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Short Note

Ethyl 3,5-Dimethyl-4-[(4-phenyl-1,3-thiazol-2-yl)carbamoyl]-1*H*-pyrrole-2-carboxylate

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Abstract: A new compound, ethyl 3,5-dimethyl-4-[(4-phenyl-1,3-thiazol-2-yl)carbamoyl]-1*H*-pyrrole-2-carboxylate (**3**) was synthesized by the amination method. The synthesized compound (**3**) was characterized by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectral data and elemental analysis.

Keywords: diethyl 3,5-dimethyl-1*H*-pyrrole-2,4-dicarboxylate; 4-phenyl-1,3-thiazol-2-amine; amination reaction

1. Introduction

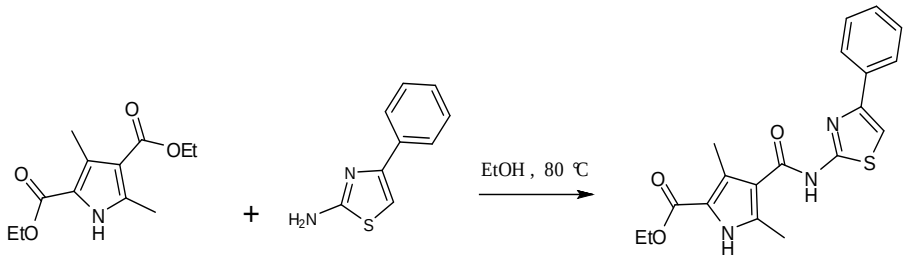
Thiazoles are an important class of natural and synthetic compounds. Thiazole derivatives display a wide range of biological activities such as anesthetic [1] and anti-inflammatory [2]. In view of their pharmaceutical applications, the synthesis of thiazoles is important. Here, the preparation and characterization of a new thiazole derivative is reported.

2. Results and Discussion

The two educts, diethyl 3,5-dimethyl-1*H*-pyrrole-2,4-dicarboxylate (**1**) and 4-phenyl-1,3-thiazol-2-amine **(2)** were synthesized according to previously reported methods [3–6]. The title compound, ethyl 3,5-dimethyl-4-[(4-phenyl-1,3-thiazol-2-yl)carbamoyl]-1*H*-pyrrole-2-carboxylate (**3)** was synthesized by an amination reaction [7,8]. The ^{1}H-NMR spectrum of compound (**1**) showed a quartet at δ 4.20 and a triplet at δ 1.30, corresponding to -COOC$\underline{H}_2$CH$_3$ and -COOCH$_2$C$\underline{H}_3$ protons in the 2- and 4-position of the pyrrole ring. The ^{1}H-NMR spectrum (Figure 2) of compound (**3**) showed a singlet at δ 8.11, corresponding to the -CON$\underline{H}$ proton in the 4-position of the pyrrole ring. A doublet observed at δ 3.87

and δ 2.18 was attributed to the CH_3 protons at 3- and 5-position in the pyrrole ring. A 1D NOE spectrum (Figure 3a and 3b) of compound (**3**) showed interactions between the amide-NH proton and the CH_3 protons at the 3- and 5-position, respectively, thus confirming that the -CONH group is located in 4-position of the pyrrole ring. No signal enhancement was obtained on irradiation of the NH proton at the 1-position of the pyrrole ring. The ^{13}C-NMR spectrum (Figure 4) of compound (**3**) showed signals at δ 156.9 and δ 166.0, corresponding to the –COOEt group at the 2-position and the –CONH group at the 4-position of the pyrrole ring. The mass spectra (EI) of compound (**3**) showed the molecular ion peak at *m/z* 370.43 (M^+ + 1, 12%), consistent with the assigned molecular formula $C_{19}H_{19}N_3O_3S$.

Scheme 1. Synthesis of the title compound (**3**).



1 **2** **3**

Scheme 2. Proposed conformation of compound (**3**).

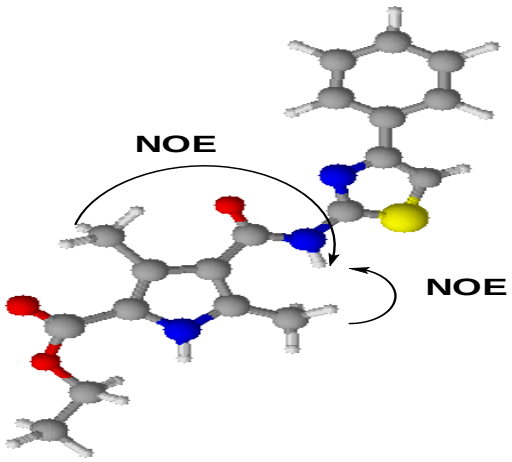


Figure 1. ^{1}H-NMR spectrum of compound (**1**) (400 MHz, DMSO-d_6).

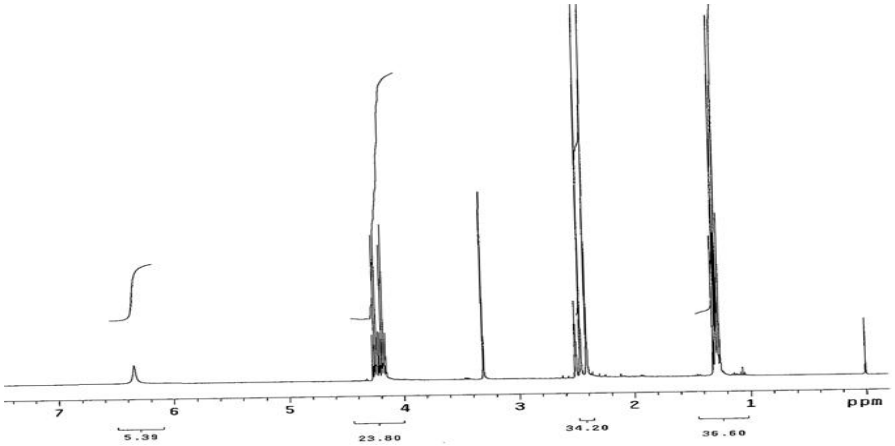


Figure 2. ¹H-NMR spectrum of compound (**3**) (400 MHz, DMSO-d_6).

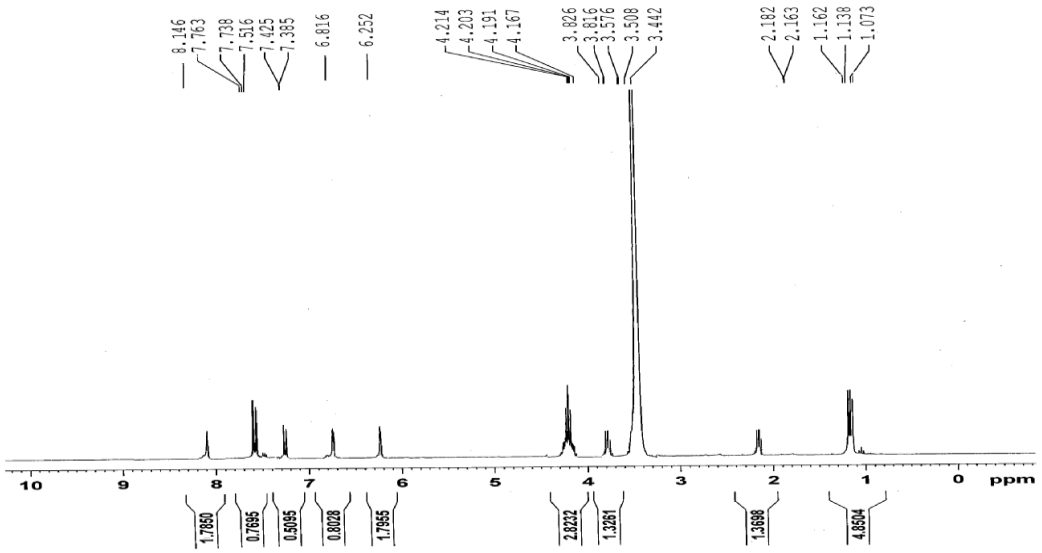
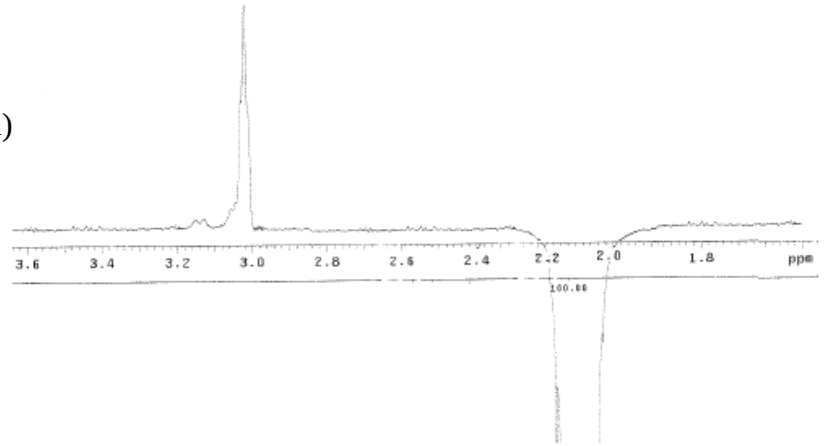


Figure 3. (a) 1D NOE NMR for CH_3 at 5-position, with irradiation of neighboring CONH proton in compound (**3**) recorded at 400 MHz in DMSO-d_6. (b) 1D NOE NMR for CH_3 at 2-position, irradiated with neighboring CONH proton in compound (**3**) recorded at 400 MHz, in DMSO-d_6.

(a)



(b)

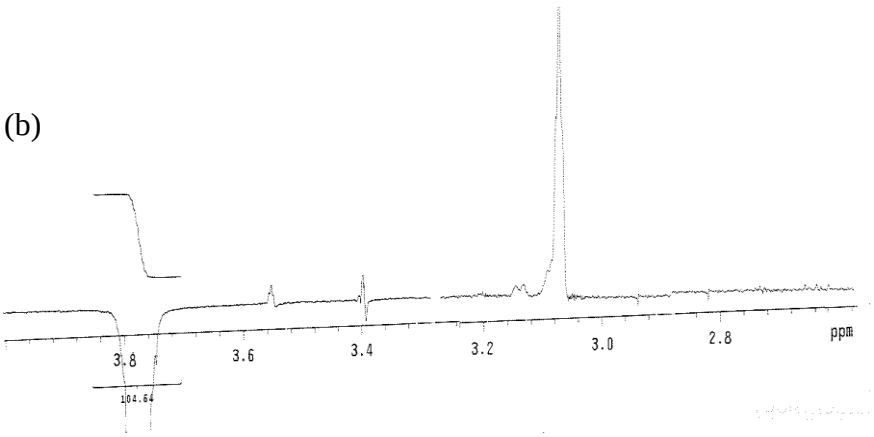


Figure 4. ^{13}C-NMR spectrum of compound (**3**) (100 MHz, DMSO-d_6).

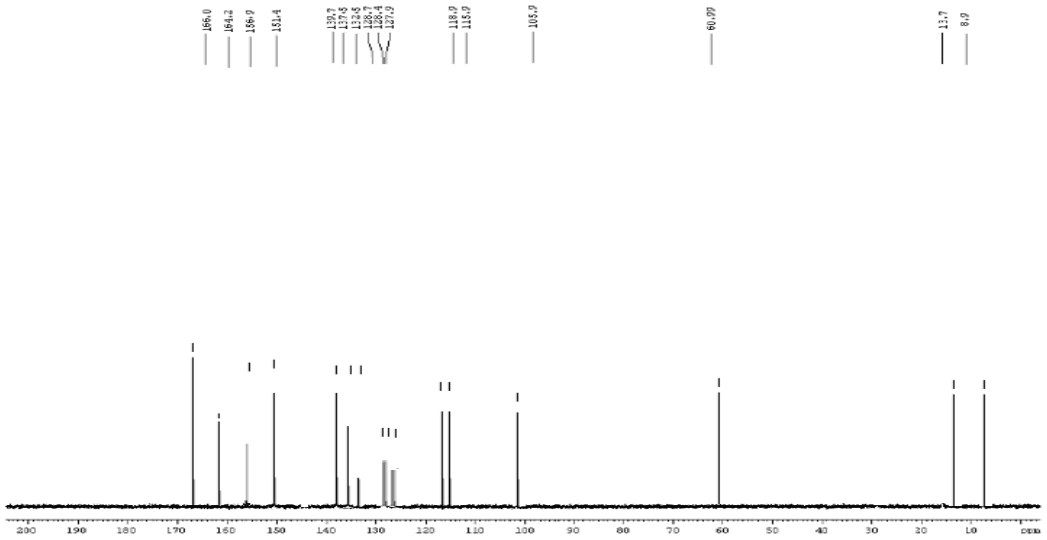
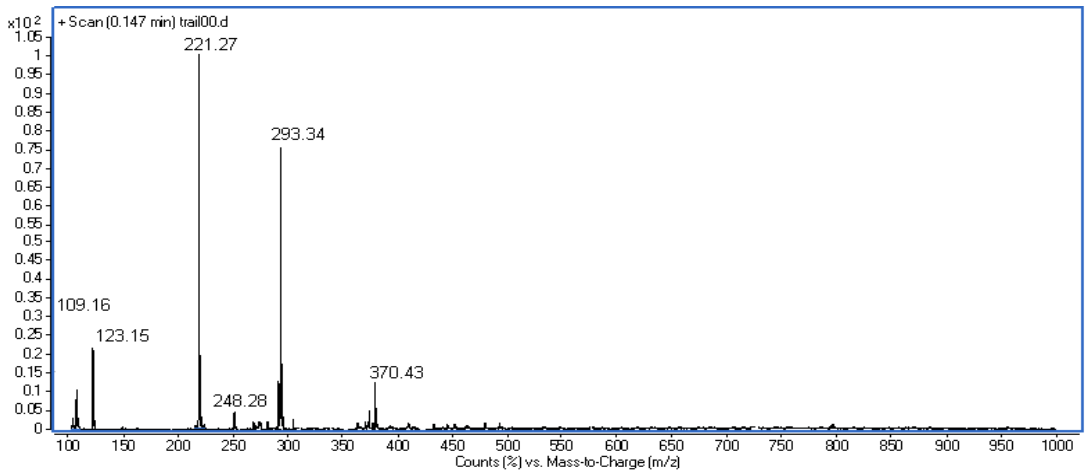


Figure 5. Mass spectrum (EI) of compound (**3**).



3. Experimental

The melting point was determined in an open capillary tube and it is uncorrected. The IR spectrum was recorded for a KBr pellet on a Shimadzu 8201pc (4000–400 cm^{-1}). The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker DRX-400 and a Varian Mercury Plus 400 at 400 MHz (^{1}H) and 100 MHz (^{13}C), respectively. The mass spectrum (EI) was recorded on a Jeol JMS D-300 spectrometer operating at 70 eV. Elemental analysis (C, H, N and S) were carried out using a Varian Elemental Analyzer EL III. The purity of the compound was checked by thin layer chromatography (TLC) with silica gel plates.

3.1. Synthesis of ethyl 3,5-dimethyl-4-[(4-phenyl-1,3-thiazol-2-yl)carbamoyl]-1H-pyrrole-2-carboxylate (**3**)

A mixture of diethyl 3,5-dimethyl-1*H*-pyrrole-2,4-dicarboxylate (**1**) (2.39 g, 0.01 mol), 4-phenyl-1,3-thiazol-2-amine (**2**) (1.78 g, 0.01 mol) and absolute ethanol (30 mL) was heated under

reflux for 48 h. The reaction mixture was cooled and poured into crushed ice. The obtained solid was filtered off and washed with water. The filtered solid was purified by recrystallisation from absolute ethanol to give the title compound (**3**) as a yellow solid (1.20 g, 28%).

Melting point: 147 ℃

IR (KBr, cm^{-1}): υ 3350 (N-H_{str}), 3050 (C-H_{str} of phenyl ring), 2953 (C-H_{str} of CH_3), 1755 (C=O, ester), 1685 (-HN-C=O), 1626 (C=N), 712 (C-S-C).

^{1}H-NMR (DMSO-d_6, 400 MHz): δ 8.11 (s, 1H, NH-CO), 7.32–7.74 (m, 5H, Ph), 6.25 (s, 1H, pyrrole NH), 6.85 (s, 1H, thiazole-H), 4.20 (q, 2H, *J* = 18.8 Hz, $OC\underline{H}_2CH_3$), 3.87 (d, 3H, *J* = 7.6 Hz, 3-CH_3), 2.18 (d, 3H, *J* = 4 Hz, 5-CH_3), 1.30 (t, 3H, *J* = 16.4 Hz, $OCH_2C\underline{H}_3$).

^{13}C-NMR (DMSO-d_6, 100 MHz): δ 166.0 (NHCO), 164.2 (thiazole 2-C), 156.9 (C-$\underline{C}$OOEt at 2-position in pyrrole ring), 151.4 (thiazole 4-C), 137.5 (pyrrole 3-C), 139.7 (pyrrole 5-C), 127.9, 128.4, 128.7, 132.1 (phenyl-C), 118.8 (pyrrole 2-C), 115.7 (pyrrole 4-C), 105.0 (thiazole 5-C), 60.2 ($O\underline{C}H_2CH_3$), 13.8 (5-CH_3), 8.9 (3-CH_3).

MS (EI): *m/z* = 370.43 (M^+ + 1, 12%), 293.34 (75%), 248.28 (5%), 221.27 (100%), 123.15 (22%), 109.16 (10%).

Elemental analysis: Calcd. for $C_{19}H_{19}N_3O_3S$ (MW = 369.45): C, 61.76%; H, 5.18%; N, 11.37%; S, 8.67%. Found: C, 61.71%; H, 5.14%; N, 11.33%; S, 8.64%.

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