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Reactions of 1-(Phenylsulphonylmethyl)benzotriazole with some Nitroarenes

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Abstract. Treatment of nitroarenes 2 - 6 with 1-(phenylsulphonylmethyl)benzotriazole 1 in the KOH - DMSO base - solvent system at room temperature results in cleavage of the phenylsulphonyl group, while the *t*-BuOK - DMF system at low temperature promotes oxidation of the reaction intermediates.

The vicarious nucleophilic substitution of hydrogen (VNS) is a versatile method for the introduction of a variety of substituents into electrophilic arenes.¹ Particularly useful carbanion precursors in this reaction are chloromethyl aryl sulphones. In conjunction with our work concerned with the nucleophilic substitution in azoles² and directed toward the synthesis of fused nitrogen heterocycles, we investigated the VNS of 1-(phenylsulphonylmethyl)benzotriazole 1³ with nitroarenes. We expected the reaction to provide us with starting materials for further cyclizations based on chemical interactions between aromatic nitro group and ortho side chain. We wondered whether the presence of the benzotriazolyl substituent instead of halogen in the aforementioned sulphones would alter the composition of the reaction mixtures.⁴ The benzotriazolate anion is regarded to be a good leaving group which can be used in place of halogen in many reactions.⁵ So, one would expect the benzotriazolate anion to leave in the course of the VNS. However, when the reactions of sulphone 1 and nitroarenes 2-6 were carried out in the KOH - dimethyl sulphoxide (DMSO) base - solvent system no usual products of the VNS, i.e. compounds with the phenylsulphonylmethyl substituent, were found in the reaction mixtures. Instead, the phenylsulphinate anion was eliminated and products 2a - 6a with the benzotriazolylmethyl residue were isolated in 48 - 72% yields (Scheme 1, Table 1).⁶ In cases of the reactions of compounds 2 - 4 and 6 also other products were detected or separated in very low yields from the reaction mixtures. They were identified as products of oxidation of the σ^{H} -adducts (2b - 4b, (6), (6,7) The latter products usually prevailed (compound 6 is the sole exception) when the syntheses were performed in the t-BuOK - dimethylformamide (DMF) system at low temperature .



Scheme 1

Table 1. Influence of experimental parameters on yields of products 2a - 6a and 2b - 6b.

Nitroarene	Yields of isolated products (in %)			
	Procedure A		Procedure B	
2	2a :49	2b : traces	2a : 11	2b : 41
3	3a :71	3b : traces	3a :4	3b : 45
4	4a : 49	4b : 2	4a :4	4b : 37
5	5a : 72	5b : 0	5a : 6	5b : 15
6	6a : 48	6b : 2	6a : 20	6b : 9

The direction of the above described reactions resembles the pattern already reported for tertiary carbanions.⁸ The phenylsulphinate anion is certainly a poorer leaving group in the VNS than is chloride,⁹ and the benzotriazolate anion seems to be even worse. So, under the conditions which are suitable for tertiary carbanions to enter the ortho-position to the nitro group (*t*-BuOK - DMF at low temperature) the oxidation products are usually the major components of the reaction mixtures. On the other hand, the transition state in the KOH - DMSO system is probably much more sterically demanding. This forces one of the carbanion substituents to leave, and this is the phenylsulphonyl group which undergoes the cleavage.

In conclusion, we have presented a simple method for introduction of benzotriazolylmethyl moiety into ortho-position of para-substituted nitroarenes. As the benzotriazole residue can be displaced in many ways, the obtained products are potentially useful intermediates for further transformations. Moreover, the carbanion derived from 1-(phenylsulphonylmethyl)benzotriazole 1 is reasonably resistant to oxidation. This fact gives us an opportunity to examine factors which effect the oxidation of the σ^{H} -adducts. This problem has not been elucidated and still awaits systematic investigation.¹⁰

TYPICAL PROCEDURES

Procedure A. To a stirred solution of sulphone 1 (2 mmol) and nitroarene (2 mmol) in dry DMSO (10 ml) under an argon atmosphere¹¹ was added finely powdered KOH (0.7 g)¹² in one portion. The resulted dark-coloured mixture was vigorously stirred for 20 min. at room temperature, quenched with 3% HCl (50 ml) and extracted with chloroform (3 x 30 ml). The organic phase was washed with water, dried over MgSO₄, and the solvent was removed *in vacuo*. Crystallisation or flash-chromatography on silica gel (hexane : ethyl acetate as an eluent) afforded pure products.

Procedure B. To a stirred cloudy solution of sulphone 1 (2 mmol) and nitroarene (2 mmol) in dry DMF (10 ml) was added a solution of *t*-BuOK (670 mg, 6 mmol) in dry DMF (3 ml), while the temperature was maintained below -30° C. Stirring was continued for 90 min. at -30° C, the reaction mixture was poured into 3% HCl (50 ml) and extracted with chloroform (3 x 30 ml). The organic phase was washed several times with water, dried over MgSO₄, the solvent was evaporated and the residue was flash-chromatographed on silica gel (hexane : ethyl acetate as an eluent).

REFERENCES AND NOTES

- Mąkosza, M.; Winiarski, J. Acc. Chem Res. 1987, 20, 282-289; Mąkosza, M. Synthesis 1991, 103-111.
- 2. Bernard, M. K.; Mąkosza, M.; Szafran, B.; Wrzeciono, U. Liebigs Ann. Chem. 1989, 545-549; Bernard, M. K.; Szoja, C.; Wrzeciono, U. Liebigs Ann. Chem. 1990, 755-759.
- 3. Compound 1 was prepared according to the known procedure : Katritzky, A. R.; Rachwal, S.; Caster, K. C.; Mahni, F.; Law, K. W.; Rubio, O. J. Chem. Soc., Perkin Trans. 1 1987, 781-789.
- 4. We also investigated the VNS of the carbanions originated from 1-(phenylsulphonylmethyl)benzimidazole and 1-(phenylsulphonylmethyl)-3,5-dimethylpyrazole with 1,3-dinitrobenzene. However, yields of products similar to those depicted above were generally lower and the reaction patterns were less consistent than that described for sulphone 1.
- Katritzky, A. R.; Rachwal, S.; Hitchings, G. J. Tetrahedron 1991, 47, 2683-2732; Katritzky, A. R.; Lan, X.; Fan, W.-X. Synthesis 1994, 445-456.
- 6. Selected physical and ¹H NMR (300 MHz, DMSO-d₆, δ in ppm) data :
 2a : m.p. 168-169 °C; δ = 6.34 (s, 2H). 7.00 (d, J=2 Hz, 1H), 7.46 (m, 1H), 7.60 (m, 1H), 7.74 (dd, J=9 and 2 Hz, 1H), 7.91 (m, 1H), 8.12 (m, 1H), 8.24 (d, J=9 Hz).
 2b : m.p. 193-195 °C; δ = 7.32-7.47 (m, 5H), 7.60-7.66 (m, 3H), 7.99 (dd, J=9 and 2 Hz, 1H), 8.09 (m, 1H), 8.17 (s, 1H), 8.20 (d, J=9 Hz, 1H), 8.84 (d, J=2 Hz, 1H).
 3a : m.p. 155.5-156.5 °C; δ = 6.51 (s, 2H), 6.96 (d, J=9 Hz, 1H), 7.47 (m, 1H), 7.59 (m, 1H), 7.90 (m, 1H), 8.14 (m, 1H), 8.46 (dd, J=9 and 2 Hz, 1H), 8.88 (d, J=2 Hz, 1H).

3b : m.p. 205-206 °C; δ = 7.29 (m, 1H), 7.37-7.48 (m, 4H), 7.61-7.70 (m, 3H), 8.08 (m, 1H), 8.25 (s, 1H), 8.81 (d, J=2 Hz, 1H), 8.88 (dd, J=9 and 2 Hz, 1H), 9.16 (d, J=9 Hz, 1H).
4a : m.p. 133-134 °C; δ = 6.41 (s, 2H), 7.32 (s, 1H), 7.48 (m, 1H), 7.62 (m, 1H), 7.93 (m, 1H), 8.12 (m, 1H), 8.96 (s, 1H).
4b : m.p. 165-167 °C; δ = 7.27 (m, 1H), 7.37-7.49 (m, 4H), 7.60-7.71 (m, 3H), 8.09 (m, 1H), 8.27 (s, 1H), 8.96 (s, 1H), 9.07 (s, 1H).
5a : m.p. 182-183 °C; δ = 4.55 (s, 3H), 6.55 (s, 2H), 7.42 (m, 1H), 7.59 (m, 1H), 7.92 (m, 1H), 8.05 (m, 1H), 8.12 (d, J=9 Hz, 1H), 8.24 (d, J=9 Hz, 1H).
5b : m. p. 183-185 °C; δ = 4.31 (s, 3H), 7.40-7.53 (m, 5H), 7.67-7.73 (m, 3H), 8.12 (m + d with J=9 Hz, 2H), 8.35 (d, J=9 Hz, 1H), 8.56 (s, 1H).
6a : m.p. 174-176 °C; δ = 6.55 (s, 2H), 7.44 (m, 1H), 7.62 (m, 1H), 7.80 (m, 1H), 7.91 (m, 1H), 8.06 (m. 1H), 8.33 (d, J=9 Hz, 1H), 8.36 (d, J=9 Hz, 1H), 8.99 (m, 1H), 9.15 (m, 1H).
6b : m.p. 197-198 °C; δ = 7.18 (m, 1H), 7.46 (m, 1H), 7.58 (m, 2H), 7.74-7.87 (m, 4H), 8.14 (m, 1H), 8.33 (d, J=9 Hz, 1H), 8.33 (s, 1H), 8.45 (d, J=9 Hz, 1H), 9.12 (m, 1H), 9.35 (m, 1H).

- 7. It should be added that if nitroarenes with free para position, like nitrobenzene or *o*-chloronitrobenzene, were used as starting materials for the reactions with the carbanion of 1, yields of the elimination products dropped considerably and the reaction mixtures were more complex.
- 8. Mudryk, B.; Mąkosza, M. Tetrahedron 1988, 44, 209-213.
- 9. Ostrowski, S.; Mąkosza, M. *Tetrahedron* **1988**, *44*, 1721-1726. In this paper the authors reported, *inter alia*, on two products resulted from the elimination of the phenylsulphinate anion. These products were obtained in 19 or 41% yields from the reaction of 6-azaquinoxaline with phenyl-thio- or 2,4-dibromophenoxy-methyl phenyl sulphone in the t-BuOK ammonia base solvent system.
- 10. Mąkosza, M. Pol. J. Chem. 1992, 66, 3-23.
- 11. If the atmospheric oxygen was not excluded the reaction mixtures contained larger amounts of the oxidation products.
- 12. Similar results were obtained when sodium hydride was used in place of potassium hydroxide.

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