



Convenient Synthesis of Aromatic Thiols from Phenols

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Abstract: Aromatic thiols were synthesised from phenols in good yield and under mild conditions by reaction of the corresponding triflates with sodium triisopropylsilylanethiolate (NaSTIPS) and subsequent deprotection.

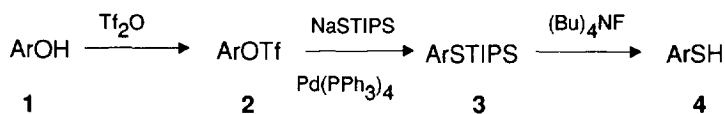
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Aryl thiols are important intermediates in chemical synthesis. Numerous synthetic methods have been developed to introduce this functional group¹⁻² either from aryl halides³⁻⁴ or from phenols;⁵⁻⁶ most of these transformations are unsatisfactory since they usually require drastic conditions which make them of little interest for functionalised molecules.

A mild conversion of aryl halides into silyl sulfides with potassium triisopropylsilylanethiolate (KSTIPS), under palladium catalysis has been recently published⁷. Since the number of elaborated phenols or methoxy analogues commercially available is greater than that of the corresponding halides, we became interested in the mild conversion of phenols into aryl thiols, for which there is no general method. Palladium catalysed coupling of aryl triflates with nucleophiles is a powerful reaction⁸ which has been successfully used to introduce the sulfide function⁹ but a convenient transformation into thiols has not been published.

We want to report here the simple transformation of phenols into aromatic thiols by palladium-catalysed coupling reaction of the corresponding triflate with sodium triisopropylsilylanethiolate (NaSTIPS) and subsequent deprotection of the silyl function.

Eight representative phenols were chosen among functionalised monocyclic or bicyclic phenols. (Table).

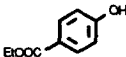
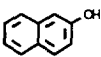
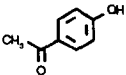
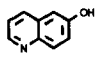
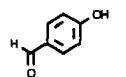
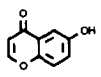
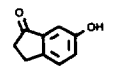
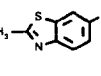


Phenols **1** were readily converted into triflates **2** by treatment with triflic anhydride.¹⁰ Triflates **2** were then reacted with NaSTIPS in the presence of tetrakis(triphenylphosphine)palladium(0) to give the silylated thiols **3** which were deprotected by treatment with tetrabutylammonium fluoride.

Conversion of **2** to **3** proceeds well (yields ranging from 40% to 86%) and is compatible with functions such as an aldehyde or an ester; it does not seem to be dependent on the electron density of the aromatic ring

since electron-deficient bicyclic phenols are just as reactive as the naphthalene analogue. Deprotection products were purified by flash chromatography and generally isolated as free thiols but rapid oxidation during purification was observed for some of them, which were therefore isolated as disulfides.

Table. Transformation of 1 into 4

Phenol 1	ArSTIPS 3	ArSH 4	Phenol 1	ArSTIPS 3	ArSH 4
	Yield % *			Yield % *	
	67	-		86	60
	60	50**		44	43**
	40	68		82	67
	60	40		76	72

* isolated product

** isolated as disulfide

In summary, we report here a convenient transformation of phenols into aromatic thiols by the Pd-catalysed reaction of the corresponding triflates with NaSTIPS followed by classical deprotection.

References and notes:

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10. **Typical procedure:** A solution of Pd(PPh₃)₄ (0.13 mmol) and NaSTIPS (1.7 mmol) in solution in THF (4 ml) was added under argon atmosphere to a solution of triflate 2⁽⁸⁾ (1.7 mmol) in dry benzene (4 ml). After 4 hours at reflux, H₂O (10 ml) and AcOEt (50 ml) were added; the organic layer was washed with water, dried over MgSO₄, concentrated and purified by flash chromatography (AcOEt / hexane) to give the silylated thiol, which was deprotected in THF at 0°C, in the presence of TBAF.

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