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A CONVENIENT SYNTHESIS OF ß-KETO PHENYL SULPHIDES FROM ALKYNES.

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Summary - ß-Keto sulphides can be conveniently prepared by BF_3-promoted reaction of 4'-nitrobenzenesulphenanilide in acetonitrile or acetic acid and subsequent hydrolysis of the resulting ß-acetamidino- or ß-acetoxy-vinyl phenyl sulphides.

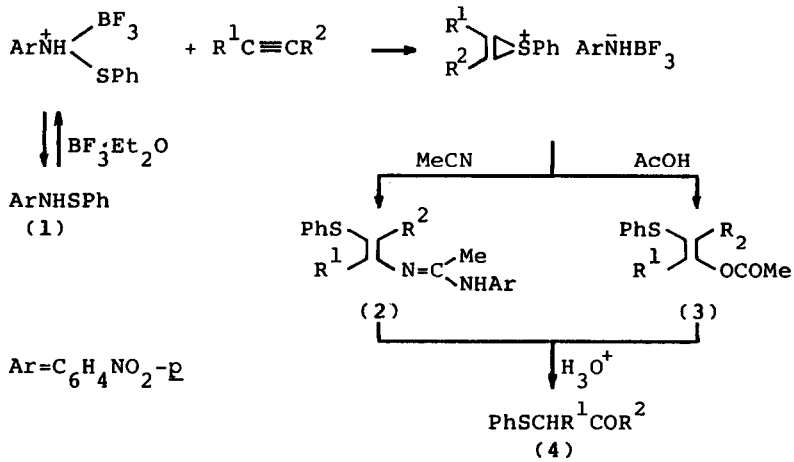
In previous papers we have shown that the boron trifluoride-promoted reaction of benzenesulphenanilides with alkenes in benzene[1] or nitrile solvents[2] provides a useful method for azasulphenylation of alkenes. These reactions are believed to involve intermediacy of episulphonium ions arising from nucleophilic displacement at the sulphur atom of an anilide-BF_3 complex.

The resulting episulphonium ions would be trapped by the liberated arylamino nucleophile to give arylamino sulphides,[1] or by the nitrile solvent ultimately leading to amidino- and amido-sulphides.[2]

More recently, we have shown that 4'-nitrobenzenesulphenanilide (1) (and its N-methyl derivative) undergoes electrophilic addition to alkynes in the presence of boron trifluoride, probably affording thiirenium ion intermediates which can be smoothly captured by acetonitrile to give eventually ß-acetamidinovinyl phenyl sulphides (2) with trans-stereo specificity and high regioselectivity (Markovnikov orientation).[3,4] Moreover, we have observed that the reaction of the anilide (1) with alkynes in acetic acid solution readily affords ß-acetoxyvinyl phenyl sulphides (3) in fair to good yields.[4] The compounds (2) and (3), which are masked ß-keto phenyl sulphides (4), undergo easy hydrolysis to give (4) in almost quantitative yields.[3,4] These results prompted us to device a simple method to effect direct conversion of alkynes to ß-keto sulphides (4), which are known to be intermediates of significant importance in synthetic organic chemistry.[5]

The general experimental procedure employed in this work is as follows.

To a stirred solution of the alkyne (10 mmol) and boron trifluoride--diethyl ether (ca 47% BF_3) (0.04 ml, 3 mmol) in acetonitrile (10 ml) (Procedure A) or acetic acid (10 ml) (Procedure B) was added a solution of 4'-nitrobenzenesulphenanilide (1) (486 mg, 2 mmol) in 10 ml of acetonitrile or acetic acid respectively. The reaction mixture was stirred at room temperature for ca. 1 h (ca. 2h in the case of terminal alkynes),



the excess of solvent and alkyne was distilled off under vacuum, and the residue dissolved in a mixture of 5M hydrochloric acid-dioxane (1:2) (15 ml). The resulting solution was refluxed for ca 20 min, then cooled to room temperature and treated with 5% aqueous potassium carbonate. The organic layer was extracted with diethyl ether, the excess solvent removed and the residue chromatographed on a silica gel column. Elution with light petroleum (b.p. 40-70°C) gave variable amounts of diphenyl disulphide; elution with light petroleum-diethyl ether (9:1) gave the appropriate ß-keto sulphide (4). Yields of products (4) are collected in the Table.

Further elution with diethyl ether gave 4-nitroaniline and N-(4-nitrophenyl)acetamidine ($ArN{=}C(Me)NH_2$) (overall yield 94-96%) (Procedure A) or 4-nitroaniline (90-95%) (Procedure B). We have observed that alkynes, particularly the aryl-substituted ones, may undergo significant conversion to the corresponding ketones upon refluxing in dioxane-hydrochloric acid; thus it is preferable to eliminate the alkyne excess before hydrolysis of the reaction mixture.

As can be seen in the Table, (i) comparable findings are generally obtained by using Procedure A or B; (ii) disubstituted alkynes lead to keto sulphides (4) in higher yields with respect to terminal alkynes; this trend reflects our previous observation[3,4] that a remarkable increase in the yields of the adducts (2) and (3) occurs on passing from terminal alkynes to disubstituted ones; (iii) alkyl- and aryl-substituted alkynes give the keto sulphides (4) expected from adducts (2) and (3) of Markovnikov type (entries 1,2,7-9); this is consistent with our earlier evidence[3,4] that the reaction of the anilide (1) with alkynes in acetonitrile or acetic acid leads to the exclusive or preferential formation of Markovnikov adducts; (iv) as expected, symmetrical dialkyl-substituted alkynes furnish a single keto sulphide (4) (entries 3,5,6), whereas a mixture of two isomeric keto sulphides in comparable yields is obtained from nonsymmetrical 2-hexyne (entry 4).

Our one-pot procedure for the conversion of alkynes to ß-keto sulphides is simple, rapid and requires 4'-nitrobenzenesulphenanilide (1) which is a readily available, quite stable, and convenient reagent.[11]

We believe that this method provides an useful alternative to the "obvious" two-step route involving hydration of alkynes[12] and subsequent sulphenylation of the resulting ketones. In fact, α-sulphenylation of

carbonyl compounds can be accomplished by using a number of different reagents, though controlled monosulphenylation is often difficult.[5,13] Our method appears to be attractive, especially when alkyl- and symmetrical dialkyl-substituted alkynes are used. Hydration of these alkynes invariably leads to nonsymmetrical dialkyl ketones, from which regioisomeric mixtures of ß-keto sulphides are normally expected to be formed. Finally, we wish to point that ß-thiovinyl arenesulphonates ($R^1SCR^2=CR^2OSO_2Ar$), particularly 2,4,6-trinitrobenzenesulphonates, have been previously shown to be suitable precursors of ß-keto sulphides.[9,14] Since thiovinyl arenesulphonates are prepared by addition of sulphenyl sulphonates (R^1SOSO_2Ar) to alkynes,[14a] the overall process might be envisioned as another synthetic route to ß-keto sulphides from alkynes. Nevertheless, these reactions, which have been generally investigated with diaryl-and dialkyl-substituted alkynes, have not found synthetic applications possibly owing to the requirements of the rather unstable and expensive sulphenyl sulphonates.

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Table. ß-Keto phenyl sulphides (4) prepared *via* BF_3-promoted reaction of 4'nitrobenzenesulphenanilide (1) with alkynes.[a]

Entry	Alkyne	ß-Keto sulphide		Yield,[b] (%)		Ref.
		R^1	R^2	A[c]	B[d]	
1	Pent-1-yne	H	n-Pr	48	-	6
2	Hex-1-yne	H	n-Bu	44	40	7
3	But-2-yne	Me	Me	63	70	6b
4	Hex-2-yne	Me	n-Pr	40	38	6
		n-Pr	Me	27	36	e
5	Hex-3-yne	Et	Et	71	84	8
6	Oct-4-yne	n-Pr	n-Pr	-	84	9
7	Phenylacetylene	H	Ph	36	48	6a
8	1-Phenylpropyne	Me	Ph	-	69	6
9	1-Phenylbut-1-yne	Et	Ph	-	81	10

a: All compounds were identified on the basis of physical and spectral data which were consistent with those reported in literature. b: Yields are for products isolated by column chromatography. c: Procedure A. d: Procedure B. e: Oily compound; m/z 208(M^+), 165,123,109,43. ^{1}H Nmr ($CDCl_3$) 0.93 (3H, t, J7Hz), 1.3-1.8(4H,m), 2.23(3H,s), 3.63 (1H,t,J7Hz), and 7.0-7.37(5H,m). Found: M^+, 208.09235. $C_{12}H_{16}OS$ requires M, 208.0922.

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