

## HETEROCYCLIC REARRANGEMENTS OF BENZOFUROXANS AND RELATED COMPOUNDS <sup>‡</sup>

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**Abstract** - Heterocyclic rearrangements of benzofuroxans, benzotriazoles, furoxans, 1,2,4-oxadiazoles, benzofuroxans, anthranils, triazoles, benzotriazoles, isoxazoles and some related compounds are reviewed in connection with the problem of benzofuroxan ring chain tautomerism. Both mono- and bicyclic rearrangements of these five-membered heterocycles and their benzo-derivatives, and related heterocyclic transformations are discussed with an emphasis on the most relevant earlier and recent studies.

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<sup>‡</sup> Submitted in Honor of the 70th Birthday of Edward C. Taylor whose example is an inspiration to all heterocyclic chemists.

## 1. Introduction

Heterocyclic rearrangements cover an enormous field of organic chemistry and have been extensively studied and reviewed.<sup>1-4</sup> Reactions of this type have been found for most heterocycles (see, e.g. ref. 4), and many new rearrangements are reported in the chemical literature each year.

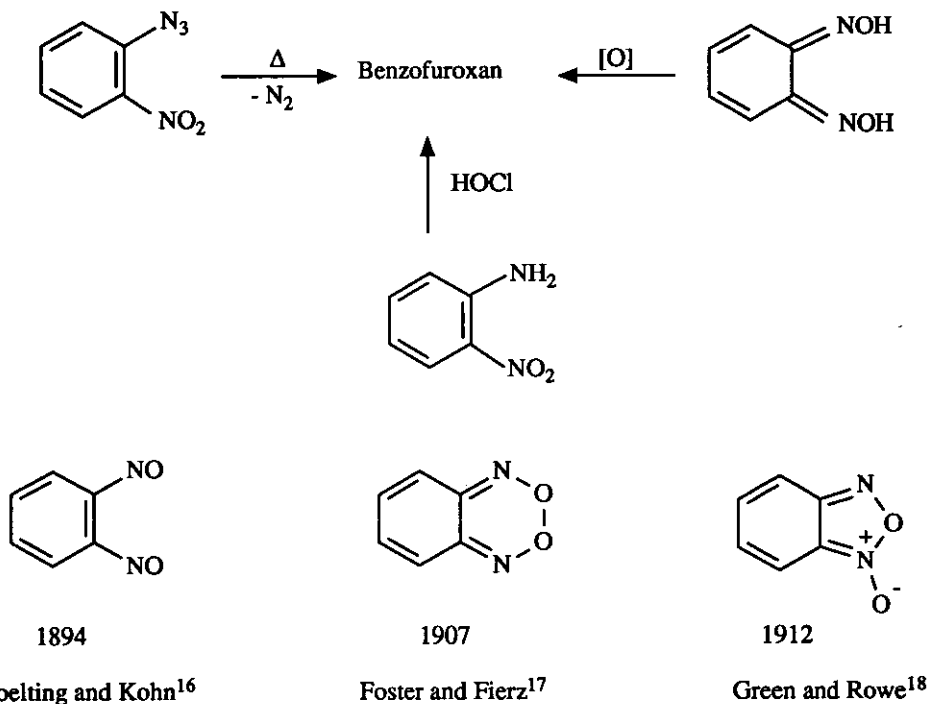
With reference to five-membered heterocycles, the best known examples include the Dimroth rearrangement of azoles,<sup>1,3,5</sup> azines<sup>3,6</sup> and azoloazines,<sup>4,6</sup> as well as Cornforth rearrangement<sup>1,3</sup> and monocyclic rearrangements.<sup>2,3</sup> The present review is concerned with heterocyclic rearrangements of benzofuroxan and related compounds. Monocyclic transformations of this type have been previously reviewed as mononuclear heterocyclic rearrangements,<sup>2,3,7</sup> and benzo-fused systems also have been covered.<sup>2,8-12</sup>

These reactions of benzofuroxans and related compounds are intimately related both mechanistically and historically with benzofuroxan tautomerism, the discovery of which led to the recognition of the generality of mono- and bicyclic rearrangements of five-membered heterocycles and their benzo-derivatives with appropriate side chains<sup>2,13,14</sup> (see below, Schemes 19 and 29). Heterocyclic transformations of benzofuroxans and related heterocycles are not limited to these two types of reactions (see, e.g., reviews<sup>12,15</sup>). In the present review, rather than an exhaustive presentation of all known examples of these transformations, we aim to present an overview of the field. The emphasis is on data which have been less discussed previously and to cover recent studies.

## 2. Ring Chain Tautomerism in Benzofuroxans and Related Bicyclic Heterocycles

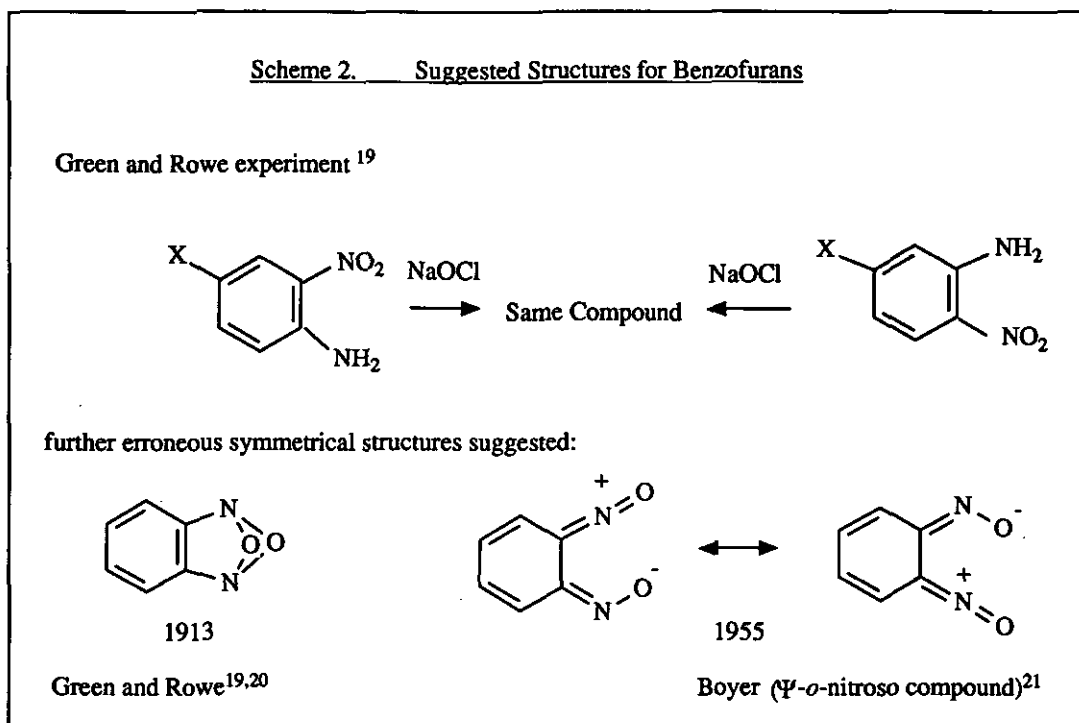
Benzofuroxan was first prepared at the end of the 19th century and was early on obtained by several different methods as shown in Scheme 1. It was assigned first the *o*-dinitroso structure,<sup>16</sup> then a peroxide structure,<sup>17</sup> and finally, in 1912, the correct structure was given to it by Green and Rowe<sup>18</sup> (Scheme 1).

**Scheme 1. Preparation and Suggested Structures for Benzofuroxan**

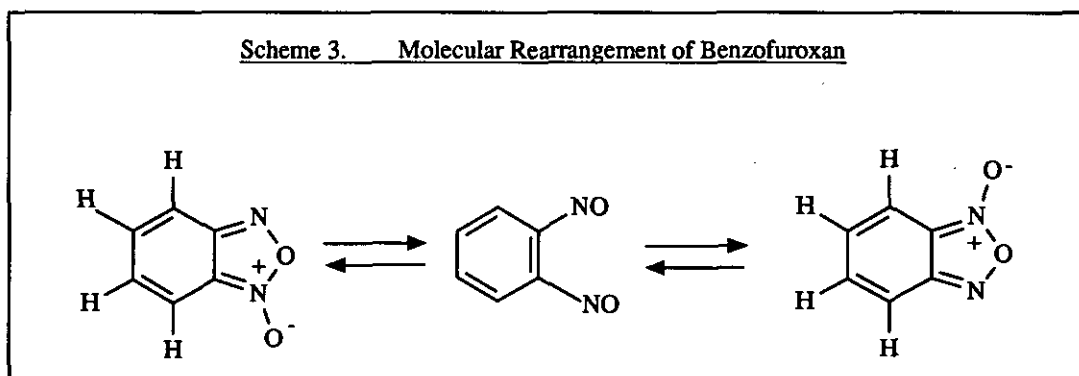


However, these same researchers attempted to prove the unsymmetrical nature of the compound and to their surprise, obtained<sup>19</sup> the same product on the sodium hypochlorite oxidation of isomeric *o*-nitroanilines shown in Scheme 2. Because of this finding, several other formulae were suggested, including the tricyclic structure<sup>19,20</sup> and the unlikely pseudo structure<sup>21,22</sup> also shown in Scheme 2.

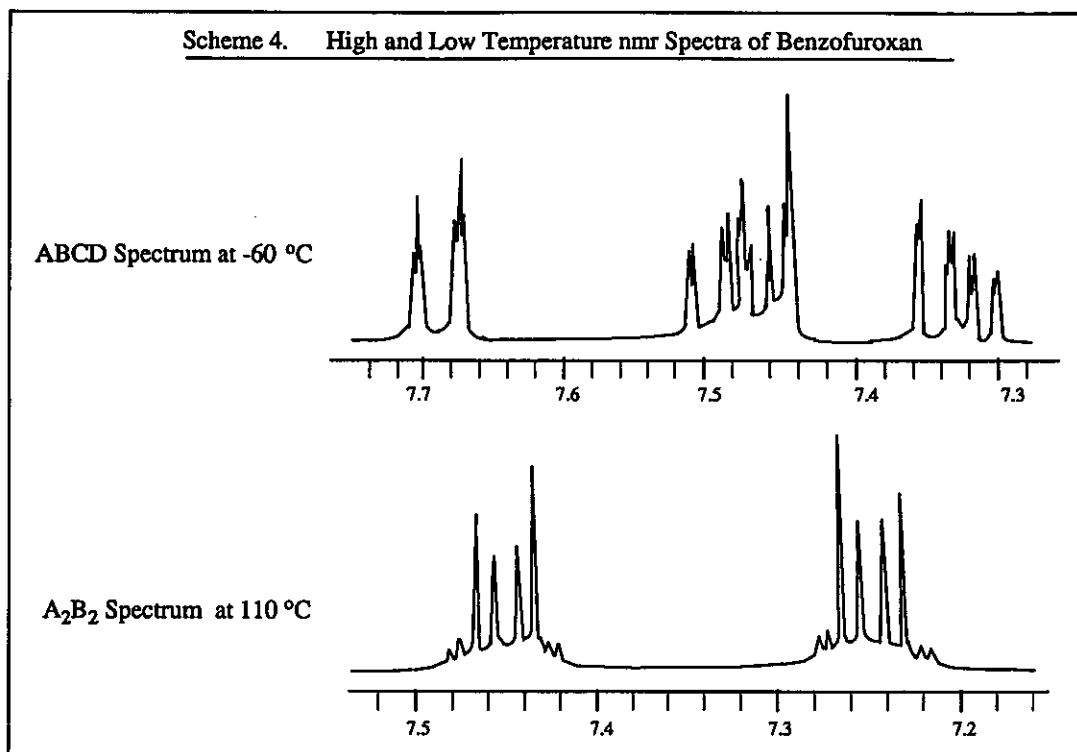
The correct explanation for this dilemma was suggested by Hammick.<sup>23</sup> It was that benzofuroxan rapidly rearranges between the two asymmetrical bicyclic structures through the ring opened dinitroso form



(Scheme 3). This postulate was later conclusively proved by nmr spectroscopy.<sup>8,24-26</sup>



In Scheme 4, <sup>1</sup>H and <sup>13</sup>C nmr spectra of benzofuroxan are shown at low and high temperature, the low temperature spectra correspond to the unsymmetrical form, and those at high temperature to the rapidly equilibrating mixture of the two equivalent unsymmetrical forms.



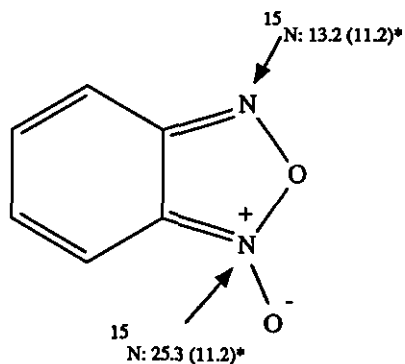
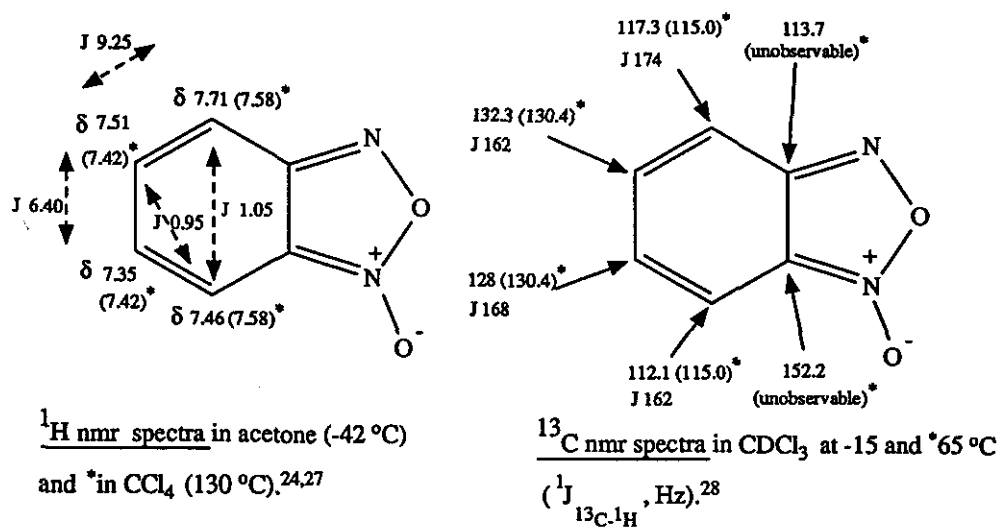
Assignments for signals and coupling constants in benzofuroxan are given in Scheme 5.

$^{17}\text{O}$  Nmr studies also indicated the presence of two non-equivalent oxygen atoms in the molecule of benzofuroxan at  $28\text{ }^{\circ}\text{C}$ , and Dnmr effects were observed at higher temperatures.<sup>31</sup>

Thus, dynamic resonance effects in  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{15}\text{N}$  and  $^{17}\text{O}$  nmr spectra all confirm the unsymmetric structure and tautomerism of benzofuroxan. A full account on the history of structural assignments in the furoxan series has been provided in an earlier review by Gasco and Boulton.<sup>12</sup>

Numerous studies on the tautomerism of furoxans and benzofuroxans show that the chemical behavior of above mentioned heterocycles is consistent with the mechanism of Scheme 3.<sup>12,15,32,33</sup> However, definitive evidence for the intermediacy of *cis*-dinitrosoalkenes and of *o*-dinitrosoarenes (Scheme 3) in these transformations was presented only in 1991 when *o*-dinitrosobenzene was isolated in Ar matrixes at  $14\text{ }^{\circ}\text{K}$  by

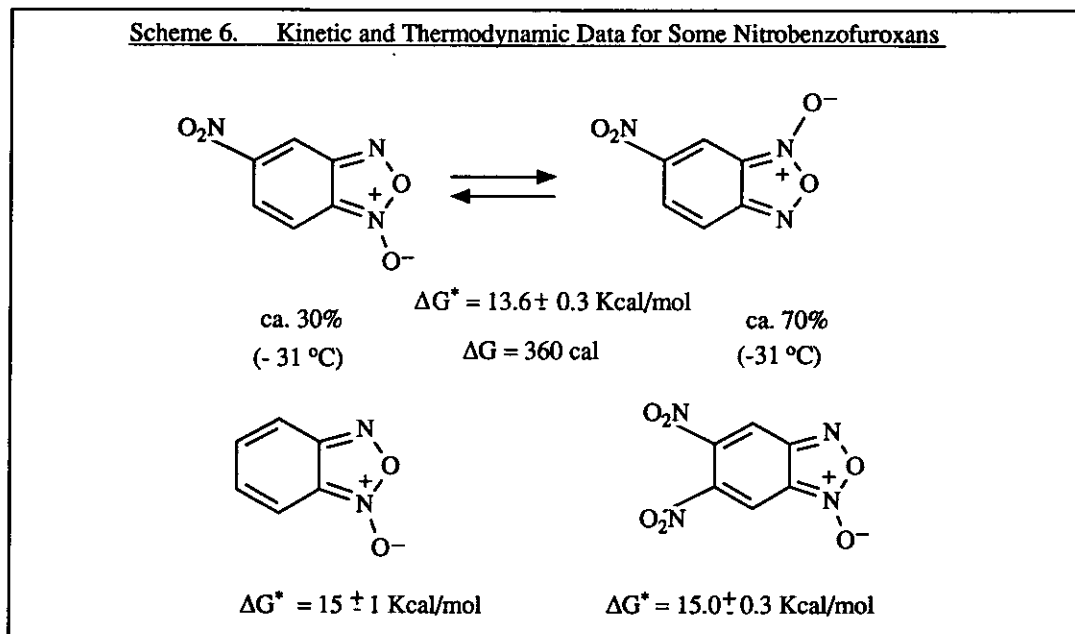
**Scheme 5. Chemical Shifts and Coupling Constants for Benzofuroxan**



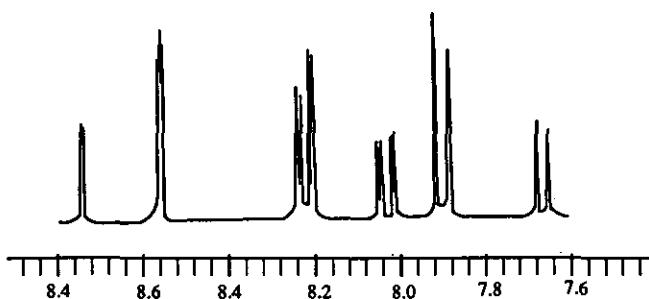
the photolysis of benzofuroxan or *o*-nitrophenyl azide, and characterized by ir and uv spectra.<sup>34</sup> Subsequent thermal and photochemical isomerization into benzofuroxan has also been observed, and supporting  $^{15}\text{N}$  labelling experiments carried out.<sup>34</sup>

The tautomerism of benzofuroxans as well as furoxans has been extensively studied by Dnmr spectroscopy. Earlier studies on this topic have been reviewed by Boulton and Ghosh,<sup>8</sup> Gasco and Boulton<sup>12</sup> and briefly by Paton.<sup>15</sup>

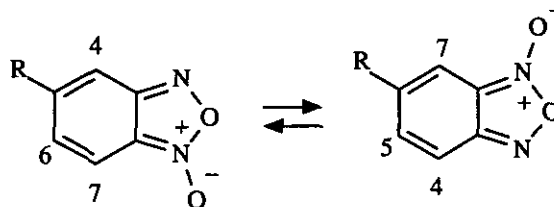
Ring chain isomerism of this type (Scheme 3) also occurs in substituted benzofuroxans. The  $\Delta G$  and  $\Delta G^*$  values for 5-nitro- and for 5,6-dinitrobenzofuroxan are shown in Scheme 6,<sup>27</sup> and the low temperature spectrum of the mixture of 5- and 6-nitrobenzofuroxan in Scheme 7. Free energy differences for the tautomeric equilibria of several substituted benzofuroxans are collected in Scheme 8.<sup>26,27,35</sup>



Scheme 7. Low Temperature Proton Spectrum of Slowly Equilibrating 5- and 6-Nitrobenzofuroxans



Scheme 8. Free Energy Differences for Benzofuroxan Tautomeric Equilibria



Tautomerism of 5 (6)-Substituted Benzofuroxans

R	$\Delta G^*$ (Kcal/mol)	$\Delta G$ (cal/mol) in favor of 6-R	R	$\Delta G^*$ (Kcal/mol)	$\Delta G$ (cal/mol) in favor of 6-R
$\text{NO}_2^a$	13.9	360	$\text{NHCOCH}_3^b$	14.1	0
5- $\text{NO}_2$ 6- $\text{CH}_3^b$	12.1	50	$\text{OCOCH}_3^b$	13.8	-100
$\text{CO}_2\text{C}_2\text{H}_5^b$	14.0	450	$\text{Cl}^b$	13.9	-200
$\text{CO}_2\text{H}^b$	14.0	320	$\text{OCH}_3^b$	14.6	-400
$\text{CH}_3^c$	-	ca. 0			

References. a: 27; b: 35; c: 26.

The equilibrium constants imply small (0-500 cal/mol) energy differences, and indicate that electron-acceptor groups favour the 6-position and electron-donor groups the 5-position.<sup>35</sup> This conclusion is in a good agreement with crystal structure determinations of 5-halobenzofuroxans by Britton and Noland.<sup>36,37</sup> Other benzofuroxans which have been studied by nmr spectroscopy include the 5,6-dinitro-,<sup>26,27</sup> 5,6- and 4,7-dichloro-,<sup>38</sup> 4,7-dibromo-,<sup>26,38</sup> 5-bromo-, 5-chloro- and 5-iodo-,<sup>39</sup>



5-chloro-4,6-dinitro-,<sup>40</sup> 7-nitro-,<sup>41</sup> 4-arenesulfinyl-7-nitro-,<sup>42</sup> 4-nitro-5-methoxy- and 4-nitro-7-methoxy-5-tosylmethyl-,<sup>43</sup> 4,6-dinitro-7-(substituted amino or amido)-benzofuroxans<sup>44</sup> and a series of 1,2-alkylenedioxybenzofuroxans<sup>45-48</sup> (see below, Scheme 18).

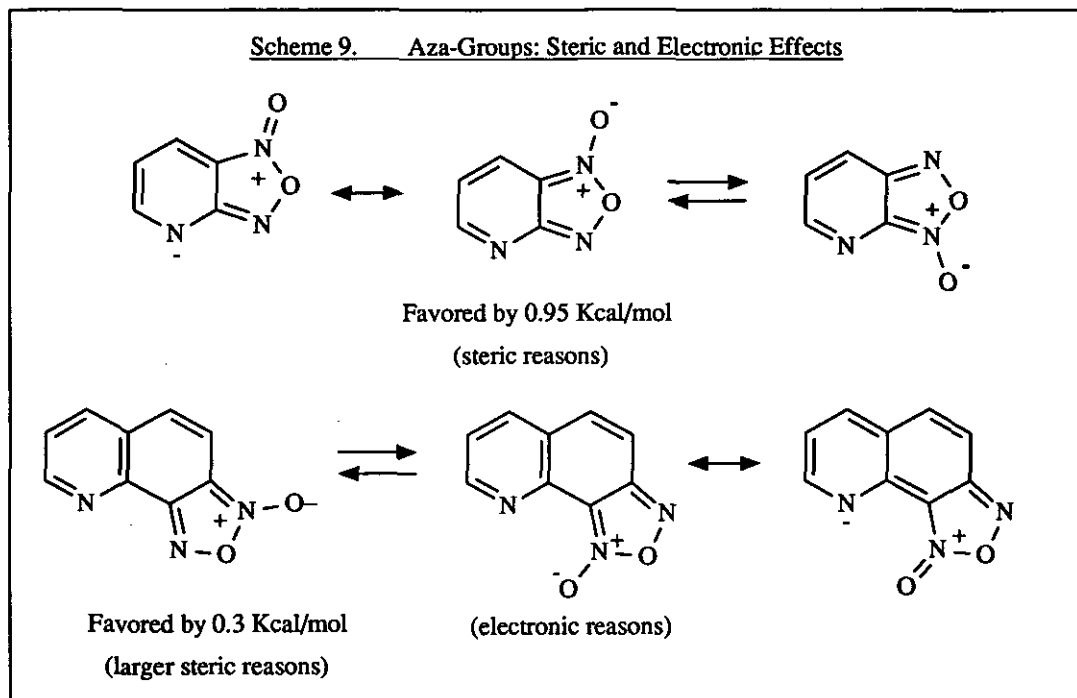
Free-energy values for the tautomerism of naphtho- and quinolinofuroxans<sup>49</sup> reflect slower isomerization for these derivatives as compared to benzofuroxans. A number of other furoxans fused to carbocyclic heterocyclic ring have also been studied (see earlier reviews<sup>12,15</sup>).  $\Delta G^*$  values for the tautomeric equilibria of furoxanobenzofuroxan and furazanobenzofuroxan have been estimated as  $21.7 \pm 0.3$  and  $22.0 \pm 0.2$  Kcal/mol, respectively.<sup>50</sup> In addition to thermal isomerization, benzofuroxans undergo analogous photochemical transformation.<sup>51</sup>

Recently reported tautomeric rearrangements in the furoxan series include those of chloro(phenyl)-,<sup>52</sup> nitro(phenyl)-,<sup>53</sup> chloro(methyl)-,<sup>54</sup> acetyl(methyl)-<sup>55</sup> and formyl(methyl)furoxan.<sup>56</sup> The isomerization of 3-phenylfuroxan to less stable 4-phenylfuroxan has been reported, but no spectral evidence was provided in the short communication.<sup>57</sup>

The tautomeric equilibria in benzofuroxans and furoxans have been the subject of several quantum mechanics investigations<sup>12,15</sup> (see also ref. 51). Recently, the overall energy of 31 mono- and di-substituted furoxans was calculated using the MINDO/3 method;<sup>58</sup> the structure of the more stable isomer was correctly predicted in each case.

An attempt to establish criteria for the direction of benzofuroxans rearrangement using molecular mechanics models has also been made.<sup>59</sup> Basing on a hypothesis that the act of rearrangement is connected with the frequency of a vibrational motion of the nitrogen atom in a five-membered ring, satisfactory agreement was achieved with known experimental data. The most stable structure was characterized by the minimum value of the frequency (in generalized coordinates). In principle, this approach could explain the effect of the conformation of a molecule on its tendency toward forward or reverse benzofuroxan rearrangement.<sup>59</sup>

The steric and electronic effects of aza-groups on the benzofuroxan equilibrium are summarized in Scheme 9.<sup>49,60</sup>



A 4(7)-aza-group exhibits considerable preference for the 4-position of the benzofuroxan skeleton, as a result of electronic repulsions between lone pairs of the oxygen and the aza-group. Energetically favorable charge delocalization can also contribute to the position of this equilibrium (Scheme 9), as is underlined by the quinolinofuroxan system,<sup>49</sup> where the "exo"-tautomer is favored by only 0.3 Kcal/mol, although the proximity is considerably increased in quinolino[8,7-*c*]furoxan over that in pyrido[6,5-*c*]furoxan (Scheme 9). Evidently, the delocalization favors quinolino[8,7-*c*]furoxan over its predominant tautomer in which no canonical form can be drawn to share the negative charge with the quinoline nitrogen.

$\Delta G^\circ$  values calculated from the monosubstituted benzofuroxans in an additive scheme can be used to predict the tautomeric equilibrium for di- and tri-substituted benzofuroxans. As shown in Scheme 10, the additivity procedure gives relatively good results.<sup>60</sup>

Scheme 10. Effects of Aza-substitution of Benzofuroxan Tautomerism

Substituents	% Named tautomer	T <sub>a</sub>	ΔG° (Kcal/mol)		
			obs <sup>b</sup>	predict <sup>c</sup>	ΔΔG <sup>d</sup>
4-CH <sub>3</sub>	75.0	- 44°	+ 0.50	---	---
5-CH <sub>3</sub>	52.4	-46	+0.05	---	---
4,6-diCH <sub>3</sub>	74.2	-46	+0.48	+ 0.45	---
4-Aza	89.1	- 45	+ 0.95	---	---
5-CH <sub>3</sub> -4-Aza	91.4	-46	+ 1.07	+ 1.00	+0.07
6-CH <sub>3</sub> -4-Aza	87.8	-45	+0.90	+ 0.90	0.00
7-CH <sub>3</sub> -4-Aza	81.6	-46	+0.67	+ 0.45	+0.22
5,7-diCH <sub>3</sub> -4-Aza	83.7	-45	+0.74	+ 0.50	+ 0.24

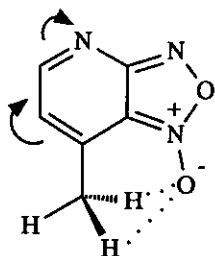
<sup>a</sup> Temperature of the determination of equilibria .

<sup>b</sup> A positive sign indicates a predominance of the tautomer indicated in the first column.

<sup>c</sup> Predicted assuming additivity of group effects, from values of 4-CH<sub>3</sub>, 5-CH<sub>3</sub> and 4-aza substituents.

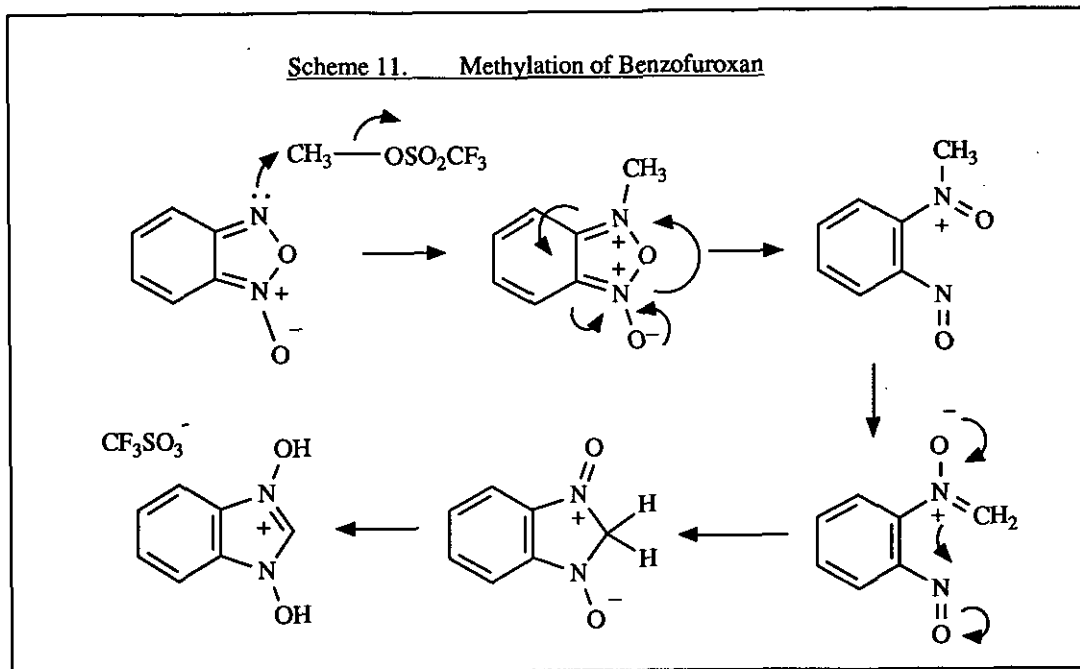
<sup>d</sup> Difference between observed and predicted values.

An extra effect noticeable for the 4-aza-7-methyl- and 4-aza-5,7-dimethylbenzofuroxans has been explained in terms of a weak hydrogen bonding between N-oxide oxygen and the methyl group hyperconjugated with the aza-nitrogen.<sup>60</sup>



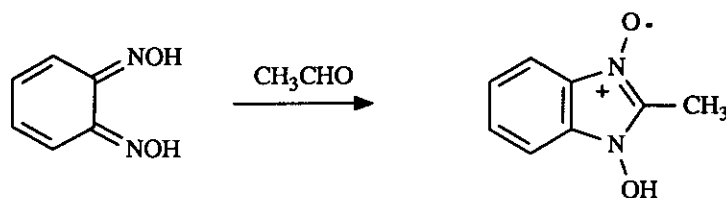
### 3. Benzofuroxan to Benzimidazole Rearrangement

The alkylation of benzofuroxan with methyl triflate leads on to an interesting isomerization.<sup>61</sup> The initial N-alkylated derivative ring opens and then a new ring closes with the carbon atom introduced by the alkylation becoming the 2-carbon of benzimidazole (Scheme 11).



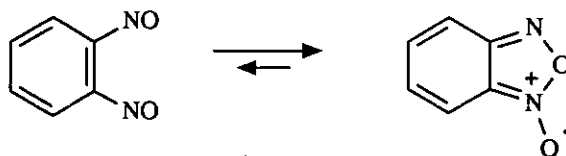
The final product is 1-hydroxybenzimidazole 3-oxide, the structure of which was confirmed by nmr and uv spectra. The uv and nmr spectra of this compound were quite compatible with those of its 2-methyl derivative prepared as shown in Scheme 12.

Scheme 12. Alkylated Benzofuroxan Rearrangement - Conformation of Structure



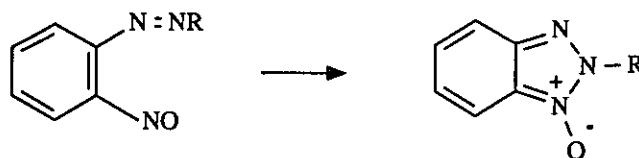
Scheme 13. Ring Chain Tautomerism of Benzotriazole Derivatives: Comparison with Benzofuroxan

benzofuroxan - in equilibrium with trace of *o*-dinitrosocompound

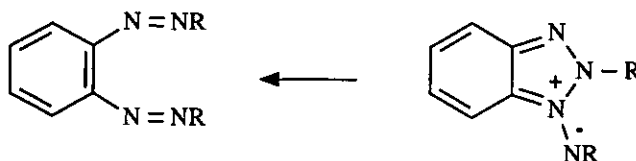


detected in Ar matrixes (14 °K) <sup>34</sup>

*o*-nitroso(aryazo)benzenes are completely cyclized



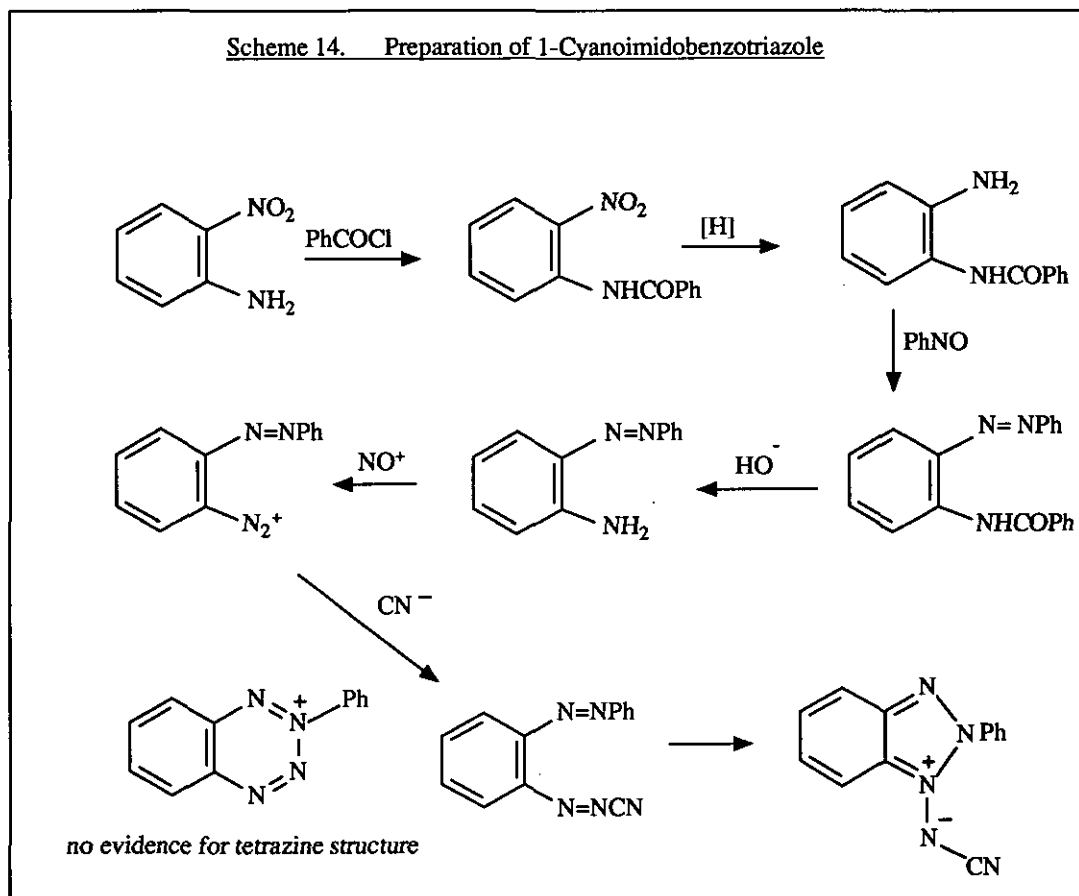
*o*-bis(azo) compounds do not cyclize

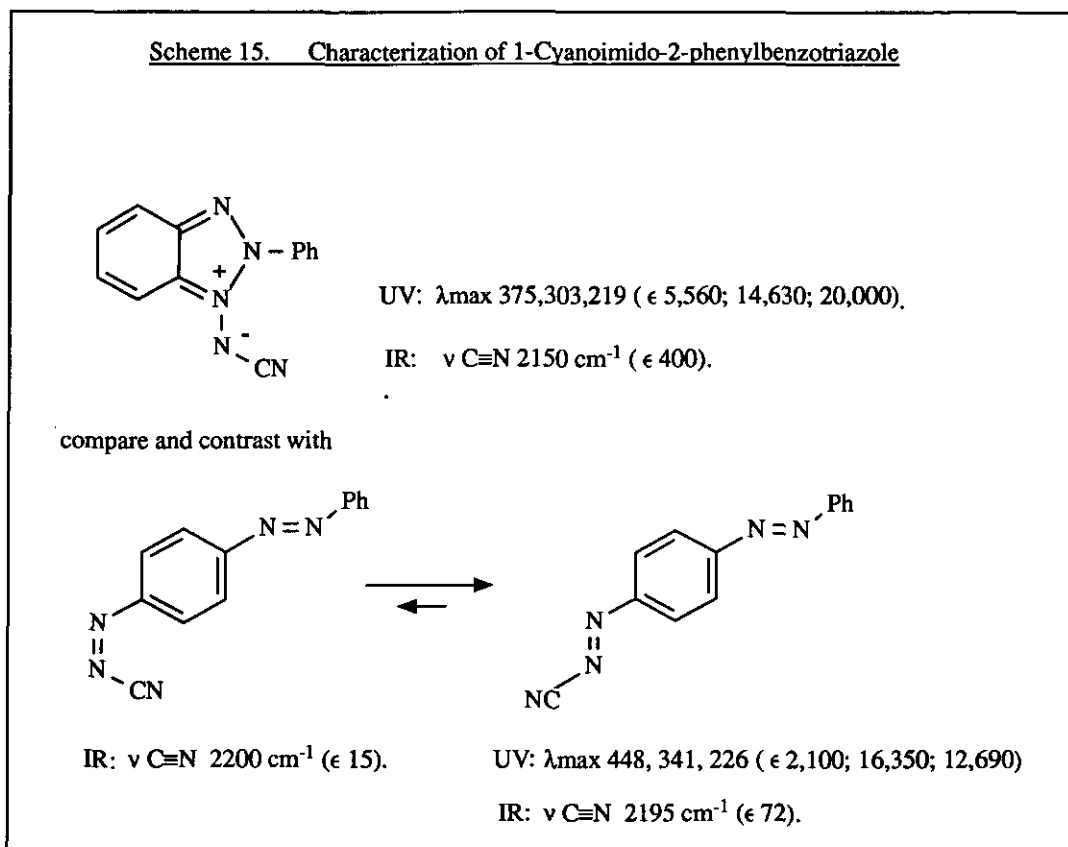


#### 4. Ring Chain Tautomerism in Benzotriazole Derivatives

The ability of benzofuroxans to isomerize via ring opening to *o*-dinitrosobenzenes is usually absent in the corresponding cyclized derivatives of *o*-nitrosoazobenzene or in *o*-bis(phenylazo)benzenes.<sup>62,63</sup> Normally, the former exists completely in the cyclized forms as benzotriazole 1-oxides, and the latter completely in the open chain form as *o*-bisazo compounds, as indicated in Scheme 13.

However, certain *o*-bisazo compounds have been shown to cyclize.<sup>63</sup> This is illustrated in Scheme 14 where the preparation is given of 1-cyanoimidobenzotriazole. Evidence that this does indeed exist in the cyclized structure is given in Scheme 15.<sup>63</sup>

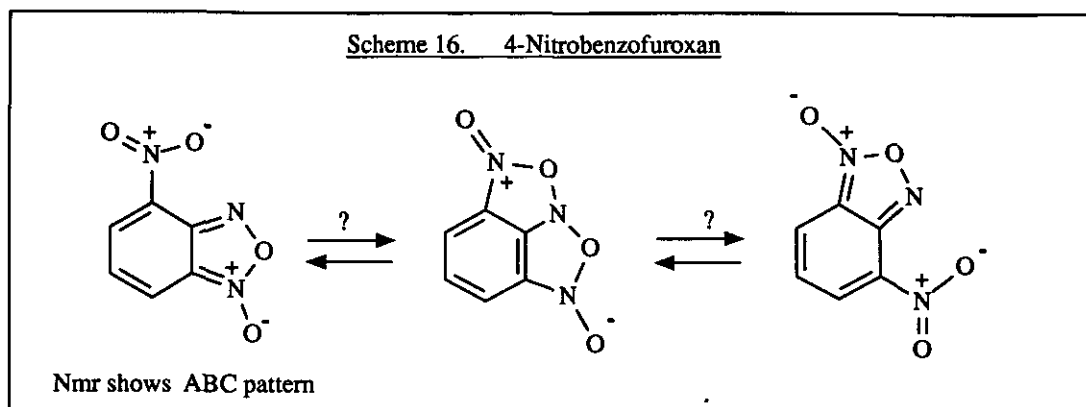


**Scheme 15. Characterization of 1-Cyanoimido-2-phenylbenzotriazole**

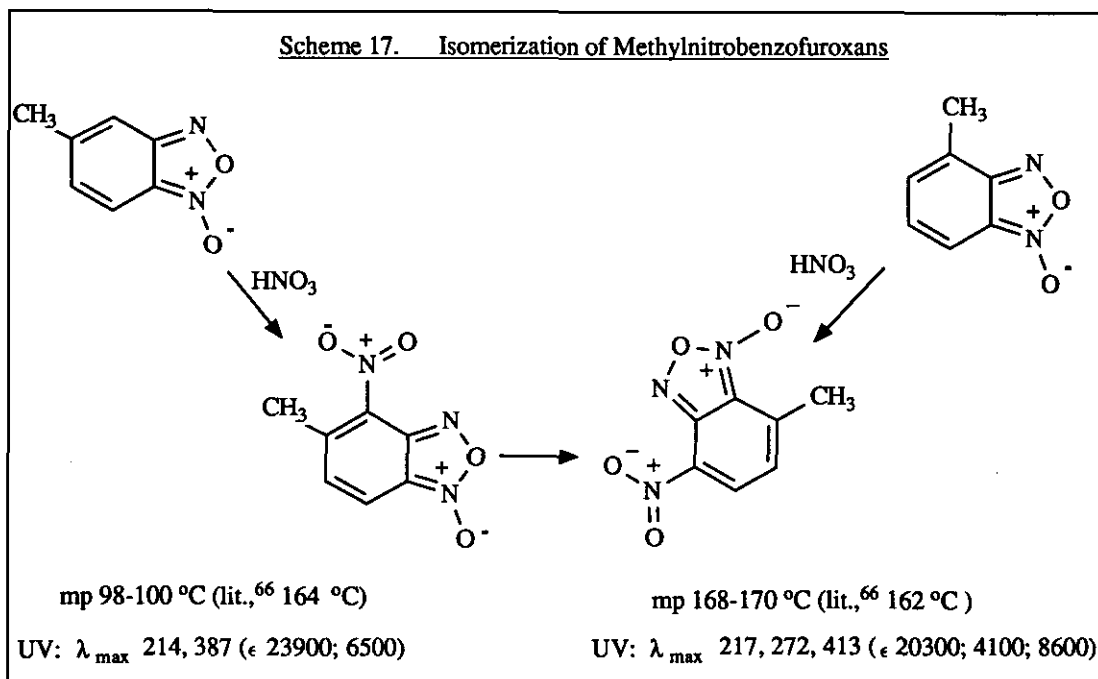
## 5. Bicyclic Rearrangements of Benzofuroxan and Related Compounds

A nitro group in the 4-position of benzofuroxan could interact with the furoxan ring as shown in Scheme 16. However, the central structure is incorrect and any rearrangement of this type is slow on the nmr time scale as the nmr spectrum of 4-nitrobenzofuroxan is an ABC pattern even at elevated temperatures.<sup>64</sup>

However, it did seem possible that isomerization could take place between the two structures. On searching the literature, it was found that the nitration of 4-methylbenzofuroxan and of 5-methylbenzofuroxan had both been investigated and that they had been reported to give different compounds. However, the literature melting points given were very similar. When this work was repeated, it was found that while the nitration



products could indeed be isolated as different compounds, on gentle heating, 4-nitro-5-methylbenzofuroxan isomerized completely to 4-nitro-7-methylbenzofuroxan which evidently has less steric hindrance<sup>64,65</sup> (Scheme 17).

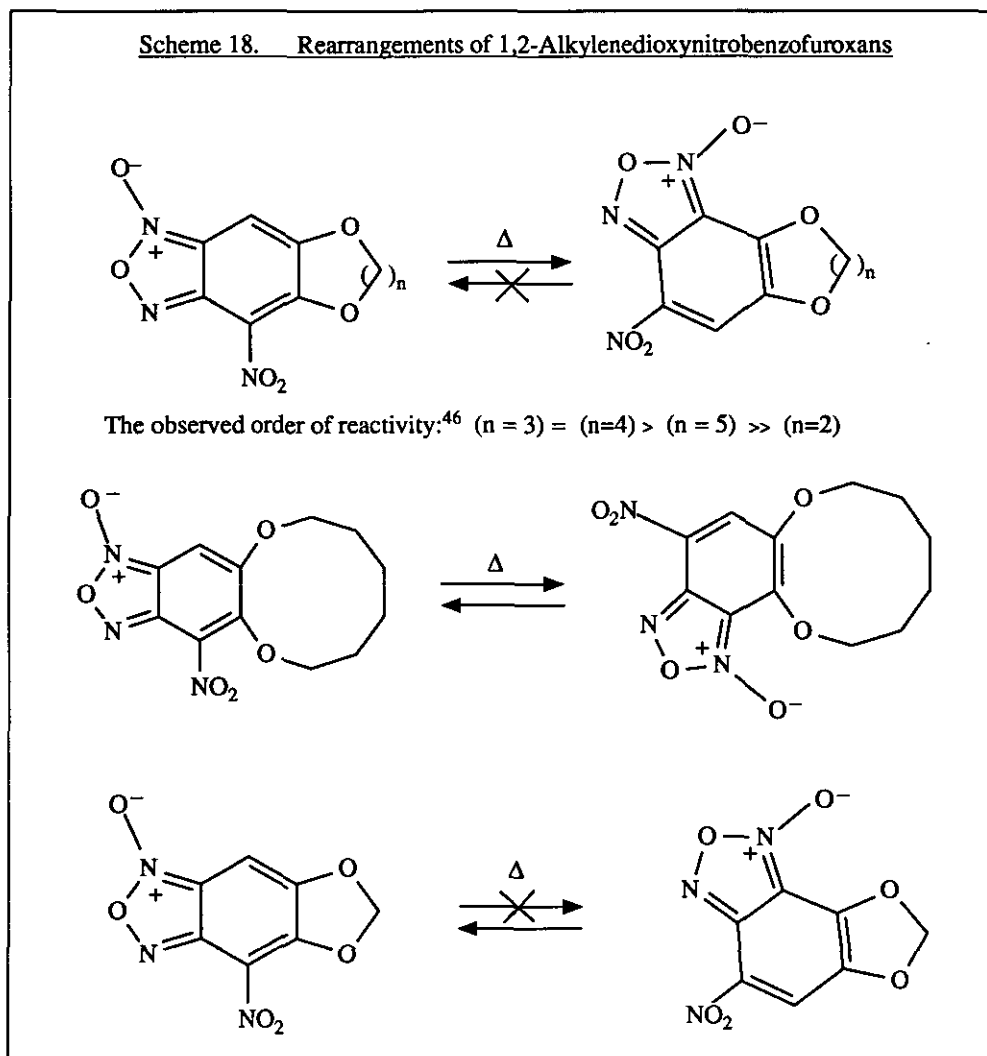


Rearrangements of 4(7)-nitrobenzofuroxans have since received much attentions and the earlier works have been reviewed.<sup>2,12,15</sup> Recently, Takakis *et al.*<sup>45,46,48</sup> studied analogous transformations in a series of 1,2-alkylenedioxynitrobenzofuroxans. Results of this works are summarized in Scheme 18.

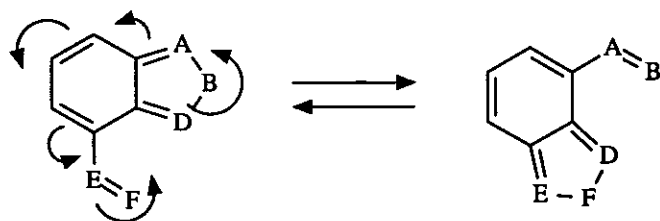


The data obtained have been rationalized in terms of a fine balance of steric, electronic, conformational and strain effects. Thus, an unexpectedly facile and irreversible transformation of 1,2-methylenedioxy-nitrobenzofuroxan to the corresponding 4-nitro-derivative (Scheme 18) has been attributed to the relief of a strain imposed by the double bond at the junction of the two rings in the starting molecule.<sup>46</sup> The initial observations<sup>64,65</sup> suggested the possibility of a class of general bicyclic rearrangements as shown in Scheme 19.<sup>14,67</sup> A few examples of possible rearrangements of this type are given in Scheme 20.

Scheme 18. Rearrangements of 1,2-Alkylenedioxy-nitrobenzofuroxans



Scheme 19. Possible Generalization of Bicyclic Rearrangement

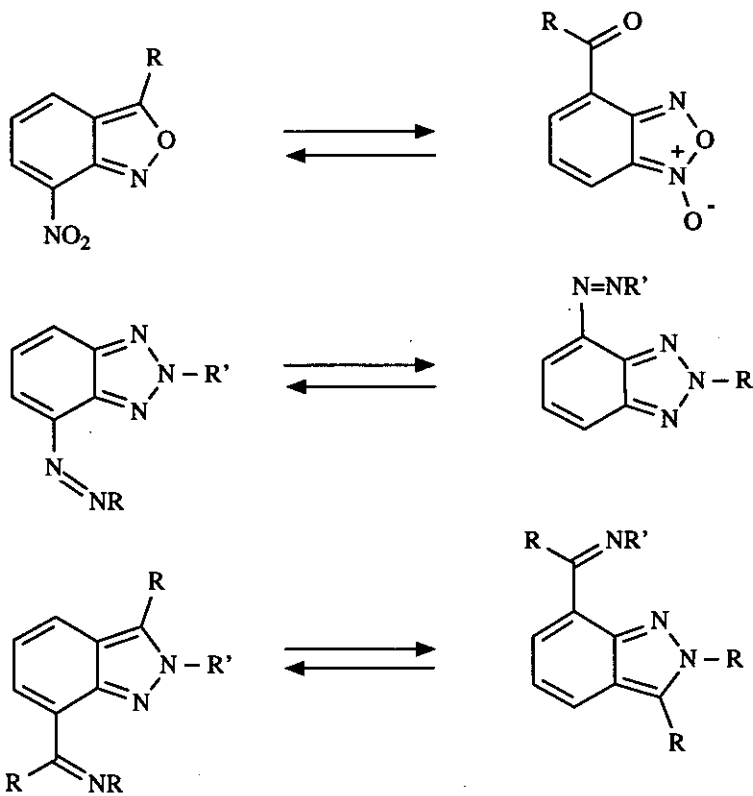


A, E = N, N-O, N-NR, CR

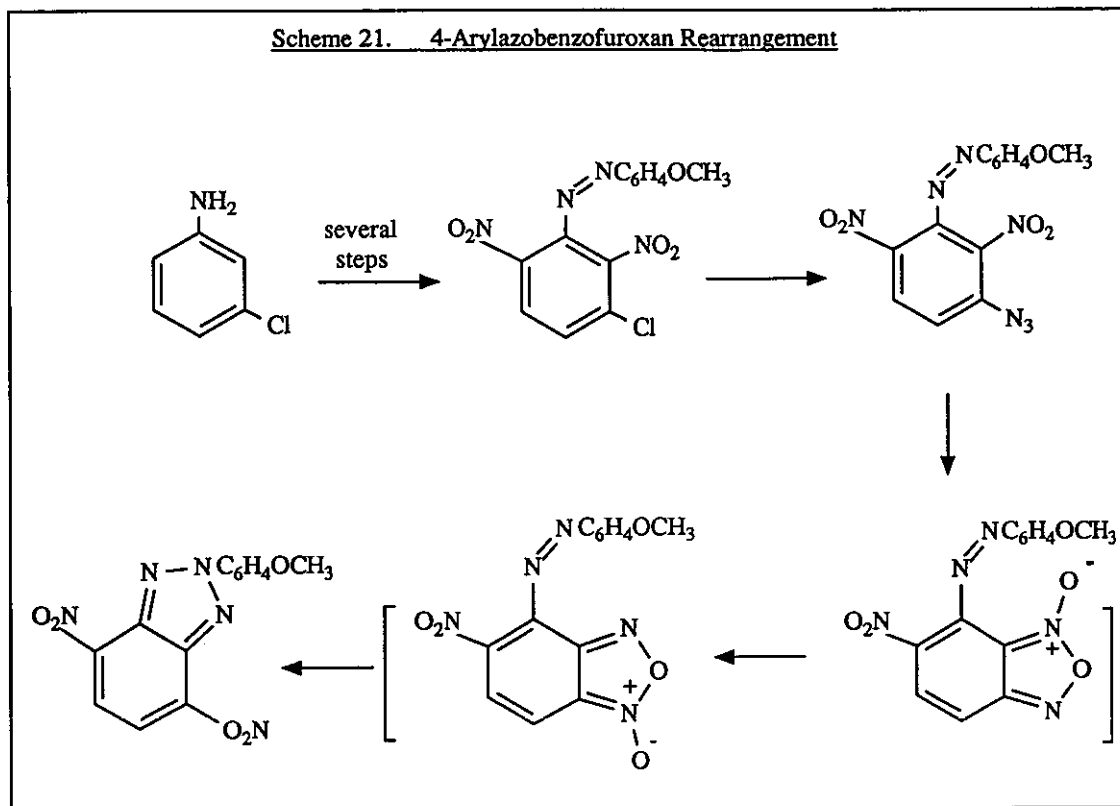
B, F = O, NR, S

D = N, CR For D = N, 21 combinations are possible

Scheme 20. Examples of Possible Bicyclic Rearrangements

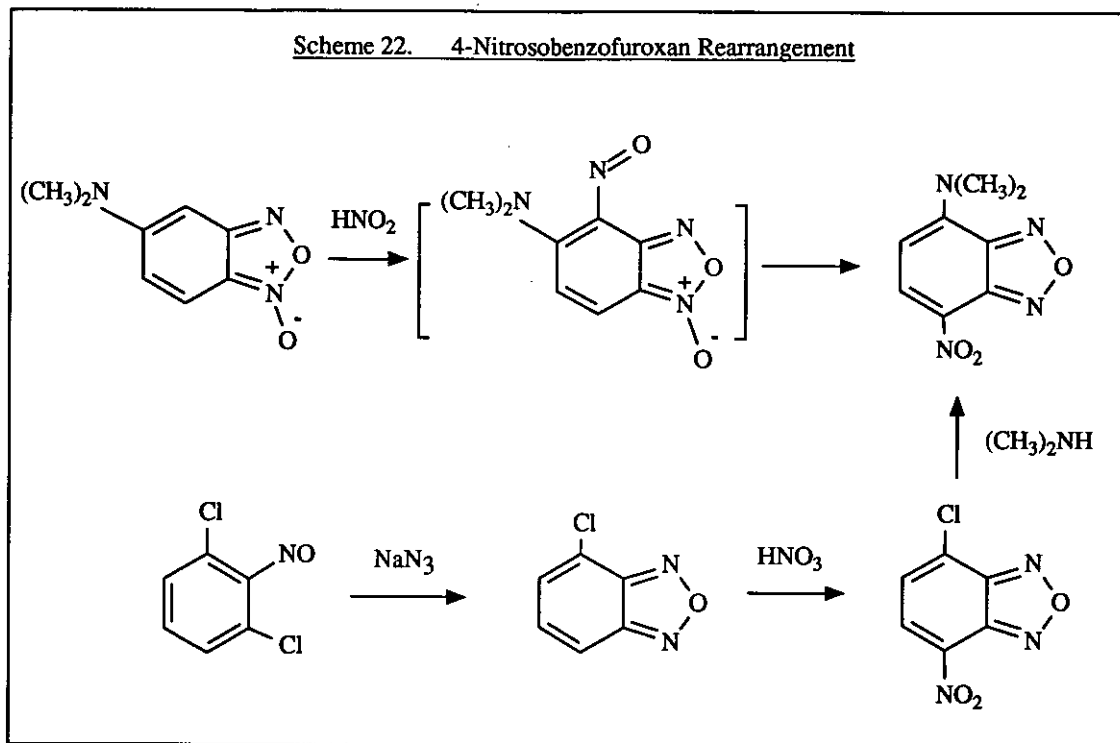


Scheme 21. 4-Arylazobenzofuroxan Rearrangement



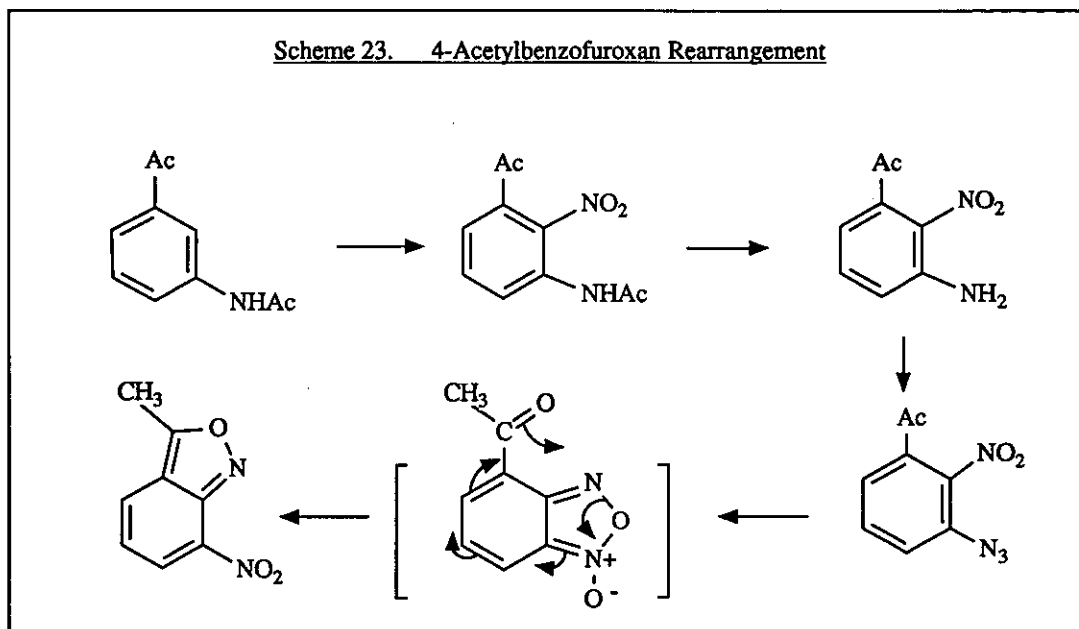
Subsequent work indeed confirmed that such rearrangements do take place, as demonstrated for the 4-arylazobenzofuroxan rearrangement to a nitrobenzotriazole in Scheme 21,<sup>67</sup> 4-nitrosobenzofuroxan rearranging to nitrobenzofurazan in Scheme 22,<sup>67</sup> 4-acylbenzofuroxan rearranging to a nitroanthranil in Scheme 23,<sup>68</sup> and a 4-iminoalkylbenzofuroxan rearranging to an indazole in Scheme 24.<sup>68</sup> The spontaneous rearrangement of 5-nitro-4-arylazobenzofuroxan into 4,7-dinitro-2-arylbenzotriazole shown on Scheme 21 involves the benzofuroxan isomerization of 6-nitro-7-arylazobenzofuroxan initially formed from the *o*-nitroaryl azide.<sup>67</sup>

The nitrosation of 5-dimethylaminobenzofuroxan is followed by spontaneous rearrangement of the intermediate 4-nitroso-derivative and leads directly to 7-nitro-4-dimethylaminobenzofurazan<sup>67</sup> (Scheme 22). The structure of this product was proved by independent synthesis from 1-nitroso-2,6-dichlorobenzene.



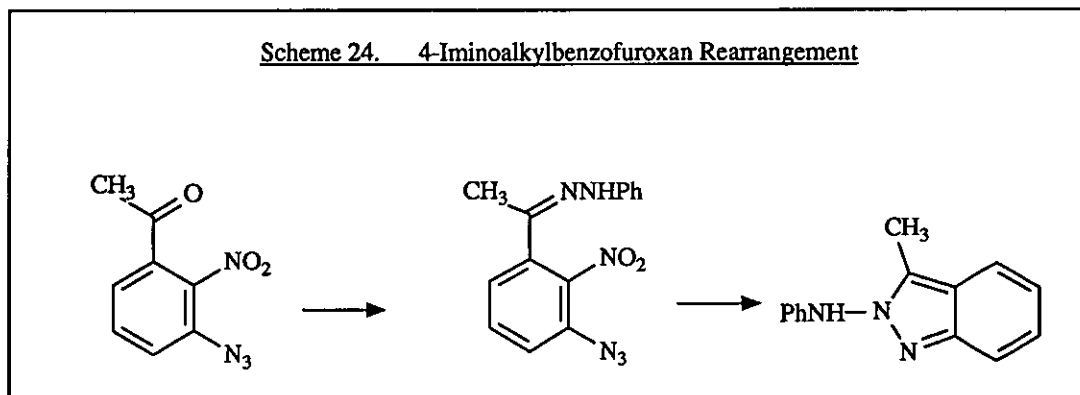
4-Acetyl- or 4-formylbenzofuroxans, prepared by nitrogen elimination from the corresponding 2-nitrophenyl azides, rearrange spontaneously to anthranils as exemplified in Scheme 23.<sup>68</sup> Attempted isolation of the intermediate benzofuroxan failed, indicating its rapid conversion under the reaction conditions.

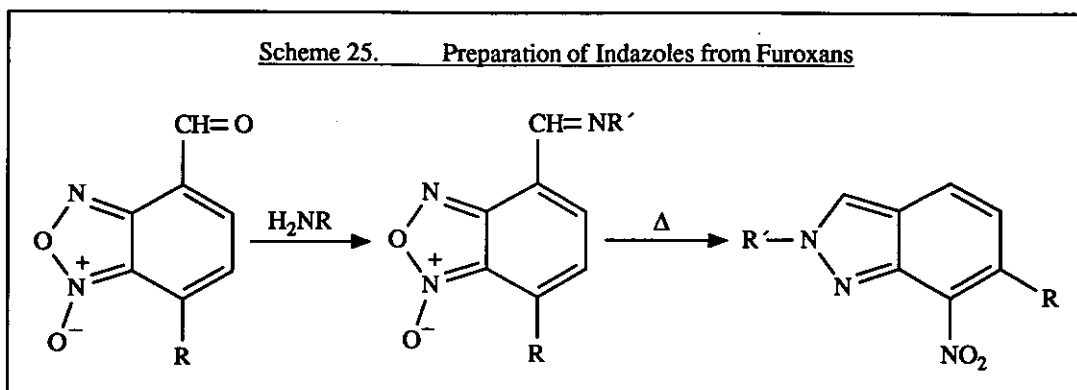
Scheme 23. 4-Acetylbenzofuroxan Rearrangement



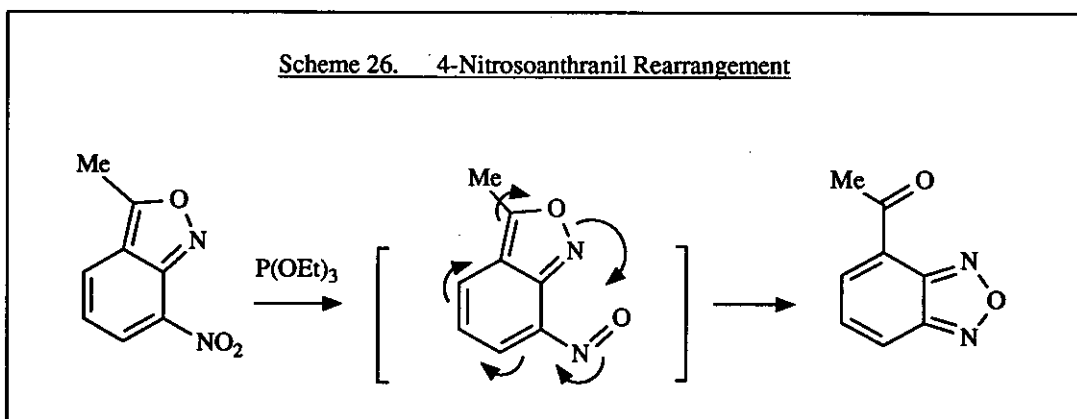
4-Iminoalkylbenzofuroxans (including hydrazone, oxime and anil derivatives) could also not be isolated on the thermolysis of their 2-nitroaryl azide precursors; instead they rearranged spontaneously into the corresponding indazoles as shown in Scheme 24.<sup>68</sup> Analogous transformations of 4(7)-iminoalkylbenzofuroxans generated *in situ* from the corresponding formylbenzofuroxans and primary amines,<sup>69</sup> hydroxylamines or hydrazones<sup>11</sup> have been applied to the synthesis of 2-substituted indazoles (Scheme 25).

Scheme 24. 4-Iminoalkylbenzofuroxan Rearrangement



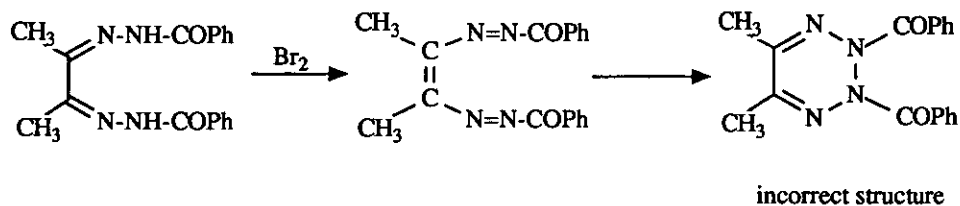


It is not only benzofuroxan rings which undergo such rearrangements. Scheme 26 shows how 4-nitrosoanthranil can rearrange to 4-acetylbenzofurazan.<sup>70,71</sup> This reaction provided early evidence for a nitroso-intermediate in the phosphite reduction of nitro-compounds.<sup>70</sup>

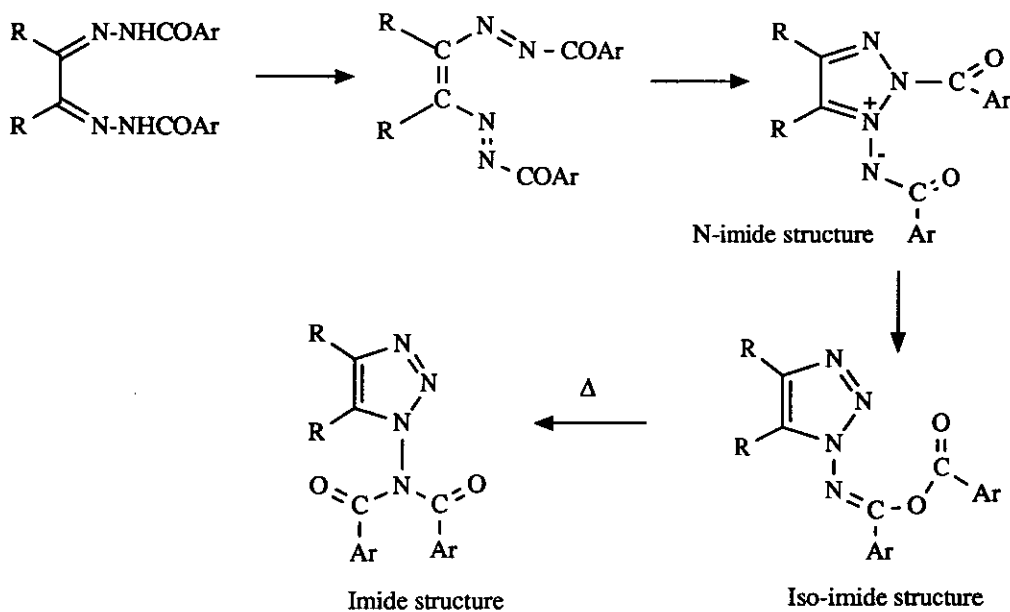


## 6. Ring Chain Tautomerism in Furoxans and Related Monoheterocycles

The oxidation of  $\alpha$ -dihydrazones was initially reported to yield dihydro-1,2,3,4-tetrazines as shown in Scheme 27.<sup>72,73</sup> However, the actual structure proved by X-ray crystallography is that of the iso-imide shown in Scheme 28. The iso-imide easily rearranges on heating to the imide structure.<sup>74</sup>

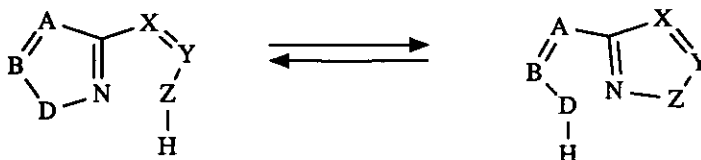
Scheme 27. The Oxidation of  $\alpha$ -Diketone Acylhydrazones

Scheme 28. Ring Chain Tautomerism of Triazoles



The existence of the above mentioned bicyclic rearrangements (Scheme 19) indicated that analogous monocyclic rearrangement should also be possible, and the general formulation that delineates these arrangements<sup>13</sup> is given in Scheme 29 (for a review see<sup>2</sup>).

## Scheme 29. Monocyclic Rearrangements - Scope



Starting Material

Product

ABD<sup>a</sup>

CCO	isoxazole
CCN	pyrrole
CNO	1,2,4-oxadiazole
NCO	1,3,4-oxadiazole
CNN	1,2,4-triazole
NCN	1,2,4-triazole
NNN	tetrazole

XYZ<sup>a</sup>

C-C=C	pyrrole <sup>b</sup>
C-C=N	pyrazole
C-N=C	imidazole <sup>b</sup>
NH-C=C	imidazole <sup>b</sup>
C-C=O	isoxazole
O-C=C	oxazole
C=N-N	1,2,3-triazole

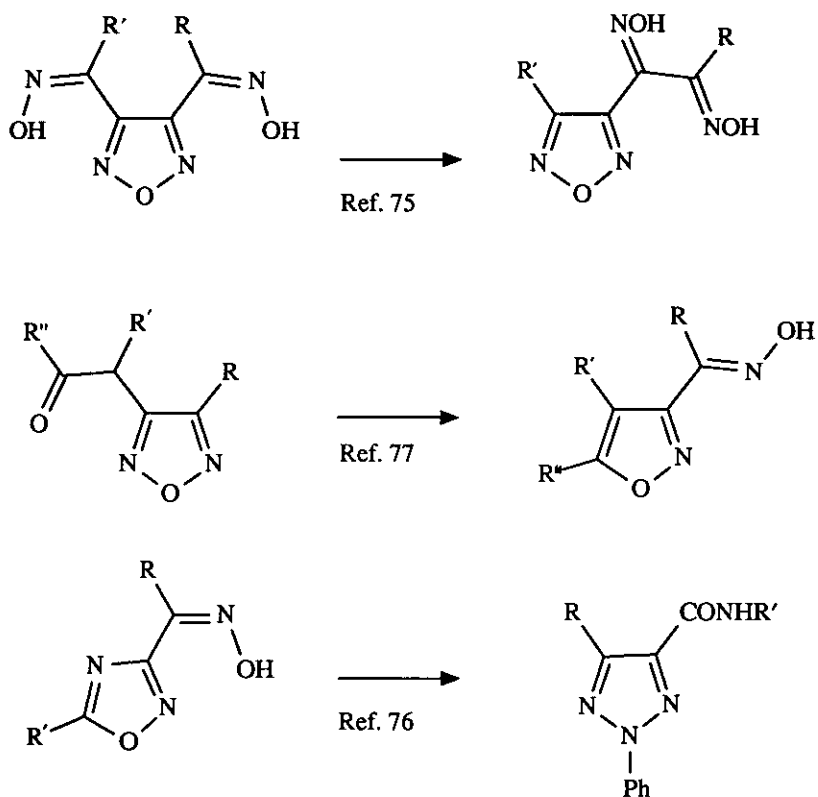
<sup>a</sup>H atoms are not shown.<sup>b</sup>Initial products undergo isomerization to a stable tautomer.

Three isolated examples of monocyclic ring transformations (or "mononuclear heterocyclic rearrangements"<sup>2</sup>) had been published prior to 1968 by various authors<sup>75-77</sup> (Scheme 30), but the generality of this rearrangement had not been recognized.

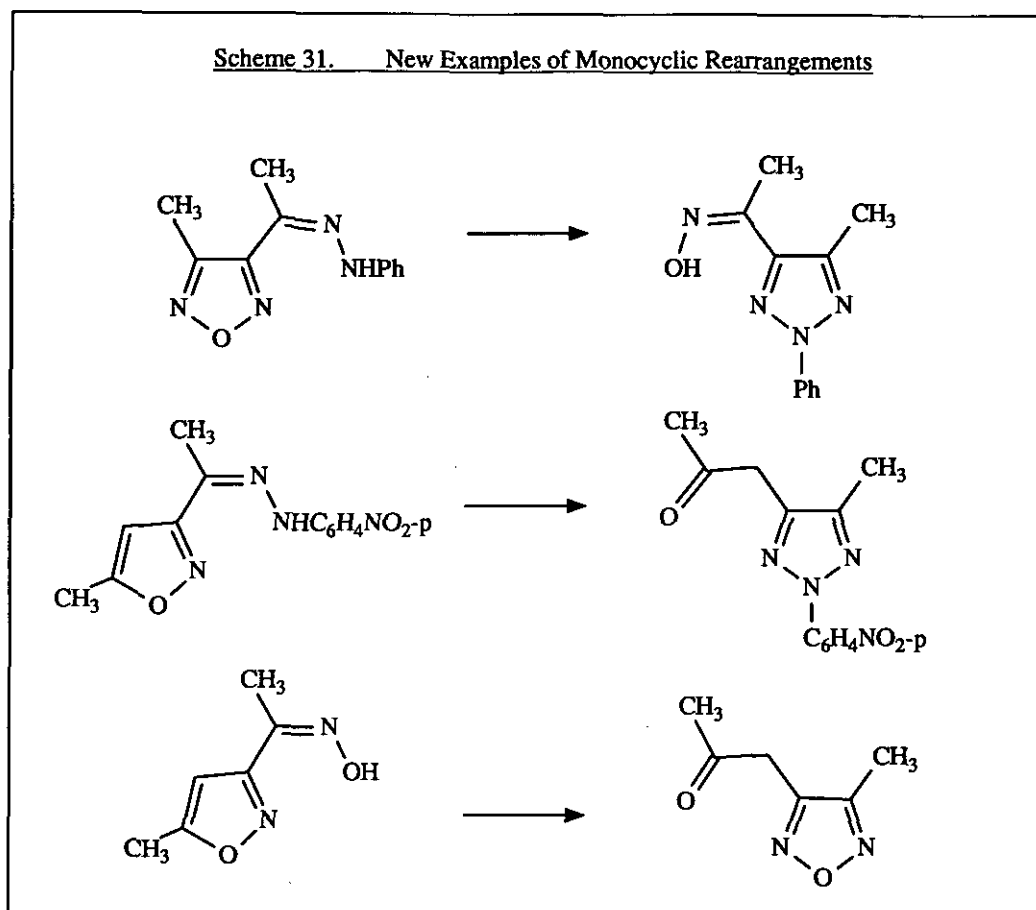
Moreover, the rearrangement of (furan-3-yl)ketones described by Cusmano and Giambrone<sup>77</sup> was reinvestigated in 1983, and their starting "ketones" proved to be in fact isoxazole oximes, which evidently were hydrolyzed under the reaction conditions.<sup>78</sup> Interestingly, the true ketones did not give any rearranged products and were recovered unchanged upon heating with ethanolic hydrochloric acid<sup>78</sup> (conditions of the ref. 77).



Scheme 30. Monocyclic Rearrangements: Early Examples



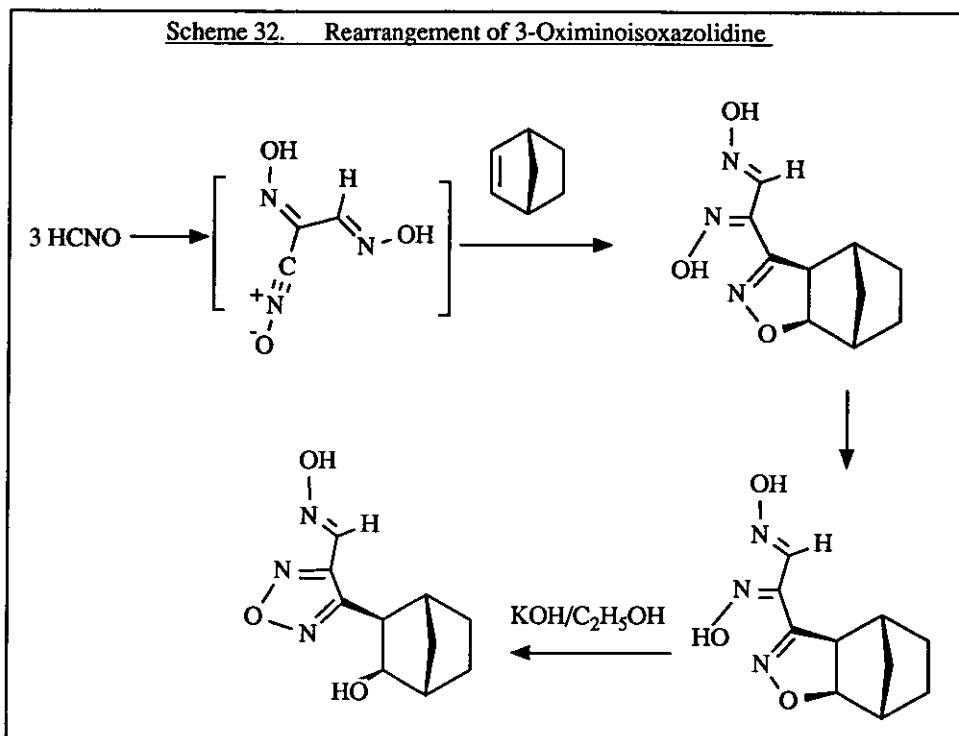
Some other typical examples of monocyclic rearrangements that were discovered after the generality of the reaction had been recognized<sup>13</sup> are shown in Scheme 31 (for a review see<sup>2</sup>).



The base-induced rearrangement of 3-acylisoxazole oximes to furazans depends strongly on the geometry of the oximes.<sup>78</sup> Not unexpectedly, compounds with the (*Z*)-configuration of the oxime chain rearrange readily, whereas a complete recovery of (*E*)-isomers was possible.

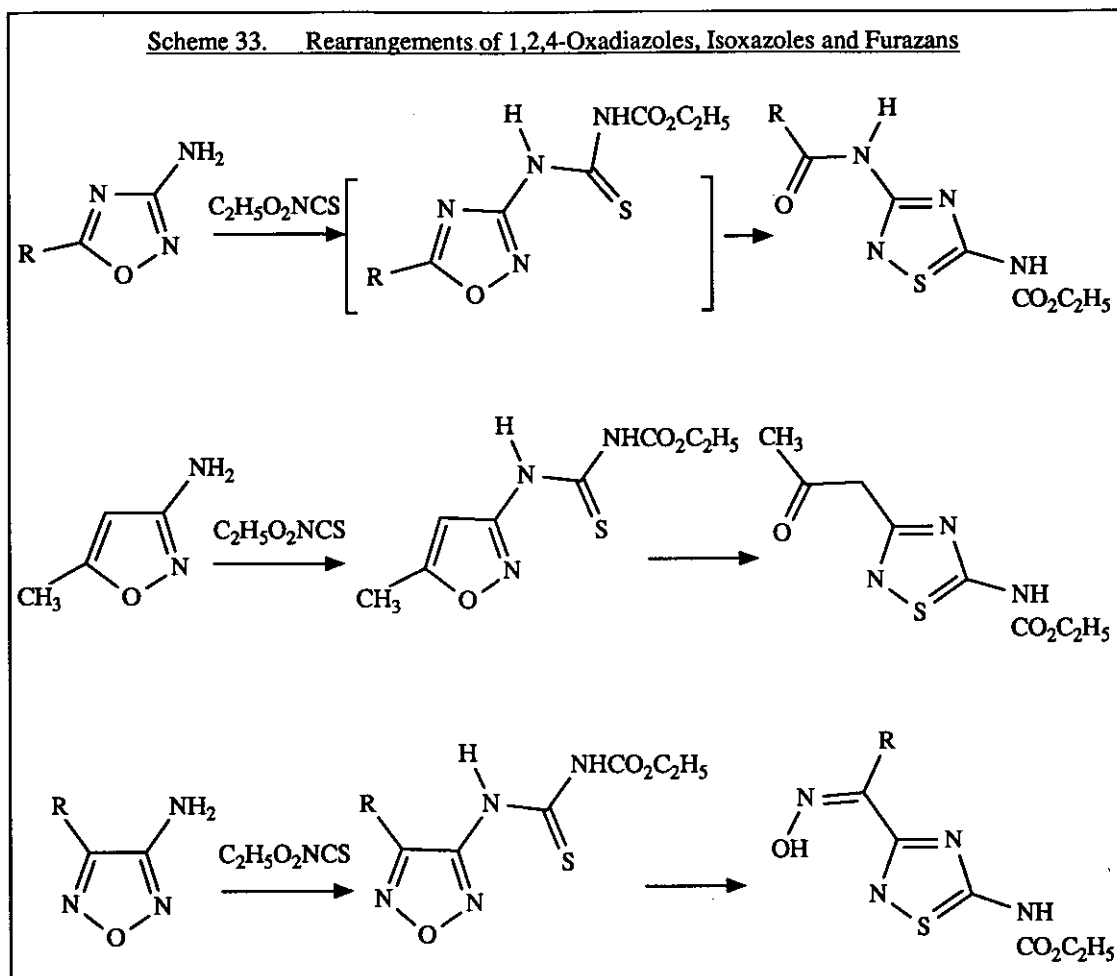
Studying reactions of fulminic acid derivatives, De Sarlo *et al.*<sup>79</sup> observed the base-induced transformation of the adduct of fulminic acid trimer and norbornene into the furazan oxime, as depicted in Scheme 32 (cf. with Scheme 29, ABD = CCO, XYZ = CNO).

This process is clearly similar to the rearrangements of 3-acylisoxazole oximes discussed above (cf. with Scheme 31), and suggests a further extension of the original Scheme 29 to analogous transformations of azoline derivatives in which an A=B bond is replaced by a saturated fragment.



The reaction of 3-amino-6-phenyl-1,2,4-oxadiazole with ethoxycarbonyl isothiocyanate initially was reported to afford the corresponding thiourea.<sup>80</sup> However, Vivona *et al.* recently reinvestigated this transformation and found that under a variety of conditions it led to 1,2,4-thiadiazole derivatives as a result of a spontaneous rearrangement of initially formed thioureas, which could not be isolated<sup>81</sup> (Scheme 33; cf. with Scheme 29, ABD = NCO, XYZ = NCS).

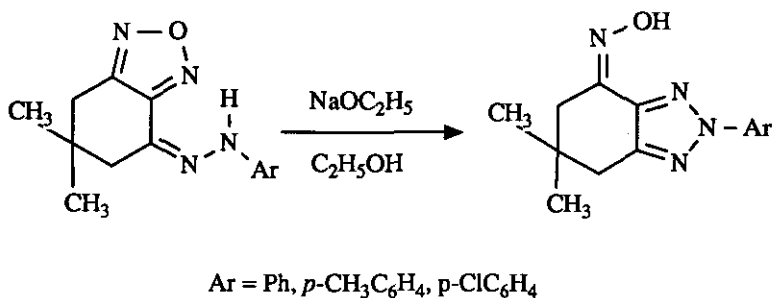
By contrast, analogous reactions of 3-amino-5-methylisoxazole and of 3-aminofurazan enabled an isolation of intermediate thioureas, further rearranged into 1,2,4-thiadiazoles (Scheme 33; cf. with Scheme 29, XYZ = NCS, ABD = CCO and ABD = CNO, respectively). The latter two transformations are facilitated by bases, deprotonation evidently enhances the nucleophilic character of the sulfur atom.<sup>81</sup>



Fused 3-acylfurazan (*Z*)-arylhyazones were rearranged under thermal basic conditions to the corresponding benzo[*d*][1,2,3]triazol-4-one oximes<sup>82</sup> (Scheme 34).

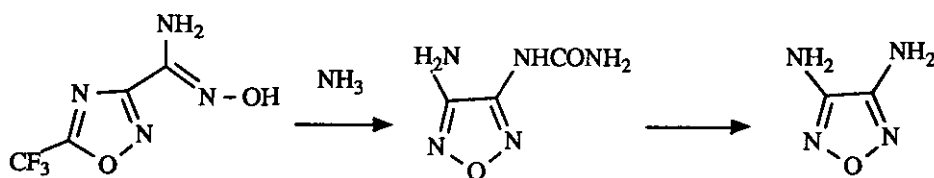
Attempts to achieve analogous photochemical transformations (photochemically allowed by the *supra-supra* process, assuming that the uncatalyzed rearrangement is a pericyclic reaction) were not successful,<sup>82</sup> nor were attempted thermal or photochemical monocyclic heterocyclic rearrangements of 2-aryl-4,5,6,7-tetrahydro-6,6-dimethyl-2H-benzo[*d*][1,2,3]triazol-4-one (*Z*)-arylhyazones.<sup>83</sup>

**Scheme 34.** Rearrangement of Fused 3-Acylisoxazole (Z)-Arylhydrazones to Benzo[d][1,2,3]triazol-4-one Oximes

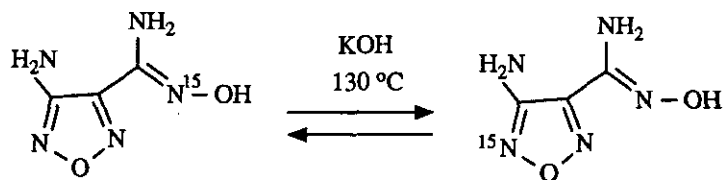


Recently, the rearrangement of 1,2,4-oxadiazoles 3-carboxamidoximes to 3-acylamino-furazans (cf. with Scheme 31, ref. 2) was extended by a similar synthesis of diaminofurazan from 5-trifluoromethyl-1,2,4-oxadiazole 3-carboxamidoxime<sup>84</sup> (Scheme 35).

**Scheme 35.** New Examples of 1,2,4-Oxadiazole and Furazan Carboxamidoximes Rearrangement



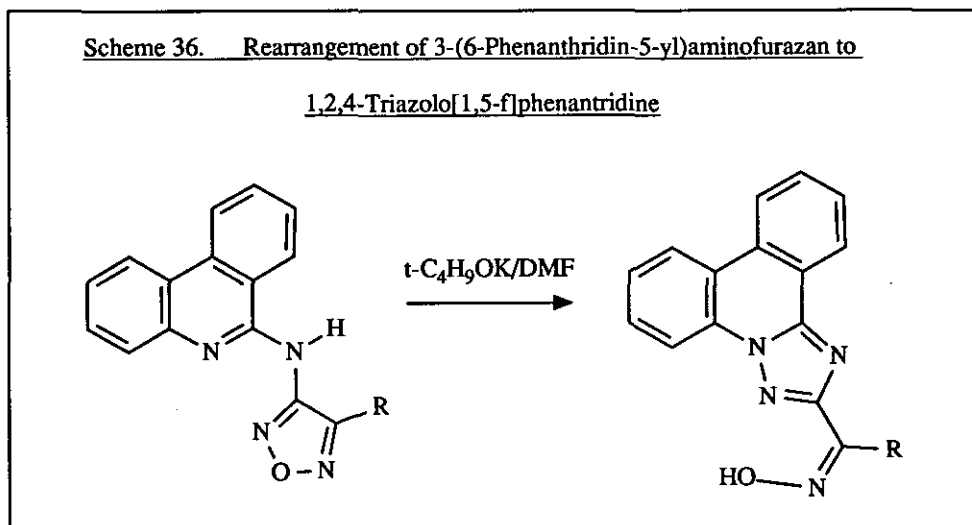
Ref. 84



Ref. 85

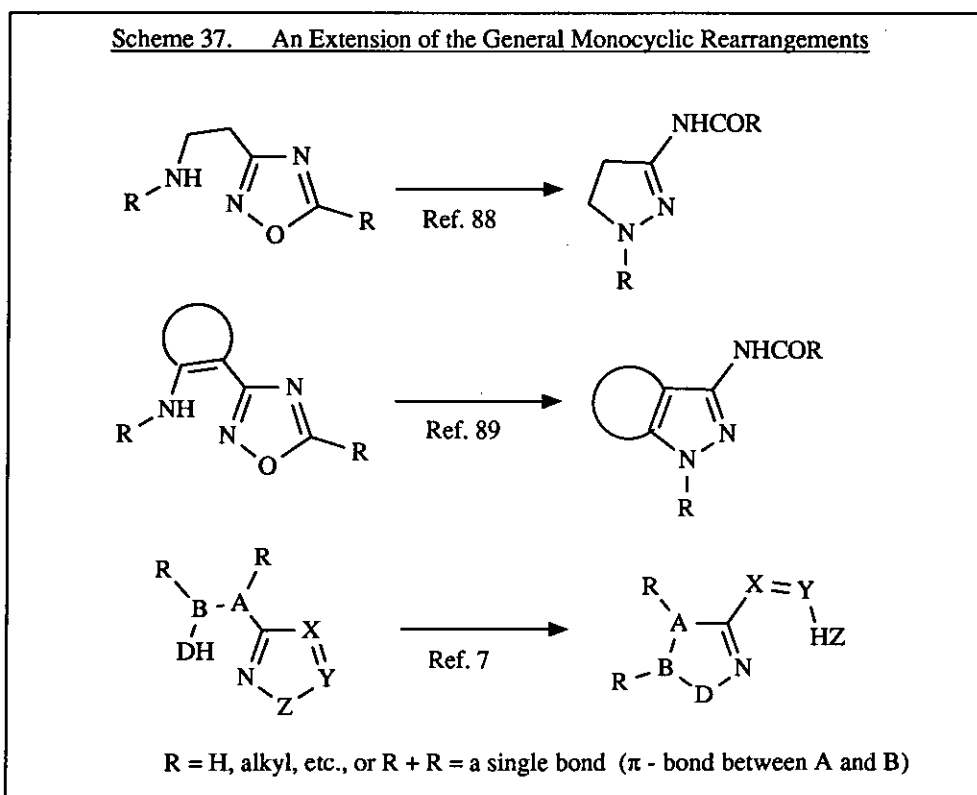
The degenerative rearrangement of  $^{15}\text{N}$ -labelled 3-aminofurazan 4-carboxamidoxime required more rigorous conditions and was studied by mass spectrometric analysis.<sup>85</sup> An analogous transformation of pentamethyleneamidoximes of 4-aminofurazan-3-carboxylic acid also has been investigated.<sup>86</sup>

Recently, Cusmano *et al.*<sup>87</sup> reported a base-catalyzed rearrangement of 3-(6-phenanthridin-5-yl)aminofurazan into 1,2,4-triazolo[1,5-f]phenanthridine (Scheme 36). This rearrangement is closely related to previously reported transformations of arylformamidinoazoles to 1,2,4-triazole derivatives.<sup>2</sup> In this case, the nucleophilic imine nitrogen of the formamidino side chain is incorporated into the heterocyclic ring. The reaction is probably the first application of the monocyclic heterocyclic rearrangement to the synthesis of a bridged nitrogen system (cf. with Scheme 29, ABD = CNO, XYZ = NCN).



The mechanisms proposed for monocyclic rearrangements have been reviewed by Ruccia *et al.*<sup>2</sup> Similarity and difference between mechanisms of transformations of Schemes 19 and 29 (referred to as "rearrangements of the first and second type", respectively) have also been analyzed by Horvatz *et al.*<sup>7</sup> In the first case (Scheme 19), the ring transformation proceeds with concomitant alteration of the electronic structure of the fused benzene ring and the side chain, and regrouping of the quinonoid  $\pi$ -electronic system is an important feature of these reactions. By contrast, no shift of the double bond is necessary in the second type of the rearrangement (Scheme 29), formally the  $\pi$ -electronic system remains unaltered, and a proton migration (or transfer of a negative charge) is involved in the process.<sup>7</sup>

An extension of the rearrangement of the second type has been suggested,<sup>7</sup> based on the transformations of 3-(2-aminoethyl)-1,2,4-oxadiazoles<sup>88</sup> and 3-(2-aminoaryl)-1,2,4-oxadiazoles<sup>89</sup> to 3-acylamino-2-pyrazolines or fused 3-acylaminopyrazoles, respectively (Scheme 37).



## REFERENCES

1. H.C.Van der Plas, 'Ring Transformations of Heterocycles,' Vol. 1,2, Academic Press, Inc., London, 1973.
2. M.Ruccia, N.Vivona, and D.Spinelli, 'Advances in Heterocyclic Chemistry', Vol. 29, ed. by A.R.Katritzky, Academic Press, Inc., London, 1981, p. 141.
3. G.L'abbé, *J. Heterocycl. Chem.*, 1984, **21**, 627.
4. 'Comprehensive Heterocyclic Chemistry', Vol. 1-8, ed. by A.R.Katritzky and C.W.Rees, Pergamon Press, Oxford, 1984.
5. O.Dimroth, *Ann. Chem.*, 1909, **364**, 183.
6. A.N.Kost, S.P.Gromov, and R.S.Sagitullin, *Tetrahedron*, 1981, **37**, 3423.
7. K.Horvath, D.Korbonits, G.Naray-Szabó, and K.Simon, *J. Mol. Str. (Theochem.)*, 1986, **136**, 215.
8. A.J.Boulton and P.B.Ghosh, 'Advances in Heterocyclic Chemistry,' Vol. 10, ed. by A.R.Katritzky, Academic Press, Inc., London, 1969, p. 1.
9. H.Balli and S.Gunzenhauser, *Helv. Chim. Acta*, 1978, **61**, 2628.
10. R.Huisgen, *Angew. Chem., Int. Edit. Eng.*, 1980, **19**, 947.
11. A.J.Boulton, T.Kan-Woon, S.N.Balasubrahmanyam, I.M.Mallick, and A.S.Radhakrishna, *J. Org. Chem.*, 1980, **45**, 1653.
12. A.Gasco and A.J.Boulton, 'Advances in Heterocyclic Chemistry', Vol. 29, ed. by A.R.Katritzky, Academic Press, Inc., London, 1981, p. 251.
13. A.J.Boulton, A.R.Katritzky, and A.Majid-Hamid, *J. Chem. Soc.(C)*, 1967, 2005.
14. A.J.Boulton, P.B.Ghosh, and A.R.Katritzky, *Angew. Chem., Int. Ed. Eng.*, 1964, 693.
15. R.M.Paton, 'Comprehensive Heterocyclic Chemistry', Vol. 6, ed. by A.R.Katritzky and C.W.Rees, Pergamon Press, Oxford, 1984, p. 393.
16. Noelting and Kohn, *Chem. Ztg.*, 1894, **18**, 1095 ('Beilstein Handbuch Der Organischen Chemie', 1925, Bd. 7, S. 601).
17. M.O.Forster and H.E.Fierz, *J. Chem. Soc.*, 1907, **91**, 1942.
18. A.G.Green and F.M.Rowe, *J. Chem. Soc.*, 1912, **101**, 2452.



19. A.G.Green and F.M.Rowe, *J. Chem. Soc.*, 1913, **103**, 897.
20. A.G.Green and F.M.Rowe, *J. Chem. Soc.*, 1913, **103**, 2023.
21. J.H.Boyer, R.F.Reinisch, M.J.Danzig, G.A.Stoner, and F.Sahhar, *J. Am. Chem. Soc.*, 1955, **77**, 5688.
22. J.H.Boyer, 'Heterocyclic Compounds', Vol. 7, ed. by R.C.Elderfield, John Wiley and Sons, New York, 1961, p. 462.
23. D.L.Hammick, W.A.M.Edwardes, and E.R.Steiner, *J. Chem. Soc.*, 1931, 3308.
24. A.R.Katritzky, S.Øksne, and R.K.Harris, *Chem. Ind.*, 1961, **41**, 990.
25. G.Englert, *Z. Anal. Chem.*, 1961, **181**, 447.
26. G.Englert, *Z. Elektrochem.*, 1961, **65**, 854 (*Chem. Abstr.*, 1962, **57**, 6771c).
27. R.K.Harris, A.R.Katritzky, S.Øksne, A.S.Bailey, and W.G.Paterson, *J. Chem. Soc.*, 1963, 197.
28. F.A.L.Anet and I.Yavari, *Org. Magn. Reson.*, 1976, **8**, 158.
29. I.Yavari, R.E.Botto, and J.D.Roberts, *J. Org. Chem.*, 1978, **43**, 2542.
30. M.Witanowski, L.Stefaniak, A.Grabowska, and G.A.Webb, *Spectr. Acta*, 1978, **34A**, 877.
31. P.Diehl, H.A.Christ, and F.B.Mallory, *Helv. Chim. Acta*, 1962, **45**, 504.
32. A.B.Bulacinsky, E.F.V.Scriven, and H.Suschitzky, *Tetrahedron Lett.*, 1975, 3577.
33. N.G.Argyropoulos, J.K.Gallos, and D.N.Nicolaides, *Tetrahedron*, 1986, **42**, 3631.
34. I.R.Dunkin, M.A.Lynch, A.J.Boulton, and N.Henderson, *J. Chem. Soc., Chem. Commun.*, 1991, 1178.
35. A.J.Boulton, A.R.Katritzky, M.J.Sewell, and B.Wallis, *J. Chem. Soc. (B)*, 1967, 914.
36. D.Britton and W.E.Noland, *Chem. Ind.*, 1962, **42**, 563.
37. D.Britton and W.E.Noland, *J. Org. Chem.*, 1962, **27**, 3218.
38. F.B.Mallory, S.L.Manatt, and C.S.Wood, *J. Am. Chem. Soc.*, 1965, **87**, 5433.
39. Sh.Uematsu and Y.Akahori, *Chem. Pharm. Bull.*, 1978, **26**, 25 (*Chem. Abstr.*, 1978, **88**, 151781y).
40. W.P.Norris, A.Chafin, R.J.Spear, and R.W.Read, *Heterocycles*, 1984, **22**, 271.
41. E.Buncel, N.Chuaqui-Offermanns, and A.R.Norris, *Can. J. Chem.*, 1979, **57**, 2512.
42. J.G.Belton, *Proc. R. Ir. Acad., Sect.B*, 1974, **74**, 185 (*Chem. Abstr.*, 1974, **81**, 152118e).

43. S.Ostrowski and K.Wojciechowski, *Can. J. Chem.*, 1990, **68**, 2239.
44. E.Gruendemann, H.J.Niclas, and B.Goehrmann, *J. Prakt. Chem.*, 1990, **332**, 931 (*Chem. Abstr.*, 1991, **115**, 114429v).
45. I.M.Takakis and P.M.Hadjimihalakis, *J. Heterocycl. Chem.*, 1991, **28**, 1373.
46. I.M.Takakis, P.M.Hadjimihalakis, and G.G.Tsantali, *Tetrahedron*, 1991, **47**, 7157.
47. I.M.Takakis and P.M.Hadjimihalakis, *J. Heterocycl. Chem.*, 1992, **29**, 121.
48. I.M.Takakis, P.M.Hadjimihalakis, G.G.Tsantali, and H.Pilini, *J. Heterocycl. Chem.*, 1992, **29**, 123.
49. Altaf-ur-Rahman, A.J.Boulton, D.P.Clifford, and G.J.T.Tiddy, *J. Chem. Soc. (B)*, 1968, 1516.
50. A.J.Boulton, A.C.G. Gray, and A.R.Katritzky, *J. Chem. Soc.*, 1965, 5958.
51. G.Calzaferrri, R.Gleiter, K.-H.Knauer, H.-D.Martin, and E.Schmidt, *Angew. Chem., Int. Edit. Eng.*, 1974, **13**, 86.
52. R.Calvino, R.Fruttero, A.Gasco, and V.Mortarini, *J. Heterocycl. Chem.*, 1982, **19**, 427.
53. N.N.Makhova, I.V.Ovchinnikov, B.N.Khasanov, and L.I.Khmel'nitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1982, 646.
54. R.Calvino, A.Gasco, E.Menziani, and A.Serafino, *J. Heterocycl. Chem.*, 1983, **20**, 783.
55. R.Calvino, B.Ferrarotti, A.Serafino, and A.Gasco, *Heterocycles*, 1985, **23**, 1955.
56. R.Fruttero, B.Ferrarotti, A.Serafino, A.Di Stilo, and A.Gasco, *J. Heterocycl. Chem.*, 1989, **26**, 1345.
57. V.A.Petrosyan, M.E.Niyazymbetov, and E.V.Kozlovskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1986, 1691.
58. V.G.Andrianov, M.A.Shokhen, A.V.Eremeev, and S.V.Barmina, *Khim. Geterotsikl. Soedin.*, 1986, 264.
59. A.V.Belik and P.V.Belousov, *Dokl. Akad. Nauk SSSR*, 1990, **313**, 1127.
60. A.J.Boulton, P.J.Halls, and A.R.Katritzky, *J. Chem. Soc. (B)*, 1970, 636.
61. A.J.Boulton, A.C.G. Gray, and A.R.Katritzky, *J. Chem. Soc. (B)*, 1967, 911.
62. D.Y.Curtin, R.J.Crawford, and D.K.Wedegaertner, *J. Org. Chem.*, 1962, **27**, 4300.
63. H.Bauer, G.R.Bedford, and A.R.Katritzky, *J. Chem. Soc.*, 1964, **148**, 751.
64. A.J.Boulton and A.R.Katritzky, *Rev. Roum. Chim.*, 1962, 691.

65. A.J.Boulton and A.R.Katritzky, *Proc. Chem. Soc.*, 1962, 257.
66. P.Drost, *Ann. Chem.*, 1900, **313**, 299.
67. A.J.Boulton, P.B.Ghosh, and A.R.Katritzky, *J. Chem. Soc. (B)*, 1966, 1004.
68. A.J.Boulton, P.B.Ghosh, and A.R.Katritzky, *J. Chem. Soc. (B)*, 1966, 1011.
69. S.N.Balasubrahmanyam, A.S.Radhakrishna, A.J.Boulton, and Thoe Kan-Woon, *J. Org. Chem.*, 1977, **42**, 897.
70. A.J.Boulton, I.J.Fletcher, and A.R.Katritzky, *J. Chem. Soc., Chem. Commun.*, 1968, 62.
71. A.J.Boulton, I.J.Fletcher, and A.R.Katritzky, *J. Chem. Soc. (C)*, 1971, 1193.
72. H.v.Pechmann and W.Bauer, *Ber.*, 1900, **33**, 644.
73. H.v.Pechmann and W.Bauer, *Ber.*, 1909, **42**, 659.
74. H.Bauer, A.J.Boulton, W.Fedeli, A.R.Katritzky, A.Majid-Hamid, F.Mazza, and A.Vaciago, *Angew. Chem., Int. Ed. Eng.*, 1971, **10**, 129.
75. G.Ponzio and F.Biglietti, *Gazz. Chim. Ital.*, 1933, **63**, 159 (*Chem. Abstr.*, 1933, **27**, 3708).
76. P.Gramantieri, *Gazz. Chim. Ital.*, 1935, **65**, 102 (*Chem. Abstr.*, 1935, **29**, 4739<sup>2</sup>).
77. S.Cusmano and S.Giambrone, *Gazz. Chim. Ital.*, 1951, **81**, 499 (*Chem. Abstr.*, 1952, **46**, 5584h).
78. N.Vivona, G.Macaluso, and V.Frenna, *J. Chem. Soc., Perkin Trans. I*, 1983, 483.
79. F.De Sarlo, A.Guarna, A.Brandi, and A.Goti, *Tetrahedron*, 1985, **41**, 5181.
80. G.Westphal and R.Schmidt, *Z. Chem.*, 1974, **14**, 94.
81. G.Macaluso, G.Cusmano, S.Buscemi, V.Frenna, N.Vivona, and M.Ruccia, *Heterocycles*, 1986, **24**, 3433.
82. S.Lefkopoulou, J.Stephanidou-Stephanatou, C.Tsoleridis, and N.E.Alexandrou, *Helv. Chim. Acta*, 1985, **68**, 1748.
83. S.Lefkopoulou, J.Stephanidou-Stephanatou, and N.E.Alexandrou, *J. Chem. Res. (S)*, 1985, **5**, 82.
84. V.G.Andrianov, A.V.Eremeev, and Yu.B.Sheremet, *Khim. Geterotsikl. Soedin.*, 1988, 856.
85. V.G.Andrianov, V.G.Semenikhina, A.V.Eremeev, and A.P.Gaukhman, *Khim. Geterotsikl. Soedin.*, 1988, 1701.
86. V.G.Andrianov, V.G.Semenikhina, and A.V.Eremeev, *Khim. Geterotsikl. Soedin.*, 1991, 122.

87. G.Cusmano, G.Macaluso, M.Gruttadauria, and S.Buscemi, *Heterocycles*, 1990, **31**, 869.
88. D.Korbonits, E.M.-Bakó, and K.Horváth, *J. Chem. Res.*, 1979, 64.
89. D.Korbonits, I.Kanzel-Szvoboda, and K.Horváth, *J. Chem. Soc., Perkin Trans. 1*, 1982, 759.

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