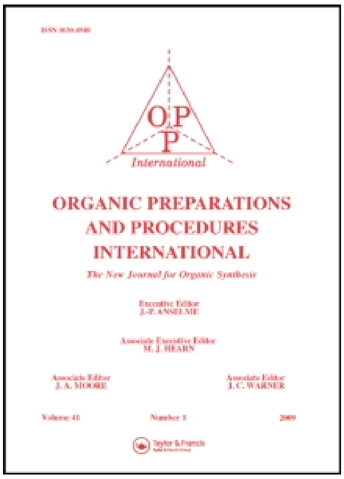

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PREPARATION OF SOME 2,3-DIHYDROBENZOTHIAZOLE-2-CARBOXAMIDES

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PREPARATION OF SOME 2,3-DIHYDROBENZOTHIAZOLE-2-CARBOXAMIDES

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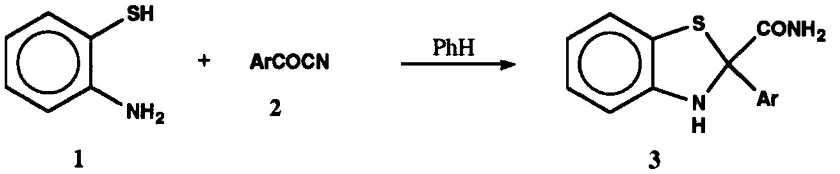
Cyclic α-aminoamides were required for another project, and we chose to prepare 2,3-dihydrobenzothiazole-2-carboxamides (**3a-c**) as model compounds because of their expected ease of handling. We discovered that the preferred method to prepare them is by the reaction of 2-aminothiophenol (**1**) with the benzoyl cyanides (**2**) to give the amides directly.



a) Ar = C_6H_5 b) Ar = p-MeC_6H_4 c) Ar = p-$NO_2C_6H_4$

Distilled **1** reacted with **2a** at room temperature in benzene solution to give an 83% yield of 2-phenyl-2,3-dihydrobenzothiazole-2-carboxamide (**3a**) in ten minutes. When commercial **1** was used without distillation, the yields were significantly lower and the crude products were less pure. Compound **3a** could also be prepared by two other more conventional methods. Treatment of the corresponding ethyl 2-phenyl-2,3-dihydrobenzothiazole-2-carboxylate (**4**) with methanolic ammonia at room temperature for two days gave a 67% yield of **3a**, which could also be obtained in 61% yield by the reaction of **1** with benzoylformamide at 135°. Compounds **3b** and **3c** were also obtained by the reaction of **1** with the 4-substituted benzoyl cyanides (**2b,c**) but in lower yields; the reactions were also slower.

EXPERIMENTAL SECTION

Chemicals were obtained from Aldrich. Melting points (Mel-Temp) are uncorrected. IR spectra were recorded on a Perkin-Elmer 1310 spectrophotometer. Mass spectra were recorded on a Hewlett-Packard 5988A (CI) or an LKB 400 (EI) spectrometer. The NMR spectrum was recorded on a Varian VXRS400 spectrometer. Elemental analyses were performed by Schwarzkopf and MicAnal Laboratories.

2-Phenyl-2,3-dihydrobenzothiazole-2-carboxamide (**3a**).- A solution of benzoyl cyanide (**2a**) (1.05 g, 8.0 mmoles) in 2 mL of benzene was added dropwise to a solution of freshly distilled 2-aminothiophenol (**1**) (1.00 g, 8.0 mmoles) in 8 mL of benzene at room temperature. Precipitation of the product began during the addition and appeared to be complete after 10 min. The product (1.7 g, 83%), mp.

175-178°, was recrystallized from ethanol-ethyl acetate to give the pure product, mp. 178-181°. IR (Nujol): 3445, 3315, 3215 (NH); 1669 (C=O) cm^{-1}. MS(NH_3-CI): m/e (%) 257.2 (M^+H, 77), 274.2 (M^+NH4, 5), 212.2 (100). ^{13}C NMR (DMSO): δ 173.3 (C=O), 145, 141, 128, 127.8, 126, 125, 124, 121, 119, 109, 82.

Anal. Calcd. for $C_{14}H_{12}N_2OS$: C, 65.60; H, 4.71; N, 10.92 Found: C, 65.77; H, 4.78; N, 10.99

From 1 and Benzoylformamide.- Compound **3a** was also prepared by heating 0.96 g (7.3 mmoles) of distilled **1** with 1.04 g (7.0 mmoles) of benzoylform amide to 135° under nitrogen for 1 hr. The solid which formed overnight was digested with ethanol and collected to give 1.1 g (61%) of crude product, mp. 167-173°. The recrystallized sample weighed 0.85 g (47%), mp. 177-180°.

From Ammonolysis of 4.- Ammonia was bubbled through a cooled solution of ethyl 2-phenyl-2,3-dihydrobenzothiazole-2-carboxylate (**4**) (0.25 g, 0.88 mmole synthesized in 78% yield, mp. 97-99°, lit.[1] 99°, by the method of Biekert, Sonnenbichler, and Hoffmann).[1] in 10 mL of methanol for 20 min.; the vessel was stoppered and left at room temperature for 2 days. The solvent was then evaporated at reduced pressure without heating. The gummy crystals which remained were recrystallized to give 0.15 g (67%) of **3a**, mp. 177-180°.

2-(4-Methylphenyl)-2,3-dihydrobenzothiazole-2-carboxamide (3b).- The *p*-toluoyl cyanide (**2b**) was prepared by the method of Dornow and Grabhofer[2] in yields of 70-80%, mp. 47-51°, lit.[3] 50-52°. A sample of **2b** (1.2 g, 8.3 mmoles) in 2 mL of benzene was added to a solution of 1.0 g (8.0 mmoles) of **1** in 8 mL of benzene at room temperature. A precipitate began to form in about 20 min. and the product (1.5 g, 68%), mp. 163-166°) was collected after 3 hrs. The recrystallized product (ethanol-ethyl acetate) melted at 167-169°. IR (Nujol): 3400, 3310 (NH); 1660 (C=O) cm^{-1}. MS: m/e (%) 270 (2), 226 (100).

Anal. Calcd. for $C_{15}H_{14}N_2OS$: C, 66.64; H, 5.22; N, 10.36 Found: C, 66.32; H, 5.14; N, 10.35

2-(4-Nitrophenyl)-2,3-dihydrobenzothiazole-2-carboxamide (3c).- The 4-nitrobenzoyl cyanide (**2c**) was prepared by the method of Dornow and Grabhofer[2] in yields of 43-67% (mp. 112-116°, lit.[2], 116°). A solution of **2c** (1.4 g, 8.0 mmole) in 15 mL of benzene was added to 1.0 g (8.0 mmoles) of **1** in 50 mL of benzene. The mixture was refluxed for 3 hrs., allowed to cool, and the precipitated product was collected. Recrystallization (benzene-ligroin) gave 1.3 g (54%), mp. 153-155°. IR (Nujol): 3435, 3400 (NH), 1695 (C=O) cm^{-1}. MS: m/e (%) 301 (3), 257 (100).

Anal. Calcd. for $C_{14}H_{11}N_3O_3S$: C, 55.80; H, 3.67; N, 13.94 Found: C, 55.70; H, 3.71; N, 13.92

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