Tetrahedron Letters,Vol.27,No.15,pp 1739-1742,1986 0040-4039/86 $3.00 + .00
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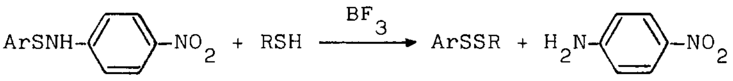
4'-NITROARENESULPHENANILIDES: THEIR USE IN THE SYNTHESIS OF UNSYMMETRICAL DISULPHIDES

L. Benati, P.C. Montevecchi, and P. Spagnolo
Istituto di Chimica Organica dell'Università
Viale Risorgimento 4, 40136 Bologna, Italy

Summary: The reaction of 4'-nitroarenesulphenanilides with thiols in the presence of boron trifluoride etherate can provide an effective route to unsymmetrical disulphides.

Sulphenamides are important intermediates in organic synthesis, which have been extensively used as sulphenyl-transfer reagents in the preparation of a variety of sulphur compounds.[1,2] In particular, the thermal reaction of thiols with sulphenamides derived from an imide such as phthalimide, succinimide, and maleimide has been found to be a useful synthetic route to symmetrical and unsymmetrical disulphides.[3] Most recently we have shown that boron trifluoride etherate transforms sulphenanilides into highly reactive electrophilic species which readily undergo nucleophilic displacement at sulphur by another sulphenanilide unit, ultimately leading to decomposition products, and/or by an alkene to give eventually β-arylamino-sulphides.[2,4] Now we wish to report that the boron-trifluoride reaction of 4'-nitroarenesulphenanilides (1) with thiols can provide a convenient synthetic method for the preparation of unsymmetrical disulphides. In fact, when the sulphenanilides (1) in dichloromethane, containing equimolar amounts of an alkanethiol, were treated with a slight excess of boron trifluoride etherate at room temperature, a smooth reaction of the starting anilide (1) took place, which was generally complete within ca. 2 min. After hydrolysis and column chromatography, the resulting aralkyl disulphides were isolated highly pure and in a nearly quantitative yield (Table, entries 1-3, 6-11). The general reaction can be depicted as follows:



(1)

Ar= C_6H_5, 4-$CH_3C_6H_4$, 4-ClC_6H_4

This method is somewhat limited for the preparation of unsymmetrical diaryl disulphides, since in all cases examined reaction of the anilides (**1**) with an appropriate arenethiol resulted in the formation of the three possible disulphides, evidently as the result of a rapid mercaptan-disulphide interchange occurring under the acid reaction conditions (Table, entries 4-5, 12-14). However, it would appear that the mixed disulphide can be obtained in a satisfactory yield at least when an arenethiol bearing a strong electron-withdrawing substituent is employed.

Table. Unsymmetrical disulphides prepared via BF$_3$-promoted reaction of 4'-nitroarenesulphenanilides (1) with thiols.[a,b]

Entry	Ar	R	Yield,[c] (%)	Ref.
1	C_6H_5	C_2H_5	96	5
2	C_6H_5	$C(CH_3)_3$	98	6
3	C_6H_5	$C_6H_5CH_2$	99	7
4	C_6H_5	4-ClC_6H_4	74[d,e]	8
5	C_6H_5	4-$NO_2C_6H_4$	75[f]	9
6	4-ClC_6H_4	C_2H_5	98	10
7	4-ClC_6H_4	n-C_3H_7	98	11
8	4-ClC_6H_4	$C(CH_3)_3$	98	-
9	4-ClC_6H_4	$C_6H_5CH_2$	99	12
10	4-$CH_3C_6H_4$	n-C_3H_7	99	13
11	4-$CH_3C_6H_4$	$C_6H_5CH_2$	92	14
12	4-$CH_3C_6H_4$	C_6H_5	51[d,g]	8
13	4-$CH_3C_6H_4$	4-ClC_6H_4	60[d,h]	15
14	4-$CH_3C_6H_4$	4-$NO_2C_6H_4$	77[i]	9

[a] Reactions were generally run in dichloromethane at room temperature for 1-2 min. [b] All compounds were identified by t.l.c. and/or g.l.c., ^1H n.m.r., and mass spectrometry. [c] Yields are for products isolated by column chromatography, unless otherwise stated. [d] Yields determined by g.l.c. [e] A mixture of disulphides (1:6:1) was isolated. [f] Phenyl disulphide (10%) and 4-nitrophenyl disulphide (8%) were also isolated. [g] A mixture of disulphides (1:2:1) was isolated. [h] A mixture of disulphides (1:3:1) was isolated. [i] 4-Tolyl disulphide (8%) and 4-nitrophenyl disulphide (6%) were also isolated.

An analogous drawback has been previously observed also in the preparation of mixed diaryl disulphides from N-arylthiophthalimides and arenethiols with no catalyst.[3b]

A typical experimental procedure is as follows. To a stirred solution of 4'-nitrobenzenesulphenanilide (246 mg, 1 mmol) and ethanethiol (62 mg, 1 mmol) in dichloromethane (10 ml) was added boron trifluoride etherate *ca.* 47% BF_3 (0.2 ml, 1.5 mmol) at room temperature. After being stirred for *ca.* 2 min the reaction mixture was treated with 5% aqueous potassium carbonate; the organic layer was then separated, the excess solvent removed and the residue chromatographed on a silica gel column. Elution with light petroleum (b.p. 40-70°C) gave ethyl phenyl disulphide (163 mg, 96%); elution with diethyl ether - light petroleum (1:1) gave 4-nitroaniline (124 mg, 90%).

Finally, we wish to point out that our procedure is simple, very rapid and requires precursor sulphenanilides (1), which are readily prepared from arenesulphenyl chlorides and 4-nitroaniline and are quite stable, crystalline solids.[16]

ACKNOWLEDGMENT

The authors gratefully acknowledge financial support form the Ministero della Pubblica Istruzione and C.N.R., Roma.

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16. 4'-Nitrobenzenesulphenanilide: see ref. 4; 4'-nitro-4-chlorobenzenesulphenanilide had m.p. 155-156°C, ν_{max} 3400 cm^{-1}, m/z 280(M^+) and 143; 4'-nitro-4-toluenesulphenanilide had m.p. 139-140°C, ν_{max} 3400 cm^{-1}, m/z 260(M^+) and 123.

(Received in UK 21 February 1986)