

Short Note

(Z)-2-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile

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Received: 12 July 2010 / Accepted: 30 July 2010 / Published: 3 August 2010

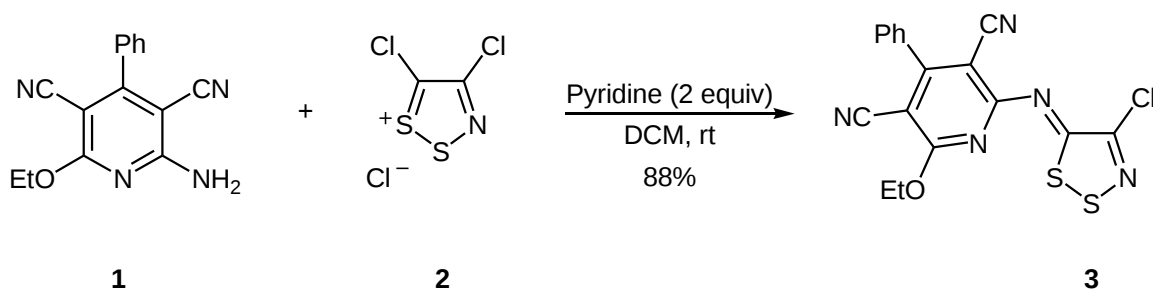
Abstract: 2-Amino-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **1** reacts with 4,5-dichloro-1,2,3-dithiazolium chloride **2** in the presence of pyridine (2 equiv.) to afford (Z)-2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **3** in 88% yield.

Keywords: pyridine; dithiazolium; dithiazolimine; Appel salt; condensation; heterocycle

N-Aryl-1,2,3-dithiazolimines show interesting antitumour [1], antifungal [2], antibacterial [3], and herbicidal activities [4]. Furthermore, these compounds are useful precursors for difficult to access cyano substituted heteroarenes [3,5]. *N*-Aryl-1,2,3-dithiazolimines are readily prepared from the condensation of anilines and 4,5-dichloro-1,2,3-dithiazolium chloride **2** commonly known as Appel's salt [6,7].

Surprisingly, there are only a few examples, of *N*-heteroazine substituted 1,2,3-dithiazolimines [7-9]. During ongoing studies of the chemistry of 4,5-dichloro-1,2,3-dithiazolium chloride **2** [10-13], we needed access to a highly substituted *N*-pyridyl-1,2,3-dithiazolimine. Fully substituted 2-amino-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **1** can be prepared from benzaldehyde and malononitrile in ethanol in the presence of base [14] and is a maxi-K channel opening agent [15].

Condensation of 2-amino-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **1** with Appel salt **2** in the presence of a tertiary amine base gave as expected the highly crystalline dithiazolimine **3**. Of the various amine bases screened (pyridine, 2,6-lutidine, DABCO, triethylamine, Hünig's base, DBU and DBN), the use of pyridine (2 equiv.) led to the highest yield (88%).



Some of the chemistry of the dithiazolimine **3** has been previously reported, but no experimental procedure for its preparation nor spectroscopic/physical data, were given [16]. These details for the preparation and full characterization of dithiazolimine **3** are now reported.

Experimental

Anhydrous Na_2SO_4 was used for drying organic extracts and volatiles were removed under reduced pressure. The reaction mixture and column eluents were monitored by TLC, using commercial glass backed thin layer chromatography (TLC) plates (Merck Kieselgel 60 F₂₅₄). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography was used, using Merck Silica Gel 60 (less than 0.063 mm). Melting point was determined using a PolyTherm-A, Wagner & Munz, Kofler-Hotstage Microscope apparatus. IR spectrum was recorded on a Shimadzu FTIR-NIR Prestige-21 spectrometer with Pike Miracle Ge ATR accessory and strong, medium and weak peaks are represented by s, m and w, respectively. ^1H NMR spectrum was recorded on a Bruker Avance 300 machine (at 300 MHz). Deuterated chloroform was used for deuterium lock and the signals are referenced to the residual undeuterated solvent peak. Low resolution (EI) mass spectrum was recorded on a Shimadzu Q2010 GCMS with a direct inlet probe. Microanalysis was performed at London Metropolitan University.

(Z)-2-(4-Chloro-5H-1,2,3-dithiazol-5-ylideneamino)-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile (**3**)

To a stirred suspension of 4,5-dichloro-1,2,3-dithiazolium chloride **2** (79 mg, 0.38 mmol) in DCM (4 mL) at *ca.* 20 °C and protected with a CaCl_2 drying tube, was added 2-amino-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **1** (100 mg, 0.38 mmol). After 1 h, to the reaction mixture was added dropwise pyridine (61.5 μL , 0.76 mmol) and the mixture was then left to stir at *ca.* 20 °C for an additional 2 h. The reaction mixture was then adsorbed onto silica and chromatography (hexane) gave S_8 (traces). Further elution (hexane/DCM, 8:2) gave 4-chloro-5H-1,2,3-dithiazole-5-thione (8.3 mg, 8%) and further elution (hexane/DCM 7:3) gave the *title compound* (133.4 mg, 88%) as yellow-orange cotton-like fibers, mp 264–265 °C (from toluene); (Found C, 51.2; H, 2.4; N, 17.5 $\text{C}_{17}\text{H}_{10}\text{ClN}_5\text{OS}_2$ requires C, 51.1; H, 2.5; N, 17.5%); λ_{max} (DCM) 229 (log ϵ 4.53), 264 (4.50), 279 inf (4.39), 301 inf (4.19), 329 inf (3.98), 403 inf (4.21), 424 (4.45), 447 (4.51), 472 (4.24); $\nu_{\text{max}}/\text{cm}^{-1}$ 3061w, 2976w, 2224m ($\text{C}\equiv\text{N}$), 1553s, 1518m, 1508s, 1468s, 1443m, 1429m, 1412m, 1373s, 1339s, 1237w, 1186m, 1165m, 1078w, 1022w, 883m, 804m, 745m, 710s; δ_{H} (300 MHz; $\text{DMSO}-d_6$) 7.64 (5H, s, Ph H), 4.71 (2H, q, J 6.8, OCH_2), 1.48 (3H, t, J 6.9, OCH_2CH_3); δ_{C} (75 MHz; $\text{DMSO}-d_6$) 164.9, 164.7, 160.5, 158.7, 149.3, 133.1, 130.8 (Ph CH), 128.8 (Ph CH), 128.7 (Ph CH), 114.4 ($\text{C}\equiv\text{N}$), 113.9 ($\text{C}\equiv\text{N}$), 98.6, 92.1, 67.0 (CH_2), 14.3 (CH_3); m/z (EI); 401 ($\text{M}^+ + 2$, 40%), 400 ($\text{M}^+ + 1$, 55), 399 (M^+ , 100), 398 (88),

372 (25), 364 (9), 336 (80), 305 (11), 278 (11), 272 (16), 246 (41), 218 (37), 191 (21), 165 (58), 138 (22), 127 (12), 125 (12), 102 (9), 91 (12), 77 (20), 70 (10), 64 (91), 51 (19).

Acknowledgements

The authors wish to thank the Cyprus Research Promotion Foundation [Grant No. TEXNOΛΟΓΙΑ/ΘΕΠΠΣ/0308(BE)/08] and the following organisations in Cyprus for generous donations of chemicals and glassware: the State General Laboratory, the Agricultural Research Institute and the Ministry of Agriculture. Furthermore we thank the A.G. Leventis Foundation for helping to establish the NMR facility in the University of Cyprus.

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