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The Synthesis of Cyclohepta[4,5]pyrrolo[2,3-*d*] thiazoles

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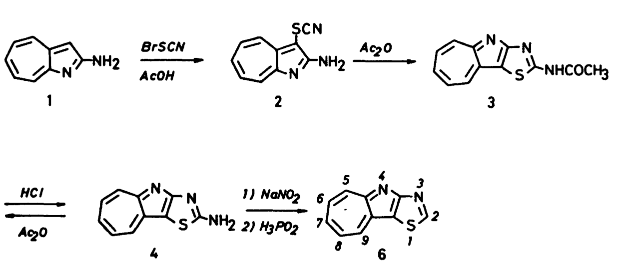
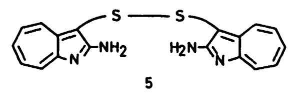
Synopsis. Cyclohepta[4,5]pyrrolo[2,3-*d*]thiazole and its amino derivatives were obtained in a few steps by starting with 2-amino-1-azaazulene.

1-Azaazulenes(cyclohepta[*b*]pyrroles) are important and interesting compounds not only as non-benzenoid analogues of indoles and isomers of quinolines, but also as azulenoid heterocyclic compounds. Several azulenoid heterocyclic compounds which consist of the 1-aza-azulene ring condensed with heterocyclic aromatics are known.[1] In a previous paper,[2] the preparation of cyclohepta[*b*]thieno[3,2-*d*]pyrrole was reported.

We now wish to report the synthesis of cyclohept[4,5]-pyrrolo[2,3-*d*]thiazole and its amino derivatives. 2-Amino-1-azaazulene (**1**),[3] on treatment with thiocyanogen bromide prepared by adding bromine to a solution of potassium thiocyanate in acetic acid and filtering off the potassium bromide, gave 2-amino-3-thiocyanato-1-azaazulene (**2**). When this compound (**2**) was cyclized by the action of acetic anhydride at the boiling point, 2-acetylaminocyclohepta[4,5]pyrrolo[2,3-*d*]thiazole (**3**) was obtained in a 78% yield. Compound (**3**), when boiled with dilute hydrochloric acid, was converted to 2-aminocyclohepta[4,5]pyrrolo[2,3-*d*]thiazole (**4**). On treatment with acetic anhydride, **4** afforded **3**. On the other hand, in the case of the treatment of **2** with concentrated hydrochloric acid in ethanol, disulfide (**5**) was obtained in an 84% yield. The structure of **5** was established on the basis of the spectral data and the results of elemental analysis (see Experimental). The mass spectrum of **5** is similar to that of 2-amino-1-azaazulene (**1**) in its fragmentation pattern below *m*/*e* 144. Compound **4** was diazotized with a concentrated aqueous sodium nitrite solution in 85% phosphoric acid, followed by treatment with phosphinic acid to give cyclohepta[4,5]pyrrolo[2,3-*d*]thiazole (**6**) as reddish purple prisms in a 41% yield.





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Experimental

All the melting points are uncorrected.

2-Amino-1-azaazulene (1). A solution of 2-chloro-1-azaazulene (6.18 g) in dry ethanol (130 ml) was saturated with ammonia and heated at 170 °C in a sealed tube for 64 h. After cooling, the reaction mixture was concentrated, diluted with water, neutralized with a 10% sodium hydroxide solution, and extracted with chloroform. The extract was dried, the solvent was removed, and the residue was chromatographed on a silica-gel column. From the methanol effluent, **1** was obtained as golden leaves (4.08 g, 75%); mp 177—178 °C (lit. 3 mp 171—172 °C); ^{1}H NMR (100 MHz, in $CDCl_3$) δ=5.54 (2H, bs, N$\underline{H}_2$), 6.54 (1H, s, H-3), 7.29—7.74 (3H, m, H-5,6,7), and 7.88—8.12 (2H, m, H-4,8); MS *m*/*e* 144 (M^+), 117, 89, and 58.5. (Found: C, 75.25; H, 5.72; N, 19.42%).

2-Amino-3-thiocyanato-1-azaazulene (2). To a stirred solution of **1** (1.00 g) in acetic acid (25 ml), thiocyanogen bromide prepared from potassium thiocyanate (1.01 g) and bromine (1.45 g) in acetic acid (35 ml) was added, drop by drop. After stirring for 2.5 h, the reaction mixture was diluted with water and neutralized with a sodium carbonate solution. The resulting precipitate was filtered off and recrystallized from ethanol to give **2** as yellow prisms (1.17 g, 84%); mp 164 °C (decomp); IR (KBr) 3464, 3304, 2162, 1644, 1513, and 1500 cm^{-1}; UV(CH_3OH) 213 (log ε 4.19), 239 (4.07), 285 (4.54), 361 (3.86), and 426 nm (3.58). Found: C, 59.78; H, 3.41; N, 21.07; S, 16.05%. Calcd for $C_{10}H_7N_3S$: C, 59.68; H, 3.51; N, 20.88; S, 15.93%.

*2-Acetylaminocyclohepta[4,5]pyrrolo[2,3-*d*]thiazole (3).* *(a)*: A mixture of **2** (400 mg) and acetic anhydride (2.50 g) was refluxed for 3 h. After cooling, the reaction mixture was poured into water and neutralized with a sodium hydrogencarbonate solution. The resulting precipitate was filtered off, dried, and recrystallized from *N*,*N*-dimethylformamide to give **3** as purple micro needles (380 mg, 78%); mp 285 °C (decomp); IR (KBr) 3304, 3157, 2912, 1695, 1515, and 1501 cm^{-1}; UV (CH_3OH) 217 (log ε 3.78), 244 (3.64), 303 (4.36), 325 (4.16), 352 (3.60), and 368 nm (3.63). Found: C, 59.48; H, 3.74; N, 17.52; S, 13.26%; M^+, 243. Calcd for $C_{12}H_9ON_3S$: C, 59.24; H, 3.73; N, 17.27; S, 13.18%; M, 243.

(b): A mixture of **4** (100 mg) and acetic anhydride (1.0 ml) was refluxed for 30 min. The reaction mixture was then treated by a method similar to that used for *(a)*. Recrystallization from *N*,*N*-dimethylformamide yielded purple micro needles (80 mg, 66%) of **3** (mp 285 °C), which was identified by a mixed-melting-point determination and by a comparison of its infrared spectrum with that of the sample prepared by means of Method *(a)*.

*2-Aminocyclohepta[4,5]pyrrolo[2,3-*d*]thiazole (4).* A mixture of **3** (280 mg) and 6 mol dm^{-3} hydrochloric acid (14 ml) in ethanol was heated at 110 °C for 3 h. After the removal of the solvent, water (50 ml) was added to the residue. When the solution was made slightly basic with a 10% sodium hydroxide aqueous solution, a precipitate separated out. The precipitate was collected by filtration, washed with water, and recrystallized from ethanol to give purple prisms (220 mg, 93%); mp 231 °C (decomp); IR(KBr) 3389, 3272, 3059, 1498, 1469, 1428, and 1407 cm^{-1}; UV(CH_3OH) 216 (log ε 4.63), 237 (4.45), 298 (5.09), 327 (4.98), 361 (4.21), 378 (4.10), and 493 nm (3.85). Found: C, 59.45; H, 3.40; N, 20.73; S, 15.97%. Calcd for $C_{10}H_7N_3S$: C, 59.68; H, 3.51; N, 20.88; S, 15.94%.

2,2′-Diamino-3,3′-dithiodi(1-azaazulene) (5). To a suspension of **2** (260 mg) in ethanol (26 ml), concentrated hydrochloric acid (2.6 ml) was added, after which the mixture was refluxed for 10 h. The reaction mixture was evaporated *in vacuo*, and the residue was diluted with water. The solution was then neutralized with a sodium carbonate aqueous solution. The resulting precipitate was filtered off, dried, and recrystallized from *N*,*N*-dimethylformamide to give red micro needles (190 mg, 84%); mp 255 °C (decomp); IR(KBr) 3457, 3382, 3288, 1640, and 1500 cm^{-1}; UV(CH_3OH) 216 (log ε 4.48), 280 (4.75), and 426 nm (3.92); MS *m/e* 350 M$^+$, 175, 144, 117, 89, and 58.5. Found: C, 61.55; H, 4.04; N, 15.94; S, 18.16%. Calcd for $C_{18}H_{14}N_4S_2$: C, 61.69; H, 4.03; N, 15.99; S, 18.30%.

*Cyclohepta[4,5]pyrrolo[2,3-d]thiazole (**6**).* A solution of **4** (1.00 g) in 85% phosphoric acid was cooled to −10 °C, after which a concentrated aqueous solution of sodium nitrite (857 mg) was slowly stirred in below the surface at such a rate as to maintain the temperature below −5 °C. To the resulting solution, prechilled (0 °C) 50% phosphinic acid was vigorously stirred in, drop by drop. The reaction mixture was then allowed to warm to room temperature with continued stirring for 1 h and then diluted with water. The resulting solution was made alkaline by adding a potassium carbonate aqueous solution, and extracted with benzene. The benzene layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was chromatographed on a silica-gel column with benzene–ethyl acetate (3 : 7). The reddish purple effluent was freed from the solvent to give **6** (374 mg, 41%) as reddish purple prisms; mp 142.5—143.5 °C; IR(KBr) 3050, 1585, 1487, 1463, and 1435 cm^{-1}; UV(cyclohexane 252 (log ε 3.96), 296 (4.80), 312 (4.10), 343 (3.80), 359 (3.86), 525 (2.90), 546 (2.85), 563 (2.84), 588 (2.61), 608 nm (2.58); ^{1}H NMR (90 MHz, in $CDCl_3$) $\delta=7.6$—8.0 (3H, m, H-6,7,8), 8.64 (1H, dm, $J=8.8$ Hz, H-9), 8.8—8.9 (1H, m, H-5), and 9.39 (1H, s, H-2); ^{13}C NMR (22.5 MHz, in $CDCl_3$) $\delta=179.6$(C-3a), 163.2(C-2), 161.9(C-4a), 137.9(C-5), 137.7(C-9a), 137.5(C-7), 133.8(C-9), 130.1(C-6), 128.5(C-8), and 115.9(C-9b). Found: C, 64.44; H, 3.25; N, 15.13; S, 17.15%; M$^+$, 186. Calcd for $C_{10}H_6SN_2$: C, 64.49; H, 3.25; N, 15.05; S, 17.22%; M, 186.

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