Synthesis of 6-Aminobenzothiazoles from *p*-Benzoquinone Imine Derivatives

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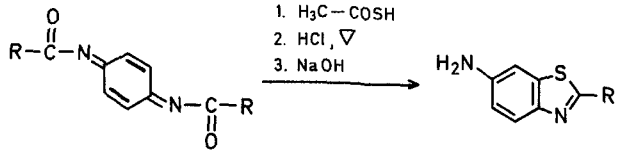
A simple synthesis of 6-aminobenzothiazoles substituted in position 2 was developed using reactions of acylated *p*-benzoquinone imines with thiolacetic acid[1]. The respective quinone imine derivatives were prepared from acylated *p*-phenylenediamines using a classical lead(IV) acetate oxidation procedure[2]. The reaction of the quinone imine derivatives **1** with thiolacetic acid proceeded rapidly at laboratory temperature. The crude products upon treatment with 20% hydrochloric acid at boiling temperature for an extended period of time and then with a dilute sodium hydroxide solution yielded 2-substituted 6-aminobenzothiazoles **2** as shown below.



1a R = CH_3
b R = C_6H_5

2a,b

The procedure was applied in the synthesis of 6-amino-2-methylbenzothiazole (**2a**; m.p. 125–127°) and 6-amino-2-phenylbenzothiazole (**2b**; m.p. 205–206°), the yields of which were moderate to good. Both **2a** and **2b** were converted into the respective 2-substituted 6-hydroxybenzothiazoles using common reactions. Thus, the newly described synthesis of benzothiazole derivatives represents a potential alternate route to existing syntheses of luciferin, e.g. Lit. [3].

Preparation of 6-Amino-2-methylbenzothiazole (2a):
To dry, ethanol-free chloroform (90 ml) is added *p*-phenylene-diacetamide (900 mg, 4.7 mmol; prepared according to the method of Adams and Anderson[2] m.p. above 300°). Lead(IV) acetate (2.5 g, 5.6 mmol) is then added and the suspension is refluxed and stirred for 2 h. The reaction mixture is then allowed to cool to room temperature and filtered into a flask containing chloroform (15 ml) and thiolacetic acid (3 ml, 42.3 mmol). After standing for 1 h at room temperature, the solvent is removed by rotary evaporation under reduced pressure to yield a crude yellow solid; yield: 650 mg. This solid is treated with constant-boiling hydrochloric acid (20 ml) for 3 h. After cooling and neutralization with 1 molar sodium hydroxide, the solution is continuously extracted with ethyl acetate. Removal of the solvent gives 6-amino-2-methylbenzothiazole; yield: 340 mg (45%); m.p. 118–121°; recrystallization from aqueous ethanol gives a colorless solid; m.p. 125–127° (Lit. [4] m.p. 125–127°).

I.R. (KBr): ν_{max} = 3380, 3305, 3203, 2920, 1630, 1465, 1230, 1170 cm^{-1}.

U.V. (methanol): λ_{max} = 220, 245, 285 nm.

M.S. (70 eV): *m/e* (relative intensity): = 164 (M^+, 100), 163 (31), 119 (5).

A sample of compound **2a** (110 mg) is converted via a diazonium salt into *6-hydroxy-2-methylbenzothiazole*; yield: 49 mg (44%); m.p. 162–163° (Lit. [5] m.p. 162–163°).

M.S. (70 eV): *m/e* = 165 (M^+).

Preparation of 6-Amino-2-phenylbenzothiazole (2b):
A mixture of *p*-benzoquinone dibenzimide (m.p. 139–140°, prepared according to Lit. [2]; 100 mg), thiolacetic acid (1 ml) and chloroform (8 ml) is reacted to give a crude product (115 mg). Hydrolysis of this with concentrated hydrochloric acid for 24 h and subsequent continuous extraction of the basified (15% sodium hydroxide) solution (pH 10) with ether gives the blue fluorescent (254, 366 nm, and U.V. light) product; yield: 35 mg (50%); m.p. 203–205°; colorless solid after recrystallization from aqueous ethanol; m.p. 205–206° (Lit. [6] m.p. 205–206°).

I.R. (KBr): ν_{max} = 3372, 3305, 3200, 1630, 1605, 1465, 1230 cm^{-1}.

U.V. (methanol): λ_{max} = 219, 233 (sh), 249 (sh), 337 nm.

M.S. (70 eV): *m/e* (relative intensity) = 226 (M^+, 100), 123 (21), 91 (25), 77 (36).

A sample of the product (**2b**; 100 mg) is converted via a diazonium salt into *6-hydroxy-2-phenylbenzothiazole*; yield: 35 mg (35%); m.p. 227–229° (Lit. [7] m.p. 227–229°).

U.V. (methanol): λ_{max} = 219, 322 nm.

M.S. (70 eV): *m/e* (relative intensity) = 227 (M^+, 26), 85 (38), 71 (56), 57 (100).

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