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Selective introduction of sulfo groups into aromatic nitro compounds

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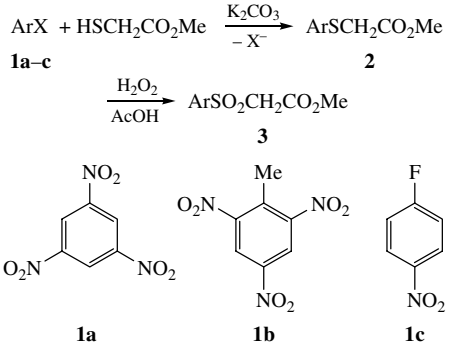
A new reaction has been found, *viz.* oxidative destruction of nitro-substituted sulfones $ArSO_2CH_2CO_2Me$ to give sulfonic acids $ArSO_3H$ on treatment with 70% HNO_3; in addition, di(arylsulfonyl)furoxans are formed as by-products.

The direct sulfonation of aromatic nitro compounds involves considerable difficulties where the benzene ring has two or more nitro groups as substituents or where sulfonation to a position deactivated by a nitro group (*e.g.*, a *para* position) is required.

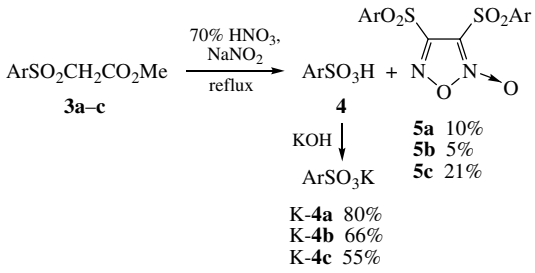
We have found a method for the selective introduction of sulfo groups into aromatic nitro compounds, where nucleophilic substitution activated by a nitro group is used at the first stage instead of hindered electrophilic substitution.



Scheme 1

The nucleofuge (NO_2, Hal) located at the benzene-ring position to which an SO_3H group needs to be introduced in the molecule of nitro compound **1** is replaced on treatment with an ester of thioglycolic acid in the presence of K_2CO_3 (in N-MP or DMF) to give *S*-arylthioglycol ester **2**. Corresponding sulfones **3** were obtained by the oxidation of sulfides **2** with aqueous H_2O_2 in acetic acid. The following examples are provided: 1,3,5-trinitrobenzene (**1a**, one NO_2 group is replaced), 2,4,6-trinitrotoluene (**1b**, only *ortho*-NO_2 is replaced) and *p*-fluoronitrobenzene (**1c**, the fluorine atom is replaced) (Scheme 1).†

We have found a new reaction (Scheme 2): the heating of sulfones **3** with 70% HNO_3 in the presence of a catalytic amount of $NaNO_2$ results in the oxidative destruction of sulfones **3** to give corresponding nitro-substituted arenesulfonic acids **4** isolated as stable potassium salts (K-**4**). The corresponding di(arylsulfonyl)furoxans **5** are also formed as by-products (Scheme 2).‡ Although Farrar[5] obtained di(arylsulfonyl)furoxans as main products of the treatment of arylsulfonylacetic acids with a mixture of HNO_3 and AcOH, they were formed in minor amounts in our case with the predominant formation of arylsulfo acids.



Scheme 2

The structure of arenesulfonic acids **4** was determined based on ^{1}H NMR data and elementary analyses of their potassium salts (K-**4**). In the case of furoxans **5**, the structure of compound **5a** was determined by X-ray diffraction analysis, while those of compounds **5b**,**c** were determined similarly to compound **5a** as well as using ^{1}H NMR data and elementary analyses.

According to X-ray diffraction data obtained from a crystal of compound **5a**,§ though the molecule has the C_1 point group, it occupies a special position, *viz.*, the C_2 axis passing through the middle of the C(1)–C(1A) bond; this leads to statistic disorder of the O(1) and O(2) atoms. Note that this disorder is not symmetry-imposed and persists also in noncentrosymmetric orthorhombic as well as in monoclinic space groups (treated as merohedral twins). In the crystal, the phenyl ring is almost

† Previously, we have already described the synthesis of sulfide **2b** and sulfone **3b** from 2,4,6-trinitrotoluene **1b**.[1] Sulfides **2a**,**c** and sulfones **3a**,**c** were obtained similarly from nitro compounds **1a**,**c**, respectively.

^{1}H NMR spectra were recorded with a Bruker AM-300 instrument. The chemical shifts in [$^2H_6$]DMSO are reported relative to TMS. The melting points of the resulting compounds were determined on a Boetius hot stage according to Koffler (the heating rate was 4 K min^{-1}).

For **2a**: yield 78%; mp 93–95 °C (from EtOH). ^{1}H NMR, δ: 8.60 (t, 1H, ^4J 1.9 Hz), 8.49 (d, 2H, ^4J 1.9 Hz), 4.30 (s, 2H), 3.69 (s, 3H). Found (%): C, 39.48; H, 2.79; N, 9.96; S, 11.49. Calc. for $C_9H_8N_2O_6S$ (%): C, 39.71; H, 2.96; N, 10.29; S, 11.78.

For **2c**: yield 85%; mp 51–52 °C (from MeOH) (lit.,[2] mp 50.9–52.4 °C). ^{1}H NMR, δ: 8.15 (d, 2H, ^3J 5.8 Hz), 7.52 (d, 2H, ^3J 5.8 Hz), 4.15 (s, 2H), 3.66 (s, 3H).

For **3a**: yield 72%; mp 81–83 °C (from AcOH–H_2O, 3:2). ^{1}H NMR, δ: 9.15 (t, 1H, ^4J 2.1 Hz), 9.03 (d, 2H, ^4J 2.1 Hz), 5.12 (s, 2H), 3.62 (s, 3H). Found (%): C, 35.75; H, 2.69; N, 8.93; S, 10.45. Calc. for $C_9H_8N_2O_8S$ (%): C, 35.53; H, 2.65; N, 9.21; S, 10.54.

For **3c**: yield 86%; mp 127–129 °C (from MeOH) (lit.,[2] mp 128.7–130 °C). ^{1}H NMR, δ: 8.47 (d, 2H, ^3J 6.0 Hz), 8.20 (d, 2H, ^3J 6.0 Hz), 4.90 (s, 2H), 3.62 (s, 3H).

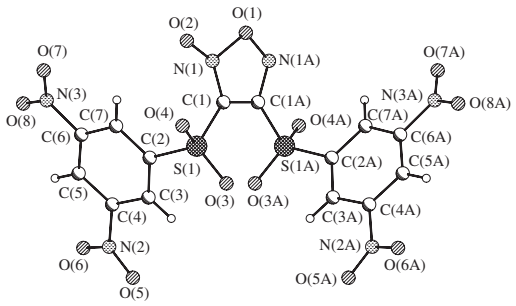


Figure 1 General view of **5a** molecule. The statistic disorder is omitted for clarity.

‡ *General procedure for the synthesis of potassium sulfonates*. Sulfone **3a–c** (1 g) was dissolved in 5 ml of 70% nitric acid and two or three crystals of $NaNO_2$ were added. The mixture was slowly heated with stirring; nitrogen oxides were evolved. The mixture was refluxed for 3 h. In the case of sulfones **3a** and **3c**, white precipitates were formed from the reaction mixture (furoxans **5a** or **5c**). After refluxing, the reaction mixture was quickly cooled. Furoxans **5a**,**c** were filtered off, washed with water and dried in air. Furoxan **5b** was obtained by pouring the reaction mixture into cold water. The white precipitate was filtered off and dried. The filtrates obtained after the separation of the furoxans were evaporated to dryness *in vacuo*. The residue was dissolved in EtOH, and a solution of an equimolar amount (with respect to compound **3**) of KOH in ethanol was added with stirring and cooling. The resulting precipitate of the potassium salt of sulfonic acid **4a–c** was filtered off and dried in air.

For K-**4a**:[3] yield 80%; mp 332–334 °C (from water). ^{1}H NMR, δ: 8.79 (t, 1H, ^4J 1.9 Hz), 8.63 (d, 2H, ^4J 1.9 Hz). Found (%, K as K_2SO_4 ash): C, 25.27; H, 1.08; N, 9.36; S, 10.92; K, 13.73. Calc. for $C_6H_3KN_2O_7S$ (%): C, 25.17; H, 1.06; N, 9.79; S, 11.20; K, 13.66.

For K-**4b**: yield 66%; mp 360 °C (from EtOH). ^{1}H NMR, δ: 8.78 (d, 1H, ^4J 2.1 Hz), 8.63 (d, 1H, ^4J 2.1 Hz), 8.63 (d, 1H, ^4J 2.1 Hz), 2.71 (s, 3H). Found (%): C, 28.35; H, 1.70; N, 9.36; S, 10.20; K, 13.45. Calc. for $C_7H_5KN_2O_7S$ (%): C, 28.00; H, 1.68; N, 9.33; S, 10.68; K, 13.02.

For K-**4c**: yield 55%; mp 360 °C (from EtOH) (lit.,[4] mp 328 °C). ^{1}H NMR, δ: 8.21 (d, 2H, ^3J 6.1 Hz), 7.86 (d, 2H, ^3J 6.1 Hz). Found (%): C, 30.08; H, 1.71; N, 5.64; S, 13.31; K, 16.38. Calc. for $C_6H_4KNO_5S$ (%): C, 29.87; H, 1.67; N, 5.81; S, 13.29; K, 16.21.

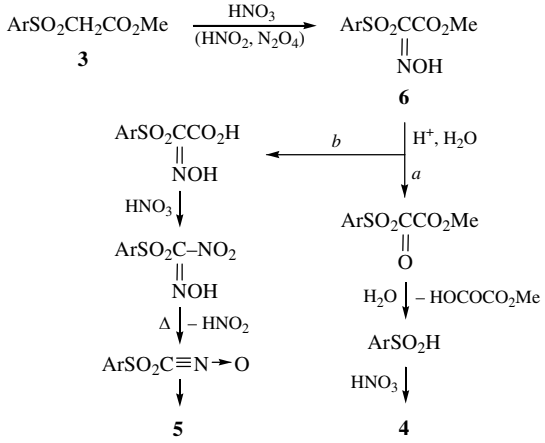
For **5a**: yield 0.092 g (10%); mp 250–252 °C. ^{1}H NMR, δ: 9.29 (t, 1H, ^4J 2.0 Hz), 9.19 (t, 1H, ^4J 2.0 Hz), 9.10 (d, 2H, ^4J 1.9 Hz), 8.88 (d, 2H, ^4J 1.9 Hz). Found (%): C, 30.81; H, 1.11; N, 15.33; S, 11.61. Calc. for $C_{14}H_6N_6O_{14}S_2$ (%): C, 30.78; H, 1.11; N, 15.38; S, 11.74.

For **5b**: yield 0.035 g (5%); mp 213–215 °C (from 1,2-dichloroethane). ^{1}H NMR, δ: 9.28 (d, 1H, ^4J 2.0 Hz), 9.21 (d, 1H, ^4J 2.0 Hz), 9.12 (d, 1H, ^4J 2.0 Hz), 9.02 (d, 1H, ^4J 2.0 Hz), 2.75 (s, 3H), 2.65 (s, 3H). Found (%): C, 33.70; H, 1.79; N, 14.39; S, 11.49. Calc. for $C_{16}H_{10}N_6O_{14}S_2$ (%): C, 33.46; H, 1.75; N, 14.63; S, 11.16.

For **5c**: yield 0.184 g (21%); mp 239–241 °C. ^{1}H NMR, δ: 8.62 (m, 4H), 8.38 (d, 2H, ^3J 5.9 Hz), 8.22 (d, 2H, ^3J 5.9 Hz). Found (%): C, 38.57; H, 1.72; N, 12.30; S, 13.95. Calc. for $C_{14}H_8N_4O_{10}S_2$ (%): C, 38.85; H, 1.77; N, 12.28; S, 14.05.

§ The crystals of compound **5a** (M = 264.24) are orthorhombic, space group *Pbcn*, at 100 K: a = 27.548(3), b = 12.0893(8), c = 12.3106(9) Å, V = 2481.5(3) Å^3, Z = 4 (Z' = 0.5), d_{calc} = 1.845 g cm^{-3}, (MoKα) = 3.66 cm^{-1}, F(000) = 1104. The intensities of 9194 reflections were measured with a Bruker SMART APEX2 CCD diffractometer [λ(MoKα) = 0.71072 Å, ω-scans, $2\theta < 58°$] and 2167 independent reflections [R_{int} = 0.0643] were used in further refinement. The structure was solved by the direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. Analysis of the Fourier synthesis revealed that the O(1) and O(2) atoms are disordered over two positions around two fold axis. The positions of hydrogen atoms were calculated geometrically. For compound **5a**, the refinement converged to wR_2 = = 0.0757 and GOF = 0.987 for all independent reflections [R_1 = 0.0389 was calculated against F for 1349 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS 5.0.

CCDC 666455 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2007.



Scheme 3

perpendicular to the furoxan ring, the dihedral angle being 77.8°. Such a mutual disposition of the rings results in the presence of a rather short intramolecular contact O(2)···O(4) [2.817(5) Å], which can lead to the observed disorder in the crystal. The nitro groups in compound **5a** are almost coplanar to the aryl ring, with the torsion angles O(5)N(2)C(4)C(3) and O(7)N(3)C(6)C(7) equal to 17°.

Analysis of the intermolecular contacts has revealed the presence of a rather rare SO_2···O_2N type of contact [O(5)···O(3) equal to 2.963(2) Å], as well as NO_2···π contact with the O(6)···C(3) distance equal to 3.178 Å.

The chemistry of the process requires an additional study; however, considering the fact that the oxidative destruction is initiated by $NaNO_2$ and nitrogen oxides are liberated during the reaction, it can be assumed that the primary step involves the nitrozation of the reactive methylene unit in sulfones **3** to give corresponding oximes **6** (Scheme 3). A possible variant that explains the formation of both arenesulfonic acids **4** and furoxans **5** is shown in Scheme 3.

Thus, the three examples above show the possibility of the selective introduction of sulfonic groups into the molecules of aromatic nitro compounds by means of nucleophilic replacement of a nitro group or a halogen substituent on treatment with an ester of thioglycolic acid, followed by oxidation of the resulting *S*-arylthioglycolic ester to the corresponding sulfone and oxidative destruction of the latter to give a nitro-substituted arenesulfonic acid. It should be noted that the use of nucleophilic substitution for introducing a sulfo group into an aromatic ring was known before.[6,7] However, this method is unsuitable for replacing a relatively weakly activated nucleofuge, as shown for trinitro derivatives **1a**,**b** with *meta*-arranged nitro groups: the nitro group in these compounds is not replaced even in dipolar aprotic solvents.

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