A Facile One-Step Synthesis of 2-Arylbenzothiazoles

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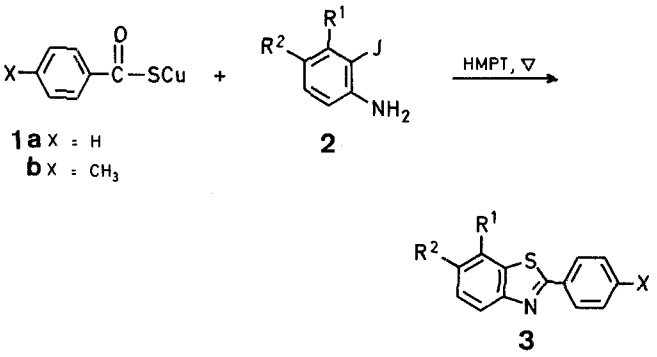
2-Substituted benzothiazoles are of increasing importance in the chemical industry[1] and in biochemistry[2], and as synthetically useful units[3], which can serve as a masked carbonyl function. Methods for the preparation of this heterocyclic nucleus, therefore, have been extensively studied[4]. Among these, the condensation of 2-aminothiophenol with carboxylic acids under acidic conditions[5] and the use of reactive carboxylic acid derivatives, e.g., acid chloride[4], acid anhydride[4], iminoester[4], or *N*-ethoxycarbonylthioamide[6] provide the most direct routes to the 2-substituted benzothiazoles. Condensations of selenoamides[7a] and (1-alkynyl)-triphenylphosphonium bromides[7b] with 2-aminothiophenol are also reported to give 2-substituted benzothiazoles. However, these methods suffer from not readily available starting materials, particularly for the synthesis of benzothiazoles substituted in the homoheterocyclic ring.

Copper(I) thiobenzoate **(1a)** which is an efficient reagent for converting aryl iodides into *S*-aryl thiobenzoates[8], also provides a straight-forward and versatile access to 2-arylbenzothiazoles, when reacted with 2-iodoanilines.

We have found that heating a mixture of **1** and 2-iodoanilines **2** at 100–110°C in hexamethylphosphoric triamide (HMPT) affords the corresponding 2-arylbenzothiazoles directly **3** (Table).



This reaction is particularly useful for the preparation of benzothiazoles substituted in the condensed six-membered ring. When applied to 2-amino-1-iodonaphthalene, the naphtho[2,1-*d*]thiazoles **(3e)** and **(3f)** were obtained in moderate yields. However, the reaction of 2-bromoaniline with **1a** at 130°C gave mainly 2-bromobenzanilide (53%) together with the desired 2-phenylbenzothiazole **(3a)** (7%), and 2-chloroaniline was quantitatively converted into 2-chlorobenzanilide under similar conditions at 150–160°C.

Because of the simple procedure, easily available starting materials, and high yields, this method provides a new, facile, one-step route to 2-arylbenzothiazoles **(3)**.

The structures of all new compounds were established by analytical data and ^{1}H-N.M.R. and I.R. spectra. All melting points are uncorrected. Copper(I) thiobenzoates **(1a)** and **(1b)**[8a], 2-iodoaniline[9a], 2-iodo-4-methylaniline[9b], and 2-amino-1-iodonaphthalene[9c], were prepared by reported methods.

Table. 2-Arylbenzothiazoles **3** prepared

Product No.	R^1	R^2	X	Yield [%][a]	m.p. [°C]	Molecular Formula[b] or Lit. m.p. [°C]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS, 60 MHz) δ [ppm]
3a	H	H	H	85	115–116°	113–114°[5c]	1480, 1440, 1320, 1230, 1075, 965, 770, 735, 690	7.1–7.5 (m, 5H); 7.7–8.3 (m, 4H)
3b	H	H	CH_3	80	84–85.5°	86°[10]	1480, 1440, 1300, 1250, 1010, 960, 750	2.35 (s, 3H); 7.3 (m, 4H); 7.55 (m, 2H); 8.05 (m, 2H)
3c	H	CH_3	H	96	124–126°	125–125.5°[11]	2900, 1480, 1440, 1310, 1220, 970, 845, 760, 680	2.40 (s, 3H); 7.0–7.5 (m, 5H); 7.8–8.1 (m, 3H)
3d	H	CH_3	CH_3	60	135–137°	$C_{15}H_{13}NS$ (239.3)	1480, 1450, 1310, 1230, 960, 820, 685	2.36 (s, 3H); 2.44 (s, 3H); 7.1–8.1 (m, 7H)
3e	—(CH=CH)$_2$—		H	50	109–110°	$C_{17}H_{11}NS$ (261.3)	1480, 1440, 930, 815, 750, 690	7.2–7.5 (m, 5H); 7.5–8.1 (m, 6H)
3f	—(CH=CH)$_2$—		CH_3	43	137–139°	$C_{18}H_{13}NS$ (275.4)	3050, 1480, 1440, 950, 810, 740, 700	2.35 (s, 3H); 7.0–7.3 (m, 2H); 7.3–7.6 (m, 3H); 7.6–8.1 (m, 5H)

[a] Yield of isolated product.

[b] Satisfactory microanalyses obtained: C ±0.29, H ±0.25, N ±0.22.

2-Phenylbenzothiazole (3a); Typical Procedure:

A stirred mixture of copper(I) thiobenzoate (**1a**; 602 mg, 3 mmol), 2-iodoaniline (**2**, $R^1=R^2=H$; 438 mg, 2 mmol), and hexamethylphosphoric triamide (5 ml) is heated under nitrogen at 100–110°C for 3 h, and is then poured into water (300 ml). The milky solution gradually deposits a brown precipitate, which is filtered off, washed with water (100 ml), sucked dry, and extracted with hexane (100 ml) using a Soxhlet extractor. The solvent is evaporated and the residue is recrystallized from ethanol to give colorless crystals of **3a**; yield: 359 mg (85%); m.p. 115–116°C (Lit.[5c], m.p. 113–114°C).

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[1] F. M. Harmer, in: *The Chemistry of Heterocyclic Compounds*, Vol. 18, A. Weissberger, Ed., Interscience, New York, 1964, Chapter 6.

[2] B. Prescott, J. M. Webb, *Antibiot. Chemother.* **8**, 33 (1958).

[3] E. J. Corey, D. L. Boger, *Tetrahedron Lett.* **1978**, 5, 9, 13.

[4] R. C. Elderfield, *Heterocyclic Compounds*, Vol. 5, John Wiley & Sons, New York, 1957, pp. 483–722.

[5] (a) D. L. Boger, *J. Org. Chem.* **43**, 2296 (1978).
(b) Y. Kanaoka, T. Hamada, O. Yonemitsu, *Chem. Pharm. Bull.* **18**, 587 (1970).
(c) D. W. Hein, R. J. Alheim, J. J. Leavitt, *J. Am. Chem. Soc.* **79**, 427 (1957).

[6] B. George, E. P. Papadopoulos, *J. Org. Chem.* **42**, 441 (1977).

[7] (a) V. I. Cohen, *J. Heterocyclic Chem.* **14**, 1321 (1977).
(b) E. E. Schweizer, S. D. Goff, *J. Org. Chem.* **43**, 2972 (1978).

[8] (a) K. P. Nair, C. G. R. Nair, *Indian J. Chem.* **9**, 706 (1971).
(b) A. Osuka, N. Ohmasa, Y. Uno, H. Suzuki, *Synthesis* **1983**, 68.

[9] (a) A. Bayer, *Ber. Dtsch. Chem. Ges.* **38**, 2761 (1905).
(b) R. Q. Brewstar, *Org. Synth. Coll. Vol.* **II**, 347 (1943).

[10] A. I. Kiparianov, I. K. Ushenko, A. L. Gershun, *J. Gen. Chem. USSR (Engl. Trans.)* **14**, 865 (1944).

[11] O. Sues, N. Tomanek, E. Lind, *German Patent* 1137625 (1962); *C. A.* **59**, 11515 (1963).