Nitration and bromination of *N*-(dimethylphenyl)methane-sulfonamides

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The orientation of the products of nitrosation:nitration and bromination of the methanesulfonamides of the six isomeric dimethylanilines have been established by ^{1}H NMR nuclear Overhauser experiments.

Keywords: dimethylanilines, sulfonamides, nitrosation: nitration, bromination

The aromatic methanesulfonamide group is an *ortho*/*para* directing group for electrophilic aromatic substitution.[1] When compared to the acetamido group, the toluene-*p*-sulfonamide group has been regarded as a more powerful directing group.[2] The nitration of the benzene-, toluene-*p*- and methane-sulfonamide derivatives of 2,6-dimethylaniline using sodium nitrite:nitric acid (nitrosation:nitration[3]) has been reported[4] to give good yields of the 4-nitro compounds free from isomeric impurities. This contrasts with the results of nitration of 2, 6-dimethylacetanilide using a nitric:sulfuric acid mixture which led to substitution at the 3-position.[5] These differences in orientation reflect mechanistic differences between these sets of conditions.[6] In the light of this we have examined the orientation of substitution in the nitrosation:nitration and bromination of the methanesulfonamides of the six isomeric dimethylanilines.

The methanesulfonamides were prepared by treatment of the dimethylaniline with methanesulfonyl chloride in pyridine. The orientation of substitution was established using nuclear Overhauser effect (nOe) enhancements based on irradiation of the sulfonamide NH and the aromatic methyl group signals in the ^{1}H NMR spectrum. The nitration products were also hydrolysed with sulfuric acid to give the known dimethylnitroanilines. The results of nitrosation:nitration using refluxing aqueous nitric acid and acetic acid mixtures containing sodium nitrite, are given in Table 1. The yields are reported in terms of crystallised products.

Whilst the nitrosation:nitration of the methane-sulfonamide of 2,6-dimethylaniline gave, as reported,[4] a high yield of the 4-nitro compound, nitration with a nitric:sulfuric acid mixture at room temperature overnight gave the 3,5-dinitro compound. Application of the nitrosation:nitration conditions to 2,6-dimethylacetanilide gave tarry material.

The bromination experiments were carried out using bromine in glacial acetic acid containing hydrobromic acid. The results are given in Table 2.

The orientation of the major substitution products was determined by the methanesulfonamide group. Many of the products crystallise more easily than those derived from the dimethylacetanilides suggesting that there may be circumstances in which it is preferable to use the substitution reactions of the sulfonamides rather than the acetanilides.

Techniques used: ^{1}H NMR spectroscopy, nuclear Overhauser effects.

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Table 1 Nitration of (dimethylpheny1)methanesulfonamides

Substrate	Product	Yield/%
(2,3-dimethylphenyl) methanesulfonamide	(2,3-dimethyl-4,6-dinitro phenyl)methanesulfonamide	70
(2,4-dimethylphenyl) methanesulfonamide	(2,4-dimethyl-6-nitrophenyl) methanesulfonamide	83
(2,5-dimethylphenyl) methanesulfonamide	(2,5-dimethyl-4,6,dinitrophenyl) methanesulfonamide	92
(2.6-dimethylphenyl) methanesulfonamide	(2,6-dimethyl-4-nitrophenyl) methanesulfonamide	84
(3,4-dimethylphenyl) methanesulfonamide	(3,4-dimethyl-2,6-dinitro phenyl) methanesulfonamide	85
(3,5-dimethylphenyl) methanesulfonamide	(3,5-dimethyl-4-nitrophenyl) methanesulfonamide	90

Table 2 Bromination of (dimethylphenyl)methanesulfonmides

Substrate	Product	Yield/%
(2,3-dimethylphenyl) methanesulfonamide	(4-bromo-2,3-dimethylphenyl) methanesulfonamide	76
(2.4-dimethylphenyl) methanesulfonamide	(6-bromo-2,4-dimethylphenyl) methanesulfonamide	83
(2,5-dimethylphenyl) methanesulfonamide	(4-bromo-2,5-dimethylphenyl) methanesulfonamide	72
(2,6-dimethylphenyl) methanesulfonamide	(4-bromo-2,6-dimethylphenyl) methanesulfonamide	86
(3,4-dimethylphenyl) methanesulfonamide	(6-bromo-3,4-dimethylphenyl) methanesulfonamide	88
(3,5-dimethylphenyl) methanesulfonamide	(2,4-dibromo-3,5-dimethyl-phenyl) methanesulfonamide	72

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