Pergamon

Tetrahedron Vol. 51, No. 26, pp. 7277-7286, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00351-7

The Vicarious Nucleophilic Substitution of Hydrogen and Related Reactions in Nitrobenzoxazoles.

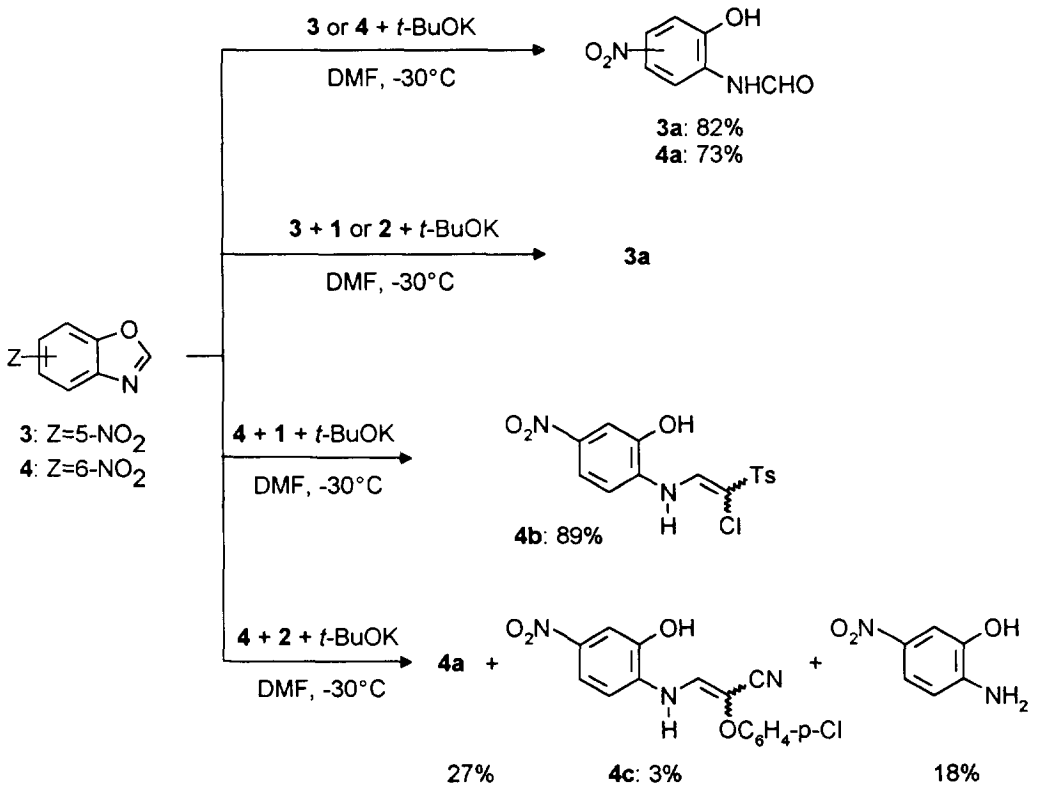
Mieczysław Mąkosza* and Jacek Stalewski

Institute of Organic Chemistry, Polish Academy of Sciences, ul. Kasprzaka 44, 01-224 Warsaw, Poland

Abstract: 5- and 6-nitrobenzoxazoles **3** and **4** react with nucleophiles exclusively at C-2, giving ring opening products. If position 2- is blocked with phenyl substituent the reaction takes place in the carbocyclic ring affording the VNS products. 2-Methylthio-5-nitrobenzoxazole **7** and its 6-nitro isomer **8** give products which result from addition of a nucleophile to the carbocyclic ring (VNS) as well as to the heterocyclic ring (S_NAr and ring cleavage). 2-Methylthiobenzoxazoles can be readily converted to the corresponding benzoxazolones via oxidative hydrolysis.

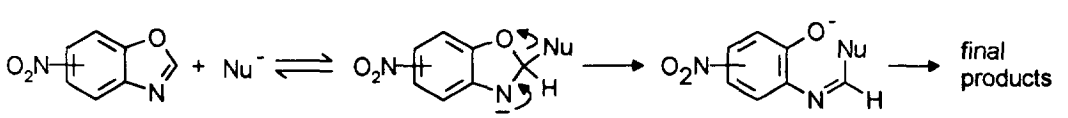
Vicarious Nucleophilic Substitution of Hydrogen (VNS) is a convenient and general way of introduction of α-functionalized substituents to electrophilic arenes.[1] The reaction proceeds *via* addition of carbanions bearing leaving group to the arenes, followed by base-induced β-elimination of HX from the formed σ^H-adducts, producing anions of the substitution products. This reaction proceeds efficiently with numerous aromatic nitro compounds, amongst them nitro derivatives of heterocycles such as furan, pyrrole, thiophene, imidazole, pyridine, quinoline and indole.[2] Also some electrophilic heterocycles without nitro group enter the VNS reaction.[3] In our work, directed towards synthesis of tetrahydropyrroloquinoline alkaloids *via* this reaction, we have expected that nitrobenzoxazole derivatives should be useful intermediates.[4] Therefore we have decided to examine their behaviour in the VNS reaction somewhat closer. It has already been shown that benzoxazole itself enters the VNS reaction with chloromethane sulfomorpholide carbanion, in this case 2-hydrogen is replaced with the carbanion moiety.[5] Thus one of the main questions in our study of the VNS reaction in 5- and 6-nitrobenzoxazoles was the site of the nucleophilic addition: C-2 or the carbocyclic ring activated by the nitro group. Standard nucleophiles for the VNS reaction, such as carbanions of chloromethyl-*p*-tolyl sulfone **1** and *p*-chlorophenoxyacetonitrile **2**, were used in these studies.

In the reactions of these C-H acids with 5- and 6-nitrobenzoxazoles **3** and **4** carried out in the presence of *t*-BuOK in DMF we have not observed formation of the VNS products, always opening of the heterocyclic ring *via* addition of the base or the carbanions took place (scheme 1).



Scheme 1

Treatment of **3** and **4** with *t*-BuOK itself resulted in the formation of 2-hydroxy-5-nitro- and 2-hydroxy-4-nitro-formanilides **3a** and **4a** respectively. In the attempted reactions of **3** with **1** or **2** in the presence of *t*-BuOK formanilide **3a** was still the only isolable product. On the other hand, under the same conditions the reaction of **4** with these C-H acids gave products which were formed *via* addition of the carbanion to the oxazole ring. Thus in the case of **1** enaminophenol **4b** was the only product, whereas **2**, besides small amount of analogous enaminophenol **4c**, gave **4a** and 2-amino-5-nitrophenol resulting apparently from hydrolysis of **4c**, accompanied by some tarry products. These results can be rationalized as follows (scheme 2):



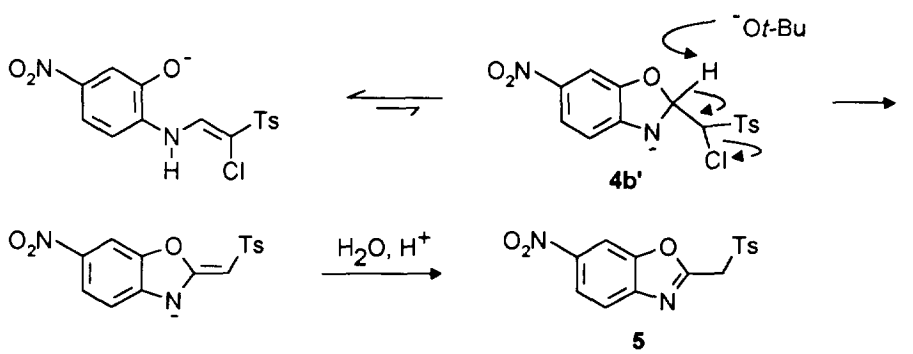
Scheme 2

In the first step a nucleophile (carbanion or *t*-butoxide anion) adds to C-2 of the nitrobenzoxazole. Then the ring opening in the intermediate adduct occurs furnishing phenolate anions, which are converted to the final products when treated with aqueous acid. Somewhat different reaction course of **3** compared to **4** can be explained in terms of HSAB

concept: **4**, being able to delocalize more efficiently the negative charge on the nitrogen atom *via* conjugation with *para* nitro group, is a relatively soft acid and therefore reaction with soft carbanions is preferred to that with hard *t*-butoxide anions. Alternatively one can suppose that the adducts of *t*-butoxide anions are formed faster than those of carbanions. Such an adduct derived from **3**, unstable itself, would undergo rapid ring opening to form the stable conjugated *p*-nitrophenolate, whereas the analogous adduct of **4** would undergo ring-opening much slower as it is better stabilized due to the negative charge delocalization, and formation of *m*-nitrophenolate would not be as favourable as formation of the *para* isomer. In this situation equilibration takes place to produce the thermodynamically favoured adducts of carbanions and finally **4b** and **4c**.

The standard analytical and spectral data were not sufficient to determine structure of compound **4b** and needed to be supported by some additional information. Thus **4b** behaves as a typical phenol - it is soluble in aqueoues alkali and can be methylated by diazomethane to give the corresponding anisole **4d**. The DEPT-135 ^{13}C NMR spectrum reveals the presence of six signals corresponding to eight methine carbon atoms (four methine carbon atoms of tosyl group give two signals), which points out the enamine structure rather than that of the tautomeric imine (the latter contains nine methine carbon atoms). Also broadening of the signal at 8.24 ppm in the ^1H NMR spectrum indicates that it is due to the hydrogen atom attached to nitrogen (enamine) rather than carbon (imine).

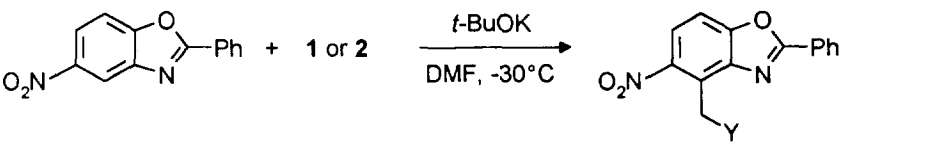
Treatment of **4b** with 2*M* *t*-BuOK at room temperature resulted in elimination of HCl and subsequently in formation of 6-nitro-2-(tolylsulfonylmethyl)-benzoxazole **5**, the expected product of the VNS reaction at position 2 of **4**. Probably, in basic media **4b** equilibrates with **4b'** via the intramolecular Michael reaction. **4b'** undergoes β-elimination to give **5**, the latter process being facilitated by high concentration of base, as shown in Scheme 3.



Scheme 3

Thus addition of nucleophilic agents to 2-unsubstituted nitrobenzoxazoles takes place exclusively at position 2 of the heterocyclic ring. One could expect that blocking this position against nucleophilic attack with some inert substituent, such as phenyl group, would promote the VNS reaction in the carbocyclic ring. Indeed, 2-phenyl-5-nitrobenzoxazole **6** reacts with **1** and **2** giving the expected products of the VNS of hydrogen in position 4-, **6a** and **6b** respectively. Such orientation of the reaction is in full agreement with that observed earlier in bicyclic nitroarenes such as 2-

nitronaphthalene, 6-nitroquinoline or 5-nitroindole,[6] i.e. substitution of hydrogen takes place at the carbon atom adjacent to the ring junction.



6a: Y=*p*-$SO_2C_6H_4CH_3$; 77%

6b: Y=CN; 82%

Scheme 4

Thus it was necessary to protect position -2 with a substituent so that the VNS reaction could occur in the carbocyclic ring. Although the phenyl substituent was efficient in preventing nucleophilic addition to position -2, it was not fully satisfactory due to expected difficulties in its removal. The more labile methylthio group seemed to be more promising in this respect yet it was not clear whether it would provide sufficient protection against nucleophilic attack at C-2. Thus 5- and 6-nitrobenzoxazole derivatives **7** and **8**, containing methylthio substituent in position -2 were prepared and subjected to the reactions with **1** and **2** in the presence of *t*-BuOK and also with *t*-BuOK itself (scheme 5).

Treatment of **7** and **8** with *t*-BuOK resulted in opening of the oxazole ring. Interestingly, although in both these experiments individual products were formed in high yields they were of different type: *N*-aryl-methylthiocarbamate **7a** and *N*-aryl-*t*-butylcarbamate **8a**. In both these cases *t*-BuOK adds at position -2 giving the correponding σ-adducts, however the fate of these adducts depends on the position of the nitro group. The adduct of **7** undergoes fast ring opening because highly stabilized *p*-nitrophenolate anion is produced. On the other hand the ring opening of the adduct of **8** should be somewhat slower because the produced phenolate anion would not be conjugated with the nitro group. Hence the departure of methylthio anion proceeds faster and results in the formation of the substitution product which *via* subsequent addition of *t*-butoxide and the ring opening gives **8a.**

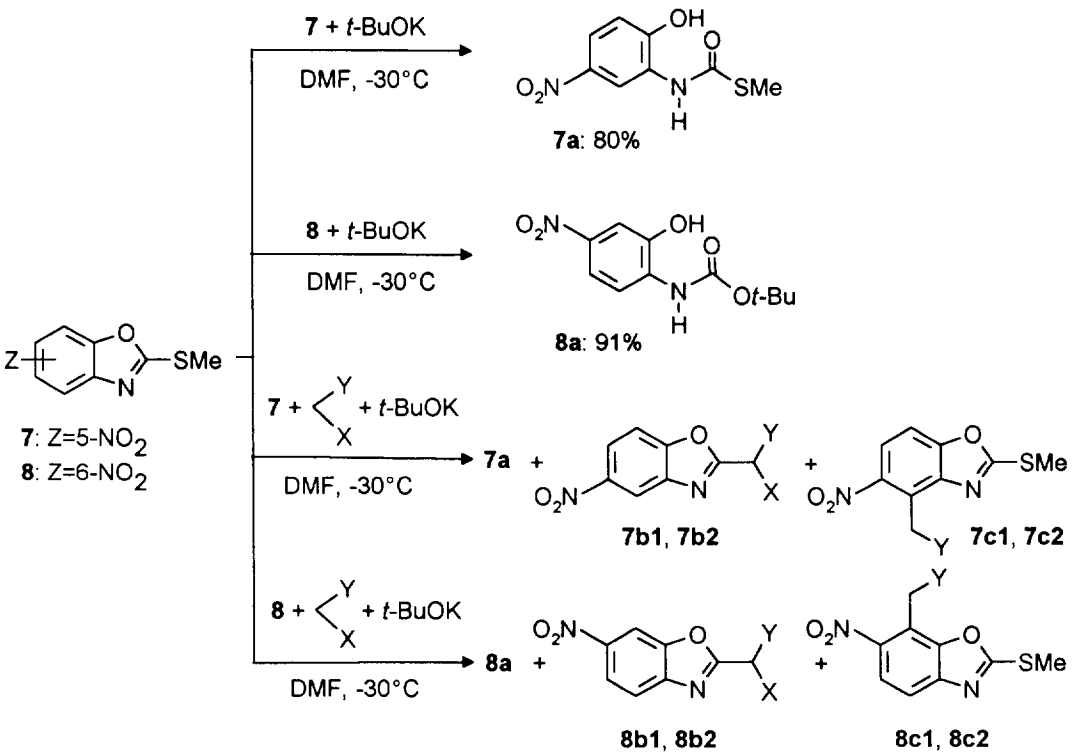
When **7** or **8** were reacted with **1** in the presence of t-BuOK, three competetive processess took place, each of them furnishing a different type of product:

a) **7a** and **8a** *via* addition of *t*-BuOK and the heterocyclic ring opening.

b) **7b1** and **8b1** *via* addition of the carbanions at C-2 and elimination of SMe group, i.e. S_NAr process in the heterocyclic ring.

c) **7c1** and **8c1** *via* the VNS reaction in the carbocyclic ring.

Ratio of the products formed *via* addition to the carbocyclic ring and the heterocyclic ring seems to be independent on the position of the nitro group. This suggest that steric reasons are involved: positions -4 and -7 in benzoxazole are much more hindered than position -2. Therefore addition of bulky carbanion of chloromethyl-*p*-tolyl sulfone to the carbocyclic ring of **7** and **8** is equally disfavoured compared to the competing processes. On the other hand



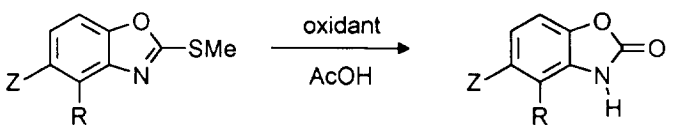
Ar	C-H acid	Y	X	type **a** product	type **b** product	type **c** product
7	**1**	Ts	Cl	**7a**; 48%	**7b1**; 18%	**7c1**; 23%
7	**2**	CN	*p*-ClC$_6$H$_4$O			**7c2**; 60%
8	**1**	Ts	Cl	**8a**; 5%	**8b1**; 58%	**8c1**; 23%
8	**2**	CN	*p*-ClC$_6$H$_4$O		**8b2**; 5%	**8c2**; 63%

Scheme 5

distribution of the two types of products **a** and **b** resulting from the addition of *t*-BuO$^-$ or carbanions at C-2 depends strongly on the position of NO_2 group and follows the pattern observed for the 2-unsubstituted nitrobenzoxazoles, i.e. the reaction with carbanions is a predominant process for the 6-nitro isomer and the reaction with alkoxide anions prevails in the case of 5-nitro- compound. This again can be explained in terms of the HSAB concept - delocalization of the negative charge in corresponding adducts and perhaps anions of final products, as in the case of **3** and **4** discussed earlier. The reaction of 7 and **8** with **2** proceeded cleanly giving the expected VNS products **7c2** and **8c2**

respectively, the latter being accompanied by a minute amount of the substitution product **8b2**. Carbanion of **2** is not as sterically demanding as carbanion of **1**, hence addition to the carbocyclic ring becomes faster than other processes, which eventually results in relatively high yields of the VNS products. Orientation of the VNS reaction in **7** and **8** is analogous to that observed in **6** and other bicyclic nitroarenes.

In order to remove SMe group, the VNS product **7c2** was subjected to oxidation. with sodium perborate hydrate and also hydrogen peroxide in acetic acid, to give in both cases benzoxazolone **8**, apparently resulting from an initial oxidation and subsequent hydrolysis. The same reaction occurred in the case of 5-nitro-2-methylthiobenzoxazole as well as 2-methylthiobenzoxazole itself, affording corresponding benzoxazolones **10** and **11** respectively (scheme 6), so this seems to be a general process for benzoxazoles containing an alkylthio substituent in 2-position.



R	Z	oxidant	product
CH_2CN	NO_2	$NaBO_3 \cdot 4H_2O$	**9**; 67%
CH_2CN	NO_2	30% H_2O_2	**9**; 98%
H	NO_2	30% H_2O_2	**10**; 96%
H	H	$NaBO_3 \cdot 4H_2O$	**11**; 75%

Scheme 6

Taking into account that 2-methylthiobenzoxazoles can be readily prepared *via* condensation of *o*-aminophenols with ethyl xanthogenates[7] followed by methylation with dimethyl sulfate[8] (actually as a one pot process), this approach can be recommended as a convenient method of synthesis of substituted benzoxazolones. This route - although lengthy - eliminates phosgene or high temperature reactions usually used in preparations of these compounds.

Conclusions

In the reactions of nucleophilic agents with 5- and 6-nitrobenzoxazoles C-2 is the preferred addition site. Fate of these adducts depends on many factors. When C-2 is occupied with a substituent, the nucleophilic addition can occur at the carbocyclic ring which can result in the VNS reaction. Benzoxazolones can be prepared under mild conditions starting from *o*-aminophenols *via* corresponding 2-methylthiobenzoxazoles.

Experimental

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded on Varian Gemini (200 MHz) instruments; chemical shifts are reported in ppm downfield from TMS as internal standard; coupling constants *J* are given in Hertz. Mass spectra were recorded on AMD 604 spectrometer. IR spectra were taken with Perkin Elmer 1640 and only noteworthy absorptions are listed. Column chromatography was performed on silica gel 70-230 or 230-400 mesh (Merck) using hexane - ethyl acetate mixtures as eluents unless indicated otherwise. The following starting materials were obtained according to known procedures: chloromethyl-*p*-tolyl sulfone **1**,[9] 4-chlorophenoxyacetonitrile **2**,[10] 5- and 6-nitrobenzoxazoles **3** and **4** respectively.[11] **6** was prepared by condensation of 2-amino-4-nitrophenol with benzoyl chloride at reflux in 94 % yield, m.p. 170 °C; ref.[12]: 172°C. Other reagents were commercially available.

Preparation of 2-methylthiobenzoxazoles: A solution of potassium salt of the corresponding benzoxazole-2-thione was prepared, as described in ref. [7] and dimethyl sulfate (20% excess based on the starting aminophenol) was added at 50 °C. After stirring for 1h the precipitate of product was collected by filtration and recrystallized from acetonitrile (**7** and **8**) or alternatively the liquid product (2-methylthiobenzoxazole itself) was extracted with ether and distilled. **7**: 70%, m.p. 157-8°C; ref.[13]: 159°C. **8**: 48%, m.p. 128-9°C, ref.[14]: 124°C. 2-Methylthiobenzoxazole: 59%; b.p. 96-9°C/3 Torr, ref.[8] 139-140°C/21 Torr.

General procedure for the reactions of nitrobenzoxazoles with nucleophiles: To a solution of *t*-BuOK (6 mmol, 673 mg) in DMF (6 ml), a solution of a nitrobenzoxazole (2 mmol), or of a nitrobenzoxazole (2 mmol), together with **1** or **2** (2 mmol) in DMF (20 ml) was added dropwise at -30°C. The reaction mixture was stirred at this temperature for 30 min and poured into ice-cold diluted hydrochloric acid. Products were isolated by filtration and recrystallization from EtOH or alternatively by extraction with ethyl acetate and further purification by column chromatography with hexane - ethyl acetate solutions as eluents.

2-Hydroxy-5-nitroformanilide (3a): M.p. 240-2°C (dec.); ref.[15]: 245 (dec.).

2-Hydroxy-4-nitroformanilide (4a): M.p. 237-8°C (dec.); ref.[15]: 235 (dec.).

1-Chloro-2-[(2-hydroxy-4-nitrophenyl)amino]ethenyl-*p*-tolyl sulfone (4b): δ_H (dmso-d_6): 2.39 (3H, s, CH_3), 7.39-7.48 (2H, m, AA' part of AA'XX' system , Ts), 7.55 (1H, X part of ABX system, H-6), 7.69, 7.75 (2H, AB part of ABX system, J_{AB}=3.0, J_{AX}=0.2, $|J_{BX}|$=9.0, H-3 and H-5), 7-76-7.84 (2H, m, XX' part of AA'XX' system, Ts), 8.24 (1H, br. d, *J*=12.8, NH), 8.53 (1H, d, *J*=12.8, HC=C), 11.32 (0.5H, br. s, OH). δ_C (dmso-d_6) (asterisk denotes methyl and methine carbon atoms): 21.07*, 104.98, 110.10*, 115.97*, 116.39*, 127.67*, 129.9*, 134.39, 136.05*, 136.29, 142.17, 142.24, 146.06. MS, m/z (%): 370, 368 (M^+, 6, 17 respectively), 334 (5), 268 (47), 222 (2), 212 (5), 179 (25), 165 (63), 155 (53), 147 (23), 139 (17), 133 (13), 119 (21), 91 (100). Elemental analysis: C 48.71, H 3.40, N 7.52; calc. for $C_{15}H_{13}ClN_2O_5S$: C 48.85, H 3.55, N 7.60.

2-(4-Chlorophenoxy)-3-[(2-hydroxy-4-nitrophenyl)amino]acrylonitrile (4c): M.p. 236-7°C. δ_H (dmso-d_6): 7.11-7.21 (2H, m, AA' part of AA'XX' system, OC_6H_4-*p*-Cl), 7.41-7.51 (2H, m, XX' part of AA'XX' system, OC_6H_4-*p*-Cl), 7.49 (1H, d, *J*=8.8, H-6), 7.63 (1H, d, *J*=2.6, H-3), 7.73 (1H, dd, *J*=8.8, *J*=2.6, H-5), 8.13 (2H, br. s, HC=C and NH).

MS, m/z (%): 333, 331 (M^+, 18, 55 respectively), 203 (13), 172 (17), 165 (100), 149 (10), 130 (23), 128 (68), 119 (13). Elemental analysis: C 54.09, H 2.74, N, 12.74; calc. for $C_{15}H_{10}ClN_3O_4$: C 54.31, H 3.04, N 12.67.

5-Nitro-2-phenyl-4-(4-tolylsulfonylmethyl)benzoxazole (6a): M.p. 202°C. δ_H ($CDCl_3$): 2.13 (3H, s, CH_3), 5.49 (2H, s, CH_2), 7.08-7.16 (2H, m, AA' part of AA'XX' system, Ts), 7.47-7.62 (5H, m, Ts and Ph), 7.62 (1H, d, *J*=8.9, H-7), 8.05-8.13 (2H, m, Ph), 8.15 (1H, d, *J*=8.9, H-6). MS, m/z (%): 408 (M^+, 2), 344 (9), 327 (8), 299 (2), 253 (100), 237 (3), 223 (7), 195 (48), 167 (5), 105 (7), 91 (5). Elemental analysis: C 61.53, H 3.78, N 6.92; calc. for $C_{21}H_{16}N_2O_5S$: C 61.76, H 3.95, N 6.86.

(5-Nitro-2-phenyl-benzoxazol-4-yl)acetonitrile (6b): M.p. 165-6°C. δ_H ($CDCl_3$): 4.59 (2H, s, CH_2), 7.53-7.66 (3H, m, Ph), 7.71 (1H, d, *J*=9.0, H-7), 8.26-8.32 (2H, m, Ph), 8.33 (1H, d, *J*=9.0, H-6). MS, m/z (%): 279 (M^+, 100), 262 (60), 206 (12), 196 (45), 105 (60). Elemental analysis: C 64.56, H 3.07, N 14.27; calc. for $C_{15}H_9N_3O_3$: C 64.52, H 3.25, N 15.05.

***N*-(2-Hydroxy-5-nitrophenyl)-(methylthio)carbamate (7a)**: M.p. 240-2°C (dec.). δ_H (dmso-d_6): 2.31 (3H, s, CH_3), 7.03 (1H, d, *J*=9.0, H-3), 7.93 (1H, dd, *J*=9.0, *J*=2.8, H-4), 8.63 (1H, d, *J*=2.8, H-6), 9.81 (1H, s, OH), 11.57 (1H, br.s, NH). MS, m/z (%): 228 (M^+, 9), 200 (2), 180 (100), 164 (5), 150 (37), 134 (29), 122 (10), 106 (26). Elemental analysis: C 42.34, H 3.71, N 12.54, calc. for $C_8H_8N_2O_4S$: C 42.10, H 3.53, N 12.27.

***N*-(2-Hydroxy-4-nitrophenyl)-*t*-butylcarbamate (8a)**: M.p. 143-5°C. δ_H ($CDCl_3$): 1.55 (9H, s, *t*-C_4H_9), 7.11 (1H, br. s, OH), 7.60-7.64 (1H, m, Ar), 7.76-7.82 (2H, m, Ar), 7.93 (1H, br. s., NH). MS, m/z (%): 254 (M^+, 3), 198 (33), 180 (100), 164 (7), 154 (18), 150 (34), 134 (18), 124 (8), 106 (37). Elemental analysis: C 51.79, H 5.61, N 11.00; calc. for $C_{11}H_{14}N_2O_5$: C 51.97, H 5.55, N 11.02.

2-[Chloro(4-tolylsulfonyl)methyl]-5-nitrobenzoxazole (7b1): M.p. 192-4°C. δ_H ($CDCl_3$): 2.50 (3H, s, CH_3), 6.01 (1H, s, aliphatic CH), 7.36-7.44 (2H, m, AA' part of AA'XX' system, Ts), 7.75 (1H, d, *J*=9.1, H-7), 7.76-7.84 (2H, m, XX' part of AA'XX' system, Ts), 8.43 (1H, dd, *J*=9.1, *J*=2.2, H-6), 8.67 (1H, d, *J*=2.2, H-4). MS, m/z (%): 368, 366 (M^+, 1, 4 respectively), 304 (3), 302 (10), 268 (29), 223 (7), 213 (9), 211 (28), 177 (12), 167 (5), 165 (16), 155 (100), 139 (5), 131 (7), 91 (67). Elemental analysis: C 49.02, H 2.77, N 7.25; calc. for $C_{15}H_{11}ClN_2O_5S$: C 49.12, H 3.02, N 7.64.

2-(Methylthio)-5-nitro-4-(4-tolylsulfonylmethyl)benzoxazole (7c1): M.p. 157-9°C. δ_H ($CDCl_3$): 2.41 (3H, s, $ArCH_3$), 2.65 (3H, s, SCH_3), 5.39 (2H, s, CH_2), 7.16-7.24 (2H, m, AA' part of AA'XX' system, Ts), 7.47 (1H, d, *J*=8.8, H-7), 7.46-7.54 (2H, m, XX' part of AA'XX' system), 8.04 (1H, d, *J*=8.8, H-6). MS, m/z (%): 378 (M^+, 3), 314 (11), 297 (10), 223 (100), 193 (5), 165 (28), 132 (11), 91 (12). Elemental analysis: C 50.76, H 3.52, N 7.36; calc. for $C_{16}H_{14}N_2O_5S_2$: C 50.78, H 3.73, N 7.40.

[2-(Methylthio)-5-nitro-benzoxazol-4-yl]acetonitrile (7c2): M.p. 151-3°C. δ_H ($CDCl_3$): 2.83 (3H, s, CH_3), 4.47 (2H, s, CH_2), 7.55 (1H, d, *J*=9.0, H-7), 8.23 (1H, d, *J*=9.0, H-6). MS, m/z (%): 249 (100), 232 (49), 216 (12), 204 (18), 191 (14), 181 (13), 175 (65), 166 (27), 160 (45), 102 (13). Elemental analysis: C 48.24, H, 2.80, N 16.72; calc. for $C_{10}H_7N_3O_3S$: C 48.19, H 2.83, N 16.86.

2-[Chloro(4-tolylsulfonyl)methyl]-6-nitrobenzoxazole (8b1): M.p. 159-160°C. δ_H ($CDCl_3$): 2.51 (3H, s, CH_3), 6.01 (1H, s, aliphatic CH), 7.37-7.45 (2H, m, AA' part of AA'XX' system, Ts), 7.76-7.84 (2H, m, XX' part of AA'XX' system, Ts), 7.92 (1H, d, *J*=8.8, H-4), 8.38 (1H, dd, *J*=8.8, *J*=2.1, H-5), 8.52 (1H, d, *J*=2.1, H-7). MS, m/z (%): 368, 366 (M^+, 1, 4 respectively), 304 (2), 302 (5), 268 (59), 213 (4), 211 (13), 177 (8), 155 (100), 147 (11), 131 (4), 119 (4), 102 (5), 91 (78). Elemental analysis: C 48.83, H 2.91, N 7.37; calc. for $C_{15}H_{11}ClN_2O_5S$: C 49.12, H 3.02, N 7.64.

2-(Methylthio)-6-nitro-7-(4-tolylsulfonylmethyl)benzoxazole (8c1): M.p. 193-5°C. δ_H ($CDCl_3$) 2.43 (3H, s, $ArCH_3$), 2.75 (3H, s, SCH_3), 5.23 (2H, s, CH_2), 7.20-7.26 (2H, m, AA' part of AA'XX' system, Ts), 7.46-7.54 (2H, m, XX' part of AA'XX' system, Ts), 7.61 (1H, d, *J*=8.7, H-4), 8.10 (1H, d, *J*=8.7, H-5). MS, m/z (%): 378 (M^+, 24), 332 (18), 223 (100), 206 (5), 178 (8), 165 (9), 134 (5), 91 (8). Elemental analysis: C 50.76, H 3.83, N 7.29; calc. for $C_{16}H_{14}N_2O_5S_2$: C 50.78, H 3.73, N 7.40.

(4-Chlorophenoxy)(6-nitrobenzoxazol-2-yl)acetonitrile (8b2): M.p. 168-9°C. δ_H ($CDCl_3$): 6.21 (1H, s, aliphatic CH), 7.02-7.20 (2H, m, AA' part of AA'XX' system, OC_6H_4-*p*-Cl), 7.30-7.43 (2H, m, XX' part of AA'XX' system, OC_6H_4-*p*-Cl), 7.99 (1H, d, *J*=8.8, H-4), 8.41 (1H, dd, *J*=8.8, *J*=2.1, H-5), 8.57 (1H, d, *J*=2.1, H-7). MS, m/z (%): 331, 329 (M^+, 5, 16 respectively), 294 (60), 202 (20), 172 (18), 156 (3), 144 (4), 129 (33), 127 (100), 99 (26). Elemental analysis: C 54.28, H 2.25, N 12.68; calc. for $C_{15}H_8ClN_3O_4$: C 54.65, H 2.45, N 12.75.

[2-(Methylthio)-6-nitro-benzoxazol-7-yl]acetonitrile (8c2): M.p. 171-3°C. δ_H ($CDCl_3$): 2.83 (3H, s, CH_3), 4.35 (2H, s, CH_2), 7.67 (1H, d, *J*=8.8, H-4), 8.29 (1H, d, *J*=8.8, H-5). MS, m/z (%): 249 (M^+, 98), 232 (100), 217 (13), 205 (13), 188 (12), 176 (12), 159 (23), 148 (4), 102 (8). Elemental analysis: C 48.28, H 2.75, N 17.00; calc. for $C_{10}H_7N_3O_3S$: C 48.19, H 2.83, N 16.86.

1-Chloro-2-[(2-methoxy-4-nitrophenyl)amino]ethenyl-*p*-tolyl sulfone (4d): To a suspension of **4b** (100 mg, 0.27 mmol) in methanol (3 ml), a solution of diazomethane (ca. 8 mmol) in ether (15 ml) was added. A clear solution was obtained which was stirred overnight and evaporated. The residue was recrystallized from MeOH to give **4d** (67 mg, 65%) as a yellow solid. M.p. 155-6°C. δ_H (dmso-d_6): 2.39 (3H, s, $ArCH_3$), 3.99 (3H, s, OCH_3), 7.39-7.47 (2H, m, AA' part of AA'XX' system , Ts), 7.62 (1H, d, *J*=8.8, H-6), 7.76-7.84 (3H, m, Ts and H-3), 7.89 (1H, dd, *J*=8.8, *J*=2.1), 8.14 (1H, br.s, NH), 8.40 (1H, s, HC=C). MS, m/z (%): 384, 382 (M^+, 38, 100 respectively), 348 (7), 318 (2), 228 (8), 226 (25), 212 (5), 183 (6), 181 (17), 168 (2), 166 (5), 139 (8), 91 (10). Elemental analysis: C 49.94, H 3.74, N 6.98; calc. for $C_{16}H_{15}ClN_2O_5S$: C 50.20, H 3.95, N 7.32.

2-(4-Tolylsulfonylmethyl)-5-nitrobenzoxazole (5): To a solution of *t*-BuOK (673 mg, 6mmol) in DMF (3 ml), **4b** (111 mg, 0.3 mmol) was added in one portion. The reaction mixture was stirred for 5 min and poured into ice-cold diluted hydrochloric acid. The product was extracted with ethyl acetate, the extract was washed with water, dried ($MgSO_4$ and evaporated. The residue was subjected to column chromatography (chloroform) to give **5** (30 mg, 30 %) as a colorless solid. M.p. 197-8°C. δ_H(dmso-d_6): 2.42 (3H, s, CH_3), 5.43 (2H, s), 7.40-7.50 (2H, m, AA' part of AA'XX' system, Ts), 7.70-7.80 (2H, m, XX' part of AA'XX' system, Ts), 7.99 (1H, d, *J*=8.8, H-4), 8.31 (1H, dd, *J*=8.8, *J*=2.2, H-5), 8.75 (1H, d, *J*=2.2, H-7). MS, m/z (%): 268 (100), 222 (2), 177 (3), 155 (43), 147 (15), 131 (7),

119 (7), 103 (8), 91 (65). MS (LSIMS), m/z: 332 (M^+). Elemental analysis: C 54.02, H 3.56, N 8.19, calc. for $C_{15}H_{12}N_2O_5S$: C 54.21, H, 3.64, N 8.43.

General procedure for oxidation of 2-methylthiobenzoxazoles to benzoxazolones: To a suspension of a 2-methylthiobenzoxazole (20 mmol) in acetic acid (80 ml), 30% H_2O_2 (18 ml, 175 mmol) or $NaBO_3{\cdot}4H_2O$ (15.4 g, 100 mmol) was added and the mixture was slowly warmed up. At ca. 50°C vigorous exothermic reaction started and at this point the external heating was removed. The reaction mixture became homogenous, the temperature rose to about 80°C and then gradually dropped to r.t. Most of the solvent was removed under reduced pressure and water was added to the residue. The precipitate formed was collected by filtration, washed with water and air dried.

(5-Nitro-2-oxo-2,3-dihydrobenzoxazol-4-yl)acetonitrile (9): M.p. 195-7°C. δ_H(aceton-d_6): 4.27 (2H, s, CH_2), 7.50 (1H, d, J=8.8, H-7), 8.08 (1H, d, J=8.8, H-6). MS, m/z (%): 219 (M^+, 48), 202 (100), 175 (40), 159 (7), 146 (5), 120 (16). IR (KBr): 1800, 1825 (C=O), 2250 (CN), 3294 (NH). Elemental analysis: C 49.49, H 2.36, N 19.04; calc. for $C_9H_5N_3O_4$: C 49.33, H 2.30, N 19.17.

5-Nitro-2(3*H*)-benzoxazolone (10): M.p. 233-4°C. ref.[16]: 231-2°C.

2(3*H*)-Benzoxazolone (11): M.p. 140-1°C. ref.[17]:142-3°C.

References:

1. Mąkosza, M.; Winiarski, J. *Acc. Chem. Res.* **1987**, *20*, 272.
2. Mąkosza, M. *Synthesis* **1991**, 103.
3. Mąkosza, M.; Glinka, T.; Ostrowski, S.; Rykowski, A. *Chem. Lett.* **1987**, 16.
4. Mąkosza, M.; Stalewski, J. *Tetrahedron*, this issue.
5. Mąkosza, M.; Goliński, J.; Rykowski, A. *Tetrahedron Lett.* **1983**, *24*, 3277.
6. Wojciechowski, K.; Mąkosza, M. *Synthesis* **1989**, 106.
7. Van Allan, J. A.; Deacon, B. D. *Org. Synt.*, **1950**, *30*, 56.
8. Beilenson, B.; Hamer, F. M. *J. Chem. Soc.* **1939**, 143.
9. Mąkosza, M.; Danikiewicz, W.; Wojciechowski, K. *Liebigs Ann. Chem.* **1987**, 711.
10. Grochowski, E.; Eckstein, Z. *Bull. Acad. Pol. Sci., Ser. Sc. Chim.* **1963**, *11*, 443.
11. Kuntz K. R.; Will Taylor, E.; Hutton, H. M.; Blackburn, B. J. *Org. Proc. Prep. Int.* **1990**, *22*, 613.
12. Stephens, F. F.; Bower, J. D. *J. Chem. Soc.* **1950**, 1722.
13. Zinner, H.; Reimann, R.,; Weber, A. *Chem. Ber.* **1960**, *93*, 2035.
14. Bower J. D.; Stephens F. F. *J. Chem. Soc.* **1951**, 325.
15. Llinares, J.; Gally, J. P.; Faure, R.; Vincent, E. J. *Can. J. Chem.* **1979**, *57*, 937.
16. Clark, R. L.; Pessolano, A. A. *J. Am. Chem. Soc.* **1958**, *80*, 1662.
17. Bywater, W. G.; Coleman, W. R.; Kamm, O., Houston Merrit, H. *J. Am. Chem. Soc.* **1945**, *67*, 905.

(*Received in UK* 28 *March* 1995; *revised* 2 *May* 1995; *accepted* 5 *May* 1995)