RELATIONS STRUCTURE-REACTIVITY AND THE POSITIVE STERIC EFFECTS OF ORTHO SUBSTITUENTS IN ARENESULFONYL CHLORIDES

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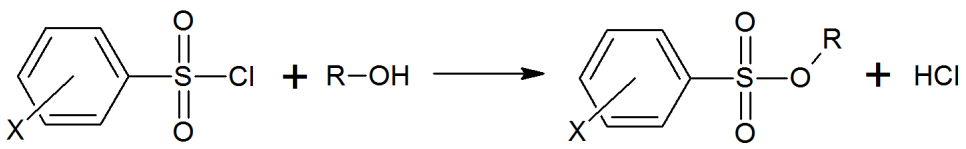
This work aims to unravel the origin of the positive *ortho*-effect in solvolysis reactions of hindered arenesulfonyl chlorides. The alcoholysis in methanol, ethanol, propanol and *iso*-propanol, at 313 K, of hindered X-ArSO$_2$Cl (X=4-Me; 4-Br-; H-; 2,4,6-Me$_3$-; 2,6-Me$_2$-4-*t*-Bu-; 2,3,5,6-Me$_4$-; 2,4,6-Me$_3$-3-NO$_2$-; 2,4,6-*i*-Pr$_3$-) was investigated. X-ray analysis was carried out in solid crystals of hindered arenesulfonyl chlorides and arenesulfonates. The hypothesis of C-H···O intramolecular interactions in these compounds was discussed. A S$_N$2-like transition state, with nucleophilic assistance of a second alcohol molecule was proposed. Empirical data support the change from nucleophile's backside attack to frontal attack when moving from unhindered compounds to *ortho*-alkyl substituted.

Nucleophilic substitution processes at tetracoordinated sulfur atoms have been the subject of detailed research for many years. Due to the electronic characteristics of the sulfur atom (heterovalent nature, participation of 3d-orbitals in the formation of chemical bonds, tetrahedricity of sulfonyl group caused by sp^3-d^2 hybridization of its atomic orbitals), sulfo-derivatives show a variety of interesting reactivity features. Between these, it is remarkable the accelerating effect of *o*-alkyl groups on nucleophilic substitution reactions at the sulfur atom. For the last 50 years a large amount of evidences of this phenomenon have been gathered.[1-5] The contradictory views about the nature of this phenomenon show the issue is still insufficiently and incompletely understood. In this respect, feasibility of uni-[1] and bimolecular mechanisms, [2] structural modifications of the S$_N$2-type transition state (TS) involving a second molecule of nucleophile (S$_N$3-mechanism),[3] stabilization of the bimolecular TS by intramolecular interactions, hyperconjugation effects[4] or stereochemical rearrangements during the nucleophilic attack[5] have been discussed. This work attempts to unravel the origin of the positive *ortho*-effect in solvolysis reactions of hindered arensulfonyl chlorides.

Results and discussion

Therefore, alcoholysis reactions of sterically hindered aromatic sulfonyl halides were studied:



where R= Me-, Et-, Pr-; *i*-Pr-.

X= 4-Me-; H-;4-Br-; 2,4,6-*i*-Pr$_3$-; 2,6-Me$_2$-4-*t*-Bu-; 2,4,6-Me$_3$-; 2,3,5,6-Me$_4$-; 2,4,6-Me$_3$-3-NO$_2$-.

Reaction kinetics were appropriately fitted by a first-order kinetic model. The processes in methanol, ethanol and propanol are quite similar (Table 1). An increase of electron withdrawing

effect of -*X* in unhindered compounds leads to lower reactivity, contrary to the prediction for typical S_N2 reactions. The kinetics of neutral *iso*-propanolysis of aromatic sulfonyl chlorides has shown the opposite tendency relative to unbranched alcohols. The following sterically-hindered compounds (X=2,4,6-Me_3-; 2,6-Me_2-4-*t*-Bu-; 2,3,5,6-Me_4-; 2,4,6-Me_3-3-NO_2-) show anomalous acceleration appropriate for all alcohols.

Table 1 - Observed rate constants for alcoholysis of arenesulfonyl chlorides at 313K

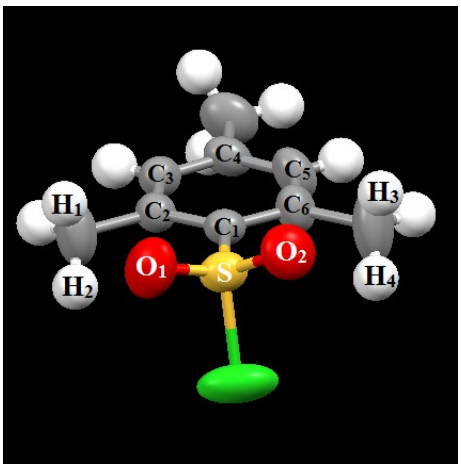
X	$k_{obs}\cdot10^4$ / s^{-1}			
	MeOH	EtOH	PrOH	*i*-PrOH
4-Me-	3.80±0.02	0.82±0.01	0.506±0.002	0.066±0.008
H-	3.76±0.01	0.91±0.01	0.488±0.003	0.08±0.01
4-Br-	3.24±0.02	0.67±0.01	0.450±0.007	0.099±0.001
2,4,6-*i*-Pr_3-	7.94±0.04	1.16±0.01	0.684±0.001	0.070±0.005
2,6-Me_2-4-*t*-Bu-	28.1±0.2	5.70±0.80	3.43±0.01	0.47±0.01
2,4,6-Me_3-	29.1±0.2	4.99±0.02	3.03±0.01	0.44±0.01
2,3,5,6-Me_4-	20.1±0.1	4.05±0.05	1.96±0.01	0.31±0.01
2,4,6-Me_3-3-NO_2-	12.8±0.2	2.76±0.01	2.00±0.02	0.38±0.03

To understand the effect of steric factors on the solvolysis of hindered arenesulfonyl chlorides, it is necessary to identify the structural features of the investigated substrates and of some reaction products.

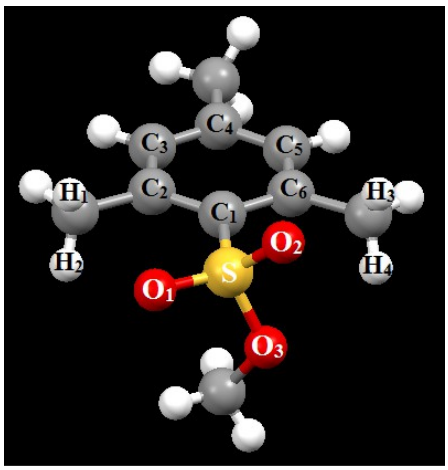
X-ray analysis was carried out in solid crystals having in mind that the structure in the solid state can differ from that of occurring in solution. Nevertheless, this information can be useful to understand the structure of the TS. Sterically hindered substrates showed the oxygen atoms of the sulfo- groups oriented toward the *ortho*-methyl groups (Fig. 1).

The distance between the hydrogen atom of the *o*-alkyl group and the nearest oxygen of the sulfonyl group, $l_{(O\cdots H)}$, (see Table 2), is comparable to the length of typical hydrogen bonds (2.30-2.70 Å) [6, 7] , thus a weak intramolecular interaction (C-H···O) may occur [8]. The value of the sum of Van der Waals radii [9] of oxygen and hydrogen atoms, Σr_W = 2.72 Å, also supports the idea about C-H···O intramolecular interactions in these compounds. In the products the angle (O_1SO_2) between the oxygens of sulfo group is retained, whereas one of the oxygens of the sulfo group keeps its orientation toward the *ortho*-methyl group, as evidenced by the low values of torsion angles (O(1)-S(1)-C(1)-C(2)) (Table 2). This may indicate that such interactions are preserved in the products and may contribute to the rearrangement of the oxygens of the sulfo group in the TS.

To understand the influence of steric factors we must take into account that the sulfonyl chloride group can freely rotate around the S-C bond in sterically unhindered substrates. The introduction of two *ortho*-alkyl groups limits this rotation significantly [10, 11]. This may promote more rapid formation of the cyclic TS [12], involving a second molecule of solvent (Fig. 2).



a.



b.

Figure 1 X-ray structure of arenesulfonyl compounds

a. 2,4,6-trimethylbenzenesulfonyl chloride; b. methyl 2,4,6-trimethylbenzenesulfonate

Table 2 – Geometrical parameters involving the oxygens of the sulfo group and the hydrogens of *ortho*-methyl groups of some derivatives of hindered arenesulfonic compounds X-ArSO$_2$-Y.

Substituent X, Y	$l_{(O1\cdots H1)}$, [Å]	$l_{(O1\cdots H2)}$, [Å]	$l_{(O2\cdots H3)}$, [Å]	$l_{(O2\cdots H4)}$, [Å]	(O_1SO_2), [°]	O(1)-S(1)-C(1)-C(2)
X=2,4,6-*i*-Pr$_3$-; Y=Cl.*	2.732	-	2.425	-	118.06	-6.39(2)
X=2,6-Me$_2$-4-*t*-Bu-; Y=Cl.	2.453	2.511	2.358	2.702	118.36	-17.5(2)
X=2,4,6-Me$_3$-; Y=Cl.	2.443	2.531	2.453	2.603	117.67	28.9(3)
X=2,4,6-Me$_3$-3-NO$_2$-; Y=Cl.	2.521	2.409	2.507	2.578	118.27	33.2(3)
X=2,6-Me$_2$-4-*t*-Bu-; Y= MeO-.	2.438	2.490	2.475	3.198	118.06	8.8(2)
X=2,6-Me$_2$-4-*t*-Bu-; Y= EtO-.	2.456	2.515	2.551	3.096	118.46	9.6(2)
X=2,6-Me$_2$-4-*t*-Bu-; Y= PrO-.	2.437	2.470	2.586	2.890	118.74	5.4(3)
X=2,6-Me$_2$-4-*t*-Bu-; Y= *i*-PrO-.	2.480	2.483	2.486	3.202	118.55	-9.8(2)
X=2,4,6-Me$_3$-; Y= MeO-.	2.473	2.540	2.475	2.903	118.30	-0.53(9)
X=2,4,6-Me$_3$-; Y= *i*-PrO-	2.281	2.660	2.538	2.887	118.61	-3.48(13)
X=2,3,5,6-Me$_4$-; Y= PrO-.	2.732	2.632	2.425	3.762	118.20	-15.08(9)
X=2,3,5,6-Me$_4$-; Y= *i*-PrO-.	2.446	2.517	2.464	3.046	117.93	-5.4(2)

*Obtained from Cambridge Structural Database[10]

The positive *ortho*-effect tends to decrease in the series MeOH – EtOH – PrOH – *i*-PrOH, and the effect on k_X/k_H is still significant even for *iso*-propanolysis where the steric interactions between bulky alkyl group of alcohol and *ortho*-methyl substitutients might take place in the TS. Thus we conclude that *o*-alkyl groups provide a common mechanism of TS stabilization for all the types of nuclephile.

We suggest that *o*-alkyl groups limit the backside approach of the nucleophile whereby creating preconditions for a frontal attack on the sulfur atom (Figs. 2 & 3). On one hand this facilitates a more compact packing of alcohol molecules in the cyclic TS, and on the other, energy is not required because the oxygens of the sulfo group do not move as it would be the case in a rear attack (Fig. 3). *Ortho*-alkyl groups may block the backside attack of the nucleophile through steric hindrance and fix the oxygens of the sulfo group by intramolecular interactions. On the other hand, frontal axial attack may assist the cyclic TS as it decreases the bond lengths in the cycle (Fig. 2).

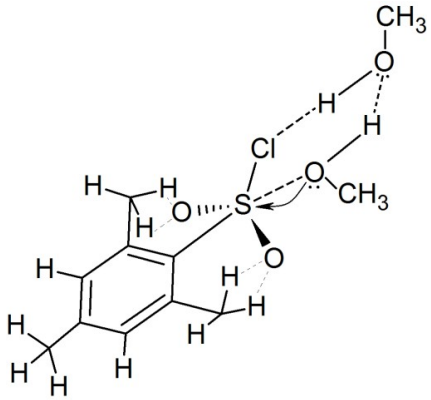
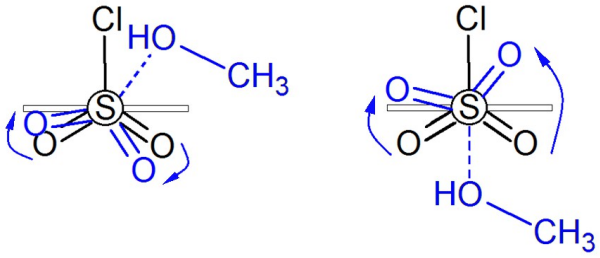


Figure 2. Cyclic transition state involving two nucleophile molecules in the methanolysis of 2,4,6-Me_3-benzenesulfonyl chloride (frontal nucleophilic attack)



a. b.

Figure 3 - Different types of nucleophilic attack at the reaction center during arenesulfonyl chloride methanolysis: a. axial attack; b. backside attack.

Intramolecular interactions between the oxygens of the sulfo group and the hydrogens of *ortho*-methyl groups may be the reason of so called "positive steric effect" and explain the abnormal reactivity of those hindered compounds.

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