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Short Note

2-(3,5-Dimethyl-1*H*-pyrazol-1-yl)thiazolo[4,5-*b*]pyridine

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Abstract: The compound 2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazolo[4,5-*b*]pyridine (**1**) was synthesized with a yield of 71% by the reaction of 1-(thiazolo[4,5-*b*]pyridine-2-yl)hydrazine and acetylacetone. The structure was characterized by a single-crystal X-ray structure determination as well as ^{1}H and ^{13}C{^{1}H} NMR spectroscopy. X-ray crystallography on **1** confirms the molecule consists of a pyridine–thiazole moiety and the pyrazole ring, and all non-hydrogen atoms are planar.

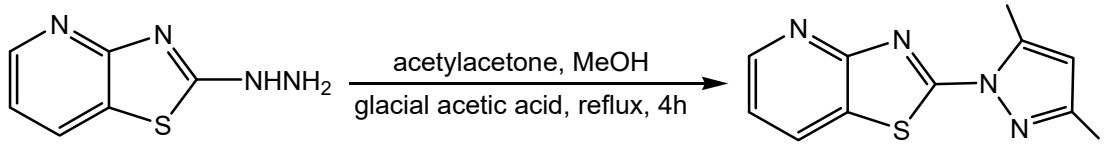
Keywords: thiazolo[4,5-*b*]pyridine; pyrazole; X-ray crystallography

1. Introduction

Heterocyclic compounds such as thiazoles and pyrazoles have attracted much research attention in the field of drug design because of their varied biological activities, such as antibacterial, antifungal, anti-inflammatory, and antitumor activities [1–4]. It is well known that the incorporation of different heterocyclic systems into a single molecule to form fused hybrids could offer access to new chemical entities with enhanced activities in comparison with their parent rings alone [5–7]. For example, some 1*H*-pyrazolyl derivatives of thiazolo[4,5-*d*]pyrimidines have exhibited promising anti-inflammatory and antimicrobial activities [8]. On the other hand, thiazolo[4,5-*b*]pyridine derivatives have been shown to possess antioxidant and anti-inflammatory activities [9,10]. In view of the abovementioned findings, a new thiazolo[4,5-*b*]pyridine–pyrazole compound was synthesized and structurally characterized.

2. Results

The title compound 2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazolo[4,5-*b*]pyridine (**1**) was easily prepared in a good yield (71%) from the hetero-cyclization of 1-(thiazolo[4,5-*b*]pyridin-2-yl)hydrazine and acetylacetone in methanol using glacial acetic acid as catalyst, as shown in Scheme 1. The reaction consists of two nucleophilic addition and dehydration processes, resulting in the pyrazolyl ring. The product was characterized by ^{1}H, ^{13}C{^{1}H}-NMR, (see Supplementary Materials for original spectra) and X-ray crystallography. An isomer of the title compound, namely 2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazolo[5,4-*b*]pyridine, has been reported before, but its detailed synthesis method was not given [11].



Scheme 1. Synthesis of 2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazolo[4,5-*b*]pyridine.

The molecular structure of compound **1** is shown in Figure 1. The asymmetric unit contains one molecule of the title compound, which is constructed by the pyridine–thiazole moiety and the dimethyl-pyrazole fragment. All non-hydrogen atoms of the title compound are almost planar

with a maximum deviation of 0.245(3) Å for C10. The C–N bond distances are in the range of 1.291(3)-1.390(3) Å, which are typical of azocompounds. The C2–S1 and C6–S1 bond lengths of 1.724(3) Å and 1.737(2) Å are intermediate between the double (~1.56 Å) and single (~1.82 Å) bonds. The shortening of the C–S bonds shows the partial double bond character, which was also observed in other pyridine-thiazole compounds [11–13]. Comparing with its isomer 2-(3,5-dimethyl-1*H*-pyrazol-1-yl)thiazolo[5,4-*b*]pyridine, the shorter C–S bond lengths show a subtle difference between the two thiazole rings. The difference may be caused by different positions of the heteroatoms.

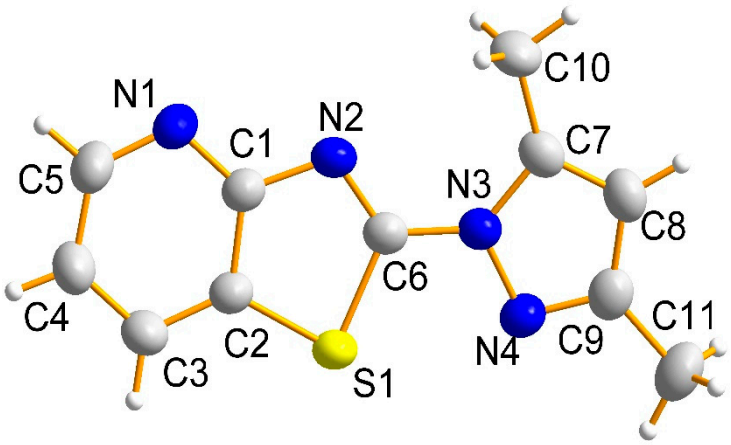


Figure 1. The molecular structure of **1** showing atom labeling and displacement ellipsoids at the 50% probability.

3. Materials and Methods

3.1. General Information

The compound 1-(thiazolo[4,5-*b*]pyridin-2-yl)hydrazine was synthesized according to the reported method [12]. All other chemicals and solvents were purchased from commercial sources and used without purification. The melting point was determined on a Beijing Keyi apparatus (Beijing synthware glass, Beijing, China). Nuclear magnetic resonance (NMR) spectra were measured on a Bruker AvanceII 400 spectrometer (Bruker BioSpin AG, Fällanden, Switzerland) operating at 400 MHz, using tetramethylsilane (TMS) as an internal standard. The X-ray diffraction data were collected at 298 K on a Bruker Smart CCD area detector (Bruker, Karlsruhe, Germany) with graphite-monochromated Mokα radiation (λ = 0.71073 Å). The structures were solved by direct methods, before further refinement with full-matrix least-squares on F^2 was obtained with the SHELXL program package [14].

3.2. Synthesis and Characterization of **1**

A mixture of 1-(thiazolo[4,5-*b*]pyridin-2-yl)hydrazine (0.166 g, 1 mmol) and acetylacetone (0.1 g, 1 mmol) in 30 mL methanol in the presence of catalytic amount of glacial acetic acid was refluxed for 4 h. Then, the mixture was left for slow evaporation under ambient conditions. Colorless crystals were collected after three days. Yield: 0.163 g, 71%. White solid; m.p. 142.5–143.6 °C. ^{1}H–NMR (400 MHz, $CDCl_3$): δ 8.60–8.62 (d, 1H, arom), 8.14–8.16 (d, 1H, arom), 7.23–7.26 (m, 1H, arom), 6.08 (s, 1H, arom), 2.83 (s, 3H, CH_3), 2.31 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 164.39, 162.88, 153.23, 147.80, 143.51, 130.23, 126.98, 119.41, 111.27, 14.21, 13.75.

Crystal data for $C_{11}H_{10}N_4S$ (**1**): M = 230.29, orthorhombic, *Pbca*, a = 11.863(7), b = 10.910(7), c = 16.519(10) Å, V = 2138(2) Å^3, Z = 8, D_x = 1.431 g cm^{-3}, F(000) = 960 and μ = 0.278 mm^{-1}. CCDC deposition number: 1941839.

Supplementary Materials: The following are available online: ^{1}H and ^{13}C{^{1}H} NMR, and crystallographic data for (**1**) in crystallographic information file (CIF) format. CCDC 1941839 also contains the supplementary

crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html.

Author Contributions: H.L. conceived and designed the experiments; M.Z. performed the experiments; M.Z., H.L. and Y.W. analyzed the data; H.L. and M.Z. wrote the paper.

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Conflicts of Interest: The author declares no conflict of interest.

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