



Synthesis and Characterisation of Novel Knoevenagel Condensation Product of Naphthofuran-2-Carbaldehyde with Barbituric Acid and Ethylcyanoacetate

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ABSTRACT

In the present study novel naphthofuran-2-carbaldehyde condensed with barbituric acid and ethylcyanoacetate motifs through base catalysed Knoevenagel condensation reaction and characterized the derivatives by spectroscopic techniques such as FTIR, ¹H NMR and mass spectral analysis to confirm the structures.

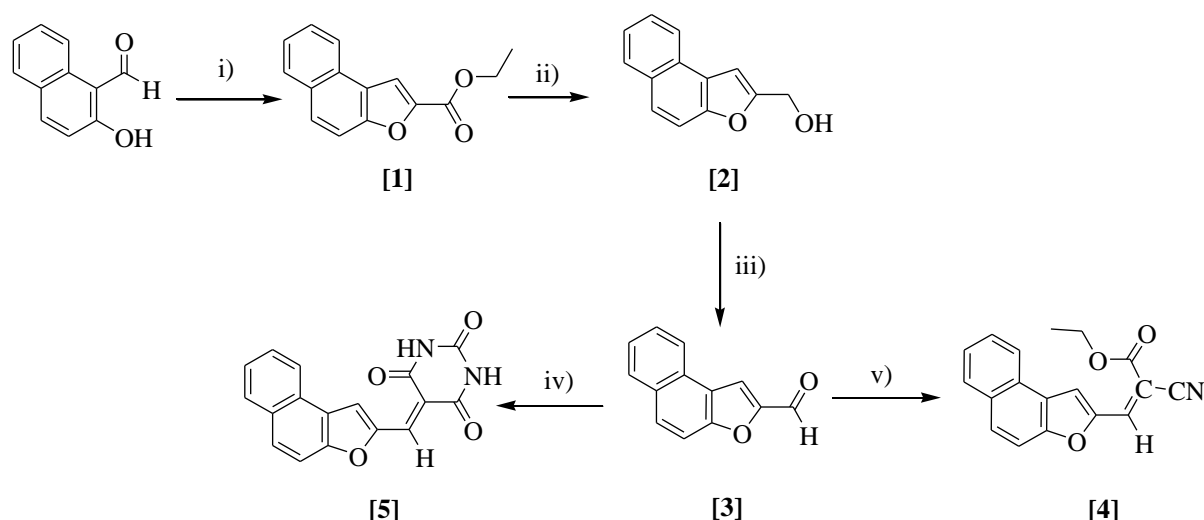
Keywords: Naphthofuran-2-carbaldehyde; Knoevenagel condensation; Barbituric acid and ethylcyanoacetate

INTRODUCTION

Naphthofuran ring containing compounds so far attracted much attention because of their diverse pharmacological as well as biological properties such as antibacterial, antitumor and antielmintic activities [1]. Number heterocyclic compounds which are potentially active contain naphthofuran motifs which play vital roles in the biological system [2,3]. The literature survey reveals that the BA derivatives are well known to possess antibacterial [4], sedatives [5], herbicides [6], fungicides [7], antitumor [8] and antimetastatic activity [9]. Furthermore benzylidene derivatives of barbituric acids known to act as potential organic oxidizers [10], as building blocks in the preparation of oxadezaflavines [11], and for the unsymmetrical synthesis of disulfides [12]. Other applications of barbiturates include nonlinear optical materials [13]. In addition chemistry of multiple bonds also plays important role in the organic synthesis. Among the C-C bond-forming reactions in organic chemistry, the Knoevenagel condensation reaction is one of the most important reaction in which active methylene group in the molecule undergoes condensation reactions with aldehydes or ketones that do not contain α -hydrogen. With their above pharmacological properties and importance of C-C bond forming reactions, we felt straight away to synthesize and characterize naphthofuran derivatives of barbituric acid as well as ethylcyanoacetate through Knoevenagel condensation reaction.

MATERIALS AND METHODS

All the chemicals used were purchased from Merck, Sigma Aldrich, SD fine and used without further purification. IR spectra were recorded in KBr pellets on a Perkin-Elmer Spectrometer. ¹H NMR (400 MHz) were run on a Bruker Avance DPX-250, FT-NMR spectrometer in CDCl₃/DMSO-*d*₆ as solvent and TMS as an internal standard. Melting points were recorded on a Stuart Scientific Apparatus SMP3 (UK) in open capillary tubes. The purity of the compounds was checked by TLC. Scheme-1: Synthetic route for the synthesis of Knoevenagel condensation products of naphthofura-2-carbaldehyde.



Reagents and Conditions

i) $\text{ClCH}_2\text{COOEt}$, K_2CO_3 , DMF, reflux; ii) LiAlH_4 , THF, 0°C ; iii) IBX, EtOAc, reflux; iv) Barbituric acid, EtOH, 70°C ; v) Ethylcyanoacetate, EtOH, 70°C .

Table 1: Physical characterization data of the synthesised compounds

Comp Name	Molecular formula	Molecular weight	Melting point ($^\circ\text{C}$)	Yield (%)
1	$\text{C}_{15}\text{H}_{12}\text{O}_3$	240.2	100	77
2	$\text{C}_{13}\text{H}_{10}\text{O}_2$	198.2	135	91
3	$\text{C}_{13}\text{H}_8\text{O}_2$	196.2	258	90
4	$\text{C}_{18}\text{H}_{13}\text{NO}_3$	291.3	145	92
5	$\text{C}_{17}\text{H}_{10}\text{N}_2\text{O}_4$	306.2	>280	94

EXPERIMENTAL

Preparation of Ethyl naphthofuran-2-carboxylate [1]

To a solution of 2-hydroxy-1-naphthaldehyde (0.03 mol) in dry N, N dimethylformamide (25 ml), ethylchloroacetate (0.03 mol) and anhydrous potassium carbonate (0.9 mol) were added and the reaction mixture was refluxed on water bath for 24 h. The reaction was monitored by TLC. After completion of reaction, the reaction mixture was then poured into ice cold water, to obtain the product ethyl naphthofuran-2-carboxylate as solid, which was collected by filtration, dried and recrystallised from ethanol.

Preparation of Naphthofuran-2-ylmethanol [2]

To a mixture of Lithium aluminum hydride (0.04 mol) in tetrahydrofuran (5 mL), the solution of ethyl naphthofuran-2-carboxylate (0.01 mol) in THF (5 mL) was added slowly with continuous stirring at 0°C . Stirring was continued for 2 h at room temperature. The completion of reaction was monitored by TLC. After completion of reaction, the reaction mixture was quenched in ammonium chloride solution. The product was extracted in ethyl acetate and purified through silica gel column chromatography.

Preparation of Naphthofuran-2-carbaldehyde [3]

Naphthofuran-2ylmethanol (0.01 mol) was dissolved in ethyl acetate (7 mL) and IBX (0.03 mol) was added. The resulting suspension was immersed in an oil bath set to 80°C and stirred vigorously with calcium chloride guard tube. After 3.5 h (TLC monitoring), the reaction was cooled to room temperature and filtered through a celite bed. The filter bed was washed with 3-2 ml of ethyl acetate (25 mL), and the combined filtrates were concentrated to obtain naphthofuran-2-carbaldehyde.

Preparation of 5-(naphthofuran-2-ylmethylene) pyrimidin-2,4,6(1H, 3H, 5H)-trione [4]

Naphthofuran-2-carbaldehyde (0.01 mol) and barbituric acid (0.02 mol) were dissolved in ethyl alcohol (10 mL) in a round-bottomed flask and the resulting mixture was refluxed at 70°C for 10 h. The completion of reaction was as indicated by TLC as well as separation of solid from reaction mixture. The separated solid product was filtered, dried and recrystallized from ethanol to get pure compound.

Preparation of Ethyl-2-cyano-3-(naphthofuran-2-yl) acrylate [5]

Naphthofuran-2-carbaldehyde (0.01 mol) and ethylcyanoacetate (0.02 mol) were dissolved in ethyl alcohol (10 mL) in a round-bottomed flask and the resulting mixture was refluxed at 70°C for 10 h. The completion of reaction was as indicated by TLC as well as separation of solid from reaction mixture. The separated solid product was filtered, dried and recrystallized from ethanol to get pure compound.

Spectral Interpretation

Ethyl naphthofuran-2-carboxylate [1]

FTIR (KBr, cm^{-1}): 3058 (ArH str), 2907 (CH str), 1724 (CO str), 1364 (C-O).

$^1\text{H NMR}$ (CDCl_3 , 400MHz, ppm): 8.46-8.44 (d, 2H, ArH), 8.08-8.02 (m, 2H, ArH), 7.88-7.86 (d, 1H, ArH), 7.70-7.057 (m, 2H, ArH), 4.41-4.36 (q, 2H, CH_2), 1.38-1.34 (t, 3H, CH_3).

MS (m/z): 242.0 (M^+)

Naphthofuran-2-ylmethanol [2]

FTIR (KBr, cm^{-1}): 3225 (OH str), 3052 (ArH), 2860 (CH str), 1381 (C-O).

$^1\text{H NMR}$ (CDCl_3 , 400MHz, ppm): 8.27-8.25 (d, 2H, ArH), 8.03-8.01 (d, 1H, ArH), 7.81-7.74 (m, 2H, ArH), 7.62-7.39 (m, 3H, ArH), 5.54-5.51 (t, 1H, OH), 4.66-4.65 (d, 1H, CH_2).

MS (m/z): 181.0 (M^+)

Naphthofuran-2-carbaldehyde [3]

FTIR (KBr, cm^{-1}): 2918 (ArH str), 2535 (CHO str), 1695 (CO str), 1324 (C-O).

$^1\text{H NMR}$ (CDCl_3 , 400MHz, ppm): 9.89 (s, 1H, CHO), 8.63 (d, 1H, ArH), 8.46--8.44 (d, 1H, ArH), 8.13-8.10 (m, 2H, ArH), 7.91-7.89 (d, 1H, ArH), 7.76-7.61 (m, 2H, ArH).

MS (m/z): 198.0 (M^+)

5-(naphthofuran-2-ylmethylene) pyrimidin-2,4,6(1H, 3H, 5H)-trione [4]

FTIR (KBr, cm^{-1}): 3035 (ArH str), 2794 (CH str), 1653 (CO str), 1312 (C-O)

$^1\text{H NMR}$ (CDCl_3 , 400MHz, ppm): 11.44-11.40 (d, 2H, CONH), 9.34 (s, 1H, C=CH), 8.39-8.37 (m, 1H, ArH), 8.16 (s, 1H, ArH), 8.11-8.09 (m, 2H, ArH), 7.86-7.84 (d, 1H, ArH), 7.72-7.70 (d, 1H, ArH), 7.63-7.61 (d, 1H, ArH).

MS (m/z): 306.27 (M^+)

Ethyl-2-cyano-3-(naphthal[2,1-b]furan-2-yl) acrylate [5]

FTIR (KBr, cm^{-1}): 3101 (ArH str), 2220 (CN str), 1709 (CO str), 1271 (C-O)

$^1\text{H NMR}$ (CDCl_3 , 400MHz, ppm): 8.20-8.18 (m, 2H, ArH), 8.14 (s, 1H, ArH), 7.97-7.90 (m, 2H, ArH), 7.70-7.67 (m, 2H, ArH), 7.57 (s, 1H, C=CH), 4.42-4.37 (q, 2H, CH_2), 1.43-1.39 (t, 3H, CH_3)

MS (m/z): 291.09 (M^+)

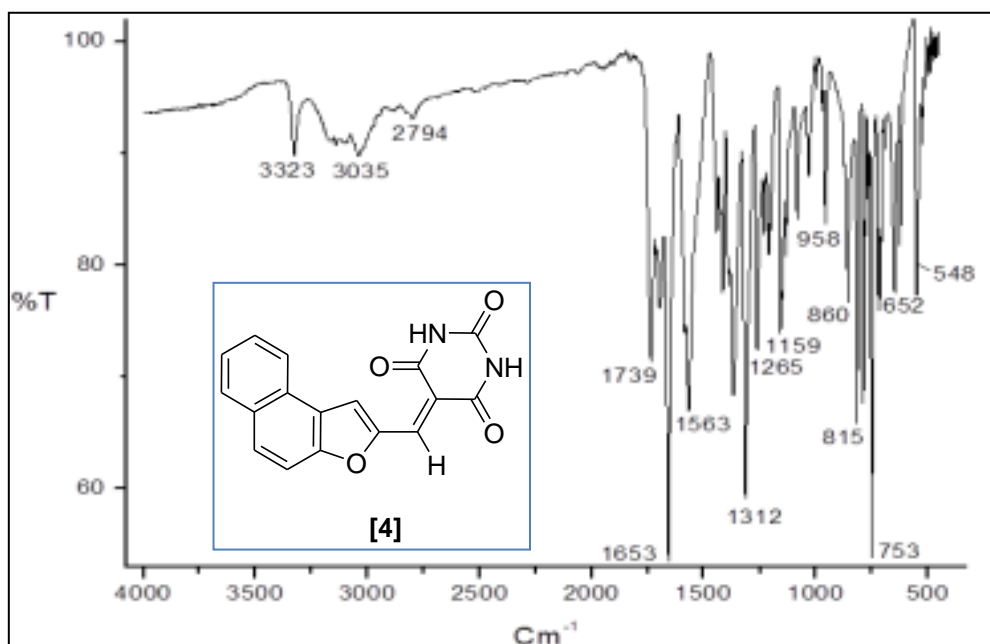


Figure 1: IR spectrum of compound [4] in KBr

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