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Short Note

1-Phenyl-3,3-di(1*H*-pyrazol-1-yl)propan-1-one

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Abstract: The title compound, 1-phenyl-3,3-di(1*H*-pyrazol-1-yl)propan-1-one, was synthesized in a 52% yield for the first time by a one-step reaction between 1*H*-pyrazole and 1-phenylprop-2-yn-1-one (their ratio being 2:1) in solid Al_2O_3 at room temperature. The product was characterized by ^{1}H-NMR, ^{13}C-NMR, IR spectroscopy, X-ray diffraction and elemental analysis.

Keywords: pyrazole; 1-phenylprop-2-yn-1-one; di(1*H*-pyrazol-1-yl)propan-1-one; Al_2O_3

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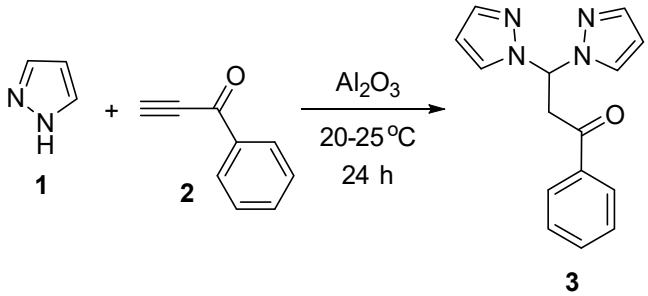
1. Introduction

Dipyrazole with a gem-disposition of pyrazole rings exhibit a wide spectrum of biological activity [1,2]. Furthermore, dipyrazolylmethanes are promising ligands [3,4]. Complex compounds with such dipyrazolyl ligands are active against the trypanosome pathogen [5], while scorpionate copper complexes of dipyrazolylmethanecarboxylic acids possess anticancer activity [6]. Complexes based on dipyrazolyl chelate ligands are active catalysts in polymerization processes [7].

Among many methods for the synthesis of compounds containing gem-dipyrrazole moieties [8], a special place is occupied by those using acetylene-derived molecules. These are the addition of pyrazoles to electron-deficient alkynes in the presence of Lewis acids [9,10] and a silver(I)-catalyzed reaction between pyrazole and propargyl acetates [11]. However, these reactions take place under rather harsh conditions (reflux during 24 h), and they require expensive catalyst salts ($Sc(OTf)_3$, $Au(OTf)_3$, AgOTf, $AgPF_4$ and $AgNO_3$).

2. Results and Discussion

We have shown that 1*H*-pyrazole (**1**) readily reacted with available 1-phenylprop-2-yn-1-one (**2**) (the ratio being 2:3, 2:1) in solid Al_2O_3 at room temperature to give a ketone with two pyrazole rings, 1-phenyl-3,3-di(1*H*-pyrazol-1-yl)propan-1-one (**3**), in a 52% yield (Scheme 1).



Scheme 1. Synthesis of 1-phenyl-3,3-di(1*H*-pyrazol-1-yl)propan-1-one (**3**).

The structure and composition of the synthesized dipyrazole were confirmed by ^{1}H, ^{13}C NMR, IR spectroscopy, X-Ray diffraction (Figure 1) and elemental analysis (see Supplementary Materials). Elemental analysis establishes the chemical formula of compound **3**. The ^{1}H NMR spectrum of **3** shows signals of the pyrazole rings at 7.65, 7.53 and 6.27 ppm,

the signal of the proton of sp^2-carbon at 7.17 ppm (C<u>H</u>CH_2) and the signal of the proton of sp^3-carbon at 4.40 ppm (CHC<u>H_2</u>). The characteristic signal of the carbonyl group is observed in the ^{13}C NMR spectrum at 194.7 ppm. The IR spectrum reveals characteristic bands of the C=O bond (1663 cm^{-1}) and C=N, C=C bonds (1570–1615 cm^{-1}).

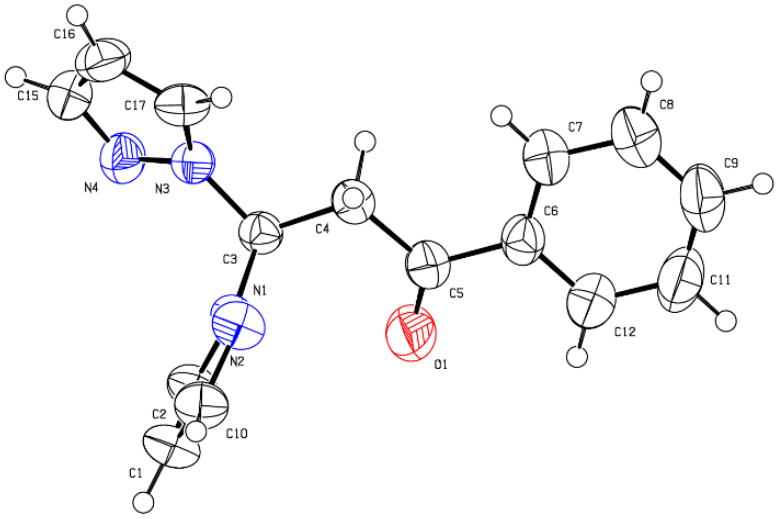


Figure 1. X-ray structure of 1-phenyl-3,3-di(1*H*-pyrazol-1-yl)propan-1-one (**3**). Thermal ellipsoids set at 50% probability.

Thus, we have synthesized a dipyrazole functionalized with a ketone group, 1-phenyl-3,3-di(1*H*-pyrazol-1-yl)propan-1-one, which contains two pharmacologically valuable counterparts (pyrazole and benzoylethyl moieties) and can be considered as a prospective tripodal scorpionate-like ligand for coordination chemistry and metal complex catalysis.

3. Materials and Methods

General. NMR spectra were recorded on a Bruker DPX-400 spectrometer (Bruker, Billerica, MA, USA) (400.1 MHz for ^{1}H and 100.6 MHz for ^{13}C) in $CDCl_3$. The internal standards were HMDS (for ^{1}H) and the residual solvent signals (for ^{13}C). Coupling constants (*J*) were measured from one-dimensional spectra, and multiplicities were abbreviated as follows: s (singlet), d (doublet), dd (doublet of doublets), q (quartet), t (triplet) and m (multiplet). The determination of the unit cell and the data collection for 1-phenyl-3,3-di(1*H*-pyrazol-1-yl)propan-1-one (**3**) were performed on a Bruker D8 VENTURE PHOTON 100 CMOS diffractometer with MoK_α radiation (λ = 0.71073) at 293.0(2) K using the ω–ϕ scan technique. A specimen of $C_{15}H_{14}N_4O$, with approximate dimensions of 0.13 mm × 0.14 mm × 0.26 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. The integration of the data using a monoclinic unit cell with a $P2_1/c$ space group yielded a total of 27,301 reflections to a maximum θ angle of 26.1° (0.81 Å resolution), of which 2675 were independent (completeness = 100.0%, Rint = 6.54%, Rsig = 2.68%) and 1826 were greater than 2σ(F2). The final cell constants of **a** = 14.6160(7) Å, **b** = 9.0561(4) Å, **c** = 10.4156(4) Å, Z = 4, volume = 1356.55(10) Å^3. Data were corrected for absorption effects using the multi-scan method (SADABS). The calculated minimum and maximum transmission coefficients (based on the crystal size) were 0.9671 and 0.9837. The structure was solved using the Bruker SHELXTL Software Package [12] and refined using the Olex2 [13] package. All H atoms were treated as riding atoms. IR spectra were recorded on a two-beam Bruker Vertex 70 spectrometer (Bruker, Billerica, MA, USA), in a KBr pellet. Elemental analyses (C, H, N) were performed on an EA FLASH 1112 Series (CHN Analyzer) instrument (Thermo Finnigan, Italy). Melting points (uncorrected) were measured on a Kofler micro hot-stage apparatus.

1*H*-Pyrazole (**1**) and Al_2O_3 were commercial ones. 1-Phenylprop-2-yn-1-one (**2**) was obtained according to the method from [14].

Synthesis of 1-phenyl-3,3-di(1H-pyrazol-1-yl)propan-1-one (**3**). 1*H*-pyrazole (**1**) (408 mg, 6 mmol) and 1-phenylprop-2-yn-1-one (**2**) (390 mg, 3 mmol) were carefully ground together with alumina (8 g, ~10-fold amount by weight) for 5 min and allowed to stay at rt for 24 h. Then, the solid reaction mixture was placed on top of an Al_2O_3-packed column and successively eluted with *n*-hexane and systems of *n*-hexane with diethyl ether (*n*-hexane/diethyl ether with a gradient from 3:1, 1:1, 1:3) to afford 1-phenyl-3,3-di(1*H*-pyrazol-1-yl)propan-1-one (**3**). Yield 415 mg (52%), yellow crystals (suitable for X-ray analysis), mp 70 °C. IR spectrum (KBr), ν, cm^{-1}: 3313, 3114, 2922, 1663 (C=O), 1615, 1570 (C=N, C=C). ^{1}H NMR ($CDCl_3$, ppm): δ 8.00–7.98 (m, 2H, *o*-Ph), 7.65–7.64 (m, 2H, H-4, pyrazole), 7.60–7.57 (m, 1H, *p*-Ph), 7.54–7.53 (m, 2H, H-5, pyrazole), 7.48–7.44 (m, 2H, *m*-Ph), 7.17 (t, *J* = 6.6 Hz, 1H, C<u>H</u>–CH_2), 6.28–6.26 (m, 2H, H-3, pyrazole), 4.39 (d, *J* = 6.6 Hz, 2H, CH–C<u>H_2</u>). ^{13}C NMR ($CDCl_3$, ppm): 194.7 (C=O), 140.3 (2C), 135.9, 133.7, 129.1 (2C), 128.7 (2C), 128.2 (2C), 106.6 (2C), 71.3, 42.2. Anal. calcd. for $C_{15}H_{14}N_4O$ (%): C, 67.65; H, 5.30; N, 21.04. Found (%): C, 67.79; H, 5.43; N, 21.19.

Supplementary Materials: The followings can be downloaded online. Copies of ^{1}H NMR, ^{13}C NMR and X-ray diffraction analysis.

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