

Short Note

[5-(1,3-Diphenyl-1*H*-pyrazol-4-yl)-3-phenyl-4,5-dihydropyrazol-1-yl](pyridin-4-yl)methanone

Darpan Kaushik *, Upasana Nagpal, Tarawanti Verma and Kapish Madan

Department of Pharmaceutical Chemistry, RITS, 4th Mile Stone, Hisar Road, Sirsa-125055, India

* Author to whom correspondence should be addressed; E-Mail: darpkash@yahoo.com.

Received: 13 December 2010 / Accepted: 4 January 2011 / Published: 11 January 2011

Abstract: A novel pyrazoline derivative **2** was synthesized by reaction of an α,β -unsaturated ketone **1** with isonicotinic acid hydrazide (INH) in glacial acetic acid. The structure of the title compound **2** was established on basis of IR, ¹H-NMR, ¹³C-NMR and mass spectral data.

Keywords: chalcone; pyrazoline; isonicotinic acid hydrazide

1. Introduction

Pyrazoline derivatives are electron-rich nitrogen heterocycles which play an important role due to their diverse biological activities [1]. They have been found to possess antimicrobial, antidiabetic, antidepressant, anticancer, hypotensive, antiamebic, anti-inflammatory and antitubercular activity [2-10]. As a part of our research programme on pyrazoline derivatives [11], we report herein the synthesis of [5-(1,3-diphenyl-1*H*-pyrazol-4-yl)-3-phenyl-4,5-dihydropyrazol-1-yl](pyridin-4-yl)methanone (**2**).

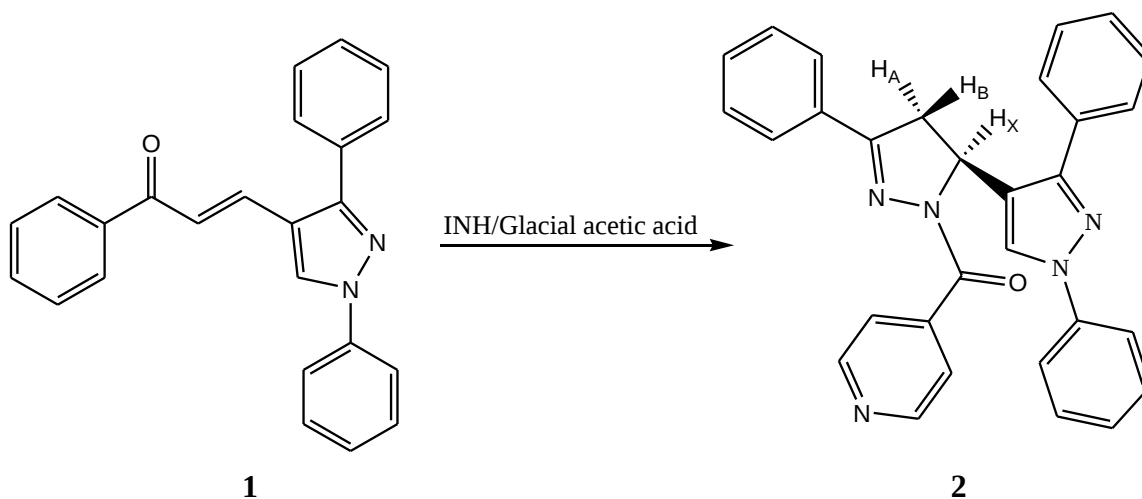
2. Results & Discussion

The title compound **2** was prepared by reaction of 3-(1,3-diphenyl-1*H*-pyrazol-4-yl)-1-phenylprop-2-en-1-one (**1**) and isonicotinic acid hydrazide in glacial acetic acid (Scheme 1). The ¹H-NMR spectrum of compound **2** displayed three characteristic signals due to diastereotopic protons (H_A, H_B and H_X). The H_A proton which is *cis* to H_X resonates upfield at δ 3.21 (center) as doublet of doublets (dd, *J* = 17.55 and 4.50 Hz), while the H_B proton which is *trans* to H_X resonates downfield at 3.71 (dd, *J* = 17.40 and 11.70 Hz). The H_X proton which is vicinal to two methylene protons (H_A and H_B) is also observed as double doublet at a δ value of 6.08 (dd, *J* = 11.55 and 4.80 Hz). The aromatic protons are

observed at the expected chemical shift and integral values. The 5-H proton of pyrazole is observed as a singlet at 8.76 ppm apparently due to deshielding caused by the pyrazoline ring.

The cyclization of chalcone **1** into pyrazoline derivative **2** was further supported by ^{13}C -NMR of prototype compound in which C_4 and C_5 carbon resonate at δ 41.49 and 53.62, respectively, while the peaks due to carbonyl carbon ($\text{C}=\text{O}$) are observed at 167.82 ppm. These values are in close agreement with reported values of carbon C_4 and C_5 in pyrazolines [12]. DEPT-135 is an important tool of ^{13}C -NMR spectroscopy in which only primary, secondary and tertiary carbons that have an attached proton give signals, but the phase of signals is different, depending on whether the number of attached hydrogens is an odd or even number. Signals arising from CH or CH_3 groups will give positive peaks, while signals arising from CH_2 groups will give negative (inverse) peaks. Here, the DEPT-135 spectrum gives positive peaks at δ 53.62 due to CH of pyrazoline (*i.e.*, C_5) and a negative (inverse) peak at 41.49 due to CH_2 of pyrazoline (C_4), respectively. The combination of ^1H -NMR, ^{13}C -NMR and DEPT-135 provides strong evidence in support of the structure assigned to this pyrazoline derivative. The MS (ESI) spectrum of compound **2** exhibits an $\text{M}+1$ peak at $m/z = 470$. The value is in complete agreement with the structure assigned. Starting material 3-(1,3-diphenyl-1*H*-pyrazol-4-yl)-1-phenylprop-2-en-1-one **1** was synthesized based on a literature method [13].

Scheme 1. Synthetic route to the title compound **2**.



3. Experimental

The melting point was determined in an open-end capillary tube on a digital melting point apparatus and is uncorrected. Infrared (IR) and proton nuclear magnetic resonance (^1H -NMR) spectra were recorded on a Nicolet 380 FT-IR (KBr) and a Bruker DRX-300 instrument, respectively. Chemical shifts are expressed in parts per million (ppm) relative to tetramethylsilane as an internal standard. The elemental analysis (C/N) was performed on a Vario EL III CHNS analyzer using sulphanilic acid as a standard. The ESI-MS spectrum was recorded on a Waters Micromass Q-TOF Micro. The homogeneity of the compounds was monitored by ascending thin-layer chromatography (TLC), visualized by iodine vapour.

Synthesis of [5-(1,3-diphenyl-1H-pyrazol-4-yl)-3-phenyl-4,5-dihydropyrazol-1-yl](pyridin-4-yl)methanone (2)

A solution of chalcone **1** (0.0025 mol) and INH (0.0031 mol) in glacial acetic acid (6 mL) was refluxed for 38 h. The reaction mixture was poured into crushed ice to give the crude product which was filtered and washed first with ethyl acetate (to remove any traces of chalcone) and then with hot water (to remove excess of hydrazide), followed by recrystallization from ethanol.

Yield: 78%; mp: 224–226 °C; buff cream amorphous solid.

IR (KBr) cm^{-1} : 2,921 (C-H), 2,847 (C-H), 1,638 (C=O), 1,613 (C=N), 1,556 (C=C).

^1H -NMR (300 MHz, CDCl_3): δ (ppm) 8.76 (s, 1H, C_5 pyrazole), 7.83–7.76 (m, 5H, Ar-H), 7.70–7.60 (m, 4H, Ar-H), 7.46–7.37 (m, 9H, Ar-H), 6.08 (dd, 1H, H_X , $J = 11.55, 4.80$ Hz), 3.71 (dd, 1H, H_B , $J = 17.40, 11.70$ Hz), 3.21 (dd, 1H, H_A , $J = 17.55, 4.50$ Hz).

^{13}C -NMR (75 MHz, CDCl_3): δ 41.49 (CH_2), 53.62 (CH), 118.26, 119.15, 125.79, 126.66, 126.85, 128.31, 128.50, 128.71, 128.82, 129.38, 130.91, 133.17, 134.61, 139.78, 140.93, 149.84, 150.10, 151.8, 167.82.

DEPT-135: 41.49 (negative peak, CH_2), 53.62 (positive peak, CH).

Anal. Calcd for $\text{C}_{30}\text{H}_{23}\text{N}_5\text{O}$: C, 76.74; H, 4.94; N, 14.92. Found: C, 76.41; H, 4.59; N, 14.31. ESI-MS: $m/z = 470$ ($\text{M}+1$) $^+$.

Acknowledgements

Authors express sincere thanks to the management of RITS, Sirsa for providing the necessary facility for the project.

References

1. Shamsuzzaman; Khan, M.S.; Alam, M. Synthesis, characterization and antimicrobial activity of new steroidal cholest-5-en-7-one derivatives fused with substituted pyrazoline ring. *J. Chil. Chem. Soc.* **2009**, *54*, 372-374.
2. Abdel-Wahab, B.F.; Abdel-Aziz, H.A.; Ahmed, E.M. Synthesis and antimicrobial evaluation of 1-(benzofuran-2-yl)-4-nitro-3-arylbutan-1-ones and 3-(benzofuran-2-yl)-4,5-dihydro-5-aryl-1-[4-(aryl)-1,3-thiazol-2-yl]-1H-pyrazoles. *Eur. J. Med. Chem.* **2009**, *44*, 2632-2635.
3. Jun, M.A.; Park, W.S.; Kang, S.K.; Kim, K.Y.; Kim, K.R.; Rhee, S.D.; Bae, M.A.; Kang, N.S.; Sohn, S.K.; Kim, S.G.; Lee, J.O.; Lee, D.H.; Cheon, H.G.; Kim, S.S.; Ahn, J.H. Synthesis and biological evaluation of pyrazoline analogues with β -amino acyl group as dipeptidyl peptidase IV inhibitors. *Eur. J. Med. Chem.* **2008**, *43*, 1889-1902.
4. Gokhan-Kelekci, N.; Koyunoglu, S.; Yabanoglu, S.; Yelekci, K.; Ozgen, O.; Ucar, G.; Erol, K.; Kendi, E.; Yesilada, A. New pyrazoline bearing 4(3H)-quinzolinone inhibitors of monoamine

- oxidase: Synthesis, biological evaluation, and structural determinants of MAO-A and MAO-B selectivity. *Bioorg. Med. Chem.* **2009**, *17*, 675-689.
5. Havrylyuk, D.; Zimenkovsky, B.; Vasylenko, O.; Zaprutko, L.; Gzella, A.; Lesyk, R. Synthesis of novel thiazolone-based compounds containing pyrazoline moiety and evaluation of their anticancer activity. *Eur. J. Med. Chem.* **2009**, *44*, 1396-1404.
 6. Turan-Zitouni, G.; Chevallet, P.; Kilic, Fatma S.; Erol, K. Synthesis of some thiazolyl-pyrazoline derivatives and preliminary investigation of their hypotensive activity. *Eur. J. Med. Chem.* **2000**, *35*, 635-641.
 7. Bhat, A.R.; Athar, F.; Azam, A. Bis-pyrazolines; Synthesis, characterization and antiamoebic activity as inhibitors of growth of *Entamoeba histolytica*. *Eur. J. Med. Chem.* **2009**, *44*, 426-431.
 8. Rathish, I.G.; Javed, K.; Ahmad, S.; Bano, S.; Alam, M.S.; Pillai, K.K.; Singh, S.; Bagchi, V. Synthesis and anti-inflammatory activity of some new 1,3,5-trisubstituted pyrazolines bearing benzene sulfonamide. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 255-258.
 9. Amir, M.; Kumar, H.; Khan, S.A. Synthesis and pharmacological evaluation of pyrazoline derivatives as new anti-inflammatory and analgesic agents. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 918-922.
 10. Shaharyar, M.; Siddiqui, A.A.; Ali, M.A.; Dharmarajan, S.; Perumal, Y. Synthesis and *in vitro* antimycobacterial activity of N¹- nicotinoyl-3-(4'-hydroxy-3'-methyl phenyl)-5-[(sub)phenyl]-2-pyrazoline. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3947-3949.
 11. Kaushik, D.; Khan, S.A.; Chawla, G.; Kumar, S. N'-[(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)methylene] 2/4-substituted hydrazides: synthesis and anticonvulsant activity. *Eur. J. Med. Chem.* **2010**, *45*, 3943-3949.
 12. Aggarwal, R.; Kumar, V.; Singh, S.P. Synthesis of some new 1-(6-fluorobenzothiazol-2-yl)-3-(4-fluoro-phenyl)-5-arylpyrazolines and their iodine (III) mediated oxidation to corresponding pyrazoles. *Indian J. Chem.* **2007**, *46B*, 1332-1336.
 13. Revanasiddappa, B.C.; Rao, N.R.; Subrahmanyam, E.V.S.; Satyanarayana, D. Synthesis and biological evaluation of some novel 1,3,5-trisubstituted pyrazolines. *E-J. Chem.* **2010**, *7*, 295-298.