

Short Note

3-Amino-6-ethoxy-4-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine-2,5-dicarbonitrile

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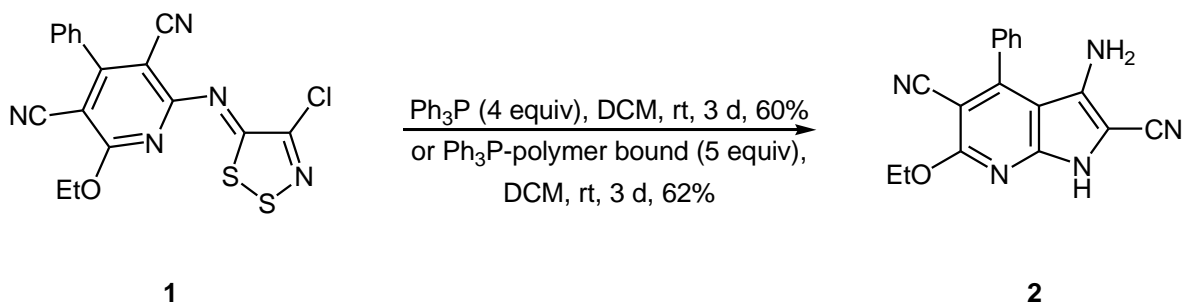
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Abstract: (*Z*)-2-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **1**, when treated with either triphenylphosphine (4 equiv.) or polymer bound triphenylphosphine (5 equiv.) in dichloromethane at room temperature for 3 days affords 3-amino-6-ethoxy-4-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine-2,5-dicarbonitrile **2** in 60–62% yields.

Keywords: pyridine; dithiazole; dithiazolimine; azaindole; indole; heterocycle; polymer bound; solid support

Neutral 1,2,3-dithiazoles, readily prepared from 4,5-dichloro-1,2,3-dithiazolium chloride **2** commonly known as Appel's salt [1], are useful precursors to often difficult to access cyano substituted heteroarenes [2-5]. Recently, we demonstrated the unexpected conversion of 2-(4-chloro-5*H*-1,2,3-dithiazolylideneamino)benzonitriles into 3-aminoindole-2-carbonitriles using triphenyl-phosphine [6].

During this study, we treated (*Z*)-2-(4-chloro-5*H*-1,2,3-dithiazol-5-ylideneamino)-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **1** [7] with triphenylphosphine (4 equiv.) in dichloromethane at room temperature for 3 days and obtained some triphenylphosphine sulfide (93%) and 3-amino-6-ethoxy-4-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine-2,5-dicarbonitrile **2** in 60% yield. By using polymer bound triphenylphosphine (5 equiv.), the chromatographic separation of the triphenylphosphine sulfide could be avoided and the desired pyrrolo[2,3-*b*]pyridine was isolated by simple filtration in 62% yield.



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.

3-Amino-6-ethoxy-4-phenyl-1H-pyrrolo[2,3-b]pyridine-2,5-dicarbonitrile (**2**)

(a) *Using free triphenylphosphine.* To a stirred solution of (*Z*)-2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **1** (100 mg, 0.25 mmol) in DCM (4 mL) at *ca.* 20 °C and protected with a CaCl_2 drying tube, was added triphenylphosphine (262 mg, 1 mmol, 4 equiv.). The mixture was then allowed to stir at *ca.* 20 °C for 3 days, until no starting materials remained (TLC). The reaction mixture was then adsorbed onto silica and chromatography (hexane/DCM, 5:5) gave triphenylphosphine sulfide (136.7 mg, 93%) as white needles, mp 161–162 °C (from cyclohexane), identical to an authentic sample. Further elution (hexane/DCM, 2:8) gave the *title compound* **2** (45.5 mg, 60%) as yellow prisms, mp 191–192 °C (from cyclohexane/EtOH); (Found: C, 67.2; H, 4.4; N, 23.0. $\text{C}_{17}\text{H}_{13}\text{N}_5\text{O}$ requires C, 67.3; H, 4.3; N, 23.1%); λ_{max} (DCM)/nm 243 (log ϵ 3.21), 276 (3.46), 314 inf (2.80), 328 (2.93), 372 inf (3.39); $\nu_{\text{max}}/\text{cm}^{-1}$ 3345m (NH), 3231m (NH₂), 2234m (C≡N), 2203s (C≡N), 1587s, 1580s, 1516m, 1489m, 1472m, 1381s, 1315s, 1180m, 1159m, 1024m, 924m, 868m, 793m, 772m, 741s, 702s; δ_{H} (300 MHz; CDCl_3) 8.31 (1H, br s, NH), 7.59–7.56 (3H, m, Ph H), 7.52–7.48 (2H, m, Ph H), 4.51 (2H, q, *J* 7.1, CH₂), 3.74 (2H, br s, NH₂), 1.47 (3H, t, *J* 7.1, CH₃); δ_{C} (75 MHz, CDCl_3) 163.7, 152.6, 146.0, 138.2, 133.1, 130.4 (Ph CH), 129.2 (Ph CH), 128.3 (Ph CH), 115.2 (C≡N), 113.8 (C≡N), 103.1, 91.2, 87.2, 63.8 (CH₂), 14.3 (CH₃); *m/z* (EI) 303 (M^+ , 84%), 275 (100), 247 (11), 219 (12), 194 (9), 165 (12), 140 (70), 51 (5).

(b) Using polymer bound triphenylphosphine. To a stirred solution of (Z)-2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)-6-ethoxy-4-phenylpyridine-3,5-dicarbonitrile **1** (100 mg, 0.25 mmol) in DCM (4 mL) at *ca.* 20 °C and protected with a CaCl₂ drying tube, was added triphenylphosphine polymer bound (328 mg, 1.25 mmol, 5 equiv.). The mixture was then allowed to stir at *ca.* 20 °C for 3 days, until no starting materials remained (TLC). Filtration of the reaction to remove the polymer, gave 3-amino-6-ethoxy-4-phenyl-1H-pyrrolo[2,3-*b*]pyridine-2,5-dicarbonitrile (**2**) (47 mg, 62%) as yellow prisms mp 191–192 °C (from cyclohexane/EtOH).

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