The Reaction of Arenesulphonyl Fluorides with Anhydrous Aluminium Chloride

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A general method is described in which arenesulphonyl fluorides can be converted into the corresponding arenesulphonyl chlorides in good yield by treatment with anhydrous aluminium chloride in boiling 1,2-dichloroethane.

SULPHONYL-CONTAINING molecules, many of which have considerable commercial importance as drugs (*e.g.* antibacterial chemotherapy and hypoglycemic agents),[1] or in photography (*e.g.* as photographic dye-releasing entities in instant photographic processes),[2] invariably utilize sulphonyl halides at some stage during the course of their syntheses. Aromatic sulphonyl chlorides are particularly useful in this context, but as the sulphonyl chloride group is not inert to a wide range of basic reagents, further modifications to a particular molecule with such reagents are ruled out, unless the readily hydrolysable sulphonyl chloride is converted into the much less reactive sulphonyl fluoride (equation (1)], by

$$ArSO_2Cl \xrightarrow[\text{dioxan } ca.\ 80°]{F^- - H_2O} ArSO_2F \qquad (1)$$

treatment with sodium or potassium fluoride in aqueous dioxan.[3] The problems posed at later stages of the syntheses will inevitably be reaction of the sulphonyl fluoride with other substrates. As the reverse reaction [equation (2)] has been little studied and its general

$$\underset{(1)}{ArSO_2F} \xrightarrow[\text{inert solvent } ca.\ 80°]{AlCl_3} \underset{(2)}{ArSO_2Cl} \qquad (2)$$

applicability has not been demonstrated, it was thought to be synthetically useful if a general method could be found to convert aromatic sulphonyl fluorides back into their corresponding more active chlorides in near quantitative yields in the presence of other functional groups.

Steinkopf and his co-workers[4] showed that aromatic hydrocarbons containing the sulphonyl fluoride group such as toluenesulphonyl fluoride and some nitro-containing derivatives such as 4-nitrotoluene-2-sulphonyl fluoride could be converted into the corresponding chlorides by treatment with anhydrous aluminium chloride in carbon disulphide at 50°. This method proved ineffective for toluene-2,4-disulphonyl fluoride and the transformation into the 2,4-disulphonyl chloride analogue was achieved by heating the reactants in nitrobenzene at 55—60° for 2 h.

In this paper, it is shown that the sulphonyl fluoride–chloride interconversion can be most conveniently carried out by dissolving or suspending the arenesulphonyl fluoride in boiling 1,2-dichloroethane followed by treatment with a 1—4 mole excess of anhydrous aluminium chloride. The reaction was found to proceed in good yield, greater than 65% in most cases (see Table). In this way the chlorides (2a—b) were prepared from the corresponding sulphonyl fluorides, except for compound (2g) which is discussed later.

The reaction could not, in general, be monitored by t.l.c., because pairs of sulphonyl fluorides and chlorides with the same aryl residue had identical R_F values in all the solvent systems examined. The sulphonyl chloride products were most easily distinguished from the starting fluorides by the strong S=O stretching frequencies of the sulphonyl halide group, which occur characteristically for the SO_2Cl group in the ranges 1 360—1 380 and 1 160—1 180 cm^{-1}, compared with 1 400—1 420 and 1 200—1 220 cm^{-1} for the SO_2F group in the compound pairs examined.[5] 1,2-Dichloroethane has advantages over nitrobenzene and carbon disulphide as the solvent of choice for the reaction. Nitrobenzene, though a good solvent for many organic compounds, has a high b.p. (210°), which after the work-up procedure can make purification of the product unnecessarily tedious and in

[1] 'Cutting's Handbook of Pharmacology', Appleton–Century–Crofts, New York, 1972, 5th edn., pp. 1—9, 35—37, and 386—389.

[2] W. T. Hanson, jun., *Photographic Science and Engineering*, 1976, **20**, 155.

[3] A. De Cat, R. Van Poucke, and M. Verbrugghe, *J. Org. Chem.*, 1965, **30**, 1498; A. De Cat and R. Van Poucke, *ibid.*, 1963, **28**, 3426; W. Davis and J. Dick, *J. Chem. Soc.*, 1931, 2104.

[4] W. Steinkopf, K. Buchkein, K. Beythein, H. Dudek, J. Eisold, J. Gall, P. Jaeger, H. Reumuth, A. Somenoff, and A. Wemme, *J. prakt. Chem.*, 1927, **117**, 1.

[5] A. D. Cross and R. A. Jones, 'An Introduction to Practical Infrared Spectroscopy', Butterworths, London, 1969, 3rd edn., p. 95, Table 30.

certain cases reduce the yield considerably, particularly if the sulphonyl chloride is temperature sensitive or readily hydrolysable. Carbon disulphide, on the other hand, has a low b.p. (48°) and a limited solvent capacity for polar organic compounds and the sulphonyl fluoride–chloride interconversion is often not possible. For example, 3-fluorosulphonylbenzoic acid can be recovered unchanged after refluxing for prolonged periods in carbon disulphide in the presence of excess of anhydrous aluminium chloride, whereas the transformation proceeds readily to 3-chlorosulphonylbenzoic acid in refluxing 1,2-dichloroethane.

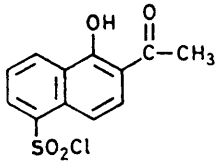
The sulphonyl fluoride–chloride interconversion can be carried out in the presence of many of the common functional groups when they comprise part of the aryl residue of the sulphonyl fluoride undergoing transformation. Included in this category are azo, amide, carboxylic acid, chloro, sulphonamido, nitro, keto, and hydroxy. Some exceptions to the generalization, however, were observed. Sulphanilyl fluoride was not converted to sulphanilyl chloride under the standard reaction condition; in this case, as might be anticipated, intractable polymeric condensates were obtained. The amino group, however, can be effectively protected by acetylation which allows the sulphonyl fluoride–chloride interconversion to proceed without complications [*cf.* (2j)]. On the other hand, the interconversion is facile for pyridyl nitrogen-containing compounds; for example, quinoline-8-sulphonyl fluoride is converted into the corresponding chloride (2l) in 58% yield.

Carbonate esters of isolated phenolic functions tend to deblock under the reaction conditions, *e.g.* 1-ethoxycarbonyloxynaphthalene-5-sulphonyl chloride was only obtained in 33% yield from the corresponding fluoride after separation by chromatography from intractable base-line material which also formed during the reaction. Acyl esters of isolated aromatic hydroxy functions can undergo concomitant Fries rearrangement with the sulphonyl fluoride–chloride interconversion. 5-Acetoxynaphthalene-1-sulphonyl fluoride was converted into 6-acetyl-5-hydroxynaphthalene-1-sulphonyl chloride (2g) in 71% yield. Compound (2g) was assigned a 1,2,5-naphthalene substitution pattern rather than the 1,4,5-substitution of the alternative isomer (3), because the i.r. spectrum of (2g) contained an absorption at 1 630 cm^{-1} typical of an *o*-hydroxyaryl ketone, whereas a typical

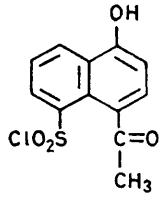
Yields, i.r. data, and m.p.s obtained from fluoride–chloride interconversion

Product [a]	Yield (%)	M.p. (°C)	I.r. absorptions assigned to SO_2F group in starting material (KBr disk) (cm^{-1})	I.r. absorptions assigned to SO_2Cl group in product (KBr disk) (cm^{-1})
Toluene-4-sulphonyl chloride (2a)	78	71	1 400	1 370
		(lit.,[6] 71)	1 200	1 170
3-Nitrobenzenesulphonyl chloride (2b)	64	61	1 415	1 385
		(lit.,[7] 61.5)	1 215	1 175
4-Nitrobenzenesulphonyl chloride (2c)	85	79	1 415	1 375
		(lit.,[7] 80)	1 215	1 175
4-Chlorobenzenesulphonyl chloride (2d)	70	51	1 405	1 375
		(lit.,[9] 53)	1 210	1 118
3-Chlorosulphonylbenzoic acid (2e)	71	136—137)	1 410	1 370
		(lit.,[10] 133—134)	1 210	1 180
5-Ethoxycarbonyloxynaphthalene-1-sulphonyl chloride (2f)	33 [b]	80	1 400	1 375
		(lit.,[11] 79)	1 220	1 175
6-Acetyl-5-hydroxynaphthalene-1-sulphonyl chloride [c] (2g)	71	148	1 400	1 370
			1 205	1 170
2,6-Dichloro-4-(4-chlorosulphonylbenzeneazo)phenol (2h)	85	146—147	1 410	1 390
			1 205	1 175
2-Chloro-5-(3-chlorosulphonylbenzeneazo)salicylamide (2i)	67	186	1 405	1 390
			1 205	1 185
4-Chlorosulphonylacetanilide (2j)	92	151	1 400	1 370
		(lit.,[8] 149)	1 210	1 175
3-Chloro-5-[3-(4-chlorosulphonylbenzenesulphamoyl)benzeneazo]-2-hydroxy-*N*-methylbenzamide (2k)	98	250 (decomp.)	1 405	1 375
			1 210	1 175
Quinoline-8-sulphonyl chloride (2l)	58	127	1 405	1 375
		(lit.,[12] 124)	1 210	1 175

[a] Starting material was the corresponding sulphonyl fluoride unless otherwise indicated. [b] After chromatography. [c] Obtained from 5-acetoxynaphthalene-1-sulphonyl fluoride.



(2g)

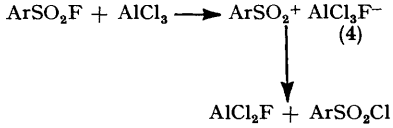


(3)

[6] 'Dictionary of Organic Compounds', Eyre and Spottiswoode, London, 1965, 4th edn., Coll. Vol. 1, p. 2072.
[7] Ref. 5, Coll. Vol. 4, p. 2433.
[8] S. Smiles and J. Stewart, *Org. Synth.*, 1951, Coll. Vol. 1, 7.
[9] Ref. 5, Coll. Vol. 2, p. 601.
[10] H. Limpricht and L. von Uslar, *Annalen*, 1858, **106**, 30.
[11] H. Rennert, *Ber.*, 1915, **48**, 462.
[12] Ref. 5, Coll. Vol. 5, p. 2845.

aryl ketone such as (3) would be expected to absorb in a higher frequency range between 1 700 and 1 680 cm^{-1}. Furthermore, the n.m.r. spectrum of (2g) show a signal for an exceptionally low field hydroxy proton at δ 14.0 as a sharp singlet exchangeable with D_2O and an aromatic splitting pattern in accord with a 1,2,5-substituted naphthalene nucleus.

An n.m.r. spectral comparison of all the sulphonyl chloride–fluoride pairs examined, with the exception of (2g), which has been discussed above, showed no alteration in the aromatic substitution pattern, indicating that no positional isomerisation of the sulphonyl halide group had taken place during the reaction. It is therefore concluded that the only bond broken during the reaction was the sulphur–halogen bond. On this basis the most reasonable mechanism for the sulphonyl fluoride–chloride interconversion is probably *via* the arenesulphonium cation complex (4) (see Scheme), by



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analogy with the formation of sulphones from arenesulphonyl esters [13] and chlorides [14] with anhydrous aluminium chloride *via* similar intermediates which are closely related to acylium cation complexes known to be intermediates in Friedel–Crafts reactions.[15]

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 157G spectrometer as KBr disks, n.m.r. spectra were recorded on a Perkin-Elmer R12B at 60 MHz, or JEOL FX-100 spectrometer at 100 Mz in deuteriochloroform with tetramethylsilane as internal standard unless otherwise stated. M.p.s are uncorrected.

The known compounds (2a—f and j) were identified by elemental analysis, i.r. and n.m.r. spectroscopy, and comparison of m.p.s with those of authentic samples.

General Procedure for Conversion of an Arenesulphonyl Fluoride into the Corresponding Chloride.—The fluoride (3×10^{-2} mol) was dissolved or suspended in 1,2-dichloroethane (*ca.* 50 ml) and anhydrous aluminium chloride powder (3×10^{-2}—1.2×10^{-1} mol) was added to the stirred solution or suspension which was then refluxed from 1—4 h. After cooling, the mixture was poured into ice-cold dilute hydrochloric acid (*ca.* 400 ml, 3N) and extracted with chloroform or ethyl acetate. The extract was dried (Na_2SO_4) and the solvent removed to give the chloride which was purified by recrystallization from a suitable solvent or in some cases by column chromatography. Yields are shown in the Table.

2,6-*Dichloro*-4-(4-*chlorosulphonylbenzeneazo*)*phenol* (2h), prepared from the corresponding fluoride by the above general method had m.p. 146—147° (from EtOAc), $\nu_{max.}$(KBr) 3 420, 1 480, 1 175, 1 140, and 800 cm^{-1}; δ 6.36br (OH), 8.09 (2 H, s), and 8.15 and 8.21 (4 H, AB, J_{AB} 6.85 Hz) (Found: C, 39.7; H, 2.1; Cl, 29.2; N, 7.6; S, 8.9. $C_{12}H_7Cl_3N_2O_3S$ requires C, 39.7; H, 1.9; Cl, 29.1; N, 7.7; S, 8.8%).

6-*Acetyl*-5-*hydroxynaphthalene*-1-*sulphonyl chloride* (2g) prepared from 5-acetoxynaphthalene-1-sulphonyl fluoride by the above general method had m.p. 148° (from AcOH), $\nu_{max.}$(KBr) 1 630, 1 460, 1 370, 1 265, 1 170, and 795 cm^{-1}; δ 2.76 (s, COMe), 7.63 (t, 3-H), 7.96 and 8.17 (AB, 7- and 8-H), 8.46 (dd, 2-H), 8.83 (dd, 4-H), and 14.0 (s, OH), $J_{7,8}$ 9.30, $J_{4,8}$ *ca.* 0.5, $J_{3,4}$ 7.80, $J_{2,4}$ 1.45, $J_{3,4}$ 8.30 Hz (Found: C, 50.9; H, 3.3; Cl, 12.3; S, 11.1. $C_{12}H_9ClO_4S$ requires C, 50.6; H, 3.2; Cl, 12.5; S, 11.25%).

3-*Chloro*-5-(3-*chlorosulphonylbenzeneazo*)*salicylamide* (2i), prepared from the corresponding fluoride. had m.p. 186° (from EtOAc). The crystals contained 0.5 mole of ethyl acetate of crystallization, $\nu_{max.}$(KBr) 3 430m, 3 360m, 1 705 (EtOAc), 1 660, 1 620, 1 470, 1 390, and 1 185 cm^{-1}; δ 6.20br ($CONH_2$), 7.80 (1 H, t), 8.11 and 8.24 (2 H, AB), 8.15 (1 H, dt), 8.27 (1 H, dt), 8.51 (1 H, t), and 12.9 (s, OH) (Found: C, 42.8; H, 2.95; Cl, 17.1; N, 10.25. $C_{13}H_9Cl_2N_3O_4S$,0.5EtOAc requires C, 43.1; H, 3.1; Cl, 17.0; N, 10.05%).

3-*Chloro*-5-[3-(4-*chlorosulphonylbenzenesulphamoyl*)*benzeneazo*]-2-*hydroxy*-N-*methylbenzamide* (2k) prepared from the corresponding fluoride had m.p. 250° (decomp.), $\nu_{max.}$(KBr) 3 420, 3 200m, 1 645, 1 590, 1 490, 1 375, 1 175, 1 165, and 1 150 cm^{-1}; δ([$^2H_6$]DMSO) 2.90 (d, collapses to s on shaking with D_2O, CH_3NH_2), 7.17 and 7.59 (4 H, A_2B_2), 7.73 (t), 7.95 (dt), 8.00 (d), 8.0 (dt, overlapping other resonances), 8.04 (t, 5 H), 8.55 (d, H), 9.48br (q, CONH), and 10.52br (s, SO_2NH) (Found: C, 44.7; H, 3.3; Cl, 12.7; N, 9.7; S, 11.5. $C_{20}H_{16}Cl_2N_4O_6S$ requires C, 44.2; H, 3.0; Cl, 13.0; N, 10.30; S, 11.8%).

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