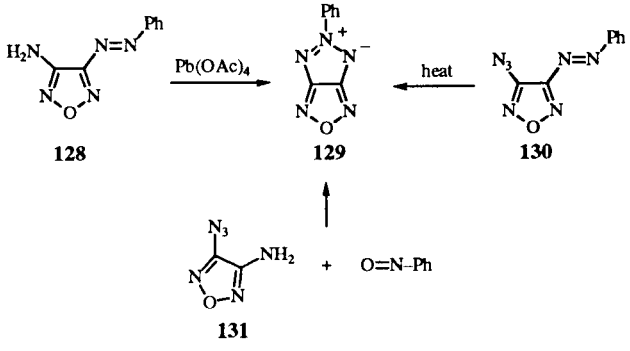
This ring system is also referred to as [1,2,3]triazolo[4,5-*c*][1,2,5]oxadiazole. The oxidation of azo



123a 122a,b 123b

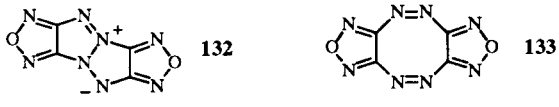
a (R = H)
b (R = CHNOH)

derivative **128** with LTA in dichloromethane afforded pentalene **129** in 28% yield [101]. The compound can also be synthesized by the thermal condensation of azide **130** (54%) or by the condensation of **131** with nitrosobenzene [102].



128 **129** **130** **131**

The X-ray photoelectron spectrum of **129** was obtained in the solid phase [103]. Theoretical investigations of compounds involving **X** as a subunit were of interest. Thus, on the basis of the computational analysis of hypothetical isomers **132** and **133,** preference was given to **133** [104].



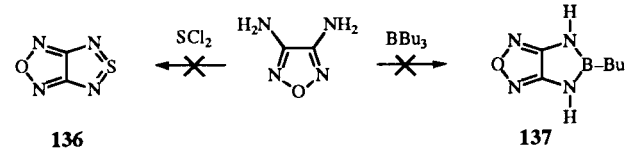
132 **133**

Other Compounds.

Tricycles involving the oxadiazolo[2,3-*b*]furazan subunit, **134** and **135**, were suggested as intermediates in the oxidation of nitrobenzofuroxans with Caro's acid [105].

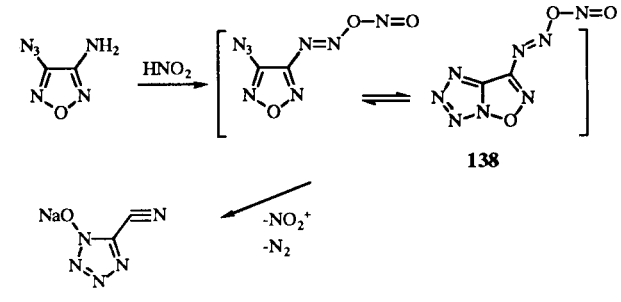
The treatment of 3,4-diaminofurazan with sulphur dichloride [106] or with tributylboron [86] did not yield **136** or **137**.

6. Furazans Fused to 5-Membered Heterocycles with Four Heteroatoms.



136 **137**

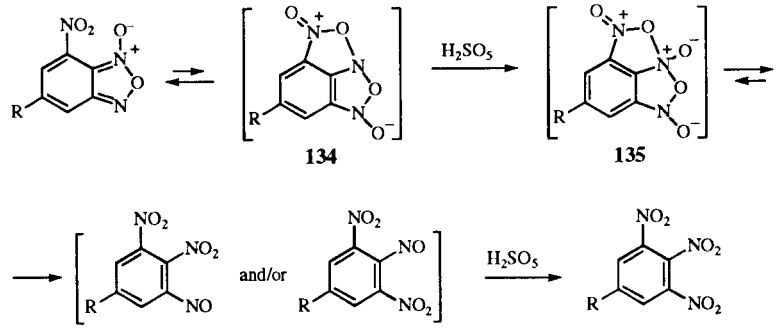
The data on stable derivatives of this series are absent from the literature. There was only one report of furazanotetrazole **138** as a possible intermediate in the transformation of the diazotization product of 3-amino-4-azidofurazan [107].



138

7. Conclusion.

In this review we have focused on syntheses of furazans condensed to five-membered rings. The number of possible combinations of furazan rings with other five-membered rings is large. However this class of compounds presently lacks many variants. Both physical, and chemical data for the bicycles synthesized are also scant. From the results described in this review several features emerge concerning the reactivity of these bicycles, induced by strain energy in the systems. Thus, lability of the nitrogen-oxygen and carbon-carbon bonds in the furazan subunit determines the ability of synchronous cleavage of both rings, producing highly active intermediate for the following reactions. The possibility of selective transformations of either furazan or cycles annelated with it is a pathway to not easily accessible compounds. The use of these bicycles as precursors awaits further systematic development. Many opportunities for discovering novel syntheses and new reactions still exist in this field.



134 **135**

We hope that this review will provide an incentive for further studies.

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