

Short Note

N'-{[2-(Piperidin-1-yl)quinolin-3-yl]methylene}pyridine-4-carbohydrazide

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Abstract: N'-{[2-(piperidin-1-yl)quinolin-3-yl]methylene}pyridine-4-carbohydrazide **2** has been synthesized through condensation of 2-(piperidin-1-yl)quinoline-3-carbaldehyde **1** with isonicotinic acid hydrazide (INH) in absolute ethanol. The structure of the title compound **2** was established on the basis of IR, ¹H-NMR, ¹³C-NMR and mass spectral data.

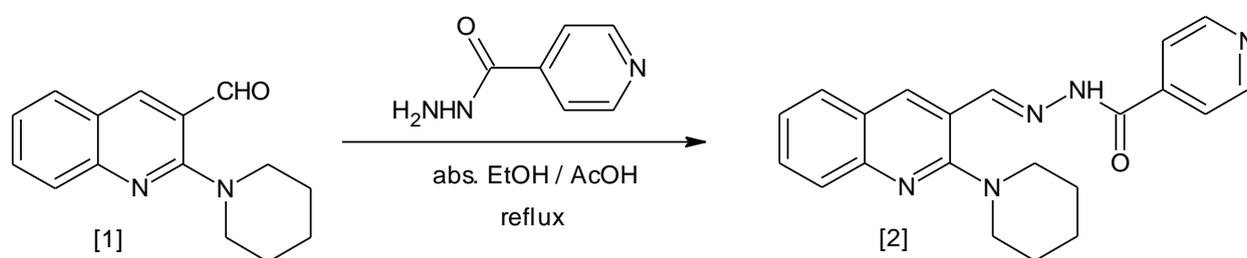
Keywords: 2-piperidinylquinoline; isonicotinic acid hydrazide

Literature review revealed that the quinoline moiety exists in a variety of biologically active compounds. They exhibit antimicrobial, anticancer, anti-inflammatory, anti-HIV, antidepressant, antidiabetic, anti-epileptic etc. activities [1–7]. The target compound of the present communication was designed based on the fact that Quipazine [2-(1-piperziny)quinoline] produces a weak inhibition of monoamine oxidase in both in-vitro and in-vivo studies [8]. The biological importance of Quipazine as antidepressant has prompted us to design and synthesize new structural analogues in which substituents could be arranged in a new molecular framework to display possible higher order of antidepressant activity. The piperazine ring in Quipazine was replaced by piperidine, as NH is isosteric with the CH₂ group. Isonicotinic acid hydrazide (INH) was clubbed to the quinoline moiety at position 3 based on the fact that INH also produces a weak inhibition of monoamine oxidase A (MAO-A) [9].

As a part of our research programme on benzofused heterocyclic compounds [10], we report herein the synthesis of N'-{[2-(piperidin-1-yl)quinolin-3-yl]methylene}pyridine-4-carbohydrazide **2** by condensation of 2-(piperidin-1-yl)quinoline-3-carbaldehyde **1** with isonicotinic acid hydrazide in absolute ethanol in the presence of catalytic amounts of glacial acetic acid.

The ^1H NMR spectrum of compound **2** showed a multiplet resonating between δ 1.6 and 1.7 ppm which was assigned to the six protons of the piperidine ring. A broad singlet (bs) was located at δ 3.2 ppm, which indicated four protons of $-\text{N}(\text{CH}_2)_2<$ of the piperidine ring. The triplet located at δ 7.3 ($J = 7.5$ Hz) indicated one aromatic H-6 proton and another at δ 7.6 ($J = 7.6$ Hz) indicated one aromatic H-7 proton. The multiplet resonating between δ 7.7 and 7.8 ppm indicated four aromatic protons, two of H-5 and H-8 and two of pyridine. The singlet located at δ 8.5 ppm indicated one aromatic H-4 proton. Another singlet appeared at δ 8.6 indicated the proton of $\text{CH}=\text{N}$. The two remaining protons of pyridine appeared as doublet at δ 8.8 ppm ($J = 4.5$ Hz). A singlet located at δ 9.5 ppm indicated the CONH proton. The IR data suggest a $\text{C}=\text{N}$ fragment due to an absorption band at $1,623\text{ cm}^{-1}$. The absorption band at $1,592\text{ cm}^{-1}$ is due to aromatic ($\text{C}=\text{C}$) stretching. Another absorption band at $1,043\text{ cm}^{-1}$ is due to ($\text{C}-\text{N}$) stretching. The presence of a carbonyl group ($\text{C}=\text{O}$) was assigned on the basis of an absorption band at $1,687\text{ cm}^{-1}$. Furthermore, the fact was also supported by the mass spectrum of compound **2** which showed a molecular ion peak (M^+) at m/z 359. These data are satisfactory for the structure assigned to the compound. Starting material 2-(piperidin-1-yl)quinoline-3-carbaldehyde **1** was synthesized based on a literature method [11].

Scheme 1. Synthesis of the title compound 2.



Synthesis of *N'*-{[2-(piperidin-1-yl)quinolin-3-yl]methylene}pyridine-4-carbohydrazide **2**

To a solution of 2-(piperidin-1-yl)quinoline-3-carbaldehyde (1 mmol, 0.240 g) and isonicotinic acid hydrazide (1 mmol, 0.137 g) in 10 mL of absolute ethanol, 2–3 drops of glacial acetic acid were added and the mixture was refluxed at 80 °C for 6 h. The content of the flask was concentrated to half of the volume and cooled. The product obtained was filtered, washed with water, dried and recrystallized from ethanol to give the pale yellow fluffy product. The progress of reaction and the purity of compound **2** was checked by TLC using toluene / ethyl acetate / formic acid (6:3.5:0.5) as mobile phase.

Yield: 94%; mp: 108–110 °C; R_f : 0.46 (toluene/ethyl acetate/formic acid, 6:3.5:0.5); pale yellow fluffy solid.

IR (KBr) cm^{-1} : 1687 ($\text{C}=\text{O}$), 1623 ($\text{C}=\text{N}$), 1592 ($\text{C}=\text{C}$), 1043 ($\text{C}-\text{N}$).

^1H NMR (300 MHz, CDCl_3): δ 1.62–1.75 (m, 6H, $\text{CH}_2 \times 3$), 3.29 (bs, 4H, N (CH_2) $\times 2$), 7.34–7.39 (t, 1H, H-6, $J = 7.5$ Hz), 7.60–7.65 (t, 1H, H-7, $J = 7.6$ Hz), 7.74–7.85 (m, 4H, Ar-H), 8.53 (s, 1H, H-4), 8.69 (s, 1H, $\text{CH}=\text{N}$), 8.81–8.83 (d, 2H, Pyridinyl H, $J = 4.5$), 9.52 (s, 1H, CONH).

^{13}C -NMR (DMSO- d_6 , 75 MHz): δ 24.1, 25.3, 49.8, 124.6, 125.93, 125.8, 126.4, 126.7, 128.0, 129.7, 130.5, 133.6, 136.9, 140.1, 148.2, 149.3, 152.4, 166.5.

FAB-MS: m/z (%): 359 (M^+ , 82), 360 ($\text{M}^+ + 1$, 30).

Anal. Calcd for $\text{C}_{21}\text{H}_{21}\text{N}_5\text{O}$: C, 70.17; H, 5.89; N, 19.48; Found : C, 70.41; H, 5.91; N, 19.54%.

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