# Journal of Chemical and Pharmaceutical Research, 2018, 10(5): 157-162



**Research Article** 

ISSN : 0975-7384 CODEN(USA) : JCPRC5

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

# M Shet Prakash<sup>\*</sup>, G Krishnaswamy, D Ravi, KN Lavanya and M Priyanka

Department of Studies and Research in Chemistry, University College of Science, Tumkur University, Tumakuru-572 103, Karnataka, India

# ABSTRACT

In the present study novel napthafuran-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 napthafuran 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 oxadeazaflavines [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  $\alpha$ -hydrogen. With their above pharmacological properties and importance of C-C bond forming reactions, we felt straight away to synthesize and characterize napthafuran 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. <sup>1</sup>H NMR (400 MHz) were run on a Bruker Avance DPX-250, FT-NMR spectrometer in  $CDCl_3/DMSO-d_6$  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 napthafura-2-carbaldehyde.



#### **Reagents and Conditions**

i) ClCH<sub>2</sub>COOEt, K<sub>2</sub>CO<sub>3</sub>, DMF, reflux; ii) LiAlH<sub>4</sub>, THF, 0°C; iii) IBX, EtOAc, reflux; iv) Barbituric acid, EtOH, 70°C; v) Ethylcyanoacetate, EtOH, 70°C.

Comp Name	Molecular formula	Molecular weight	Melting point (°C)	Yield (%)
1	$C_{15}H_{12}O_3$	240.2	100	77
2	$C_{13}H_{10}O_2$	198.2	135	91
3	$C_{13}H_8O_2$	196.2	258	90
4	$C_{18}H_{13}NO_3$	291.3	145	92
5	$C_{17}H_{10}N_2O_4$	306.2	>280	94

Table 1: Physical characterization data of the synthesised compounds

# 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-(naphthafuran-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-(naphthafuran-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<sup>-1</sup>): 3058 (ArH str), 2907 (CH str), 1724 (CO str), 1364 (C-O). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400MHz, ppm): 8.46-8.44 (d, 2H, ArH), 8.08-8.02 (m, 2H, ArH), 7.88-7.86 (d, 1H, ArH), 7.70-7057 (m, 2H, ArH), 4.41-4.36 (q, 2H, CH<sub>2</sub>), 1.38-1.34 (t, 3H, CH<sub>3</sub>). MS (m/z): 242.0 (M+)

Naphthofuran-2-ylmethanol [2] FTIR (KBr, cm<sup>-1</sup>): 3225 (OH str), 3052 (ArH), 2860 (CH str), 1381 (C-O). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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<sub>2</sub>). **MS (m/z):** 181.0 (M+)

# Naphthofuran-2-carbaldehvde [3]

FTIR (KBr, cm<sup>-1</sup>): 2918 (ArH str), 2535 (CHO str), 1695 (CO str), 1324 (C-O). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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-(naphthafuran-2-vlmethylene) pyrimidin-2.4.6(1H, 3H, 5H)-trione [4]

FTIR (KBr, cm<sup>-1</sup>): 3035 (ArH str), 2794 (CH str), 1653 (CO str), 1312 (C-O) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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<sup>-1</sup>): 3101 (ArH str), 2220 (CN str), 1709 (CO str), 1271 (C-O) <sup>1</sup>H NMR (CDCl<sub>3</sub>, 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<sub>2</sub>), 1.43-1.39 (t, 3H, CH<sub>3</sub>) MS (m/z): 291.09 (M+)



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



Figure 2: 1H NMR spectrum of compound [4] in CDCl3



Figure 3: IR spectrum of compound [5] in KBr



Figure 4: 1H NMR spectrum of compound [5] in CDCl3

#### **RESULTS AND DISCUSSION**

Synthesis of novel Knoevenagel condensation product of naphthofuran-2-carbaldehydes with barbituric acid and ethylcyanoacetate is depicted in the scheme-1. The key starting material for the synthesis Ethylnaphthofuran-2-carboxylate [1] was obtained by the reaction of 2-hydroxy-1-naphthaldehyde with ethylchloroacetate in presence of base under reflux condition. Further, reduction of [1] with LAH gave corresponding reduction product alcohol [2] and further the obtained compound [2] was oxidized with IBX to get naphthofuran-2-carbaldehyde [3]. Finally, compound [3] underwent base catalyzed Knoevenagel condensation reaction with barbituric acid and ethylcyanoacetate to give corresponding condensation products [4] and [5] respectively. Physical characterization data of the synthesised compounds along with yield are tabulated in Table 1.

The FT IR spectrum (Figure 1) of compound [4] show decrease in the CO stretching, whereas compound [5] shows characteristic absorption band for CN stretching indicates the formation (Figure 2). <sup>1</sup>H NMR of the both compounds showed absence of aldehyde proton. Compound showed amide NH proton at  $\delta$  11.44-11.40 ppm (Figure 3), whereas compound [5] showed quartet and triplet respectively for ester group at  $\delta$  4.42-4.37 and 1.43-1.39 ppm (Figure 4) confirms the condensation reaction took place. The mass spectral analysis of both the compounds further confirmed the formation of condensation products. From the above spectroscopic characterization confirms the assigned structures of the compound.

# CONCLUSION

In summary we have synthesized Knoevenagel condensation product of naphthofuran-2-carbaldehydes with barbituric acid and ethylcyanoacetate. The synthetic procedure followed is very simple as no specialised equipment's, reagents, or purification techniques are needed. Sspectroscopic characterization such as FTIR, <sup>1</sup>H NMR and mass spectral analysis confirms the assigned structures of the compound. The newly synthesised compounds may be of biologically interest and also serves as an intermediate for the organic synthesis.

## ACKNOWLEDGEMENTS

The authors are thankful to Department of Studies and Research in Chemistry, UCS, Tumkur university, Tumakuru and also thankful to Tumkur University for providing the laboratory facilities.

## REFERENCES

- [1] HM Vagdevi; VP Vaidya. Indian J Heterocyclic Chem. 2001, 10, 253.
- [2] A Goel; M Dixit. Tetrahedron Lett. 2004, 45, 8819.
- [3] H Hagiwara; K Sato; T Suzuki; M Ando. Heterocycles. 1999, 51, 497

- [4] LK Akopyan; AS Adzhibekyan; GA Porkinyan; EA Tumasyan; Bilzh A. 1976, 29, 80; Chem Abstr. 1976, 85, 72068.
- [5] S Senda; H Fugimura; H Izumi. Japan Patent, 1968, 193, 6824, Chem Abstr. 1969, 70, 78001.
- [6] SL Katz; AW Gay; US Patent; 1982, 352, 806, Chem Abstr. 1983, 98, 215603.
- [7] WG Brouwer; EE Felauerand; AR Bell; US Patent. 1990, 779, 982, Chem Abstr. 1991, 114, 185539.
- [8] S Hasegawa; S Imamura; M Muto; Y Okamoto. Che Abstract. 1990, 112:132466x.
- [9] GD Cillis; F Grams; HW Krell; V Livi; E Menta; A Oliva. Patent. 1998, WO1998058925 A1.
- [10] K Tanaka; X Cheng; T Kimura; F Yoneda. Chem Pharm Bull. 1986, 34, 3945. 138
- [11] JD Figueroa-Villar; CE Rangel; LN Dos Santos. Synth Commun. 1992, 22 (8), 1159.
- [12] K Tanaka; X Cheng; F Yoneda. *Tetrahedron*. **1988**, 44, 3241.
- [13] A Ikeda; Y Kawabe; T Sakai; K Kawasaki. Chem Lett. 1989, 1803.