889. *The Action of Aluminium Chloride on Some* o-*Alkylbenzenesulphonic Acids and* o-*Alkyldiphenyl Sulphones.*

By G. Holt and B. Pagdin.

o-Alkylbenzenesulphonic acids and *o*-alkyldiphenyl sulphones isomerise when fused with aluminium chloride, to give products which are frequently not readily available by other means. Conversion of 2,4,6-trimethylbenzenesulphonic acid into the 3,4,5-isomer followed by desulphonation is a simple procedure for the preparation of 1,2,3-trimethylbenzene. In the sulphone series rearranged products were obtained only when two *o*-methyl groups were present but one sufficed in the sulphonic acids. The greater mobility of the ethyl group is demonstrated by the rearrangement of both sulphonic acids and of sulphones containing one such *ortho*-substituent.

The literature contains no references to the action of aluminium chloride on alkylbenzenesulphonic acids or on alkylated diphenyl sulphones. Baddeley[1] has shown that *o*-alkylated aromatic ketones undergo a variety of irreversible isomerisations when fused with aluminium chloride to provide benzene derivatives which in some instances are not readily

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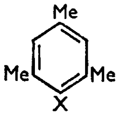
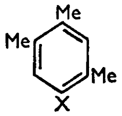
[1] Baddeley, *Quart. Rev.*, 1954, **8**, 355.

available by other means because of the unusual orientation of the substituents. For example, 3,4,5-trimethylacetophenone has been obtained from its readily available 2,4,6-isomer. Migration of alkyl groups in alkylbenzenesulphonic acids (the Jacobsen reaction [2]) occurs only when the aromatic ring has at least four alkyl substituents. We now report the migration of alkyl groups in the aromatic sulphonic acids and sulphones in which the aromatic ring has three and in some instances only two alkyl substituents.

With aluminium chloride at 200° 2,4,6- and 2,4,5-trimethyldiphenyl sulphone (I and II; X = SO_2Ph) afforded the 3,4,5-isomer (III; X = SO_2Ph) in substantially the same yield (26%):



(I)



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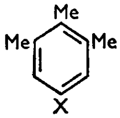

(III)

The greater influence of two *o*-alkyl groups than of one on these reactions is illustrated by the observation that 2,4,6-trimethyldiphenyl sulphone yields the 2,4,5-isomer at 140° (65%) and that even after prolonged heating at this temperature none of the 3,4,5-isomer could be isolated although the latter is formed at 200°. Even at this higher temperature, 2-methyl- and 2,5-dimethyl-diphenyl sulphone failed to rearrange. In view of the recognised greater mobility of ethyl groups 2,5-diethyldiphenyl sulphone was fused with aluminium chloride at 150°: it gave 3,5-diethyldiphenyl sulphone in 45% yield.

Fusion of the corresponding sodium alkylbenzenesulphonates with aluminium chloride provided somewhat similar results but, in general, isomerisation proceeded more readily. The results are shown in the Table.

Alkylbenzenesulphonic acid	Fusion temp.	Reaction time (hr.)	Rearrangement product
2,4,6-Me_3 (I; X = SO_3H)	140°	5	2,4,5-Me_3 (73%) *
,, ,,	200	10	3,4,5-Me_3 (60%)
2,4,5-Me_3 (II; X = SO_3H)	200	10	3,4,5-Me_3 (16%)
2,5-Me_2	200	12·5	3,5-Me_2 (59%)
2,5-Et_2	150	5	3,5-Et_2 (30%)
2,4,6-Et_3	150	5	3,5-Et_2 (30%)

* Based on 1,2,4-trimethylbenzene obtained by hydrolysis of the sulphonic acid.

The isolation of 3,5-dimethylbenzenesulphonic acid when the 2,5-isomer is fused with aluminium chloride at 200° demonstrates the greater mobility of alkyl groups in sulphonic acids than in sulphones since no rearranged product was isolated from 2,5-dimethyldiphenyl sulphone under similar conditions. In the Jacobsen reaction both intramolecular and intermolecular migration of alkyl groups is encountered. No products of intermolecular alkyl group migration have been isolated in the present work although it is possible that these were formed in small amounts and remained undetected. That alkyl groups can be lost in the aluminium chloride-catalysed isomerisation of sulphonic acids is shown by the isolation of 3,5-diethylbenzenesulphonic acid when 2,4,6-triethylbenzenesulphonic acid is fused at 150°. Presumably the two *o*-alkyl groups migrate to the corresponding *meta*-positions and an ethyl group is eliminated from the first formed 3,4,5-isomer.

In view of the experimental difficulties involved in the isolation of the sulphonic acids the yields claimed are conservative. A more accurate assessment of the yield was obtained in some instances by hydrolysis of the products and isolation and identification of the resulting benzene homologues: thus fractional hydrolysis of the sulphonic acids

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[2] "Organic Reactions," Adams, New York, John Wiley & Sons Inc., 1942, Vol. I, Compilation of References, p. 370.

given by 2,4,6-trimethylbenzenesulphonic acid when heated with aluminium chloride at 140° for 5 hours gave mesitylene (2%) and 1,2,4-trimethylbenzene (73%), whereas the corresponding 2,4,5-trimethylbenzenesulphonic acid was isolated, as the sulphonamide, in only 56% yield. This hydrolysis procedure was not always so satisfactory; *e.g.*, fractional hydrolysis of the product obtained when the above fusion was carried out at 200° gave 1,2,3-trimethylbenzene in only 30% yield although its sulphonic acid, as the sulphonyl chloride, was isolated in 60% yield. This difference is a consequence of the difficulty of hydrolysing benzenesulphonic acids which do not have an *o*-alkyl substituent.

The results outlined above make it clear that: (i) the migration of one *o*-alkyl group is facilitated by a second alkyl group in the other *o*-position; (ii) an ethyl group is more mobile than a methyl group; (iii) isomerisation of a sulphone is more difficult than that of the corresponding sulphonic acid; and (iv) isomerisation of both sulphones and sulphonic acids is more difficult than that of the corresponding alkyl aryl ketones.[3,4]

Several of the isomerisations described above make available new sulphonic acids and sulphones. An example is 3,4,5-trimethylbenzenesulphonic acid, obtained from the readily available 2,4,6-isomer. Sulphonation of 1,2,3-trimethylbenzene provides, of course, 2,3,4-trimethylbenzenesulphonic acid.[5] Again, the preparation of 3,5-dimethylbenzenesulphonic acid by isomerisation of the 2,5-isomer is much simpler than procedures described previously.[6]

EXPERIMENTAL

Fusion of Sulphones with Aluminium Chloride.—The sulphone (1 part) was added in small portions to a stirred melt of aluminium chloride (10 parts) and sodium chloride (1 part). After being heated for the time and at the temperature indicated below, the melt was cooled to 120° and poured cautiously with stirring into ice and dilute hydrochloric acid. The resulting mixture was extracted with ethylene dichloride, and the extracts were washed with water and with sodium hydroxide solution and dried (K_2CO_3). The solvent was distilled off and the residue purified as described below.

(*a*) 2,4,6-Trimethyldiphenyl sulphone [7] (2 g.) on fusion at 140° for 9 hr. gave a pale brown solid (1·6 g.) which, on crystallisation from ethanol, provided fern-like crystals (1·3 g., 65%) of 2,4,5-trimethyldiphenyl sulphone,[7] m. p. and mixed m. p. 136—137°. Attempts to effect a more efficient separation by chromatography on alumina were unsuccessful.

(*b*) 2,4,5-Trimethyldiphenyl sulphone (5 g.) on fusion at 200° for 10 hr. gave a crude product (4·25 g.; m. p. 104—110°) which on fractional crystallisation from ethanol yielded 3,4,5-trimethyldiphenyl sulphone [7] (1·3 g., 26%), m. p. and mixed m. p. 159—161°, and unchanged starting material (0·3 g.). The same sulphone on fusion in a sealed tube at 250° for 5 hr. yielded only carbonaceous material and intractable tar.

(*c*) 2,5-Dimethyldiphenyl sulphone [7] (2 g.) on fusion at 200° for 10 hr. gave a pale brown oil (1·6 g.), fractional crystallisation of which from light petroleum (b. p. 60—80°) afforded only unchanged starting material (0·6 g.), m. p. and mixed m. p. 108—110°.

(*d*) 2-Methyldiphenyl sulphone [7] (5 g.) on fusion at 200° for 48 hr. gave a black semi-solid mass (4·2 g.), extraction of which with light petroleum (b. p. 0—40°) yielded only unchanged starting material (1·3 g.), m. p. and mixed m. p. 79—80°.

(*e*) 2,5-Diethyldiphenyl sulphone [7] (2 g.), m. p. 84—86°, on fusion at 150° for 5 hr. gave a sticky product which was extracted with light petroleum (b. p. 40—60°). The extract, on cooling and partial removal of the solvent, yielded a solid which on crystallisation from benzene–light petroleum gave 3,5-*diethyldiphenyl sulphone* (0·9 g., 45%), m. p. 84—86° (Found: C, 70·2; H, 6·6; S, 11·7. $C_{16}H_{18}O_2S$ requires C, 70·1; H, 6·6; S, 11·7%). This depressed the m. p. of the starting material and yielded on oxidation by nitric acid an acid, m. p. 236°, identical (mixed m. p.) with the acid similarly obtained by oxidation of 3,5-dimethyldiphenyl sulphone.

Fusion of Sodium Sulphonates with Aluminium Chloride.—The sodium sulphonate (1 part) was added in small portions to a stirred melt of aluminium chloride (10 parts) and sodium

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[3] Baddeley, *J.*, 1944, 232.

[4] Varma, Ph.D. Thesis, Manchester, 1955.

[5] Auwers and Weiners, *Ber.*, 1925, **58**, 2815.

[6] Moschner, *Ber.*, 1901, **34**, 1260.

[7] Holt and Pagdin, *J.*, 1960, 2508.

chloride (1 part). After being heated for the time and at the temperature indicated below the melt was cooled to 120° and poured cautiously with stirring into a mixture of ice and water. The resulting mixture was filtered to remove carbonaceous material, heated to boiling, and rendered just neutral to litmus by the addition of sodium hydroxide solution. The precipitated aluminium hydroxide was coagulated by further heating, filtered off, and washed with hot water. The combined filtrate and washings were evaporated and the dry mixture of sodium sulphonates and sodium chloride was treated with phosphorus pentachloride and phosphorus oxychloride. The crude sulphonyl chloride was treated as indicated below. Alternatively, the mixture of sulphonic acids was subjected to fractional hydrolysis and the resulting hydrocarbons were collected and characterised.

(*a*) Sodium 2,4,6-trimethylbenzenesulphonate (5 g.) after reaction at 140° for 5 hr. and subsequent working up provided a sulphonyl chloride (3·84 g., 78%, m. p. 47—58°). The latter yielded a mixture of sulphonamides from which 2,4,5-trimethylbenzenesulphonamide (56%; m. p. 181°) was isolated by virtue of the insolubility of its sodium salt in water. The mixture of sulphonic acids resulting from a similar fusion of sulphonate (10 g.) was subjected to fractional desulphonation. Hydrolysis of the small amount of unchanged 2,4,6-trimethylbenzenesulphonic acid by the procedure of Smith and Cass [8] provided 1,3,5-trimethylbenzene (0·15 g., 2%; b. p. 160—164°) (sulphonamide,[9] m. p. and mixed m. p. 144°). The residual 2,4,5-trimethylbenzenesulphonic acid was hydrolysed by passing steam through its solution in 50% sulphuric acid at 140°. 1,2,4-Trimethylbenzene (3·9 g., 73%; b. p. 166—169°, n_D^{20} 1·5035) (sulphonamide m. p. and mixed m. p. 181°) was isolated from the distillate. No further hydrocarbon could be isolated even though the temperature of the mixture was raised to 200° whilst superheated steam was passed through it.

Isomerisation of sodium 2,4,6-trimethylbenzenesulphonate at 200° for 10 hr. gave sodium 3,4,5-trimethylbenzenesulphonate, isolated as the *sulphonyl chloride* (60%) which separated from light petroleum (b. p. 0—40°) in parallelepipeds, m. p. 119—121° (Found: C, 49·2; H, 5·3. $C_9H_{11}ClO_2S$ requires C, 49·4; H, 5·3%). The *sulphonamide* separated from ethanol in needles, m. p. and mixed m. p. 171—173° (Found: C, 54·6; H, 6·4; N, 7·3. $C_9H_{13}NO_2S$ requires C, 54·3; H, 6·5; N, 7·0%). When fused with potassium hydroxide according to Hartmann's method [10] the above sulphonyl chloride gave 3,4,5-trimethylphenol,[11] m. p. and mixed m. p. 102—104°.

(*b*) Sodium 2,4,5-trimethylbenzenesulphonate, after reaction at 200° for 15 hr., gave a mixture of sodium salts and thence an oily sulphonyl chloride (10 g., 51%). The solid (3 g.) obtained by triturating this oil with light petroleum yielded a sulphonamide which did not depress the m. p. (171—173°) of 3,4,5-trimethylbenzenesulphonamide. The oily portion of the sulphonyl chloride on treatment with ammonia provided a mixture of sulphonamides which could not be separated. The mixture of sulphonic acids produced in this reaction was subjected to fractional hydrolysis with phosphoric acid as described below for the 2,4,6-isomer. 1,2,4-Trimethylbenzene (8·5%) and 1,2,3-trimethylbenzene (16·5%) were obtained and characterised as their sulphonamides.

(*c*) Sodium 2,5-dimethylbenzenesulphonate (20 g.), after reaction at 200° for 12 hr., gave a sulphonyl chloride (11·7 g., 59%; m. p. 82—88°) which on crystallisation from light petroleum (b. p. 60—80°) yielded 3,5-dimethylbenzenesulphonyl chloride, m. p. 91—92° (Found: C, 47·0; H, 4·3. Calc. for $C_8H_9ClO_2S$: C, 46·9; H, 4·4%). The sulphonamide (Found: C, 52·1; H, 6·1; N, 7·4. Calc. for $C_8H_{11}NO_2S$: C, 51·9; H, 6·0; N, 7·6%) prepared from this chloride did not depress the m. p. (135·5°) of authentic 3,5-dimethylbenzenesulphonamide.[6] The sulphonyl chloride, on fusion with potassium hydroxide, provided 1,3,5-xylenol,[12] m. p. and mixed m. p. 64°, which was further characterised as its toluene-*p*-sulphonate, m. p. 84°.

(*d*) Sodium 2,5-diethylbenzenesulphonate (20 g.), after reaction at 150° for 5 hr., gave a dark brown oily sulphonyl chloride (14·4 g., 69%). The latter (2 g.) afforded 3,5-*diethylbenzenesulphonamide* (0·55 g., 30%), m. p. 93° (Found: C, 56·3; H, 7·0; N, 6·6; S, 14·5. $C_{10}H_{15}NO_2S$ requires C, 56·5; H, 7·1; N, 6·6; S, 15·0%). No identifiable products were obtained by crystallisation or chromatography of the material contained in the benzene–light petroleum

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[8] Smith and Cass, *J. Amer. Chem. Soc.*, 1932, **54**, 1603.
[9] Gibson, *J.*, 1920, **117**, 953.
[10] Hartmann, *Org. Synth.*, 1923, **3**, 37.
[11] Baddeley, *J.*, 1943, 527.
[12] Ipatiew and Petrow, *Ber.*, 1927, **60**, 1963.

mother liquor from the crystallisation of this sulphonamide. Attempts to purify the crude sulphonyl chloride by fractional distillation were unsuccessful.

(*e*) Sodium 2,4,6-triethylbenzenesulphonate (5 g.), after reaction at 150° for 5 hr., gave an oily sulphonyl chloride (3·2 g., 65%) which, with ammonia, provided an oily sulphonamide (3 g.). The latter on trituration with ethanol yielded a sticky solid (0·5 g.) which was extracted with light petroleum (b. p. 60—80°); the extracts slowly deposited a white solid (0·33 g.), m. p. 89—91°. Recrystallisation from light petroleum (b. p. 60—80°) gave 3,5-diethylbenzenesulphonamide (0·3 g.) as needles, m. p. 91—92° (Found: C, 56·1; H, 7·0; S, 15·0%). This material did not depress the m. p. (91—92°) of the 3,5-diethylbenzenesulphonamide obtained in the previous experiment. When the fusion was carried out at 120° for 1·5 hr. the product appeared to be extremely complex and no solid sulphonamide was obtained.

Preparation of 1,2,3-*Trimethylbenzene from* 2,4,6-*Trimethylbenzenesulphonic Acid.*—Sodium 2,4,6-trimethylbenzenesulphonate (50 g.) was fused with aluminium chloride (200 g.) and sodium chloride (16 g.) at 200° for 10 hr. The cooled melt was decomposed by water (2 l.) and after the addition of phosphoric acid (1 l.; *d* 1·750) the mixture was heated whilst steam was passed through it. When the temperature inside the flask reached 140° hydrocarbon began to pass over with the steam and distillation was continued at this temperature until oily drops no longer passed over. The distillate was neutralised and extracted with chloroform, and the dried (K_2CO_3) extracts were concentrated. Distillation of the residue provided 1,2,4-trimethylbenzene (2·3 g., 8·5%; b. p. 164—165°) (sulphonamide, m. p. and mixed m. p. 179—181°). The temperature inside the flask was raised until, at 170°, oil again appeared in the steam-distillate. The oil was removed from the distillate by extraction with chloroform, and the residue obtained on concentration of the dried chloroform extracts was distilled to provide 1,2,3-trimethylbenzene (8 g., 30%; b. p. 168—172°) (sulphonamide,[5] m. p. and mixed m. p. 194—196°).

Alternative Syntheses.—3,5-*Dimethylbenzenesulphonamide.* The neutral sulphate of 2,4-dimethylaniline was heated under reduced pressure,[13] providing 2-amino-3,5-dimethylbenzenesulphonic acid (56%). The latter on deamination [14] provided 3,5-dimethylbenzenesulphonic acid which was converted into the sulphonamide (m. p. 135·5°) in the usual manner.

3,4,5-*Trimethylbenzenesulphonamide.* 3,4,5-Trimethylacetophenone oxime [3] on Beckmann rearrangement with polyphosphoric acid afforded 3,4,5-trimethylacetanilide in virtually quantitative yield. Hydrolysis of this acetyl derivative gave 5-amino-1,2,3-trimethylbenzene [15] (90%) which was diazotised and converted [16] into the corresponding sulphinic acid (23%). Treatment of the latter with chlorine and ammonia afforded the required sulphonamide (60%), m. p. 169—172° (from ethanol) (Found: C, 54·6; H, 6·4; N, 7·3. Calc. for $C_9H_{13}NO_2S$: C, 54·3; H, 6·5; N, 7·0%).

Separation of 2,4,5- *and* 2,4,6-*Trimethylbenzenesulphonamide.*—To an intimate mixture of 2,4,6-trimethylbenzenesulphonamide (1 g.) and 2,4,5-trimethylbenzenesulphonamide (1 g.) was added 2N-sodium hydroxide (10 ml.). The sodium 2,4,6-trimethylbenzenesulphonamide was dissolved by warming the stirred mixture to 60°. The cooled (10°) suspension was filtered, the solid was washed with a few drops of 2N-sodium hydroxide, and the combined filtrate and washings (A) were collected. The solid (1·13 g.) was taken up in the minimum volume of hot water and acidified with 2N-sulphuric acid. The sulphonamide which crystallised from the cooled solution was separated, washed with cold water until sulphate-free, and dried (0·85 g., 85%; m. p. 175—178°). One recrystallisation from aqueous ethanol gave 2,4,5-trimethylbenzenesulphonamide [8] as white needles, m. p. and mixed m. p. 180—181°.

The combined filtrate and washings (A) were acidified with 2N-sulphuric acid, and the solid was separated, washed free from sulphate, and dried, giving material (1·02 g.) of m. p. 139—143°. Recrystallisation from aqueous alcohol provided pure 2,4,6-trimethylbenzenesulphonamide,[8] m. p. and mixed m. p. 143—144°.

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[13] Junghahn, *Ber.*, 1902, **35**, 3750.
[14] Wallingford and Krueger, *Org. Synth.*, Coll. Vol. II, p. 353.
[15] Horning and Stromberg, *J. Amer. Chem. Soc.*, 1952, **74**, 2680.
[16] Gattermann, *Ber.*, 1899, **32**, 1136; Haworth and Lapworth, *J.*, 1923, **123**, 2982.