

Short Note

## ***tert*-Butyl 1-(Furan-2-yl)-4-oxo-2,3,7-triazaspiro[4.5]dec-1-ene-7-carboxylate**

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**Abstract:** A simple and novel route for synthesis of new spirocyclic compound is developed. The present work involves condensation of ethyl nipecotate with 2-furaldehyde followed by the MnO<sub>2</sub> oxidation to give the  $\beta$ -keto ester which upon reaction with hydrazine hydrate gives the spiro pyrazolone.

**Keywords:** spirocyclic; pyrazolone; ethyl nipecotate

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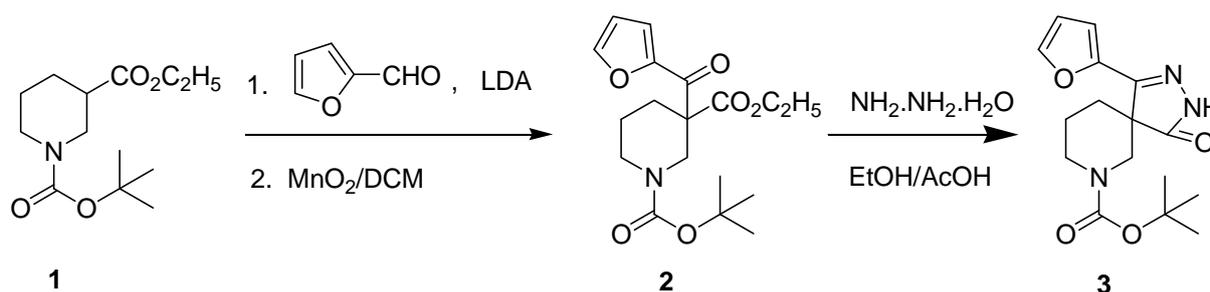
### **Introduction**

Spirocyclic compounds have attracted the attention of organic chemists due to their unique structural and reactivity pattern. These compounds represent an important class of naturally occurring substances characterized by their highly pronounced biological activities [1,2]. The spiro functionality shown in countless phytochemicals, such as in alkaloids, lactones, terpenoids, and clinically valuable compounds has been known for a long time. Arguably among the most challenging structural motifs to synthesize, all-carbon spirocyclics have inspired chemists for decades [3]. At present, spirocyclic compounds play a very important role in many fields such as chiral medicine, chiral LCD materials, macromolecule bulking agent and biological pesticides [4–6]. Because of the promising biological activity of spirocyclic compounds it was decided to prepare a new spiro-heterocyclic compound.

## Results and Discussion

The title compound, *tert*-butyl 1-(furan-2-yl)-4-oxo-2,3,7-triazaspiro[4.5]dec-1-ene-7-carboxylate (**3**), was prepared by the condensation of 1-*tert*-butyl 3-ethyl 3-(furan-2-carbonyl)piperidine-1,3-dicarboxylate (**2**) with hydrazine hydrate in acidic medium (Scheme 1). The intermediate **2** was in turn prepared by the condensation of ethyl nipecotate (**1**) with furfuraldehyde in presence of lithium diisopropyl amide (LDA) followed by MnO<sub>2</sub> oxidation [7–9]. The final product was well characterized by using NMR, IR and mass spectral data.

**Scheme 1.** Synthesis of *tert*-butyl 1-(furan-2-yl)-4-oxo-2,3,7-triazaspiro[4.5]dec-1-ene-7-carboxylate.



The IR spectrum of compound (**3**) showed a wide absorption band at 3,412 cm<sup>-1</sup> due to the presence of NH in the molecule. Two sharp bands at 1,693 and 1,624 cm<sup>-1</sup> was due to Boc carbonyl and carbonyl group respectively. In <sup>1</sup>H-NMR spectrum, the signals of the respective protons of the title compound (**3**) were verified on the basis of their chemical shifts, multiplicities, and coupling constants. A broad singlet observed at δ 11.4 ppm was due to the proton of pyrazolone NH. Nine protons of three methyl groups in Boc side chain resonated at δ 1.3 ppm as a doublet. The eight protons of piperidine ring resonated in the region at δ 1.4–3.75 ppm as different signals due to chemical non-equivalence of these protons. The three protons of furan ring resonated at δ 6.65, 7.06 and 7.84 ppm as a multiplet and two singlets respectively. The mass spectrum showed a peak at *m/z* 220 corresponding to M<sup>+</sup>-Boc group as the Boc group gets cleaved during the mass spectral conditions. Elemental analysis and <sup>13</sup>C-NMR spectrum also gave satisfactory results for the title compound.

## Experimental

Melting point was taken in open capillary tube and was uncorrected. The purity of the compound was confirmed by thin layer chromatography using Merck silica gel 60 F<sub>254</sub> coated aluminium plates. IR spectrum was recorded on Shimadzu-FTIR Infrared spectrometer in KBr (max in cm<sup>-1</sup>). <sup>1</sup>H-NMR (400 MHz) spectrum was recorded on a Bruker AMX 400 spectrometer, with 5 mm PABBO BB -1H TUBES and <sup>13</sup>C-NMR (100 MHz) spectrum was recorded for approximately 0.03 M solutions in DMSO-d<sub>6</sub> at 100 MHz with TMS as internal standard. LCMS was obtained using Agilent 1200 series LC and Micromass zQ spectrometer. Elemental analysis was carried out by using VARIO EL-III (Elementar Analysensysteme GmbH).

The condensation of ethyl nipecotate (**1**) with furfuraldehyde in THF in the presence of lithium diisopropyl amide (LDA) at -78 °C yielded 1-*tert*-butyl 3-ethyl 3-(furan-2-yl(hydroxy)methyl)

piperidine-1,3-dicarboxylate [7,8] which on oxidation by  $\text{MnO}_2$  yielded the intermediate, 1-*tert*-butyl 3-ethyl 3-(furan-2-carbonyl)piperidine-1,3-dicarboxylate (**2**) [9].

To a solution of **2** (3.79 g, 10.78 mmole) in ethanol (20 mL), hydrazine hydrate, (99%, 5.0 mL, 100 mmole) was added followed by 0.3 mL of acetic acid. The reaction mixture was stirred at the ambient temperature for 6 h. After the completion of reaction as indicated by TLC, the reaction mixture was cooled to 0–5 °C and filtered. The product was washed with chilled ethanol (10 mL) followed by ether (10 mL) and dried to afford the title compound. Yield was 3.0 g, 87.2%.

Melting point: 229–232 °C.

LCMS:  $m/z = 220$ , ( $\text{M}^+$ -Boc) + 1.

IR (KBr):  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ), 3412 (NH), 3097 (Furyl C-H), 2927 (aliphatic CH), 1693 (Boc C=O), 1624 (amide C=O), 1595 (C=N).

$^1\text{H-NMR}$  (400 MHz,  $\text{DMSO-d}_6$ ):  $\delta$  ppm, 1.3 (s, 9H, Boc- $\text{CH}_3$ ), 1.4 (d, 2H, Piperidine-H,  $J = 12.4$  Hz), 1.95 (m, 2H, Piperidine-H), 2.95 (m, 1H, Piperidine-H), 3.45 (d, 1H, Piperidine-H,  $J = 13.6$  Hz), 3.75 (m, 2H, Piperidine-H), 6.65 (m, 1H, Furyl-H), 7.06 (s, 1H, Furyl-H), 7.84 (s, 1H, Furyl-H), 11.4 (s, broad, 1H, pyrazolone –NH).

$^{13}\text{C-NMR}$  (100 MHz,  $\text{DMSO-d}_6$ ):  $\delta$  ppm, 17.95 ( $\text{CH}_2$  of piperidine), 27.96 (*t*-butyl- $\text{CH}_3$ ), 43.29, 45.53, 46.74, 47.63 (Piperidine C's), 78.58 (Boc- $\text{CMe}_3$ ), 111.18, 111.57, 145.81, 144.63 (Furyl), 150.65 (Pyrazolone-C), 153.35 (Boc-CO), 177.05 (pyrazolone CO).

Elemental analysis: Calculated for  $\text{C}_{16}\text{H}_{21}\text{N}_3\text{O}_4$ , C, 60.17%; H, 6.63%; N, 13.16%; Found: C, 60.13%; H, 6.64%; N, 13.13%.

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