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# Vicarious Nucleophilic Substitution of Hydrogen in Nitrophenyl Toluenesulfonates

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***Abstract:*** Toluenesulfonates of nitrophenols react with carbanions possessing leaving groups giving products of the vicarious nucleophilic substitution of hydrogen. The yields and orientation depend on the reaction conditions and the structure of the reagents. The products obtained can be easily hydrolyzed to the corresponding phenols or - in certain cases - to hydroxynitrobenzaldehydes.
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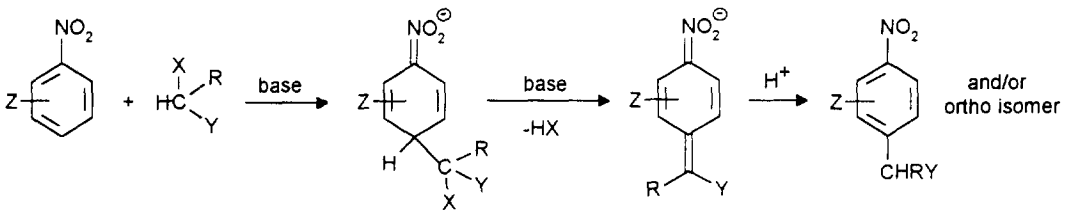
Vicarious nucleophilic substitution of hydrogen (VNS, Scheme 1) is a general process in respect to nitroarenes which can contain a practically unlimited variety of substituents[1] The reaction however does not proceed with nitrophenols because under strongly basic conditions they are in the form of nitrophenolates unable to behave as electrophilic partners in the reaction with carbanions. The presence of the second nitro group attached to the aromatic ring compensates this effect therefore dinitrophenols enter the VNS reaction.[2]




Scheme 1

Vicarious substitution of hydrogen in mononitrophenols is nevertheless possible provided the OH function is protected. Numerous examples of such reaction have been reported in which an alkyl substituent such as methyl, benzyl or allyl was used as the formal protecting groups.[3-16] This way of protection is, however, often inconvenient because cleavage of the C-O bond in ethers to form the phenolic products usually requires drastic conditions so this solution is applicable to a limited variety of functional groups present in the VNS products. Moreover, alkoxy substituents decrease the electrophilicity of the nitroaromatic ring, thus in many cases the VNS reaction does not

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proceed satisfactorily.[10,16] Therefore we studied the possibility of the VNS in nitrophenols protected with the toluenesulfonic group which is eletronwithdrawing and is easily removable under mild, basic conditions.

*Ortho*-, *meta*- and *para*-nitrophenyl toluenesulfonates **1-3** can be considered as typical polyfunctional electrophiles in which the nucleophilic attack can be directed on: (i) unsubstituted aromatic carbon *ortho* or *para* to the nitro group resulting in the VNS reaction, (ii) position substituted with OTs leading to $S_NAr$ process and (iii) the sulfur atom resulting in liberation of nitrophenolate anion.

Results of the reaction of **1**, **2** and **3** with carbanions of 1-chloroalkyl aryl sulfones, acetonitrile derivatives and also haloforms in various base/solvent systems are given in Table 1.

Nucleophilic substitution of $TsO^-$ with carbanions, possible in the case of *o*- and *p*-nitrophenyl tosylates **1** and **3**, was not observed at all, even under conditions (low base concentration or the carbanion as the only base; procedures A, C, F; see footnotes to table 1) disfavoring the VNS process. Substitution on the sulfur atom with *tert*-butoxide leading to desulfonylation of the starting sulfonates was observed commonly but in most cases it proceeded to a small extent and no more than 10% of the parent nitrophenols was formed. Noticeably faster desulfonylation was observed in the reactions of **1**, especially when procedure B or D was used.

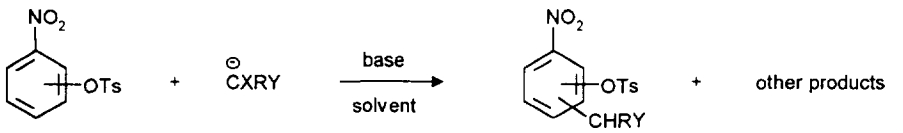
The results collected in table 1 show, that in many cases the vicarious substitution of hydrogen in **1-3** proceeded in satisfactory to very good yields. Procedure A in which the base was slowly added to the other reagents in DMF was found to be the most general and suitable. Tosylates **2** and **3** reacted satisfactorily also in THF (procedure D) whereas *o*-nitrophenyl tosylate **1** gave under these conditions large amounts of side products. For the reactions of **1-3** with haloforms optimal reaction conditions were elaborated earlier[10] and here they were applied with minor modifications.

As we have expected, tosylated nitrophenols are more active than alkylated ones in the reactions with carbanions. The reactions of **2** with chloromethyl aryl sulfones and also acetonitrile derivatives proceeded with considerably higher yields than with 3-methoxynitrobenzene.[7,8] The yield of the reaction of **2** with 1-chloroethyl phenyl sulfone (entry *14*), although rather moderate (45%), is also noteworthy, because tertiary carbanions have been known to react very poorly, if at all, in *tert*-BuOK/THF system, valuable for its *ortho*-directing effect.[7]

The increased reactivity of the tosylated nitrophenols as compared with the alkylated analogs is especially apparent in the dihalomethylation reaction of **3**. Trihalomethyl carbanions being very unstable species can be used as test reagents for the reactivity of the electrophilic arenes.[10] It was found earlier that 4-methoxynitrobenzene did not react with chloroform and bromoform, 4-benzyloxy nitrobenzene reacted only with chloroform to give the VNS product with moderate yield,[10] whereas *p*-nitrophenyl tosylate **3** reacted satisfactorily with both these trihalomethyl carbanions (entry *23*, *24*).

Much more complicated was, however, the course of the attempted dichloromethylation of **1**. Cleavage of the sulfur-oxygen bond in **1** was the prevailing process and the expected product of dichloromethylation was formed only to small extent (7% yield) along with *o*-nitrophenol and the unexpected product **19** (34%, scheme 2). The formation of the later can be rationalized by the VNS reaction in **1** with dichloromethyl tolyl sulfone

**Table 1** Reactions of Tosylated Nitrophenols with Carbanions



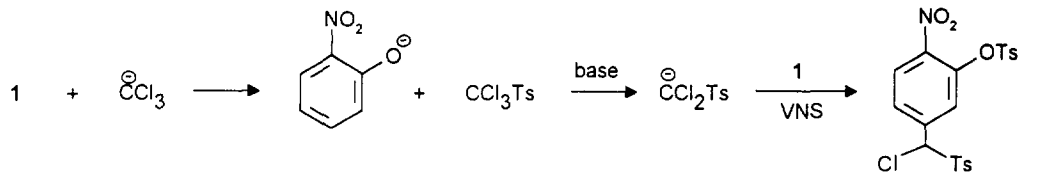

2-TsO,**1**; 3-TsO, **2**; 4-TsO, **3**.

| Reaction No. (Entry) | Nitro-arene | X | Y | R | Proce-dure[a] | VNS product | | | Other identified products[g] (yield %) |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | No. | yield[b] (%) | 2:4:6 isomer ratio[c,d] | |
| *1* | **1** | Cl | Ts | H | A | **4** | 70 | - / 60 /40 | |
| *2* | **1** | Cl | Ts | H | B | **4** | 40 | - / 63 / 37 | |
| *3* | **1** | Cl | Ts | H | C | **4** | 67 | - / 89 / 11 | |
| *4* | **1** | Cl | Ts | H | D | **4** | 44 | - / 9 / 91 | **17**[h] (38 ) |
| *5* | **1** | Cl | Ts | H | F | **4** | 46 | - / 94 / 6 | |
| *6* | **1** | Cl | $PhSO_2$ | Me | A | **5** | 58 | - / 100 / 0 | |
| *7* | **1** | Cl | Cl | Cl | E | **6** | 7 | - / 100 / 0 | **19**[i] (34) |
| *8* | **1** | *p*-$ClC_6H_4O$ | CN | H | A | **7** | 32 | - / 32 / 68 | |
| *9* | **1** | *p*-$ClC_6H_4O$ | CN | H | D[e] | **7** | 4 | - / 0 / 100 | **20**(58) |
| *10* | **2** | Cl | Ts | H | A | **8** | 86 | 14 / 50 / 36 | |
| *11* | **2** | Cl | Ts | H | C | **8** | 89 | 0 / 63 / 37 | |
| *12* | **2** | Cl | Ts | H | D | **8** | 89 | 29 / 8 / 63 | |
| *13* | **2** | Cl | $PhSO_2$ | Me | A | **9** | 70 | 0 / 86 / 14 | |
| *14* | **2** | Cl | $PhSO_2$ | Me | D | **9** | 45 | 0 / 24 / 76 | **2** (21) |
| *15* | **2** | Cl | Cl | Cl | E | **10** | 63[c] | 40 / 20 / 40 | **18**[i] (3) |
| *16* | **2** | *p*-$ClC_6H_4O$ | CN | H | A | **11** | 82 | 56 / 10 / 34 | |
| *17* | **2** | *p*-$ClC_6H_4O$ | CN | H | D[e] | **11** | 79 | 37 / 10 / 53 | |
| *18* | **2** | *p*-$ClC_6H_4O$ | CN | H | F | **11** | 25 | 57 / 22 / 21 | |
| *19* | **3** | Cl | Ts | H | A | **12** | 84 | - | |
| *20* | **3** | Cl | Ts | H | B | **12** | 70 | - | |
| *21* | **3** | Cl | Ts | H | D | **12** | 83 | - | |
| *22* | **3** | Cl | $PhSO_2$ | Me | A | **13** | 51 | - | |
| *23* | **3** | Cl | Cl | Cl | E | **14** | 50 | - | **18**[i] (~3) |
| *24* | **3** | Br | Br | Br | E | **15** | 48 | - | |
| *25* | **3** | *p*-$ClC_6H_4O$ | CN | H | D[e] | **16** | 73 | - | **21**(14), **20**(5) |
| *26* | **3** | *p*-$ClC_6H_4O$ | CN | H | A | **16** | 56 | - | **21**(3), **20**(2) |
| *27* | **3** | Cl | CN | H | B | **16** | 27 | - | |
| *28* | **3** | Cl | CN | H | B[f] | **16** | 31 | - | |

*a)* A: *tert*-BuOK added slowly to the reagents in DMF at -40°; B: the reagents added slowly to *tert*-BuOK in DMF at -40°C; C: the carbanion added slowly to the nitroarene in DMF at r.t.; D: *tert*-BuOK added to the reagents in THF at -40°C; E: DMF/THF/-78°C, *tert*-BuOK (see experimental); F: KOH/DMSO/r.t. *b)* isolated yields of the isomer mixture (if applicable). *c)* from $^1H$ NMR of the crude products mixture. *d)* refering to the nitro group position (1). *e)* at -20°C. *f)* THF was used instead of DMF. *g)* nitrophenols not specified. *h)* chloroditosylmethane. *i)* see scheme 2.

carbanion **18**$^-$ formed apparently *via* tosylation of trichloromethyl anion with **1**, followed by dehalogenation of trichloromethyl tolyl sulfone with base[17] (*tert*-BuO$^-$ or $CCl_3^-$) in a halophilic-type reaction (scheme 2).

This hypothetical explanation can be supported by isolation of small amounts of **18** also in the dichloromethylation reactions of **2** and **3** (entry *15* and *23*). Tertiary anion **18**$^-$ enters the VNS reaction in **2** and **3** less readily than in **1**, probably for steric reasons (with **1** only *para* isomer was formed), thus it remains in the reaction mixture and after protonation **18** can be isolated. The low yields of **18** in these reactions prove the much higher reactivity of the sulfonate function in *ortho* (**1**) than *meta* (**2**) and *para* (**3**) position in the nitroarene molecule.

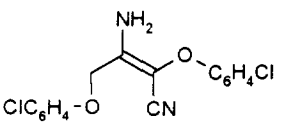



**18**$^-$ **19**

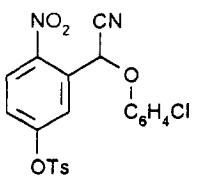
Scheme 2

A similar transfer of the tosyl group from **1** to the chloromethyl tolyl sulfone carbanion was a considerable side process in the reaction of these reagents in THF (procedure D, entry *4* ) and produced chloroditosylmethane (**17**) which was isolated in 38% yield. Its highly stabilized, inactive anion is apparently unable to enter the VNS reaction under the applied conditions.

Introduction of the cyanomethyl moiety to the nitrophenols derivatives *via* the VNS process is an important method giving an access to valuable intermediates in the synthesis of hydroxyindoles derivatives.[8,14,15] Chloroacetonitrile, the simplest reagent widely used for cyanomethylation of active nitroarenes,[5] undergoes rapid decomposition in a strong basic medium and is useless in the VNS in less active nitroarenes substituted with alkoxy groups.[16] . Nitrophenyl tosylate **3** can be however cyanomethylated with chloroacetonitrile (entry *27* and *28*), although the yields are not high (procedure B was found the best one for this reaction), proving again the higher reactivity of the *O*-tosylated than *O*-alkylated nitroarenes. More stable *p*-chlorophenoxyacetonitrile also used for cyanomethylation of nitroarenes reacted satisfactorily with **1-3**, although the product of the Thorpe condensation **20**[18] was often observed, in one case being the main product of the reaction (entry *9*). Another side product in the cyanomethylation reaction of **3** was **21** - formed *via* the oxidative substitution of hydrogen, a process competing with the VNS reaction when the carbanions posses relatively poor leaving groups.[19]




**20**




**21**

Orientation of the substitution of hydrogen is one of the most intriguing questions in the VNS reaction. Electronic and also steric effects of substituents influence the rate of the $\sigma^H$-adducts formation in different activated positions, their equilibrium concentrations and the rate of the subsequent β-elimination process, differentiating the observed reactivity of certain positions, hence the final composition of the product mixture. It is a difficult task to evaluate contributions of the particular factors in the observed orientation of VNS, this problem is now a subject of our extensive studies.

The orientation of the VNS reaction in **1** and **2** with α-chlorosulfone carbanions is strongly affected by the reaction conditions - the base concentration, solvent system and temperature. The *para* substitution (in respect to the nitro group) is favored in reactions carried out at room temperature when carbanions are the only base soluble in the reaction mixture (procedure C and F). Under such conditions the HX elimination is slow - relatively to the addition/dissociation step. The resulting domination of the *para* orientation apparently reflects higher concentration of the *para*-σ adduct thus it corresponds to the thermodynamical control. One can not exclude however, that the HCl elimination from this adduct proceeds faster compared with that in *ortho* position.

At lower temperature variation of the base concentration (diverse order of the reagents and base addition) do not affect the orientation pattern (entry *1* and *2*). This may suggest, that under such conditions, the elimination step - strongly depended on the base concentration - does not play a decisive role in differentiation of the ring positions, thus this step must be faster than the σ-adduct dissociation and consequently, the observed 4/6 isomer ratio reflects the ratio of the σ-adducts formation in both positions.

The use of THF (procedure D) instead of DMF strongly favors the *ortho* substitution (entry *4*, 9, *12* and *14* *vs* *1*, *8*, *10* and *13* resp.) which is a well known feature of the *tert*-BuOK/THF system.[7] This phenomenon is however hardly observed in the cyanomethylation of **2** (entry *17* vs *16*). Although aryloxyacetonitrile carbanions are known to react predominantly in the position *ortho* to the nitro group even in KOH/DMSO[5] and *tert*-BuOK/DMF[8] systems, formation of the *para* isomer **11.4** was expected to be markedly suppressed in THF.

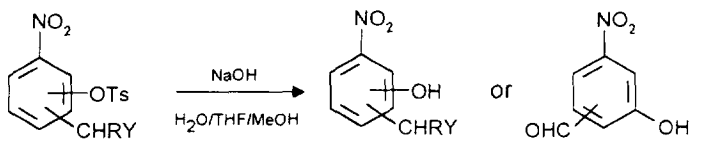
The influence of the tosyl group, when compared with the alkyl one, on the directing effect of the oxygen-bonded substituent depends on its position in the aromatic ring. In the VNS reactions with chloromethyl phenyl sulfone in *ortho* substituted nitrobenzenes both *o*-nitroanisole [7] and **1** gave very similar isomer ratios in THF ( 9/91 *vs.* 7/93) as well as in the KOH/DMSO system (94/6 *vs.* 96/4 ) respectively. Apparently, conjugation of lone electron pairs of the oxygen substituent with the nitro group, which is possible in the former nitroarene and can be rather excluded in the later one, does not play any role in the directing effect of such groups.

Orientation of the VNS reaction in 3-tosyloxynitrobenzene (**2**) differs substantially from that observed for the 3-methoxy derivative, especially in the *tert*-BuOK/THF system (85/0/15 isomer ratio[7]). Although the general preference for the *ortho* substitution (positions 2 and 6) was held, the 2/6 ratio was reversed, the 6-substitution being the main reaction course in the former case. It is difficult to decide which factors - steric or electronic - are decisive for this result, which resembles that of 3-iodo- (34/5/61) and also of 3-cyanonitrobenzene (23/14/63).[7] After all, steric factors could not explain why in the case of **2** substitution of hydrogen in the vicinity of the TsO

substituent (position 4) also takes place, which was not observed for the much smaller MeO group.[7]

The cyanomethylation of **2** with *p*-chlorophenoxyacetonitrile according to the procedure A proceeds less regioselectively than with the corresponding 3-alkoxynitrobenzene, which reacted almost exclusively in position 2 regardless of the size of the alkyl group connected with the oxygen.[8] Thus, the effect on orientation is apparently of an electronic nature.

Despite some difficulties in rationalization of the orientation pattern, the VNS reaction of the tosylated nitrophenols (**1-3**) may be a valuable method for functionalization of the aromatic ring in nitrophenols, especially in the cases of sufficient enough regioselectivity. Tosylates **1-3** exhibit higher reactivity, as compared to the *O*-alkylated analogs, and the products can be very easily deprotected to recover the phenolic function.




**22 - 27** **28**

A typical deprotection procedure consists in treatment of the tosylated products with diluted NaOH solution in MeOH/$H_2O$/THF mixture at room temperature for 30 min, giving almost quantitative yields of the phenolic products (table 2). In the case of dichloromethyl derivatives **10** in which dichloromethyl and phenolic functions are situated in conjugated positions, the labile chlorides undergo further hydrolysis and the corresponding aldehydes **28** are formed. Usually, dichloromethylated nitroarenes require much more drastic conditions to be hydrolyzed.[10] Thus, the dichloromethylation of tosylated *meta*-nitrophenol gives a simply access to the three hydroxynitrobenzaldehydes, which can be separated after the hydrolysis of the crude mixture of the VNS products **10**.

**Table 2.** Hydrolysis of the selected VNS Products.

| VNS product[a] | Nitro-phenol[a] | Isolated yield (%) |
|---|---|---|
| **4.4** | **22.4** | 90 |
| **4.6** | **22.6** | 90 |
| **8.6** | **23.6** | 98 |
| **8.4** | **23.4** | 93 |
| **9.4** | **24.4** | 90 |
| **12** | **25** | 98 |
| **14** | **26** | 96 |
| **16** | **27** | 95 |
| **10**[b] | **28.2** | 15[c] |
| **10**[b] | **28.4** | 7[c] |
| **10**[b] | **28.6** | 19[c] |

*a)* the digit after the dot means the substitution position (ref. to $NO_2$) when more then one isomer is possible. *b)* the crude reaction mixture of all isomers was hydrolyzed, then separated. *c)* yield of two steps, based on **2**.

## EXPERIMENTAL

Melting points are uncorrected. $^1$H NMR spectra were recorded on a Varian Gemini (200 MHz) and a Brucker AM 500 (500 MHz) instruments. Chemical shifts are expressed in ppm referred to TMS used as the internal standard, coupling constants in hertz. Mass spectra were obtained on a AMD-604 spectrometer. Silica gel Merck 60 70-230 mesh was used for column chromatography. Silica gel Merck $60GF_{254}$ was used for thin-layer preparative chromatography.

The following starting materials were prepared according to the published procedures: chloromethyl p-tolyl sulfone,[6] 1-chloroethyl phenyl sulfone,[7] (4-chlorophenoxy)acetonitrile,[20] 2-nitrophenyl 4-toluenesulfonate (**1**),[21]

4-nitrophenyl 4-toluenesulfonate (**2**),[21] 3-nitrophenyl 4-toluenesulfonate (**3**).[22] Remaining materials were commercial and were purified when necessary. DMF, DMSO and THF were dried by conventional methods and distilled.

**Reactions of carbanions with nitroarenes.**

***General reaction procedures:***

**A.** To a stirred solution of the nitrocompound (0,68 mmol, 0,2 g) and the CH-acid (0,68 mmol) in DMF (1 mL) cooled to -40°C a solution of *tert*-BuOK (2 mmol, 0,23 g or in the case of reactions no. *23* and *25* 2.7 mmol, 0,3 g) in DMF (3 mL) was added dropwise during 2-4 min. and the reaction mixture was stirred for about 20 min.

**B.** To a stirred solution of the *tert*-BuOK (2 mmol, 0,23 g) in DMF (2 mL) cooled to -40°C a solution of the nitrocompound (0,68 mmol, 0,2 g) and the CH-acid (0,68 mmol) in DMF (3 mL) was added dropwise for about 3 min. and the reaction mixture was stirred for about 15 min.

**C.** A solution of the carbanion prepared by addition of *tert*-BuOK (2 mmol, 0,23 g) in DMF (2 mL) to $CH_2ClTs$ (2 mmol, 0,42 g) dissolved in DMF (2 mL) was added dropwise during 15-20 min. to a stirred solution of the nitrocompound (0,68 mmol, 0,2 g) in DMF (3 mL) at room temperature and the reaction mixture was stirred for 30 min. (reaction no.*3*) or 50 min. (reaction no. *11*).

**D.** To a stirred solution of the nitrocompound (0,68 mmol, 0,2 g) and the CH-acid (0,68 mmol) in THF (1 mL) cooled to -40°C (-20°C in the case of reactions no. *9*, *17* and *25*) a solution of *tert*-BuOK (2 mmol, 0.23 g or 2,7 mmol, 0.3 g in the case of reactions no. *9*, *17* and *25*) in THF (3 mL) was added dropwise during 2-4 min. and the reaction mixture was stirred for 10-15 min.

**E.** To a stirred solution of the nitrocompound (0.68 mmol, 0.2 g) and the CH-acid (0.68 mmol or 1 mmol in the case of reaction *15*) in THF/DMF 1/1 v/v (1 mL) cooled to -70°C a solution of the *tert*-BuOK (2 mmol, 0.23 g or 2.7 mmol, 0.3 g in the case of reaction *15*) in THF/DMF 1/1 v/v (3 mL) was then added dropwise during 30-60 min. and the reaction mixture was stirred or 2-4 min.

**F.** To a stirred solution of the nitrocompound (0.68 mmol, 0.2 g) and $CH_2ClTs$ (0.68 mmol, 0.14 g) in DMSO (3 mL) powdered KOH (5 mmol, 0.28 g) was added and the reaction mixture was stirred and cooled with water-bath at room temperature for 30 min.

***General procedure for work-up and products isolation:***

The reaction mixture was quenched at the reaction temperature with 2% hydrochloric acid (10 mL,) or AcOH/MeOH 1/3 v/v (2 mL) for the procedure **E**, then it was poured into water, extracted with methylene chloride (3x20 mL), the extract was washed with water, dried over $Na_2SO_4$ and the solvent was evaporated. In the case of the cyanomethylation with (4-chlorophenoxy)acetonitrile the extract was washed with diluted NaOH first, to remove 4-chlorophenol. The column chromatography (using appropriate hexane/AcOEt mixture as an eluent) of the crude product allowed the isolation of the side products and the mixture of the VNS products which was analyzed by $^1H$ NMR technique to estimate the isomers ratio. Samples of the pure, individual isomers were obtained by additional (one or more) column or preparative TLC chromatography.

**2-Nitro-5-(toluene-4-sulfonylmethyl)phenyl toluene-4-sulfonate (4.4)**: mp 144-5°C (AcOEt); $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.47 (s, 3H), 4.34 (s, 2H), 7.22 (dd, 1H, J=8.3, J=1.8), 7.24 (d, 1H, J=1.8), 7.32 ( 2H, AA'XX'), 7.36 (AA'XX', 2H), 7.57 (AA'XX', 2H), 7.75 (AA'XX', 2H), 7.82 (d, 1H, J=8.3); MS EI 70eV m/z (%): 461 ($M^+$, 13), 443 (0.5), 397 (3), 306 (27), 291 (1), 276 (3), 260 (18), 242 (8), 225 (6), 195 (2), 181 (2), 155 (70), 152 (10), 139 (55), 135 (7), 122 (5), 107 (5), 91 (100), 77 (8), 65 (16), 51 (5); HRMS found

461.060388 (M+); calc. for $C_{21}H_{19}NO_7S_2$ 461.060296.

**2-Nitro-3-(toluene-4-sulfonylmethyl)phenyl toluene-4-sulfonate (4.6)**: mp 180-1°C (acetone); $^1$H NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.46 (s, 3H), 4.43 (s, 2H), 7.27 (AA'XX', 2H), 7.34 (AA'XX', 2H), 7.43-7.54 (m, 5H), 7.72 (AA'XX', 2H); MS EI 70eV m/z (%): 461 ($M^+$,1), 443 (0.3), 431 (0.3), 415 (1.1), 397 (0.7), 379 (0.3), 306 (43), 276 (5), 258 (4), 155 (85), 152 (15), 139 (16), 91 (100); HRMS found 461.060388 ($M^+$); calc. for $C_{21}H_{19}NO_7S_2$ 461.060296.

**2-Nitro-5[1-(phenylsulfonyl)ethyl]phenyl toluene-4-sulfonate (5)**: oil, $^1$H NMR (500 MHz, $CDCl_3$) δ 1.72 (d, 3H, J=7.1), 2.47 (s, 3H), 4.30 (q, 1H, J=7.1), 7.25 (ddd, 1H, J=8.4, J=1.9, J=0.3), 7.29 (d, 1H, J=1.9), 7.36 (AA'XX', 2H), 7.49-7.66 (m, 5H), 7.77 (AA'XX', 2H), 7.81 (d, 1H, J=8.4); MS EI 70eV m/z (%): 461 ($M^+$, 0.1), 445 (0.05), 391 (0.06), 351 (0.1), 320 (100), 274 (10), 166 (11), 156 (21), 149 (19), 139 (40), 91 (38), 77 (8), 65 (8); HRMS found 461.059478 ($M^+$); calc. for $C_{21}H_{19}NO_7S_2$ 461.060296.

**5-Dichloromethyl-2-nitrophenyl toluene-4-sulfonate (6.4)**: oil, $^1$H NMR (200 MHz, $CDCl_3$) δ 2.48 (s, 3H), 6.68 (s, 1H), 7.37 (AA'XX', 2H), 7.59 (d, 1H, J=2.0), 7.63 (dd, 1H, J=8.4, J=2.0), 7.79 (AA'XX', 2H), 7.96 (d, 1H, J=8.4); MS EI 70eV m/z (%): 375 ($M^+$, 4), 340 (2.5), 294 (0.3), 186 (1), 167 (0.9), 155 (100), 149 (2), 139 (6), 111 (2), 91 (66), 65 (9); HRMS found 374.972781 ($M^+$); calc. for $C_{14}H_{11}Cl_2NO_5S$ 374.97350.

**5-Cyanomethyl-2-nitrophenyl toluene-4-sulfonate (7.4)**: oil, $^1$H NMR (500 MHz, $CDCl_3$) δ 2.48 (s, 3H), 3.86 (s, 2H), 7.38 (AA'XX', 2H), 7.42-7.45 (m, 2H), 7.79 (AA'XX', 2H), 7.96 (d, 1H, J=8.3); MS EI 70eV m/z (%): 332 ($M^+$, 2), 268 (9), 155 (100), 149 (4), 91 (93), 77 (3), 65 (13); HRMS found 332.046978 ($M^+$); calc. for $C_{15}H_{12}N_2O_5S$ 332.046693.

**3-Cyanomethyl-2-nitrophenyl toluene-4-sulfonate (7.6)**: oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 2.48 (s, 3H), 3.78 (s, 2H), 7.37 (AA'XX', 2H), 7.53 (dd, 1H, J=7.8, J=1.8), 7.57 (dd, 1H, J=7.8, J=1.8), 7.60 (dd, 1H, J=7.8, J=7.8), 7.76 (AA'XX', 2H); MS EI 70eV m/z (%): 332 ($M^+$, 0.2), 309 (0.1), 302 (0.3), 289 (0.2), 268 (9), 251 (1), 155 (100), 139 (2), 132 (5), 91 (87), 77 (3), 65 (12), 51 (3); HRMS found 332.046316 ($M^+$); calc. for $C_{15}H_{12}N_2O_5S$ 332.046693.

**3-Nitro-2-(toluene-4-sulfonylmethyl)phenyl toluene-4-sulfonate (8.2)**: mp 170-1°C (AcOEt); $^1$H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H), 2.50 (s, 3H), 4.90 (s, 2H), 7.20 (AA'XX', 2H), 7.40 (dd, 1H, J=8.3, J=1.3), 7.40 (AA'XX', 2H), 7.48 (AA'XX', 2H), 7.50 (dd, 1H, J=8.3, J=8.3), 7.75 (AA'XX', 2H), 7.93 (dd, 1H, J=8.3, J=1.3); MS EI 70eV m/z (%): 461 ($M^+$, 1.5), 443 (0.1), 431 (0.4), 415 (0.2), 381 (0.4), 306 (76), 155 (100), 139 (12), 91 (85), 77 (6), 65 (10); HRMS found 461.061298 ($M^+$); calc. for $C_{21}H_{19}NO_7S_2$ 461.060295.

**5-Nitro-2-(toluene-4-sulfonylmethyl)phenyl toluene-4-sulfonate (8.4)**: oil; $^1$H NMR (500 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.43 (s, 3H), 4.31 (s, 2H), 7.13 (AA'XX', 2H), 7.32 (AA'XX', 2H), 7.41 (AA'XX', 2H), 7.60 (d, 1H, J=8.5), 7.64 (AA'XX', 2H), 7.69 (d, 1H, J=2.3), 8.04 (dd, 1H, J=8.5, J=2.3); MS EI 70eV m/z (%): 461 ($M^+$, 1.5), 306 (90), 290 (14), 276 (4), 242 (8), 156 (100), 139 (10), 129 (5), 91 (95), 77 (8), 65 (15), 51 (5); HRMS found 461.060388 ($M^+$); calc. for $C_{21}H_{19}NO_7S_2$ 461.060295.

**3-Nitro-4-(toluene-4-sulfonylmethyl)phenyl toluene-4-sulfonate (8.6)**: mp 155-6°C (AcOEt); $^1$H NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.48 (s, 3H), 4.85 (s, 2H), 7.27 (AA'XX', 2H), 7.32 (dd, 1H, J=8.5, J=2.5), 7.38 (AA'XX', 2H), 7.43 (d, 1H, J=8.5), 7.52 (AA'XX', 2H), 7.58 (d, 1H, J=2.5), 7.74 (AA'XX', 2H); MS EI 70eV m/z (%): 461 ($M^+$, 0.9), 431 (0.1), 397 (0.3), 381 (0.17), 306 (85), 276 (3), 225 (2), 155 (100), 139 (7), 91 (73), 77 (4), 65 (12), 51 (3); HRMS found 461.061298 ($M^+$); calc. for $C_{21}H_{19}NO_7S_2$ 461.060295.

**5-Nitro-2-[1-(phenylsulfonyl)ethyl]phenyl toluene-4-sulfonate (9.4)**: mp 143-4°C (AcOEt); $^1$H NMR (500 MHz, $CDCl_3$) δ 1.64 (d, 3H, J=7.1), 2.50 (s, 3H), 4.74 (q, 1H, J=7.1), 7.39-7.61 (m, 8H), 7.72 (AA'XX', 2H), 7.87 (d, 1H, J=8.7), 8.16 (ddd, 1H, J=8.7, J=2.3, J=0.4); MS EI 70eV m/z (%): 461 ($M^+$, 0.1), 320 (80), 165 (4),

155 (100), 139 (3), 125 (3), 91 (67), 77 (13), 65 (13), 51 (4); HRMS (LSIMS) found 462.067719 ($M+H^+$); calc. for $C_{21}H_{20}NO_7S_2$ 462.068120.

**3-Nitro-4-[1-(phenylsulfonyl)ethyl]phenyl toluene-4-sulfonate (9.6)**: Not obtained in a pure state. Following data obtained from the mixture of **9.6** and **9.4**: $^1H$ NMR (200 MHz, $CDCl_3$)δ 1.77 (d, 3H, J=7.0), 2.49 (s, 3H), 5.373 (q, 1H, J=7.0), 7.35 (dd, 1H, J=8.7, J=2.5), 7.35-7.50 (m, 5H), 7.58-7.64 (m, 3H), 7.74 (AA'XX', 2H), 7.77 (d, 1H, J=8.7); MS LSIMS (NBA) m/z (%): 945 ($2M+Na^+$, 1.3), 923 ($2M+H^+$, 1.3), 615 (NBA+M+$H^+$, 1.8), 484 ($M+Na^+$, 17), 462 ($M+H^+$, 18), 391 (3), 320 (75), 166 (12), 155 (53), 120 (14), 107 (30), 91 (47); HRMS (LSIMS) found 462.068373 ($M+H^+$); calc. for $C_{21}H_{20}NO_7S_2$ 462.068120.

**2-Dichloromethyl-3-nitrophenyl toluene-4-sulfonate (10.2)**: Not obtained in a pure state. Following data obtained from the mixture of **10.2** and **2**: $^1H$ NMR (200 MHz, $CDCl_3$) 2.49 (s, 3H), 7.04 (s, 1H), 7.42 (AA'XX', 2H), 7.58 (dd, 1H, J=8.2, J=8.2), 7.69 (dd, 1H, J=8.2, J=1.6), 7.80 (dd, 1H, J=8.2, J=1.6), 7.90 (AA'XX', 2H); MS EI 70eV m/z (%): 375 ($M^+$, 1.2), 340 (1.2), 304 (0,5), 185 (13), 155, 91; HRMS found 374.973043 ($M^+$); calc. for $C_{14}H_{11}Cl_2NO_5S$ 374.973500.

**2-Dichloromethyl-5-nitrophenyl toluene-4-sulfonate (10.4)**: oil; $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.50 (s, 3H), 6.85 (s, 1H), 7.42 (AA'XX', 2H), 7.83 (AA'XX', 2H), 7.98 (d, 1H, J=2.2), 8.09 (d, 1H, J=8.7), 8.22 (dd, 1H, J=8.7, J=2.2); MS EI 70eV m/z (%): 375 ($M^+$, 1.4), 340 (1.3), 327 (2.3), 185 (2.5), 155 (100), 139 (3), 111 (2), 91 (63), 75 (2.5), 65 (8); HRMS found 374.973148 ($M^+$); calc. for $C_{14}H_{11}Cl_2NO_5S$ 374.97350.

**4-Dichloromethyl-3-nitrophenyl toluene-4-sulfonate (10.6)**: oil; $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.49 (s, 3H), 7.39 (AA'XX', 2H), 7.46 (dd, 1H, J=8.8, J=2.5), 7.51 (s, 1H), 7.62 (d, 1H, J=2.5), 7.77 (AA'XX', 2H), 8.16 (d, 1H, J=8.8); MS EI 70eV m/z (%): 375 ($M^+$, 0.1), 340 (0.2), 304 (0.15), 291 (0.2), 263 (0.15), 155 (99), 139 (18), 91 (100), 65 (38), 51 (6); HRMS found 374.973148 ($M^+$); calc. for $C_{14}H_{11}Cl_2NO_5S$ 374.97350.

**2-Cyanomethyl-3-nitrophenyl toluene-4-sulfonate (11.2)**: oil; $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.50 (s, 3H), 3.95 (s, 2H), 7.43 (AA'XX', 2H), 7.56 (dd, 1H, J=8.3, J=7.7), 7.59 (dd, 1H, J=8.3, J=1.9), 7.84 (AA'XX', 2H), 8.07 (dd, 1H, J=7.7, J=1.9); MS EI 70eV m/z (%): 332 ($M^+$, 12), 268 (2), 155 (100), 91 (96), 65 (12); HRMS found 332.049626 ($M^+$); calc. for $C_{15}H_{12}N_2O_5S$ 332.046693.

**2-Cyanomethyl-5-nitrophenyl toluene-4-sulfonate (11.4)**: oil; $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.52 (s, 3H), 3.85 (s, 2H), 7.44 (AA'XX', 2H), 7.77 (d, 1H, J=8.5), 7.79 (d, 1H, J=2.4), 7.81 (AA'XX', 2H), 8.21 (dd, 1H, J=8.5, J=2.4); MS EI 70eV m/z (%): 332 ($M^+$, 8), 155 (100), 147 (3), 91 (98), 77 (4), 65 (16); HRMS found 332.047309 ($M^+$); calc. for $C_{15}H_{12}N_2O_5S$ 332.046693.

**4-Cyanomethyl-3-nitrophenyl toluene-4-sulfonate (11.6)**: oil; $^1H$ NMR (200 MHz, $CDCl_3$) δ 2.49 (s, 3H), 4.18 (s, 2H), 7.38 (AA'XX', 2H), 7.40 (dd, 1H, J=8.5, J=2.6), 7.71 (d, 1H, J=8.5), 7.75 (AA'XX', 2H), 7.82 (d, 1H, J=2.6); MS EI 70eV m/z (%): 332 ($M^+$, 5), 279 (14), 185 (13), 167 (44), 155 (87), 149 (97), 113 (13), 91 (100), 83 (9), 71 (22), 65 (19), 57 (25), 43 (15); HRMS found 332.046316 ($M^+$); calc. for $C_{15}H_{12}N_2O_5S$ 332.046693.

**4-Nitro-3-(toluene-4-sulfonylmethyl)phenyl toluene-4-sulfonate (12)**: mp 158-9°C (Hexane/AcOEt); $^1H$ NMR (200 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.47 (s, 3H), 4.82 (s, 2H), 7.18-7.23 (m, 2H), 7.28 (AA'XX', 2H), 7.38 (AA'XX', 2H), 7.52 (AA'XX', 2H), 7.77 (AA'XX', 2H), 7.91-7.95 (m, 1H); MS EI 70eV m/z (%): 461 ($M^+$, 4), 415 (6), 306 (58), 276 (5), 155 (77), 139 (16), 134 (10), 91 (100), 77 (4), 65 (15); HRMS found 461.060388 ($M^+$); calc. 461.06029.

**4-Nitro-3-[1-(phenylsulfonyl)ethyl]phenyl toluene-4-sulfonate (13)**: mp 140-2°C (Hexane/AcOEt); $^1H$ NMR (200 MHz, $CDCl_3$) δ 1.64 (d, 3H, J=7.0), 2.47 (s, 3H), 5.36 (q, 1H, J=7.0), 7.23 (dd, 1H, J=8.9, J=2.6), 7.38 (d, 1H, J=2.6), 7.37-7.50 (m, 4H), 7.56-7.66 (m, 3H), 7.78 (d, 1H, J=8.9), 7.79 (AA'XX', 2H); MS EI 70eV m/z (%): 461 ($M^+$, 0.4), 415 (0.5), 320 (100), 290 (3), 155 (49), 135 (6), 125 (4), 91 (50), 77 (7), 65 (7); HRMS found

461.060388 ($M^+$); calc. for $C_{21}H_{19}NO_7S_2$ 461.060296.

**3-Dichloromethyl-4-nitrophenyl toluene-4-sulfonate (14)**: mp 78-9°C (Hexane/AcOEt); $^1H$ NMR (200 MHz, $CDCl_3$) δ 2.47 (s, 3H), 7.32 (dd, 1H, J=9.0, J=2.6), 7.38 (AA'XX', 2H), 7.48 (s, 1H), 7.61 (d, 1H, J=2.6), 7.75 (AA'XX', 2H), 8.02 (d, 1H, J=9.0); MS EI 70eV m/z (%): 375 ($M^+$, 3), 340 (2), 155 (100), 150 (5), 91 (60), 65 (8); HRMS found 374.973148 ($M^+$); calc. for $C_{14}H_{11}Cl_2NO_5S$ 374.973499.

**3-Dibromomethyl-4-nitrophenyl toluene-4-sulfonate (15)**: mp 109-10°C (Hexane/AcOEt); $^1H$ NMR (200 MHz, $CDCl_3$) δ 2.46 (s, 3H), 7.27 (dd, 1H, J=9.0, J=2.6), 7.38 (AA'XX', 2H), 7.38 (s, 1H), 7.66 (d, 1H, J=2.6), 7.75 (AA'XX', 2H), 7.95 (d, 1H, J=9.0); MS EI 70eV m/z (%): 464 ($M^+$, 0.7), 384 (7), 155 (100), 150 (22), 91 (85), 65 (10); HRMS found 462.87209 ($M^+$); calc. for $C_{14}H_{11}Br_2NO_5S$ 462.872466.

**3-Cyanomethyl-4-nitrophenyl toluene-4-sulfonate (16)**: oil; $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.48 (s, 3H), 4.14 (s, 2H), 7.28-7.30 (m, 2H), 7.39 (AA'XX', 2H), 7.76 (AA'XX', 2H), 8.18-8.20 (m, 1H); MS EI 70eV m/z (%): 332 ($M^+$, 5), 316 (0.2), 302 (0.2), 268 (0.3), 225 (0.1), 192 (0.1), 178 (0.3), 161 (1), 155 (90), 147 (2), 91 (100), 77 (3), 65 (20), 51 (3); HRMS found 332.046978 ($M^+$); calc. for $C_{15}H_{12}N_2O_5S$ 332.0466935.

**Chlorobis(toluene-4-sulfonyl)methane (17)**: mp 167-8°C ($CHCl_3$); $^1H$ NMR (200 MHz, $CDCl_3$) δ 2.48 (s, 6H), 5.54 (s, 1H), 7.40 (AA'XX', 4H), 7.91 (AA'XX', 4H); MS EI 70eV m/z (%): 358 ($M^+$, 3), 294 (0.3), 203 (1.5), 167 (1), 155 (100), 139 (21), 91 (68); HRMS found 358.010407 ($M^+$); calc. for $C_{15}H_{15}ClO_4S_2$ 358.010030.

**5-[Chloro(toluene-4-sulfonyl)methyl]-2-nitrophenyl toluene-4-sulfonate (19)**: mp 126-8°C (AcOEt); $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.46 (s, 3H), 2.47 (s, 3H), 5.67 (s, 1H), 7.36 (AA'XX', 4H), 7.50 (d, 1H, J=1.9), 7.51 (dd, 1H, J=8.6, J=2.0), 7.67 (AA'XX', 2H), 7.77 (AA'XX', 2H), 7.88 (d, 1H, J=8.0); MS EI 70eV m/z (%): 495 ($M^+$, 3), 461 (1), 340 (45), 306 (4), 294 (10), 276 (2), 260 (4), 195 (3), 155 (38), 139 (100), 91 (50), 77 (6), 65 (13); HRMS found 495.021397 ($M^+$); calc. for $C_{21}H_{18}ClNO_7S_2$ 495.021323.

**3-Amino-2,3-bis(4-chlorophenoxy)acrylonitrile (20)**: $^1H$ NMR (200 MHz, $CDCl_3$) δ 4.7 (s, 2H), 4.86 (s, 2H), 6.89-6.98 (m, 4H), 7.25-7.36 (m, 4H); $^{13}C$ NMR (50.3 MHz, $CDCl_3$) δ 64.33, 102.19, 115.43, 116.25, 116.76, 127.51, 128.50, 129.74, 129.79, 145.70, 154.31, 155.61; MS EI 70eV m/z (%): 334 ($M^+$, 35), 207 (80), 190 (4), 179 (10), 172 (51), 153 (100), 144 (6), 128 (12), 111 (24), 99 (7), 75 (18); HRMS found 334.026896 ($M^+$); calc. for $C_{16}H_{12}Cl_2N_2O_2$ 334.027583.

**3-[(4-Chlorophenoxy)cyanomethyl]-4-nitrophenyl toluene-4-sulfonate (21)**: mp 135-6°C ($CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.45 (s, 3H), 6.50 (s, 1H), 6.99 (AA'XX', 2H), 7.34 (AA'XX', 2H), 7.37 (AA'XX', 2H), 7.42 (dd, 1H, J=9.0, J=2.6), 7.62 (d, 1H, J=2.6), 7.75 (AA'XX', 2H), 8.26 (d, 1H, J=9.0); MS EI 70eV m/z (%): 458 ($M^+$, 3), 441 (0.2), 423 (0.3), 415 (0.2), 377 (0.2), 363 (1), 331 (30), 307 (5), 155 (100), 152 (7), 127 (13), 108 (9), 99 (10), 91 (92), 65 (17), 57 (7); HRMS found 458.033908 ($M^+$); calc. for $C_{21}H_{15}ClN_2O_6S$ 458.03393.

**Hydrolysis of the VNS products, general procedure.**

To a stirred solution of VNS product (0,4 mmol) in THF/MeOH/THF 1/1/1 v/v (2mL) a solution of NaOH (4 mmol, 0,16 g) in $H_2O$ (1 mL) was added and the reaction mixture was stirred at room temperature and then diluted (2%) hydrochloric acid (10 mL) was added. The product was extracted with methylene chloride (20 mL) the extract washed, dried and the solvent evaporated. The solid products were recrystallized.

The VNS products mixture **10** was hydrolyzed as above, then the products were separated using column chromatography (hexane/AcOEt) and additional procedures for **28.4** ($SiO_2$, hexane/$CH_2Cl_2$) to remove 3-nitrophenol and for **28.2** (dissolved in 10% NaOH, washed with $CH_2Cl_2$ then acidified and isolated conventionally) to separate from unreacted chloromethyl tolyl sulfone.

**2-Nitro-5-(toluene-4-sulfonylmethyl)phenol (22.4)**: oil, $^1H$ NMR (200 MHz, $CDCl_3$) δ 2.45 (s, 3H), 4.30 (s,

2H), 6.78 (dd, 1H, J=8.6, J=1.9), 6.91 (d, 1H, J=1.8), 7.31 (AA'XX', 2H), 7.59 (AA'XX', 2H), 8.02 (d, 1H, J=8.6), 10.5 (s, 1H); MS EI 70eV m/z (%): 307 ($M^+$, 35), 243 (15), 155 (95), 152 (100), 139 (10), 135 (55), 122 (37), 107 (12), 94 (25), 91 (90), 77 (12), 65 (20), 51 (12); HRMS found 307.052044 ($M^+$); calc. for $C_{14}H_{13}NO_5S$ 307.051444.

**2-Nitro-3-(toluene-4-sulfonylmethyl)phenol (22.6)**: oil, $^1$H NMR (200 MHz, acetone-$d_6$ + $D_2O$) δ 2.45 (s, 3H), 4.65 (s, 2H), 6.81 (dd, 1H, J=7.6, J=1.3), 7.17 (dd, 1H, J=8.3, J=1.3), 7.33 (dd, 1H, J=8.3, J=7.6), 7.43 (AA'XX', 2H), 7.62 (AA'XX', 2H); MS EI 70eV m/z (%): 307 ($M^+$, 8), 261 (5), 186 (6), 155 (10), 152 (100), 139 (5), 135 (8), 121 (7), 106 (10), 94 (10), 91 (36),78 (11); HRMS found 307.051434 ($M^+$); calc. for $C_{14}H_{13}NO_5S$ 307.051444.

**5-Nitro-2-(toluene-4-sulfonylmethyl)phenol (23.4)**: mp 243°C dec. (MeOH); $^1$H NMR (200 MHz, DMSO) δ 2.38 (s, 3H), 4.64 (s, 2H), 7.34-7.39 (m, 3H), 7.50 (d, 1H, J=2.4), 7.55 (AA'XX', 2H), 7.65 (dd, 1H, J=8.4, J=2.4), 10.6 (s, 1H); MS EI 70eV m/z (%): 307 ($M^+$,18), 152 (100), 139 (52), 122 (18), 106 (16), 94 (57), 91 (42), 77 (26), 65 (27), 51 (22); HRMS found 307.050519 ($M^+$); calc. for $C_{14}H_{13}NO_5S$ 307.051444.

**3-Nitro-4-(toluene-4-sulfonylmethyl)phenol (23.6)**: mp 192-4°C (MeOH); $^1$H NMR (200 MHz, acetone-$d_6$) δ 2.42 (s, 3H), 4.90 (s, 2H), 7.07 (dd, 1H, J=8.4, J=2.5), 7.19 (d, 1H, J=8.4), 7.38 (AA'XX', 2H), 7.44 (d, 1H, J=2.4), 7.54 (AA'XX', 2H), 9.6 (s, 1H); MS EI 70eV m/z (%): 307 ($M^+$, 4), 152 (100), 139 (6), 135 (6), 121 (7), 105 (7), 94 (73), 91 (31), 77 (24), 65 (36), 51 (24); HRMS found 307.051129 ($M^+$); calc. for $C_{14}H_{13}NO_5S$ 307.051444.

**5-Nitro-2-[1-(toluene-4-sulfonyl)ethyl]phenol (24.4)**: mp 215-7°C dec. (AcOEt); $^1$H NMR (200 MHz, DMSO-$d_6$) δ 1.60 (d, 3H, J=7.3), 4.93 (q, 1H, J=7.3), 7.44 (d, 1H, J=2.3), 7.48-7.73 (m, 7H), 10,7 (s, 1H); MS EI 70eV m/z (%): 307 ($M^+$, 3), 166 (100), 150 (4), 142 (6), 135 (7), 125 (6), 120 (17), 108 (29), 102 (16), 91 (34), 77 (36), 65 (32), 51 (24); HRMS found 307.050824 ($M^+$); calc. for $C_{14}H_{13}NO_5S$ 307.051444.

**4-Nitro-3-(toluene-4-sulfonylmethyl)phenol (25)**: mp 205-6°C (AcOEt); $^1$H NMR (200 MHz, acetone-$d_6$/$CDCl_3$) δ 2.44 (s, 3H), 4.67 (s, 2H), 6.87 (d, 1H, J=2.7), 6.96 (dd, 1H, J=9.0, J=2.7), 7.31 (AA'XX', 2H), 7.57 (AA'XX', 2H), 7.96 (d, 1H, J=9.0); MS EI 70eV m/z (%): 307 ($M^+$, 0.3), 277 (3), 261 (52), 155 (13), 152 (100), 139 (15), 121 (10), 107 (8), 94 (21), 91 (45), 80 (7), 65 (17); HRMS found 307.051129 ($M^+$); calc. for $C_{14}H_{13}NO_5S$ 307.051444.

**3-Dichloromethyl-4-nitrophenol (26)**: oil, $^1$H NMR (200 MHz, acetone-$d_6$) δ 7.08 (dd, 1H, J=9.1, J=2.7), 7.60 (d, 1H, J=2.7), 7.77 (s, 1H), 8.06 (d, 1H, J=9.1), 10.1 (s, 1H); MS EI 70eV m/z (%): 221 ($M^+$, 10), 204 (10), 186 (53), 176 (6), 158 (48), 155 (41), 150 (100), 139 (12), 128 (25), 120 (22), 115 (11), 111 (16), 105 (21), 99 (8), 91 (55), 80 (19), 75 (20), 65 (22), 51 (29); HRMS found 220.9646 ($M^+$); calc. for $C_7H_5Cl_2NO_3$ 220.964648.

**(5-Hydroxy-2-nitrophenyl)acetonitrile (27)**: mp 185°C (MeOH); $^1$H NMR (200 MHz, acetone-$d_6$) δ 4.30 (s, 2H), 7.02 (dd, 1H, J=9.0, J=2.7), 7.17 (d, 1H, J=2.7), 8.16 (d, 1H, J=9.0); MS EI 70eV m/z (%): 178 ($M^+$, 32), 161 (100), 134 (45), 106 (32), 77 (54), 65 (20), 51 (34); HRMS found 178.037158 ($M^+$); calc. for $C_8H_6N_2O_3$ 178.037842.

**2-Hydroxy-6-nitrobenzaldehyde (28.2)**: mp 52-53°C (AcOEt) (lit.[23] 54-55°C); $^1$H NMR (200 MHz, $CDCl_3$) 7.30 (dd, 1H, J=8.0, J=1.6), 7.56(dd, 1H, J=7.9, J=1.6), 7.64 (dd, 1H, J=8.0, J=7.9), 10.34 (s, 1H), 12.11 (s, 1H); MS EI 70eV m/z (%): 167 ($M^+$, 30), 149 (52), 137 (100), 120 (29), 109 (16), 92 (31), 81 (46), 75 (6), 65 (20), 53 (12); HRMS found 167.02141 ($M^+$); calc. for $C_7H_5NO_4$ 167.02186.

**2-Hydroxy-4-nitrobenzaldehyde (28.4)**: mp 133-135°C (hexane/$CH_2Cl_2$) (lit.[24] 134-135°C); $^1$H NMR (200 MHz, acetone-$d_6$) 7.77 (d, 1H, J=2.1), 7.85 (dd, 1H, J=8.4, J=2.1), 8.08 (d, 1H, J=8.4), 10.28 (s, 1H); MS EI 70eV m/z (%): 167 ($M^+$, 100), 149 (8), 136 (4), 121 (12), 108 (4), 103 (7), 93 (6), 81 (5), 75 (6), 65 (46), 53 (6). HRMS

found 167.02125 ($M^+$); calc. for $C_7H_5NO_4$ 167.02186.

**4-Hydroxy-2-nitrobenzaldehyde (28.6)**: mp 133-135°C ($CH_2Cl_2$) (lit.[25] 136-137°C); $^1H$ NMR (200 MHz, acetone-$d_6$) δ 7.29 (ddd, 1H, J=8.5, J=2.4, J=0.6), 7.44 (d, 1H, J=2.4), 7.91 (d, 1H, J=8.5), 10.13 (d, 1H, J=0.6); IR(KBr): 3235, 1672, 1605, 1568, 1531, 1450,1358 $cm^{-1}$; MS EI 70eV m/z (%): 167 ($M^+$, 4), 150 (2), 137 (100), 120 (25), 109 (15), 92 (30), 81 (33), 69 (16), 53 (12); HRMS found 167.02172; calc. for $C_7H_5NO_4$ 167.02186.

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## REFERENCES

1. Mąkosza, M; Winiarski, J. *Acc. Chem. Res.* **1987**, *20*, 282; Mąkosza, M. *Chimia* **1994**, *48*, 499.
2. Mąkosza, M.; Ludwiczak, S. *J. Org. Chem.* **1984**, *49*, 4562.
3. Goliński, J.; Mąkosza, M. *Synthesis* **1978**, 823.
4. Goliński, J.; Mąkosza, M. *Tetrahedron Lett.* **1978**, 3495.
5. Mąkosza, M.; Winiarski, J. *J. Org. Chem.* **1984**, *49*, 1494.
6. Mąkosza, M.; Goliński, J.; Baran, J. *J. Org. Chem.* **1984**, *49*, 1488.
7. Mąkosza, M. Glinka, T.; Kinowski, J. *Tetrahedron* **1984**, *40*, 1863.
8. Mąkosza, M.; Danikiewicz, W.; Wojciechowski, K. *Liebigs Ann. Chem.* **1988**, 203.
9. Mudryk, B.; Mąkosza, M. *Tetrahedron* **1988**, *44*, 209.
10. Mąkosza, M.; Owczarczyk, Z. *J. Org. Chem.* **1989**, *54*, 5094.
11. Wojciechowski, K.; Mąkosza, M. *Synthesis* **1992**, 571.
12. Mąkosza, M.; Sypniewski, M. *Phosphorus, Sulfur and Silicon* **1993**, *80*, 89.
13. Mąkosza, M.; Hoser H. *Heterocycles* **1994**, *37*, 1701.
14. Mąkosza, M.; Stalewski, J. *Tetrahedron* **1995**, *51*, 7263.
15. Harino, J.P.; Hurt, C. *Synth. Commun.* **1994**, *24*, 839.
16. Mąkosza, M.; Wenall, M.; Goliński, J.; Kinowski, A. *Bull. Pol. Acad. Chem.* **1985**, *33*, 427.
17. For example: Paquette, L.A.; Wittenbrok, L.S. *J. Am. Chem. Soc.* **1968**, *90*, 6790
18. Contrary to the *imino* form of the dimer presented in the ref. 8 we surely found the *enamino* structure for compound **20.**
19. Ostrowski, S.; Mąkosza, M. *Tetrahedron* **1988**, *44*, 1721; Mąkosza, M.; Winiarski, J. *J Org. Chem.* **1984**, *49*, 1494; Mąkosza, M.; Winiarski, J. *Chem. Lett.* **1984**, 1625.
20. Grochowski, E.; Eckstein, Z. *Bull. Acad. Pol. Sci., Ser. Sci. Chim.* **1963**, *11*, 443.
21. Suttle, A.N.; Williams, A. *J. Chem. Soc. Perkin Trans. 2* **1983**, 1563-67.
22. Bell, F. *J. Chem. Soc.* **1930**, 1981-84.
23. Ashley, J.N.; Perkin, W.H.; Robinson, R. *J. Chem. Soc.* **1930**, 382, 394.
24. Seggeser, J.R.; Calvin, M. *J. Am. Chem. Soc.* ***1942***, 64, *825.*
25 Suvorov, N.N.; Fedotova, M.W.; Orlova, L.M.; Ogareva, O.B. *J. Gen.Chem. USSR (Engl.Transl.)* **1962**, *32*, 2325. Different data (mp 104°C, IR(KBr): 3420, 2922, 2852, 1736, 1604, 1532, 1464, 1344 $cm^{-1}$) were also reported for the compound claimed to be 4-hydroxy-2-nitrobenzaldehyde: Kaupp, G.; Shmeyers, J. *J. Org. Chem.* **1995**, *60*, 5494.

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