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Aspects of tautomerism. Part 16. Influence of the γ-keto function on the reactions of sulphonic acids

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Abstract. Reaction of sodium 2-formylbenzenesulphonate (1) with thionyl chloride or phosphorous pentachloride gives a mixture of pseudo (2) and normal (3) sulphonyl chlorides. Whereas ammonium 2-carboxybenzenesulphonate (6) gives only the normal sulphonyl chloride (7) on reaction with thionyl chloride, a mixture of normal (7) and pseudo (8) isomers are formed on reaction with phosphorous pentachloride. Sodium 2-benzoylbenzenesulphonate (15), on the other hand, gives the corresponding normal sulphonyl chloride (16) on reaction with both of the reagents mentioned above. Based on these observations it is concluded that γ-keto sulphonic acids are amenable to the influence of γ-carbonyl group as in the case of γ-keto carboxylic acids but to a lesser extent.

Keywords. Ring–chain tautomerism; neighbouring group effect; neighbouring group participation.

1. Introduction

It is customary in classical organic chemistry to discuss the properties of compounds in terms of their functional groups. In a multifunctional molecule, the properties of a particular functional group are affected by other functional groups present. Such changes have been described in terms of electronic, steric and field effects. Quantitative work carried out in the last fifty years or so has resulted in a fairly adequate description of these effects. When two or more functional groups are in close proximity, certain complex reactivity patterns – not displayed by the individual groups themselves – are observed. Not only are there quantitative changes of reactivity, but more often they are of a qualitative nature. A part of such reactivity patterns are referred to as neighbouring group participation. There exists a large body of observations wherein a functional group influences the reactivity patterns of its neighbour by mechanisms other than neighbouring group participation. We have designated these broader patterns of interaction of neighbouring groups as "neighbouring group effects". In the previous papers of this series, changes in reactivity patterns of a carboxylic acid derivative due to the presence of a neighbouring carbonyl group were studied.

The reactions of keto carboxylic acids with reagents like thionyl chloride, oxalyl chloride, phosphorous pentachloride etc. give rise to pseudo acid chloride and/or

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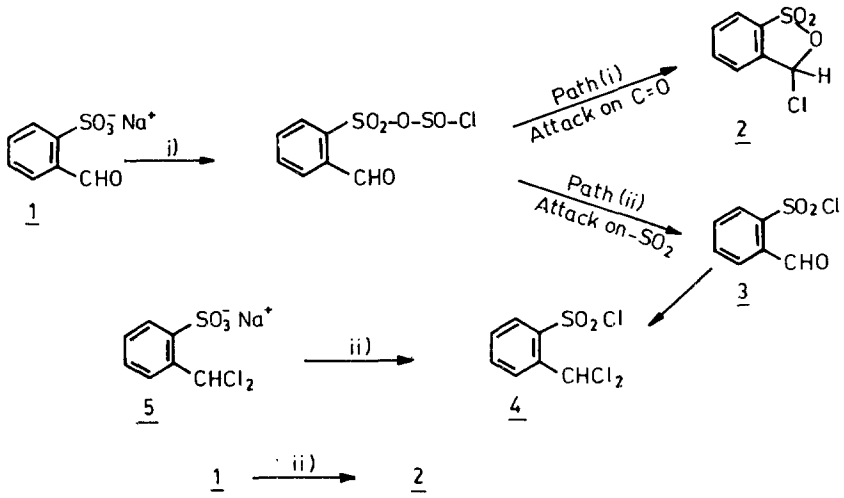
normal acid chlorides. Their formation from γ-keto carboxylic acids is fairly well understood. From a survey of available literature of γ-keto carboxylic acid chlorides, we have concluded (Bhatt *et al* 1980) that γ-keto acids, as a rule, give exclusively pseudo acid chlorides irrespective of the reagent used. There are very few exceptions to this rule. However, the situation with regard to γ-keto sulphonic acids is not defined. In the present paper we have examined this question and also the broader issue of change in the reactivity pattern of the sulphonic acid function, brought about by the presence of a carbonyl group in its neighbourhood.

2. Results and discussion

Reaction of sodium 2-formylbenzenesulphonate 1 with thionyl chloride and ambient temperature gave 3-chlorobenzoxathiole-1,1-dioxide 2 as the only product. However, when 1 was refluxed with thionyl chloride in the presence of dimethylformamide for three minutes, a mixture of 2-formylbenzenesulphonyl chloride 3 and its pseudo isomer 2 was formed in the ratio 4:7, along with 2-dichloromethylbenzenesulphonyl chloride 4 (use of longer reaction times, 1 h, gives 2 and 4 only). This is contrary to the earlier report (King *et al* 1971) that exclusively 3 is formed under the same reaction conditions. Formation of the pseudo sulphonyl chloride 2 in larger proportion must be due to the preference of path (i) over that of path (ii) (scheme 1).



Scheme 1.

When the normal sulphonyl chloride 3 was heated to 150–160° in a vacuum sealed tube, it was converted to the pseudo isomer 2. But 2 and 3 are stable and are not interconvertible at ambient temperature. That they do not display tautomerism is shown by their infrared and nuclear magnetic resonance spectra (see experimental section) which do not change.

Furthermore, the normal sulphonyl chloride 3 remained unaffected when stirred with thionyl chloride in the presence of dimethylformamide at ambient temperature. But when the reaction mixture was refluxed, the dichloride 4 was obtained. Also,

2 was not affected by thionyl chloride in the presence of dimethylformamide either at ambient temperature or under reflux. Thus pseudo 2 and normal 3 sulphonyl chlorides do not isomerise under the conditions used for their preparation.

The reaction of sodium 2-dichloromethylbenzenesulphonate 5 with thionyl chloride gave 4, without a trace of 2. This finding rules out the possibility of the formation of the pseudo isomer 2, by the intramolecular nucleophilic displacement of chlorine in 5.

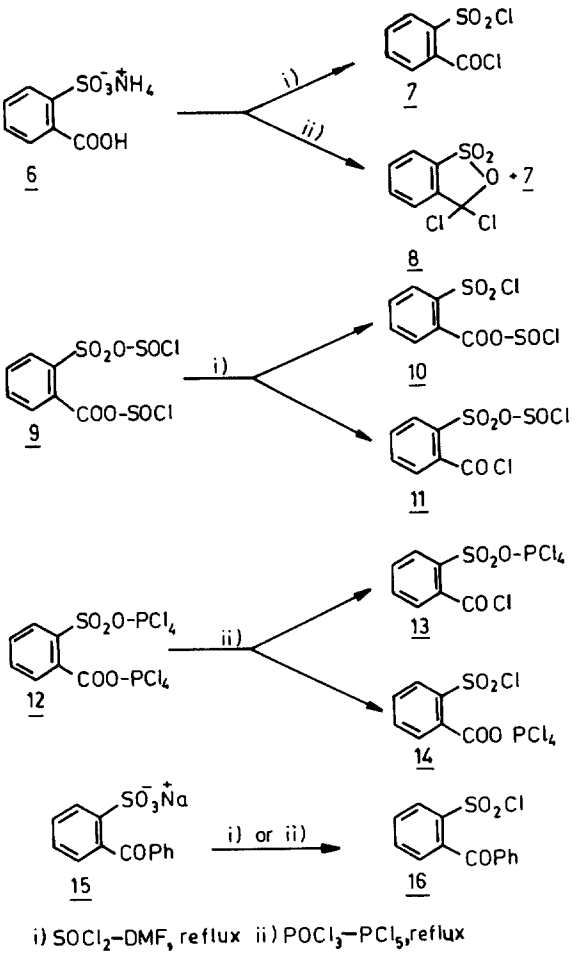
From the foregoing it is seen that pseudo and normal isomers 2 and 3 are formed by two independent competing pathways. However, the fact that path (i) is preferred over path (ii) is shown by the exclusive formation of 2 at lower temperature and in larger proportion at higher temperatures. Previous studies (Shashidhar and Bhatt 1986; Newman and Courduvelis 1966) have established that the pseudo acid chlorides are formed from δ- and γ-keto acids by means of cyclic transition states and not by displacement of the chlorosulphite ester or its analogues by the chloride ion. This concerted reaction was originally described as a 3,2,1-bicyclic pathway (Newman and Courduvelis 1966; Newman *et al* 1966). We have designated it as a $2_\sigma + 2_\pi + 2_\sigma$ concerted pathway using modern terminology (Shashidhar and Bhatt 1986), path (i) is therefore by analogy with γ-keto-acids, in all probability a $2_\sigma + 2_\pi + 2_\sigma$ concerted reaction.

Formation (Goldberger 1916) of 2 by the action of phosphorous pentachloride on 1 has been attributed to the ring–chain tautomerism of 2-formylbenzenesulphonic acid (Freeman and Ritchie 1957). Its infrared spectrum shows the presence of carbonyl group (ν_{max} 1690 cm^{-1}) and ^1H NMR spectrum (D_2O) shows only the peaks due to aldehydic (10·7 δ) and aromatic hydrogens (7·6–8·2 δ). The putative tautomerism, therefore, does not exist. However, it is interesting to note that, 2-formylbenzenesulphinic acid by contrast, exists completely in the cyclic form (King *et al* 1971).

Heating dry potassium 2-carboxy benzene sulphonate with phosphorous pentachloride at 150° for about five hours, Remsen (1903) had obtained in good yield a mixture of 7 and the pseudo acid chloride 8 (scheme 2). They believed that the major product m.p. 40° (80–90% yield) was 8 and the minor product m.p. 79° (10–20% yield) was 7 (see also List and Stein 1898). These assignments were based on chemical reactions, which are unreliable methods of establishing structures of closely related compounds. Spectroscopic methods, particularly IR spectroscopy is useful for identification in the present case. The carbonyl stretching frequency at 1780 cm^{-1} (typical of a carboxylic acid chloride) for the 40° melting isomer and its absence in the 79° melting isomer makes it necessary to reverse Remsen's assignments. Other spectroscopic data fully corroborate this view.

When ammonium 2-carboxybenzenesulphonate 6 was refluxed with thionyl chloride (b.p. 79°) in the presence of dimethylformamide, 2-chlorocarbonylbenzenesulphonyl chloride 7 was obtained. On the other hand, when 6 was refluxed in phosphorous oxychloride (b.p. 105°) with phosphorous pentachloride, a mixture of 7 and its pseudo isomer 8 in the ratio 4:1 was obtained. When pure samples of 7 and 8 were independently refluxed with thionyl chloride in presence of dimethylformamide or with phosphorous pentachloride, in phosphorous oxychloride, they remained unaffected. Clearly 7 and 8 are not interconvertible under the conditions used for their preparation. In contrast to the 2-formyl derivative 1, formation of the normal isomer is preferred over the pseudo isomer.

The behaviour of 2-carboxybenzenesulphonic acid differs from that of γ-keto

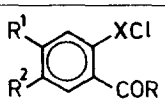


Scheme 2.

carboxylic acids in another feature. Whereas the products obtained from the former depend on the nature of the reagent used, the latter, as a rule gives the pseudo isomer, independent of the reagent used. This variation could arise from the differences in relative rates of reaction of thionyl chloride and phosphorous pentachloride towards sulphonyl and carboxylic acid groups. It can be seen that once the sulphonyl–chloride function is generated, it does not get transformed to the pseudo form. On the contrary, if the carboxylic acid chloride function is formed before formation of the sulphonyl chloride as in 13, it could assist in the cleavage of the sulphur–oxygen bond, resulting in the formation of the pseudo derivative 8. This possibility is realized only in the case of PCl_5 and that too to a minor extent. We have rationalised these observations on the basis of a reasonable assumption that $SOCl_2$ reacts with sulphonic acid faster than with carboxylic acid. Although the same is true with PCl_5, the competing reaction of formation of 13, takes place to a minor extent, which in turn leads to formation of the pseudo derivative 8.

Reaction of sodium 2-benzoylbenzenesulphonate 15 with thionyl chloride in the

Table 1. Structure of some γ-keto carboxylic acid chloride and the corresponding sulphonyl chlorides.

	Structure of the acid chloride		
	X = CO	X = SO_2	References
R = R^1 = R^2 = H	Pseudo	Pseudo/ normal	King *et al* (1971); Renson (1961)
R = C_6H_5, R^1 = R^2 = H	Pseudo	Normal	Newman and Courduvelis (1966); Abramovitch *et al* (1978); Bhatt *et al* (1971)
R = $PCH_3C_6H_4$, R^1 = R^2 = H	Pseudo	Normal	Newman and Courduvelis (1966); Abramovitch *et al* (1978); Bhatt *et al* (1971); Somayaji (1980)
R = C_6H_5, R^1 = H, R^2 = CH_3	Pseudo	Normal	Newman and Courduvelis (1966); Abramovitch *et al* (1978); Bhatt *et al* (1971); Somayaji (1980)
R = Cl, R^1 = R^2 = H	Normal/ pseudo	Normal/ pseudo	Remsen (1903); Hollis (1900); Oddo and Tognacchini (1923); Bhatt *et al* (1980); Dart and Holt (1974)
R = Cl, R^1 = NO_2, R^2 = H	Normal	Normal/ pseudo	Bhatt *et al* (1980); Remsen (1903); Hollis (1900)

presence of dimethylformamide (at ambient temperature or under reflux) resulted in the formation of 2-benzoylbenzenesulphonyl chloride 16. Neither the pseudo derivative nor the dichloride could be detected. The same result was obtained when phosphorous pentachloride was used. This is in contrast to the behaviour of 1 and 6, which is perhaps due to the reduced reactivity of the ketone as compared to the aldehyde and chlorocarbonyl groups. In table 1 are compared the structures of products obtained from some of the γ-ketosulphonic acids and the corresponding γ-keto carboxylic acids.

In conclusion, the behaviour of γ-ketosulphonic acids bear close similarity to their carboxylic acid analogues, i.e., normal and pseudo acid chlorides are formed by two independent competing pathways. Furthermore, there is no tautomerism between the normal and pseudo forms. However, participation by the keto group is much more facile in carboxylic acids than in sulphonic acids.

3. Experimental

Melting points are uncorrected. ^{1}H NMR (PMR) spectra were recorded on either Varian T-60 or Jeol FX-900 spectrometers. Chemical shifts are referred to internal tetramethylsilane. IR spectra were recorded on a Perkin-Elmer 781 spectrometer. Chromatographic separations were carried out using silica gel (60–120 mesh).

3.1 *Reaction of sodium 2-formylbenzenesulphonate 1 with thionyl chloride*

3.1a *At ambient temperature*: Sodium 2-formylbenzenesulphonate 1 (2·5 g) was stirred with thionyl chloride (6 ml) and DMF (15 drops) for 24 h. Reaction mixture was decomposed with ice, and extracted with methylene chloride. Organic extract was washed with a solution of sodium bicarbonate, followed by water and dried. Solvent was removed by distillation. The product was crystallized from a benzene–hexane mixture. Pseudo sulphonyl chloride 2 was obtained 1·34 g, 54·5%, m.p. 111–2 [Lit. (Goldberger 1916) m.p. 113–4°] IR ν_{max}(nujol): 1600, 1380, 1330, 1300, 1260, 1240,

1210, 1190 cm^{-1} PMR ($CDCl_3$): δ 7·13 (*s*, 1H, ArCH), 7·6–8·0 (*m*, 4H, ArH).

The TLC and IR spectra of the sample before and after crystallization were identical.

3.1b *At reflux*: Sodium 2-formylbenzenesulphonate 1 (5 g) and DMF (0·5 ml) were refluxed with thionyl chloride (18 ml) at 100°C for three minutes. The reaction was quenched with ice and the product extracted into methylene chloride (50 ml × 2). The combined organic extract was washed with water, then sodium bicarbonate solution (till the aqueous layer remains basic) and again with water. Methylene chloride layer was dried and the solvent was distilled off. The oily liquid obtained was treated with pentane, when a solid was thrown out. It was crystallized from a benzene–hexane mixture and 2 was obtained. 1·68 g, 34·1%, m.p. 112–3° [Lit. (Goldberger 1916) m.p. 113–4°].

The pentane extract showed two products on TLC (eluent: hexane). They were separated by column chromatography.

Fraction 1: Eluent: hexane, 2-(dichloromethyl) benzenesulphonyl chloride 4, 0·23 g, 3·7%, m.p. 50–2° [Lit. (King *et al* 1971) m.p. 54–5°]. IR ν_{max}(nujol): 1440, 1180, 1120, 1060, 1040 cm^{-1}. PMR ($CDCl_3$): δ 7·38 (*s*, 1H, CHCl), 7·0–8·4 (*m*, 4H, ArH).

Fraction 2: Eluent: 30% benzene-hexane, 2-formylbenzene sulphonyl chloride 3, oily liquid, 0·80 g, 16·3% IR_{max}(neat): 1700, 1580, 1370, 1260, 1180, 1110 cm^{-1}. PMR (CCl_4): δ 7·6–8·4 (*m*, 4H, ArH), 10·8 (*s*, 1H, CHO).

3.1c *At reflux when reaction times are longer*: The above experiment was repeated using the sodium sulphonate 1 (1 g), DMF (0·2 ml) and thionyl chloride (5 ml). Time of reflux was 3 h. TLC of the product showed two spots. It was treated with pentane. The solid thrown out was 2, 0·3 g, 30·5%, m.p. 112–3° [Lit. (Goldberger 1916) m.p. 113–4°]. The pentane solution gave 4, 0·24 g, 19·2%, m.p. 52–3° [Lit. (King *et al* 1971) m.p. 54–5°].

3.2 *Reaction of 2-formylbenzenesulphonyl chloride 3 with thionyl chloride*

3.2a *At room temperature*: The sulphonyl chloride 3 (0·12 g, 0·5 mmol) and DMF (5 drops) were stirred in thionyl chloride (3 ml) for 12 h. It was decomposed with ice and extracted with methylene chloride. Methylene chloride layer was washed with a solution of sodium bicarbonate followed by water and dried. Solvent was removed by distillation. Starting material was recovered 0·10 g, 98%.

3.2b *At reflux*: The above reaction was carried out at reflux temperature for 0·5 h. 4 was obtained as the only product. 0·127 g, 98%, m.p. 51–3° [Lit. (King *et al* 1971) m.p. 54–5°].

3.3 *Reaction of sodium 2-(dichloromethyl)benzenesulphonate 5 with thionyl chloride*

The sulphonyl chloride 4 (0·26 g, 1 mmol) was solvolyzed with water in acetone for 24 h. The acid was neutralised with sodium bicarbonate to obtain the sodium salt 5. The salt so obtained was stirred with thionyl chloride (3 ml) and DMF (5 drops) for 12 h at ambient temperature. Reaction mixture was decomposed with ice and extracted with methylene chloride. The organic layer was washed with a solution of

sodium bicarbonate and water. It was then dried and the solvent was removed by distillation. 4 was obtained, 0·25 g, 96·1%, m.p. 50–2° [Lit. (King *et al* 1971) m.p. 50–2°].

3.4 *Isomerization of normal 2-formylbenzenesulphonyl chloride 3 to its pseudo isomer 2*

The normal sulphonyl chloride 3 (0·120 g, 0·5 mmol) was heated to 150–155° in a vacuum sealed tube for 6 h. The sealed tube was cooled and opened. The contents were dissolved in chloroform and the solution was filtered through a short column of silica gel. Chloroform was removed by distillation, 2 was obtained, 0·55 g, 54%, m.p. 113–4° [Lit. (Goldberger 1916) m.p. 114°].

3.5 *Reaction of ammonium 2-carboxylbenzenesulphonate 6 with thionyl chloride*

Ammonium salt 6 (1·1 g, 5·02 mmol) and DMF (10 drops) were refluxed in thionyl chloride (5 ml) for 3 h (solid slowly goes into solution which finally turns red). The reaction mixture was decomposed with ice and the product was extracted into methylene chloride (within 2 minutes). Organic layer was washed with dilute $NaHCO_3$ solution followed by water and dried. Methylene chloride was removed by distillation. An oily product was obtained which solidified on cooling to -5°C. TLC of the product showed a single spot (eluent; benzene–hexane mixture and benzene). It was crystallized from petroleum ether (40–60°). 2-Chlorocarbonylbenzenesulphonyl chloride 7 was obtained, 1 g, 83%, m.p. 37–9° [Lit. (Remsen 1903) m.p. 40°]. IR ν_{max}(neat): 1780, 1560, 1550, 1420, 1360, 1280, 1160, 1110, 1040 cm^{-1}.

3.6 *Reaction of the ammonium salt 6 with phosphorous pentachloride*

Ammonium salt 6 (5 g, 22·8 mmol) and phosphorous oxychloride (6 ml) were heated to reflux and phosphorous pentachloride (10 g, 48 mmol) was added in four portions over a period of 2 h. Refluxing was continued for another hour. The reaction mixture was decomposed with ice and the product was extracted into methylene chloride. Organic layer was washed with a solution of sodium bicarbonate and then with water. The solution was dried and the solvent was distilled off. An oily product was obtained which showed two spots on TLC. They were separated by column chromatography.

Fraction 1: Eluent: 30% benzene–hexane, 7, 3·007 g, 55%, m.p. 38–9° [Lit. (Remsen 1903) m.p. 40°]. IR ν_{max}(neat): 1780, 1560, 1550, 1420, 1360, 1280, 1160, 1110, 1040 cm^{-1}.

Fraction 2: Eluent: benzene, 8, 0·733 g, 13.4%, m.p. 76–8° [Lit. (Remsen 1903) m.p. 79°]. IR ν_{max}(nujol): 1560, 1440, 1300, 1180, 1120, 1050 cm^{-1}.

3.7 *Reaction of sodium 2-benzoylbenzenesulphonate 15 with thionyl chloride*

2-Benzoylbenzenesulphonyl chloride 16 (0·5 g, 1·78 mmol) was heated on a water bath for 6 h in aqueous dioxane. Dioxane was distilled off and the aqueous solution was neutralized with sodium bicarbonate. Water was removed as an azeotrope of benzene. The sodium salt obtained was stirred with thionyl chloride (4 ml) and DMF (10 drops)

at ambient temperature for 12 h. It was then decomposed with ice and extracted with methylene chloride. The organic layer was washed with a solution of sodium bicarbonate followed by water and dried. The solvent was removed by distillation. Normal 2-benzoylbenzenesulphonyl chloride 16 was obtained as the only product, 0·48 g, 96%, m.p. 96–7° [Lit. (Dart and Holt 1974) m.p. 98–9°]. IR ν_{max}(nujol): 1660, 1590, 1580, 1310, 1270, 1250, 1180 cm^{-1}.

3.8 *Reaction of sodium 2-benzoylbenzenesulphonate 15 with phosphorous pentachloride*

16 (0·5 g, 1·78 mmol) was solvolyzed and neutralized as above. The sodium salt 15 so obtained was heated to reflux in phosphorous oxychloride (3 ml) with phosphorous pentachloride (1 g, 4·8 mmol) for 2 h. It was then decomposed with ice and worked up as above. 16 was obtained as the only product, 0·457 g, 91·4%, m.p. 95–7° [Lit. (Dart and Holt 1974) m.p. 98–9°].

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