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INTRAMOLECULAR VICARIOUS NUCLEOPHILIC SUBSTITUTION OF HYDROGEN[1]

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Summary: N-Methyl-N-m-nitrophenyl-(and m-nitrobenzyl-) chloromethanesulfonamides when treated with a strong base form corresponding α-chlorocarbanions which replace intramolecularly hydrogen according to the vicarious substitution scheme.

The vicarious nucleophilic substitution of hydrogen in nitroarenes is a general reaction concerning types of carbanions $R\text{-}\bar{C}XY$ and substituents in the nitroarene ring.[2] The reaction proceeds via fast and reversible addition of the carbanions to the nitroarenes to form σ-complexes (fig.1a) followed by base induced β-elimination of HX.[3] The HX elimination step is very sensitive to steric factors since in the transition state the σ-complex must attain the configuration assuring antiperiplanar orientation of the C-H and C-X bonds (fig.1a). Analyzing possibilities to afford the intramolecular reaction the situation on fig.1b should be considered. Inspection of the Dreiding molecular models has shown feasibility to attain the transition state for six - and substantial difficulties for five membered rings.

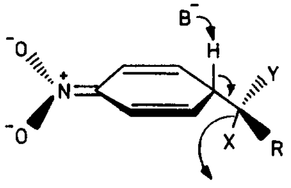


fig.1a

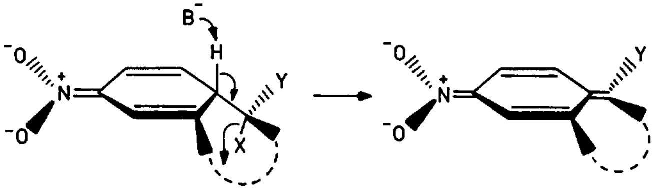
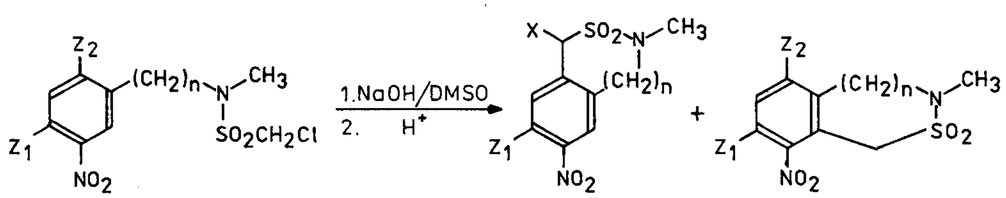


fig.1b

As the simplest models for studies of the intramolecular vicarious nucleophilic substitution of hydrogen we have chosen N-methyl-N-(m-nitrophenyl) chloromethane sulfonamides 1a-c for five membered rings and N-methyl-N-(m-nitrobenzyl)-chloromethane sulfonamides 1d,e for six membered rings.

The starting materials were easily prepared in the reaction of chloromethanesulfonyl chloride with corresponding m-nitroanilines followed by methylation and N-methyl-m-nitrobenzylamines Compounds 1a-e reacted readily in the presence of powdered NaOH in DMSO to form products of the intramolecular vicarious nucleophilic substitution of hydrogen in position ortho- and para- to the nitro group 2 and 3 respectively.[4] In a standard procedure, to a vigorously stirred solution of 1 (1.0g) in dimethylsulfoxide (20ml), powdered sodium hydroxide (2.0g) was added. The mixture was stirred at ambient temperature for 1/2 hr, then poured into 10% hydrochloric acid with ice. Ratio of the products in the crude mixture was determined by NMR spectroscopy, then the products isolated using column chromatography (silica gel, hexane-ethyl acetate 4:1). All compounds gave satisfactory elemental analysis. Results are given in the table.



1 a-e 2 a-e 3 a-e

	n	Z_1	Z_2	X	Total yield	2/3	melting point (°C)	
					(%)	ratio	2	3
a	0	H	H	H	86	1:4	140-142	218-220
b	0	H	Cl	H	71	-	-	141-143
c	0	H	F	Cl	76	5:3[x]	145-146[xx]	126-128
d	1	H	H	H	88	1:4	167-168	177-179
e	1	Br	H	H	78	3:7	146-148	181-182

[x] when an excess of t-BuOK in DMSO was used the mixture of 2a and 3c (1:1 ratio) was formed; 2a was produced by dechlorination of 2c, such processes are often observed in similar systems[5]

[xx] decomposition

In our previous paper we have shown that if there is a halogen ortho- or para- to the nitro group the vicarious nucleophilic substitution of hydrogen usually dominates over the conventional nucleophilic substitution of halogen. Only in the case of the fluoronitroarenes do both of these processes compete and this competition was used to clarify the mechanism of the vicarious substitution.[3] The same observations we have made now in the intramolecular process. When 1b was treated with the base product of the substitution of hydrogen 3b was exclusively formed, whereas in the case of 1c both processes - replacement of fluorine and the vicarious substitution of hydrogen compete. In the latter case we were unable to suppress the substitution of fluorine using a great excess of base as it was possible in the intermolecular reaction. This can be a piece of evidence that there are steric obstacles in the HCl elimination step from the five membered σ-complex thus the substitution of hydrogen is disfavoured as compared to the substitution of fluorine.

Detailed results of the studies on the intramolecular vicarious substitution of hydrogen will be published later.

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