



An unusual cleavage of a C–S bond with concurrent *S*-arylation under palladium–copper catalysis

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Received 17 May 2000; revised 13 July 2000; accepted 20 July 2000

Abstract

3-[2-(*N*-*p*-Toluenesulfonyl)aminophenylthio]prop-1-yne (**4**) reacted with aryl iodides **5–14** under palladium–copper catalysis to afford (2-arylthio)-*p*-toluenesulfonanilide (**15–23**) in moderate to good yields (54–64%) through unusual depropargylation and *S*-arylation reactions. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: palladium–copper catalysis; depropargylation; *S*-arylation.

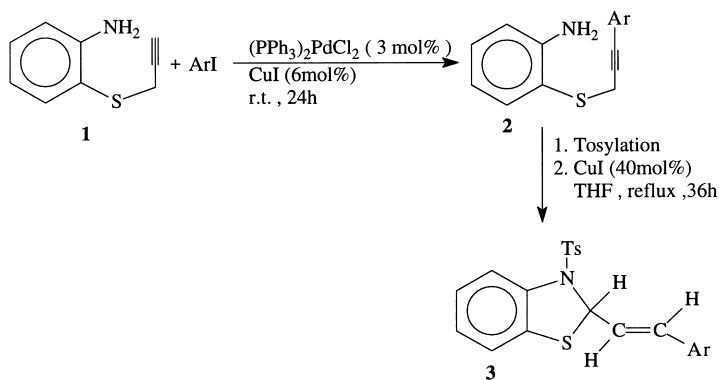
Over the last few decades, palladium–copper-catalysed reactions¹ have been found to have extremely good synthetic utility for both carboannulation² and heteroannulation³ processes. Our interest in this area has led us to synthesise different heterocyclic structures of biological interest, e.g. benzofurans,^{4a} phthalides,^{4b} isoindolines,^{4c} benzodioxanes,^{4d} benzoxazines^{4e} and others^{4f} through palladium–copper catalysis using terminal alkynes.

Recently, using a two-step procedure, e.g. (i) carbon–carbon bond formation with bistrisphenylphosphine palladium(II) chloride (3 mol%) and cyclisation with excess copper(I) iodide (40 mol%), we have developed a novel strategy for the synthesis of benzothiazolines (**3**)⁵ from 3-(2-aminophenylthio)prop-1-yne (**1**) (Scheme 1).

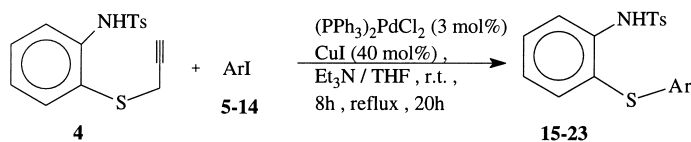
In order to make the process a single-step operation, we reacted **4** with aryl iodides (**5–14**), (PPh₃)₂PdCl₂ (3 mol%) and excess CuI (40 mol%)⁶ in THF for 20 h under reflux. To our surprise, we found that instead of any benzothiazolines being formed, **4** underwent smooth depropargylation and subsequent *S*-arylation leading to the diaryl sulfides (**15–23**) (Scheme 2 and Table 1) in moderate to good yields.

It is evident from Table 1 that the sulfides **15–23** are obtained in good yields by treatment of a THF solution of alkyne **4** with the aryl iodides **5–14** in triethylamine with 3 mol% (PPh₃)₂PdCl₂ and 40 mol% CuI at room temperature for 8 h followed by reflux for 20 h. Both palladium(II)

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Scheme 1.

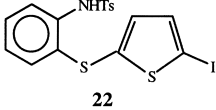
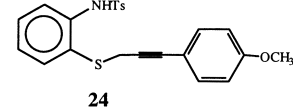
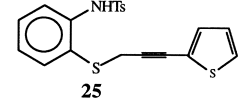


Scheme 2.

and copper(I) catalysts are essential since none of the desired products were formed without any of these two reagents (entries 11 and 12). Excess CuI was necessary to get the optimum yields as it was found that by lowering the amount of CuI, the yields became poorer.⁷ Though the methodology is generalised for a large number of aryl iodides, in the case of *p*-anisyl and 2-thienyl iodides disubstituted alkynes were also formed.⁸ All the compounds obtained were well characterised by spectral (¹H NMR, ¹³C NMR, IR) and analytical data.⁹ A typical reaction procedure is as follows: *m*-Chloriodobenzene (0.82 mmol) in THF (10 ml) was stirred at room temperature with (PPh₃)₂PdCl₂ (0.025 mmol, 3 mol%) and CuI (0.33 mmol, 40 mol%) in presence of Et₃N (3.28 mmol) in an argon atmosphere for 0.5 h. Acetylenic compound (**4**) was added to the reaction mixture and stirring was continued for 8 h at room temperature followed by reflux for 20 h. After removal of the solvent and Et₃N under reduced pressure, the residue was diluted with water (10 ml) and extracted with CHCl₃ (3×25 ml). The organic layer was washed with H₂O (3×5 ml) and dried (anh. Na₂SO₄). The crude product obtained after removal of solvent was purified by chromatography on silica gel (60–120 mesh) with the eluant being 5% ethyl acetate in light petroleum (60–80°C), to furnish pure sulfide **19** in 62% yield, m.p. 89°C [CHCl₃–pet. ether (60–80°C)].

In conclusion, we report a novel observation on depropargylation of an *S*-propargyl group through carbon–sulfur bond scission with a palladium catalyst and excess CuI reagent. A concurrent *S*-arylation under the reaction conditions led to the formation of diarylsulfides. Although a number of methods for the preparation of sulfides,¹⁰ as well as for the cleavage of the C–S bond are known,¹¹ ours is probably the first report of depropargylation and arylation in a single step operation with palladium–copper reagents. Also, the diaryl sulfides are formed in good yields from readily available starting materials under mild and easy to operate reaction conditions. Since aryl sulfides are very useful chemical intermediates in organic syntheses¹² the procedure described here could be of considerable interest to many chemists from a synthetic viewpoint.

Table 1
Palladium–copper-catalysed depropargylation with subsequent *S*-arylation leading to the disulfides **15–23**
(Scheme 2)

Entry	Aryl Iodide (Ar)	Products	Yields(%) ^a
1	Phenyl (5)	15	61
2	C ₆ H ₄ Me- <i>p</i> (6)	16	56
3	C ₆ H ₄ Me- <i>o</i> (7)	17	62
4	1-naphthyl (8)	18	63
5	C ₆ H ₄ Cl- <i>m</i> (9)	19	62
6	4-dimethoxypyrimidin- -5-yl (10)	20	54
7	C ₆ H ₄ CO ₂ Me- <i>o</i> (11)	21	64
8	5-iodothiophenyl (12)		55
9	C ₆ H ₄ OMe- <i>p</i> (13)	23 + 	56 (3:1)
10	2-thienyl (14)		59
11 ^b	C ₆ H ₄ Me- <i>p</i> (6)	no product	0
12 ^c	C ₆ H ₄ Me- <i>p</i> (6)	no product	0

^a Yields are based on **4**

^b Reaction was carried out without (PPh₃)₂PdCl₂

^c Reaction was carried out without CuI.

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6. Use of catalytic amounts of Pd-catalyst and CuI did not give any product.
7. Use of CuI (10%) gave only a 5% yield, whereas 20% and 30% of CuI gave 15% and 20% yields of the product, respectively.
8. In the case of *p*-anisyl iodide, the disubstituted alkyne was formed in 13% yield along with the sulfide, whereas 2-iodothiophene gave the disubstituted alkyne exclusively (59%).
9. Typical ¹H NMR data for compound **19** (300 MHz, CDCl₃, TMS): δ 2.34 (3H, s, ArCH₃), 6.69 (1H, s, ArH), 6.76–6.80 (1H, m, ArH), 7.04–7.11 (5H, m, ArH), 7.38–7.45 (2H, d, J = 9 Hz, ArH), 7.53 (2H, d, J = 9 Hz, ArH), 7.67 (1H, s, NH), 7.76–7.79 (1H, m, ArH). ¹³C NMR (75 MHz, CDCl₃, TMS): δ 21.51, 119.63, 124.88, 125.01, 126.23, 126.28, 127.01, 129.57, 130.08, 131.55, 135.01, 135.50, 137.35, 137.77, 139.25, 144.07. IR (KBr): ν_{max} 3277, 1590, 1580, 1562 cm⁻¹. Calculated for C₁₉H₁₆ClNO₂S₂: C, 58.51%; H, 4.14%; N, 3.59%. Found: C, 58.68%; H, 4.12%; N, 3.67%.
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