Methanolysis of *ortho*- and *para*-formylbenzenesulfonates in basic media: evidence for the intramolecular nucleophilic catalysis by the carbonyl group†

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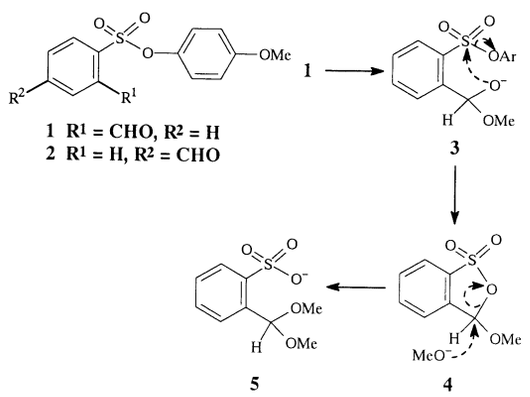
Methanolysis of *p*-methoxyphenyl 2-formylbenzenesulfonate, in the presence of anhydrous potassium carbonate at ambient temperature gives the dimethyl acetal of 2-formylbenzenesulfonic acid in excellent yield. *p*-Methoxyphenyl 4-formylbenzenesulfonate under identical conditions remains unaffected. These results provide evidence for the catalytic involvement of the neighbouring aldehyde carbonyl group and operation of intramolecular nucleophilic catalysis during the nucleophilic substitution at sulfonyl sulfur.

Assistance by neighbouring groups in organic chemical reactions is well known in the literature. Rates of reactions such as hydrolysis, solvolysis, cleavage of ethers, *etc.* are known to be enhanced by suitably placed functional groups in close proximity.[1] Often compounds exhibiting neighbouring group catalysis have been used as model systems to obtain information on the catalytic mechanisms of enzymes that bring about analogous reactions[2] and for the development of new protecting groups for organic synthesis.[3] Catalysis of hydrolysis of carboxylic acid esters by a neighbouring carbonyl group has been studied extensively.[2b] However, direct evidence for the nucleophilic catalysis by the carbonyl group, such as isolation of intermediates, is available only in a few cases.[4] In contrast, intramolecular catalysis in the case of sulfonic acid analogues[5] is not well documented. We had earlier reported[6] the enhancements in the rates of hydrolysis of phenyl 2-formylbenzenesulfonates by a neighbouring carbonyl group. We present evidence for the intramolecular nucleophilic catalysis by the *ortho* formyl group during the base catalysed methanolysis of phenyl 2-formylbenzenesulfonates.

Results and discussion

p-Methoxyphenyl sulfonates **1** and **2** (Scheme 1) were prepared by the reaction of 2-formylbenzenesulfonyl chloride[7] and 4-formylbenzenesulfonyl chloride[8] with *p*-methoxyphenol in the presence of triethylamine. Methanolysis of **1** and **2** (separately) in the presence of anhydrous potassium carbonate, monitored by TLC, showed the absence of the *ortho* isomer **1** after 30 min, whereas most of the *para* isomer **2** remained unaffected. Working up of the reaction mixture under non-aqueous conditions (see Experimental for details) yielded the acetal **5** in 87% yield. This is one of the unusual cases of formation of an acetal or a ketal from a carbonyl compound under basic conditions, which is not normally possible. Formation of a ketal under basic conditions has previously been observed during the methanolysis of 2-acetylphenyl mesitoate[4c,4d] and (9-oxobenzonorbornen-*exo*-2-yl) bromomethanesulfonate.[9] The methanolysis of this bromo compound involved nucleophilic substitution at the saturated carbon with cleavage of the alkyl–oxygen bond. However, in the present work, the nucleophilic substitution is at the sulfonyl sulfur with cleavage of the sulfur–oxygen bond.

Aryl benzenesulfonates undergo basic hydrolysis by nucleophilic substitution at the sulfonyl sulfur (S_N2 type of reaction) with S–O bond cleavage.[10] We had earlier shown[6] that the 2-formyl group enhances the rate of hydrolysis of aryl benzenesulfonates by *ca.* 10^6. We had also studied the effect of the leaving group[6] on the hydrolysis of 2- and 4-formylbenzenesulfonates. The Hammett ρ values were 0.1 (5 °C) and 1.59 (45 °C), respectively for 2- and 4-formylbenzenesulfonates. Importance of the bond breaking process for the hydrolysis of aryl benzenesulfonates was revealed by the comparatively large Hammett ρ value for 4-formyl derivatives. This implied that, normally, the overall rate of the reaction for the nucleophilic substitution at sulfonyl sulfur is influenced by the nature of the leaving group. However, the observed Hammett ρ for 2-formyl derivatives indicated that the leaving group has minimal influence on overall rate of hydrolysis of phenyl 2-formylbenzenesulfonates. These kinetic experiments do not however indicate the nature of the intermediates involved nor whether hydrated aldehyde functioned as an intramolecular nucleophile (Path A, Scheme 2) or a general base (Path B, Scheme 2) or a general acid (Path C, Scheme 2), but, it is relevant to note that the low Hammett ρ value for the alkaline hydrolysis of phenyl 2-acetylbenzoates has been shown to be consistent with the rate-determining attack of the hydroxide ion on the carbonyl group, followed by rapid intramolecular cyclisation.[11]



Scheme 1 *Reagents and conditions:* $MeOH–K_2CO_3$

Isolation of the acetal **5** clearly establishes the operation of intramolecular nucleophilic catalysis (Path A, Scheme 2) during the solvolysis–hydrolysis of 2-formylbenzenesulfonates. This reaction involves the initial addition of methoxide to the aldehyde carbonyl group to generate the anion **3**, which undergoes

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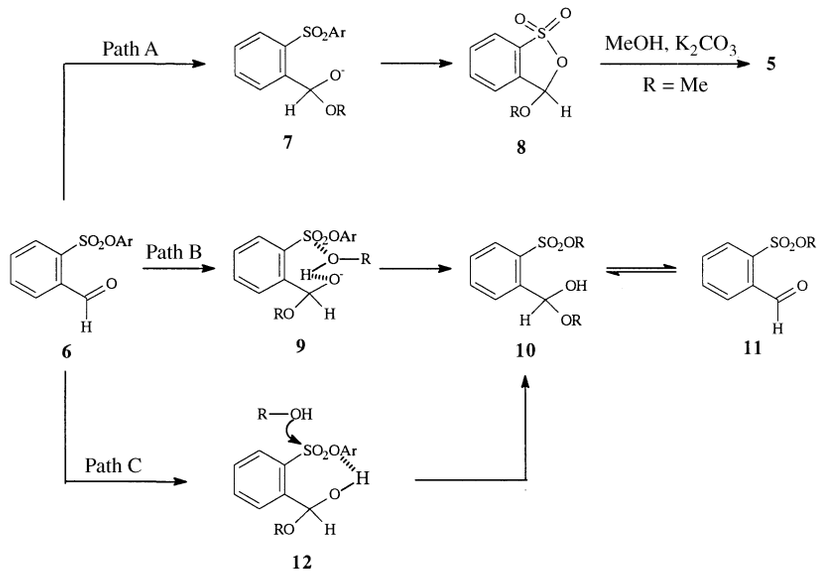

Scheme 2

intramolecular nucleophilic substitution on sulfonyl sulfur leading to the formation of the cyclic sulfonate **4**. The cyclic sulfonate intermediate **4**, being a benzyl sulfonate, undergoes further methanolysis to the acetal **5** with ease. Hence formation of the dimethyl acetal **5** is a result of two successive substitutions, one each on sulfonyl sulfur (formation of the cyclic sulfonate **4**) and the benzylic carbon (methanolysis of **4**). If the reaction proceeds by the direct nucleophilic substitution (by methanol or methoxide in the present case) at the sulfonyl sulfur, wherein the hydrated aldehyde functions as a general base or a general acid (Path B or C, Scheme 2), the end product must necessarily by the aldehyde **11**. The possibility of methanolysis of the phenyl sulfonate and formation of the acetal as being two independent parallel reactions can be ruled out since the 4-formyl derivative **2** remained unaffected under identical conditions for the formation of the acetal **5** from the 2-formyl derivative **1**.

In conclusion, the present work clearly establishes the intramolecular nucleophilic catalysis by the aldehyde carbonyl group during the hydrolysis–solvolysis of 2-formylbenzenesulfonates and shows that the phenomenon of catalytic assistance by a neighbouring carbonyl group is as important in the hydrolysis of sulfonic acid derivatives as in the case of carboxylic acid derivatives.

Experimental

General

4-Formylbenzenesulfonyl chloride was prepared by the reaction of the corresponding sulfonic acid with thionyl chloride. 4-Formylbenzenesulfonic acid was prepared[8] by the oxidation of toluene-*p*-sulfonyl chloride. Sodium 2-formylbenzenesulfonate (Aldrich) was used as received. All reagents and solvents used were purified according to literature procedures.[12] Melting points reported are uncorrected. All the NMR chemical shifts reported are with reference to internal $SiMe_4$.

Preparation of sulfonates. General procedure

2-Formyl- or 4-formyl-benzenesulfonyl chloride and *p*-methoxyphenol were dissolved in chloroform (10–15 ml) and triethylamine was added dropwise. The reaction mixture was allowed to stand at ambient temperature for 8–10 h. It was then diluted with chloroform, washed with dilute hydrochloric acid followed by sodium hydroxide (0.1 M) solution. The organic layer was washed several times with water and dried over anhydrous sodium sulfate. Chloroform was removed by distillation and the residue was crystallized from light petroleum or benzene–light petroleum.

(*p*-Methoxyphenyl) 2-formylbenzenesulfonate (1). Yield, 77.8%, mp 60–61 °C, ν_{max}(Nujol)/cm^{-1} 1700. δ_H($CDCl_3$) 3.7 (s, 3 H), 6.8 (d, 4 H), 7.6–8.4 (m, 4 H), 10.7 (s, 1 H). δ_C($CDCl_3$) 55.3, 114.6, 122.8, 129.16, 130.3, 133.4, 134.0, 134.5, 136.1, 142.2, 158.4, 188.9 (Found: C, 58.01; H, 4.25. $C_{14}H_{12}O_5S$ requires C, 57.53; H, 4.11%).

(*p*-Methoxyphenyl) 4-formylbenzenesulfonate (2). Yield, 85%, mp 131–132 °C, ν_{max}(Nujol)/cm^{-1} 1700. δ_H($CDCl_3$) 3.7 (s, 3 H), 6.8 (d, 4 H), 7.9 (s, 4 H), 10.0 (s, 1 H). δ_C[$(CD_3)_2SO$] 55.5, 114.6, 123.1, 129.3, 130.0, 139.8, 140.2, 142.7, 158.5, 190.6 (Found: C, 57.84; H, 4.20. $C_{14}H_{12}O_5S$ requires C, 57.53; H, 4.11%).

2-Formylbenzenesulfonic acid dimethyl acetal (5). The sulfonate **1** (0.1 g, 0.34 mmol) and anhydrous potassium carbonate in dry methanol (1 ml) were stirred at ambient temperature for 0.5 h, after which TLC analysis showed the absence of the starting sulfonate **1**. The reaction mixture was centrifuged and the residue was washed with dry methanol (2 × 1 ml). The combined centrifugate was evaporated to obtain a solid (130 mg). It was repeatedly washed with dichloromethane and dried (80 mg, 87%). δ_H(D_2O) 3.52 (s, 6 H), 6.25 (s, 1 H), 7.50–7.70 (m, 3 H), 7.94 (d, 1 H). δ_C(D_2O) 56.8, 103.2, 127.9, 130.5, 133.0, 136.5, 146.1, 164.0.

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References

1 (*a*) J. L. Garcia Ruano, A. M. Martin Castro and J. H. Rodriguez Ramos, *Tetrahedron Lett.*, 1996, **37**, 4569; (*b*) K. Endo, H. Takahashi and M. Aihara, *Heterocycles*, 1996, **42**, 589; (*c*) M. T. Epperson, C. E. Hadden and T. G. Waddel, *J. Org. Chem.*, 1995, **60**, 8113; (*d*) A. J. Kirby and R. Stromberg, *J. Chem. Soc., Chem. Commun.*, 1994, 709; (*e*) C. Eaborn, P. D. Lickiss and A. D. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1994, 1809; (*f*) K. Bowden and F. P. Malik, *J. Chem. Soc., Perkin Trans 2*, 1993, 7; (*g*) A. K Yatsimirsky, G. M. Kazankov and A. D. Raybov, *J. Chem. Soc., Perkin Trans. 2*, 1992, 1295; (*h*) A. J. Chandler and A. J. Kirby, *J. Chem. Soc., Chem. Commun.*, 1992, 1769; (*i*) T. Irie and H. Tanida, *J. Org. Chem.*, 1980, **45**, 1795.

2 (*a*) A. J. Kirby, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 707; (*b*) K. Bowden, *Adv. Phys. Org. Chem.*, 1993, **28**, 171.

3 (*a*) Y. Watanabe, M. Ishimaru and S. Ozaki, *Chem. Lett.*, 1994, **11**, 2163; (*b*) M. S. Shashidhar and M. V. Bhatt, *J. Chem. Soc., Chem. Commun.*, 1987, 654; (*c*) J. B. Chattopadyaya, C. B. Reese and A. H. Todd, *J. Chem. Soc., Chem. Commun.*, 1979, 987.

4 (*a*) M. L. Bender, J. A. Reinstein, M. S. Silver and R. Mikulak, *J. Am. Chem. Soc.*, 1965, **87**, 4545; (*b*) M. L. Bender and M. S. Silver, *J. Am. Chem. Soc.*, 1962, **84**, 4589; (*c*) H. D. Burrows and R. M. Topping, *J. Chem. Soc., Chem. Commun.*, 1969, 904; (*d*) H. D. Burrows and R. M. Topping, *J. Chem. Soc.* (*B*), 1970, 1323.
5 S. Thea, G. Guanti, A. R. Hopkins and A. Williams, *J. Org. Chem.*, 1985, **50**, 3336.
6 M. V . Bhatt and M. S. Shashidhar, *Tetrahedron Lett.*, 1986, **27**, 2165.
7 (*a*) M. S. Shashidhar and M. V. Bhatt, *Proc. Ind. Acad. Sci.* (*Chem. Sci.*), 1989, **101**, 319; (*b*) J. F. King, B. L. Huston, A. Hawson, J. Komery, D. M. Deaken and D. R. K. Hardinge, *Can. J. Chem.*, 1971, **49**, 936.
8 Manivel, PhD Thesis, Indian Institute of Science, Bangalore, India, 1980.
9 H. Tanida, T. Nishiya and T. Irie, *J. Org. Chem.*, 1979, **44**, 3337.
10 J. March, *Advanced Organic Chemistry, Reactions, Mechanisms and Structure*, McGraw-Hill Kogakusha Ltd, Tokyo, Japan, 2nd edn., 1977, p. 449 and references cited therein.
11 F. Anvia and K. Bowden, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1805.
12 D. D. Perrin and W. L. F. Armarego, *Purification of Laboratory Chemicals*, Pergamon Press, 2nd edn., 1988.

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