Synthesis of *NN*-Diaryltoluene-4-sulphonamides

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The copper-catalysed reaction of *N*-arylsulphonamides with aryl bromides gives moderate to good yields of *NN*-diarylsulphonamides. The effect on yield of substituents is examined and the use of the synthesis as a route to unsymmetric diphenylamines is discussed.

In the course of an investigation of the oxidation of diphenylamines we required a series of unsymmetrically substituted *NN*-diaryltoluene-4-sulphonamides. Unsymmetric diphenylamines are usually prepared by the copper-catalysed reaction of aryl halides with arylamines (the Ullmann reaction) or with *N*-acylarylamines (the Goldberg reaction) but yields are poor to moderate unless the aryl halide bears strongly electron-withdrawing groups.[1] However, the resulting weakly nucleophilic diphenylamines form sulphonamides with difficulty.[2] The Chapman rearrangement [1] of aryl *N*-arylbenzimidates gives a wider range of *N*-benzoyldiphenylamines but the reaction conditions are often critical and the resulting amide must be hydrolysed before the desired diphenylamine is available for sulphonamide formation.

Since primary sulphonamides in the presence of copper salts react with suitably activated aryl halides to give *N*-arylsulphonamides,[3] the direct synthesis of *NN*-diarylsulphonamides by an analogous reaction of aryl bromides with *N*-arylsulphonamides was investigated. In general a moderate to good yield of *NN*-diarylsulphonamide can be obtained (see Table) by heating an *N*-arylsulphonamide with an aryl bromide in the presence of copper bronze and anhydrous potassium carbonate, provided that there is an alkoxy-substituent in the secondary sulphonamide and a nitro- or alkoxy-substituent in the bromide.

It may be that the mesomeric effect of the alkoxy-substituent enhances the nucleophilicity of the sulphonamide anion. In agreement with this, the 4-nitrobenzenesulphonamides of aniline and of 4-anisidine (the anions of which should be less nucleophilic than those of the corresponding toluene-4-sulphonamides) when treated with 4-bromoanisole gave respectively 12 and 51% yields of corresponding tertiary sulphonamide; this is a poor yield when the ease of isolation of the highly crystalline products is considered.

It is less easy to explain the effect of the substituent in

[1] (*a*) J. W. Schulenberg and S. Archer, *Org. Reactions*, 1965, **14**, 1; (*b*) K. Nakamura, A. Ohno, and S. Oka, *Synthesis*, 1974, 883.

[2] P. Mesnard, B. Gibirila, and M. Bertucat, *Bull. Soc. pharm. Bordeaux*, 1963, **102**, 17.

[3] P. Ruggli and F. Brandt, *Helv. Chim. Acta*, 1944, **27**, 274; F. Ullmann, *Ber.*, 1910, **43**, 536; F. Ullmann and H. Bincer, *ibid.*, 1916, **49**, 732; F. Ullmann and P. Ochsner, *Annalen*, 1911, **381**, 1.

the aryl bromide. Although the nitro-group is the most effective for increasing the yield of *NN*-diarylsulphonamide, the good results obtained with phenyl- and alkoxy-substituted bromobenzenes may reflect the stability of the final product rather than electronic effects in the bromide.

After these studies were completed, it was reported [4] that if *N*-phenylbenzenesulphonamide was converted into its sodium salt with sodium hydride in dimethylacetamide, and the product was then heated with bromobenzene and copper(I) iodide in the same solvent, a poor yield of *NN*-diphenylbenzenesulphonamide was obtained. Because of the extensive decomposition of the toluidine sulphonamides which resulted from our experimental method, we examined the reaction under these alternative conditions of the toluene-4-sulphonamide of 4-toluidine with bromobenzene and with 4-bromoanisole. The results, given in parentheses in the Table, suggest that this route is a useful alternative for the synthesis of alkyl-substituted *NN*-diarylsulphonamides not accessible by the simple Ullmann procedure.

Reaction of sulphonamides, $RC_6H_4\cdot NH\cdot SO_2\cdot C_6H_4Me$-4, with bromides, $R'C_6H_4Br$

R	R′	Yield of *NN*-diarylsulphonamide (%)	M.p. (°C)
4-MeO	4-Me	45	96—97
4-Me	4-MeO	29 (73)	
4-MeO	4-MeO	82	129—130
4-MeO	2-MeO	63	106—106.5
2-MeO	4-MeO	84	
2-MeO	4-Ph	85	169—170
2-MeO	4-MeO, 2-Me	76	136—137
4-$PhCH_2O$	4-MeO	67	147—148
2-$PhCH_2O$	4-$PhCH_2O$	76	134—135
H	4-NO_2	91	161—162
4-Me	4-NO_2	64	148—149
4-MeO	4-NO_2	84	100—101
3-MeO	4-NO_2	86	103—104
4-$PhCH_2O$	4-NO_2	74	132—133
4-$PhCH_2O$	2-NO_2	98	147—148
4-MeO	H	70	92.5—93
H	4-OMe	14	
2-MeO	4-Cl	20	122—123
H	4-Me	12	120—121
4-Me	H	7 (44)	
4-Me	4-Me	9	141—142
H	H	9	141—142 †
4-NO_2	H	0 [b]	
4-NO_2	4-Me	0 [c]	

[a] With extensive decomposition. [b] 4-Nitrotriphenylamine (7%) isolated. [c] 4,4′-Dimethyl-4″-nitrotriphenylamine (6%) isolated.

† Lit., 141° (F. Reverdin and P. Crepieux, *Ber.*, 1902, **35**, 1441).

Although this work has been primarily concerned with the synthesis of asymmetric *NN*-diarylsulphonamides, the ready cleavage of such compounds with sodium 3-methylbutoxide [5] means that the corresponding diphenylamines can now easily be prepared: *e.g.* we have obtained 2,4′-dimethoxydiphenylamine in 60% overall yield from 2-bromoanisole and the toluene-4-sulphonamide of 4-anisidine.

EXPERIMENTAL

Melting points are corrected. All the tertiary sulphonamides showed an absence of N–H absorption in their i.r. spectra, and had n.m.r. spectra consistent with their proposed structures. Analytical data are available as Supplementary Publication No. SUP 21473 (2 pp.).*

General Preparation of NN-*Diarylsulphonamides.*—All reactants were carefully dried before use, as water seriously reduced the yield of tertiary sulphonamide.

An intimate mixture of *N*-aryltoluene-4-sulphonamide (0.01 mol), aryl bromide (0.012 mol), anhydrous potassium carbonate (0.012 mol), and copper bronze (2 g) was heated for 24 h under an air condenser at 180 °C; during the heating the mixture was swirled periodically. The excess of aryl bromide was then removed at 180° and 1 mmHg, the residue was extracted with chloroform (3 × 50 cm^3), and the filtered extract was washed exhaustively with aqueous M-sodium hydroxide, then water, and dried (Na_2SO_4). Evaporation usually gave a black gum, which was taken up in toluene and treated repeatedly with activated charcoal; the solution was finally diluted with petroleum (b.p. 80—100°) to give a precipitate of crystalline tertiary sulphonamide.

NN-*Diaryl*-4-*nitrobenzenesulphonamides.*—These were prepared by the general method described for the toluene sulphonamides. N-4-*methoxyphenyl*-N-*phenyl*-4-*nitrobenzenesulphonamide* formed needles, m.p. 151—152° (from ethanol) (Found: C, 59.2; H, 4.0; N, 7.5. $C_{19}H_{16}NO_5S$ requires C, 59.3; H, 4.2; N, 7.3%); NN-*bis*-(4-*methoxyphenyl*)-4-*nitrobenzenesulphonamide* afforded needles, m.p. 141—142° (from ethanol) (Found: C, 57.7; H, 4.3; N, 6.7. $C_{20}H_{18}NO_6S$ requires C, 58.0; H, 4.3; N, 6.8%).

Triarylamines.—Bromobenzene was treated with *N*-4-nitrophenyltoluene-4-sulphonamide as described in the general method. The neutral fraction obtained after removal of the bromobenzene and secondary sulphonamide was shown by t.l.c. (silica gel; benzene or chloroform) to contain no tertiary sulphonamide. Crystallisation of this fraction from ethanol yielded 4-nitrotriphenylamine (7%), m.p. 142—143° (lit.,[6] 144°) (Found: C, 74.4; H, 4.9; N, 9.8. Calc. for $C_{18}H_{14}N_2O_2$: C, 74.5; H, 4.8; N, 9.7%). By using 4-bromotoluene in place of bromobenzene, there was obtained 4,4′-*dimethyl*-4″-*nitrotriphenylamine* (6%), m.p. 162—163° (from ethanol) (Found: C, 75.1; H, 5.7; N, 8.8. $C_{20}H_{18}N_2O_2$ requires C, 75.4; H, 5.7; N, 8.8%).

2,4′-*Dimethoxydiphenylamine.*— *N*-2-Methoxyphenyl-*N*-4-methoxyphenyltoluene-4-sulphonamide (3.8 g, 0.01 mol) was added to a solution of sodium (1.05 g, 0.045 mol) in 3-methylbutan-1-ol (16 g, 0.18 mol) and the mixture was heated under reflux for 24 h. Hydrochloric acid (0.5M; 40 cm^3) and ether (50 cm^3) were then added and the organic layer was washed with water, dried (Na_2SO_4), and evaporated. The residual gum was extracted thoroughly with hot hexane; concentration of the extract yielded 2,4′-*dimethoxydiphenylamine* (60%) as needles, m.p. 71—72° (Found: C, 72.8; H, 6.7; N, 6.2. $C_{14}H_{15}NO_2$ requires C, 73.4; H, 6.5; N, 6.1%).

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* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1974, Index issue.

[4] R. G. R. Bacon and A. Karim, *J.C.S. Perkin I*, 1973, 278.
[5] D. Klamann and H. Bertsch, *Chem. Ber.*, 1952, **91**, 1427.
[6] S. Gambarjan, *Ber.*, 1908, **41**, 3510.