

Short Note

2-**{[5-(Diphenylmethyl)-1,3,4-oxadiazol-2-yl]sulfanyl}-N-(pyrazin-2-yl)acetamide**

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Abstract: S-Alkylation of 5-(diphenylmethyl)-1,3,4-oxadiazole-2(3*H*)-thione (**3**) by 2-chloro-*N*-(pyrazin-2-yl)acetamide (**2**) affords the title compound, 2-**{[5-(diphenylmethyl)-1,3,4-oxadiazol-2-yl]sulfanyl}-N-(pyrazin-2-yl)acetamide** (**4**). The intermediate (**2**), in turn, was prepared by the acetylation of 2-aminopyrazine (**1**) with chloroacetyl chloride. The structure of the newly synthesized compound is characterized by IR, NMR and mass spectral data.

Keywords: 1,3,4-oxadiazole; pyrazine; S-alkylation; thioether

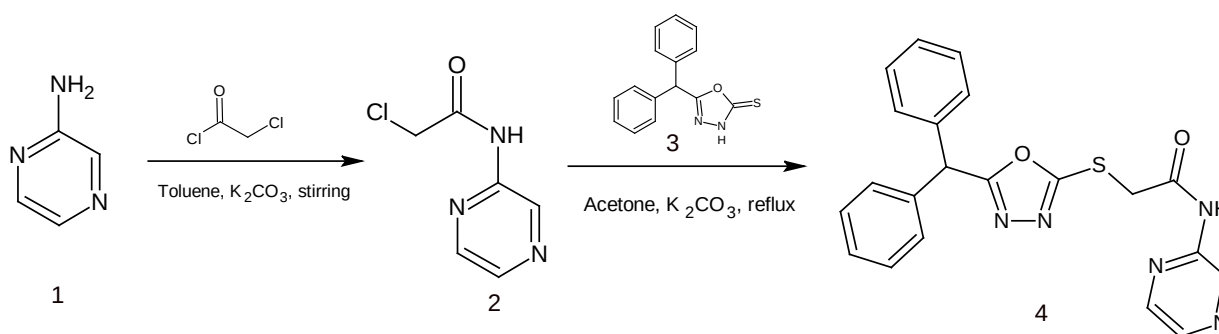
Introduction

Thioethers have emerged as preeminent classes of organic compounds, which hold useful applications as key reagents in organic synthesis, bioorganic, medicinal, and heterocyclic chemistry [1–4]. Thioether derivatives have been the subject of investigation due to their different properties such as antibacterial [5] and antifungal [6] activities. Literature survey reveals that pyrazine derivatives showed pronounced antiauxin [7], antimycobacterial [8], antimicrobial, and anticancer [9] activities. On the other hand, a wide range of biological activities like, antiinflammatory [10], analgesic [11], antimicrobial [12,13] *etc.*, have been attributed to the compounds containing 1,3,4-oxadiazole ring system [14–17]. In view of the importance of thioethers, pyrazines and 1,3,4-oxadiazoles, it was aimed to synthesize the title compound, with the combination of three pharmacophore groups.

Results and Discussion

The title compound, 2-[[5-(diphenylmethyl)-1,3,4-oxadiazol-2-yl]sulfanyl]-*N*-(pyrazin-2-yl)acetamide (**4**), was prepared by the regioselective *S*-alkylation of 5-(diphenylmethyl)-1,3,4-oxadiazole-2(3*H*)-thione (**3**) with 2-chloro-*N*-(pyrazin-2-yl)acetamide (**2**) (Scheme 1). The intermediate **2**, in turn, was prepared by the reaction of 2-aminopyrazine (**1**) with 2-chloroacetylchloride in the presence potassium carbonate [16]. The other intermediate, 5-(diphenylmethyl)-1,3,4-oxadiazole-2(3*H*)-thione (**3**) was synthesized from diphenyl acetic acid according to the method described in our earlier work [17]. The title compound (**4**) was characterized by NMR, IR and mass spectral data.

Scheme 1. Synthesis of 2-[[5-(diphenylmethyl)-1,3,4-oxadiazol-2-yl]sulfanyl]-*N*-(pyrazin-2-yl) acetamide, **4**.



The formation of 2-[[5-(diphenylmethyl)-1,3,4-oxadiazol-2-yl]sulfanyl]-*N*-(pyrazin-2-yl)acetamide (**4**) was confirmed by its NMR and mass spectral data. A singlet integrating for two protons at δ 4.53 in the 1H -NMR spectrum of compound (**4**) was due to -S-CH₂ linkage. Another singlet observed at δ 5.93 ppm was due to the proton attached the carbon for which two phenyl groups were substituted. The signals of aromatic protons merged in the regions δ 7.22–7.36 ppm and 8.38–8.41 ppm as multiplets. NH proton appeared as a singlet at δ 11.15 ppm as a singlet. Mass spectrum showed a molecular ion peak at m/z 404.5 ($M^+ + 1$) corresponding to the molecular formula of $C_{21}H_{17}N_5O_2S$. Elemental analysis and ^{13}C -NMR spectrum also gave satisfactory results for the title compound.

Experimental

The melting point was taken in an open capillary tube and was uncorrected. The purity of the compound was confirmed by thin layer chromatography using Merck silica gel 60 F₂₅₄ coated aluminium plates. IR spectrum was recorded on Shimadzu-FTIR Infrared spectrometer in KBr (ν_{max} in cm^{-1}). 1H -NMR (400 MHz) spectrum was recorded on a Varian 400 spectrometer, with 5 mm PABBO BB-1H TUBES and ^{13}C -NMR (100 MHz) spectrum was recorded for approximately 0.03 M solutions in DMSO at 100 MHz with TMS as internal standard. LCMS was obtained using an Agilent 1200 series LC and Micromass zQ spectrometer. Elemental analysis was carried out by using VARIO EL-III (Elementar Analysensysteme GmbH).

The synthesis of 2-chloro-*N*-(pyrazin-2-yl)acetamide (**2**) was carried out by the reaction of 2-aminopyrazine (**1**) with 2-chloroacetyl chloride in the presence of K_2CO_3 [18]. The other

intermediate, 5-(diphenylmethyl)-1,3,4-oxadiazole-2(3*H*)-thione **3** was synthesized by adopting the method described in our earlier work [19].

To a solution of 5-(diphenylmethyl)-1,3,4-oxadiazole-2(3*H*)-thione **3** (0.44 g, 1.65 mmol) in dry acetone (25 mL), anhydrous potassium carbonate (0.27 g, 1.98 mmol) and 2-chloro-*N*-(pyrazin-2-yl)acetamide **2** (0.34 g, 1.98 mmol) were added and the resulting solution was heated to reflux for 4 hours. After the completion of reaction as indicated by TLC, the reaction mixture was cooled to room temperature and quenched into ice cold water. The resulting precipitate was filtered and recrystallized from ethanol. The yield was 0.73 g, 71%.

Melting point: 210–212 °C.

LCMS: $m/z = 404.5$ ($M^+ + 1$).

IR (KBr): $\nu_{\max}$ (cm^{-1}), 3201 (N-H), 3041 (Ar-H), 1699 (alkyl-CO-NH), 1555 (C=N, Ar C=C).

^1H -NMR (400 MHz, $\text{DMSO}-d_6$): δ ppm, 4.53 (s, 2H, S-CH₂), 5.93 (s, 1H, Ph₂-CH), 7.22–7.36 (m, 11H, Ar-H), 8.38–8.41 (m, 2H, Ar-H), 11.15 (s, 1H, NH).

^{13}C -NMR (100 MHz, $\text{DMSO}-d_6$): δ ppm, 168.52 (C=O), 166.41, 163.89 (oxadiazole C's), 148.75, 143.11, 140.54, 139.07, 136.55, 129.14, 128.75, 127.82 (aromatic C's), 47.61 (S-CH₂), 36.78 (Ph₂-CH).

Elemental analysis: Calculated for C₂₁H₁₇N₅O₂S, C, 62.52%; H, 4.25%; N, 17.36%; Found: C, 62.49%; H, 4.28%; N, 17.32%.

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