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Oxidative cyclization of 3-oxopropanenitriles with α,β-unsaturated amides by manganese(III) acetate. Regio- and stereoselective synthesis of 4-cyano-2,3-dihydrofuran-3-carboxamides

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Abstract—4-Cyano-2,3-dihydrofuran-3-carboxamides were obtained from the oxidative cyclization of 3-oxopropanenitriles with unsaturated amides using manganese(III) acetate. Treatment of 3-oxopropanenitriles with (2*E*)-3-(5-methyl-2-furyl)acrylamide and (2*E*)-3-(2-thienyl)acrylamide gave 2-(5-methyl-2-furyl) and 2-(2-thienyl) substituted 4-cyano-2,3-dihydrofuran-3-carboxamides in moderate yields, respectively. However, (2*E*)-3-(2-furyl)acrylamide and (2*E*)-3-phenylacrylamide did not produce any product under the same conditions. On the other hand, reaction of a dienamide such as (2*E*,4*E*)-5-phenylpenta-2,4-dienamide with 3-oxopropanenitriles gave diastereomeric mixtures of 2-(2-vinylphenyl)-4-cyano-2,3-dihydrofuran-3-carboxamides. Mechanisms are proposed for the formation of all of these compounds.

1. Introduction

Dihydrofurans belong to an important class of compounds which show a wide range of biological activities and form the basic structure of many natural products.[1] These compounds can be produced by the reactions of diazo compounds or iodonium ylides with alkenes via Rh(II) catalysis.[2] More commonly, they are produced from reactions of active methylene compounds (1,3-dicarbonyl, β-ketoester and 3-oxopropanenitrile) with alkenes by using transition metal salts (e.g., Mn^{+3}, Ce^{+4}, Co^{+3}, Cu^{+2}). Among these metal salts, manganese(III) acetate[3] and cerium(IV) ammonium nitrate[4] have very important roles, and they allow the formation of highly functionalized products such as furans,[3c–f,5] dihydrofurans,[3g–p] γ-lactones,[6] β-lactams[7] and natural products.[3c,r,8]

Recently, we reported the synthesis of 3-trifluoroacetyl-4,5-dihydrofurans and 3-(dihydrofuran-2(3*H*)-ylidene)-1,1,1-trifluoroacetones by the treatment of trifluoromethyl-1,3-dicarbonyl compounds with conjugated alkenes.[3n] The oxidative cyclization of 3-oxopropanenitriles with 1,1-diarylethylenes and their reaction mechanism have been reported by Nishino et al.[9] Previously, we have studied oxidative cyclization of 3-oxopropanenitriles with conjugated alkenes containing phenyl and 2-thienyl groups using manganese(III) acetate.[3o] Recently, we have also reported the synthesis of 4,5-dihydrofurans and naphthalene derivatives including carboxamides due to the reaction of 1,3-dicarbonyls with α,β-unsaturated amides such as acrylamide and methacrylamide.[3l]

Up to now, reactions of α,β-unsaturated amides with 3-oxopropanenitriles have not been studied. Here, we describe the oxidative cyclizations of various 3-oxopropanenitriles **1a**–**h** with α,β-unsaturated amides containing 2-thienyl, 2-furyl, 2-(5-methylfuryl), phenyl and phenylvinyl groups by using manganese(III) acetate. As a result of these reactions, we have obtained 4-cyano-2,3-dihydrofurans containing carboxamides.

2. Results and discussion

(2*E*)-3-(5-Methyl-2-furyl)acrylamide **2a**, (2*E*)-3-(2-furyl)-acrylamide **2b**, (2*E*)-3-(2-thienyl)acrylamide **2c**[10] and (2*E*,4*E*)-5-phenylpenta-2,4-dienamide **2e** were obtained from the reaction of ammonia with the acyl chloride (obtained by the reaction of the carboxylic acids with $SOCl_2$).

Keywords: Manganese(III) acetate; Oxidative cyclization; Radical addition; 2,3-Dihydrofuran; Carboxamide; 3-Oxopropanenitrile; Unsaturated amide.
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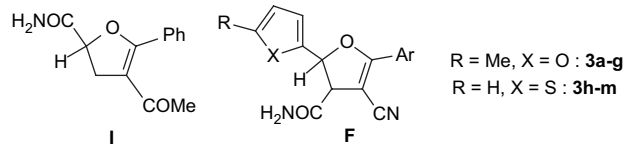
All 3-oxopropanenitriles (except **1d**) were prepared by the condensation of suitable esters with acetonitrile and NaH in PhMe.[11]

The mechanism we propose for the oxidative cyclization of α,β-unsaturated amides **2a–d** with 3-oxopropanenitriles is explained in Scheme 1. According to this mechanism, interaction of $Mn(OAc)_3$ with the enol form of 3-oxopropanenitrile **A** gives a manganese(III)–enolate complex **B**. In complex **B**, an α-carbon radical **C** is formed on 3-oxopropanenitrile while Mn^{+3} is reduced to Mn^{+2}. This α-carbon radical attacks the unsaturated amide, and compound **D** can be formed following pathway ***i***, or compound **G** can be formed following pathway ***ii***. Structure **D** is oxidized to carbocation **E** by $Mn(OAc)_3$ and intramolecular cyclization of **E** forms 2,3-dihydrofuran-3-carboxamide **F**. Structure **G** following the same two steps forms 2,3-dihydrofuran-2-carboxamide **H**.

Radical intermediate product in structure **D** is more stable than **G** since it is conjugated with an aromatic group. Consequently, we have obtained 2,3-dihydrofuran-3-carboxamides **F** regio- and stereoselectively, but the other product **G** is not produced. These two compounds were differentiated by the chemical shift values of the H-2 protons. We had reported the chemical shift value of the H-2 proton of 4-acetyl-5-phenyl-2,3-dihydrofuran-2-carboxamide **I** as δ_H=5.01 ppm (Fig. 1).[3l] However, the chemical shift values for the H-2 protons and H-3 protons are 5.73–6.56 ppm and 3.86–4.32 ppm, respectively, in the ^{1}H NMR spectra of isolated compounds **3a–m**. Thus, we concluded that these compounds are 2,3-dihydrofuran-3-carboxamides **F** formed via pathway ***i***.

While no product was obtained in the oxidative cyclization of 3-oxopropanenitriles with (2*E*)-3-(2-furyl)acrylamide **2b** using manganese(III) acetate, the reaction of **1a–g** with (2*E*)-3-(5-methyl-2-furyl)acrylamide **2a** formed 2,3-dihydrofuran-3-carboxamides **3a–g** in moderate yields

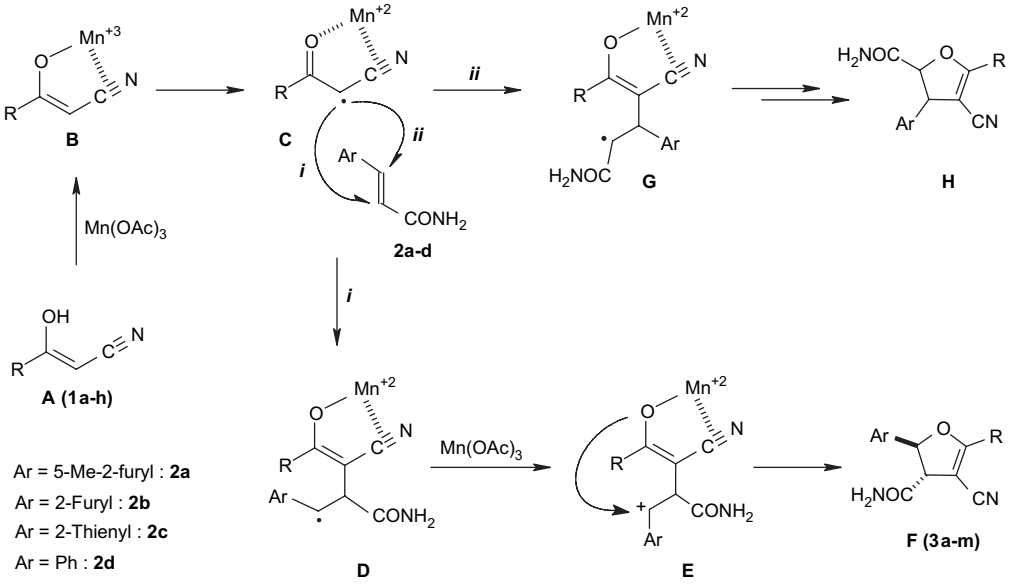


I **F**

Figure 1.

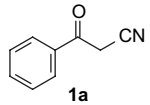
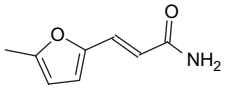
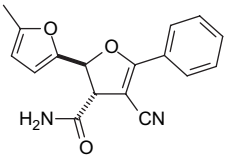
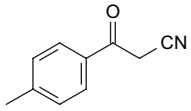
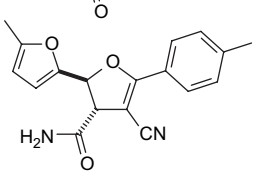
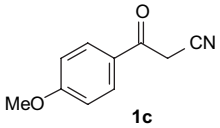
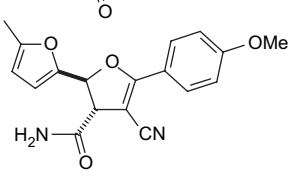
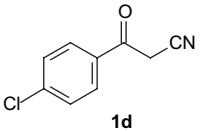
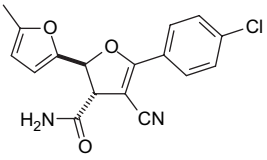
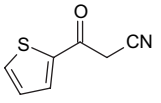
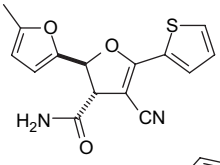
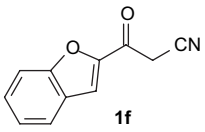
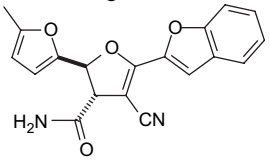
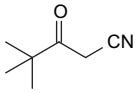
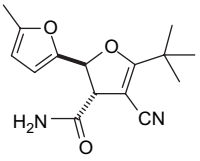
(Table 1). Treatment of 3-phenyl-3-oxopropanenitrile **1a** with **2a** gave the product 2,3-dihydrofuran **3a** in 56% yield. Additionally, 4-cyano-2,3-dihydrofuran-3-carboxamides **3b–d** were obtained via the oxidative reaction of **2a** with derivatives of **1a** such as 4-Me **1b**, 4-MeO **1c** and 4-Cl **1d** in 42, 64 and 55% yields, respectively. We have also obtained **3e** (53%) and **3f** (49%) in moderate yields, respectively, in the oxidative cyclization of 3-oxopropanenitriles **1e** and **1f** containing heterocyclic group with **2a**. In addition, the treatment of 4,4-dimethyl-3-oxopentanenitrile **1g** with **2a** formed 2,3-dihydrofuran-3-carboxamide **3g** in 42% yield. The ^{1}H NMR spectra of 2-(5-methyl-2-furyl) substituted 4-cyano-2,3-dihydrofuran-3-carboxamides **3a–g** show that the 5-methylfuryl and carboxamide groups are in trans position since the coupling constant between H2 and H3 protons of these compounds J_{trans}=6.4–7.6 Hz. It is reported that the coupling constant between these protons in same structures are given as J_{cis}=8–9 Hz, in literature.[12]

Oxidative cyclizations of (2*E*)-3-(2-thienyl)acrylamide **2c** with 3-oxopropanenitriles produced 2-(2-thienyl) substituted 2,3-dihydrofuran-3-carboxamides **3h–m** in moderate yields similar to the ones of **2a** (Table 2). We obtained 2,3-dihydrofurans **3h** (47%) and **3i** (49%) in the reactions of **2c** with **1a** and **1c**, respectively. The reaction of **1e** with **2c** gave 4-cyano-2,5-di-2-thienyl-2,3-dihydrofuran-3-carboxamide **3j** in 43% yield. Similarly, **3k** (34%) and **3l** (45%) were produced as a result of radical cyclization of 3-oxopropanenitriles containing 2-furyl (**1h**) and 2-benzofuryl (**1f**) groups with **2c**, respectively. Coupling constant between



Scheme 1. Mechanism for formation of 2,3-dihydrofuran-3-carboxamides.

Table 1. Synthesis of 2-(5-methyl-2-furyl)-4-cyano-2,3-dihydrofuran-3-carboxamides **3a–g**

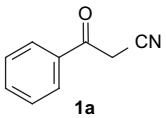
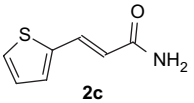
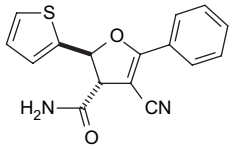
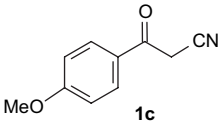
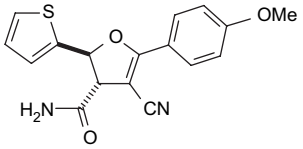
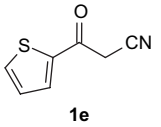
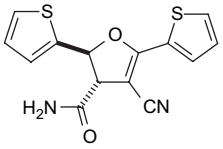
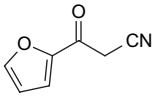
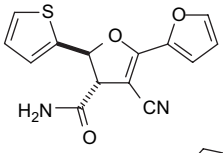
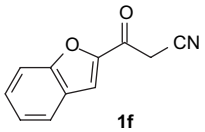
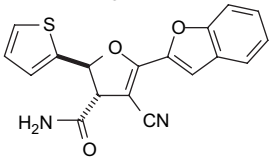
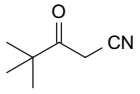
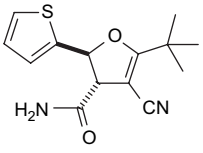
Entry	3-Oxopropanenitrile	α,β-Unsaturated amide	4-Cyano-2,3-dihydrofuran-3-carboxamide	Product and yield,[a] %
1	 **1a**	 **2a**		**3a**, 56
2	 **1b**	**2a**		**3b**, 42
3	 **1c**	**2a**		**3c**, 64
4	 **1d**	**2a**		**3d**, 55
5	 **1e**	**2a**		**3e**, 53
6	 **1f**	**2a**		**3f**, 49
7	 **1g**	**2a**		**3g**, 42

[a] Yield of isolated product based on the alkene **2a**.

H2 and H3 protons of **3h–m** J_{trans}=6.0–6.6 Hz, so 2-thienyl and carboxamide groups are in trans position.

2,3-Dihydrofurans containing heterocycles are produced in the reactions of 3-oxopropanenitriles using manganese(III) acetate with **2a** and **2c** but no product is formed in the reactions of **1a–h** under the same experimental conditions with (2*E*)-3-phenylacrylamide **2d**. On the other hand, in the cyclization reactions of (2*E*,4*E*)-5-phenylpenta-2,4-dienamide **2e**, which is an α,β,γ,δ-unsaturated amide, we obtained dihydrofuran-3-carboxamides as a mixture of diastereomers. An α-carbon radical formed from 3-oxopropanenitrile via manganese(III) acetate can be added into **2e** in four different ways and as a result of these different paths, different cyclization products can be formed. The proposed reaction mechanism is given in Scheme 2. According to this mechanism, adding the α-carbon radical in **2e** by pathway ***i*** forms **J**, which is an allylic radical intermediate product. 2-Vinylphenyl substituted 2,3-dihydrofuran-3-carboxamide **L** is produced as a result of cyclization of carbocation **K**. Allylic radical intermediate product **M** formed by the reaction of **C** with **2e** via pathway ***ii*** is oxidized to carbocation **N** with manganese(III) acetate, and compound **O** is formed by the intramolecular cyclization following this. Similarly, the secondary radical intermediate product **P** and benzylic radical intermediate product **R** are formed by the addition of α-carbon radical to **2e** via pathways ***iii*** and ***iv***, respectively. These intermediate products form 2,3-dihydrofurans **Q** and **S** as a result of the same two steps as explained above. The H2 protons of **Q** and **S** are expected to be seen as doublet peaks, whereas, triplet peaks are observed in the ^{1}H NMR spectra of isolated compounds. Thus, we decided that **Q** and **S** compounds are not formed. On the other hand, it is difficult to determine these two compounds

Table 2. Synthesis of 2-(2-thienyl)-4-cyano-2,3-dihydrofuran-3-carboxamides **3h–m**

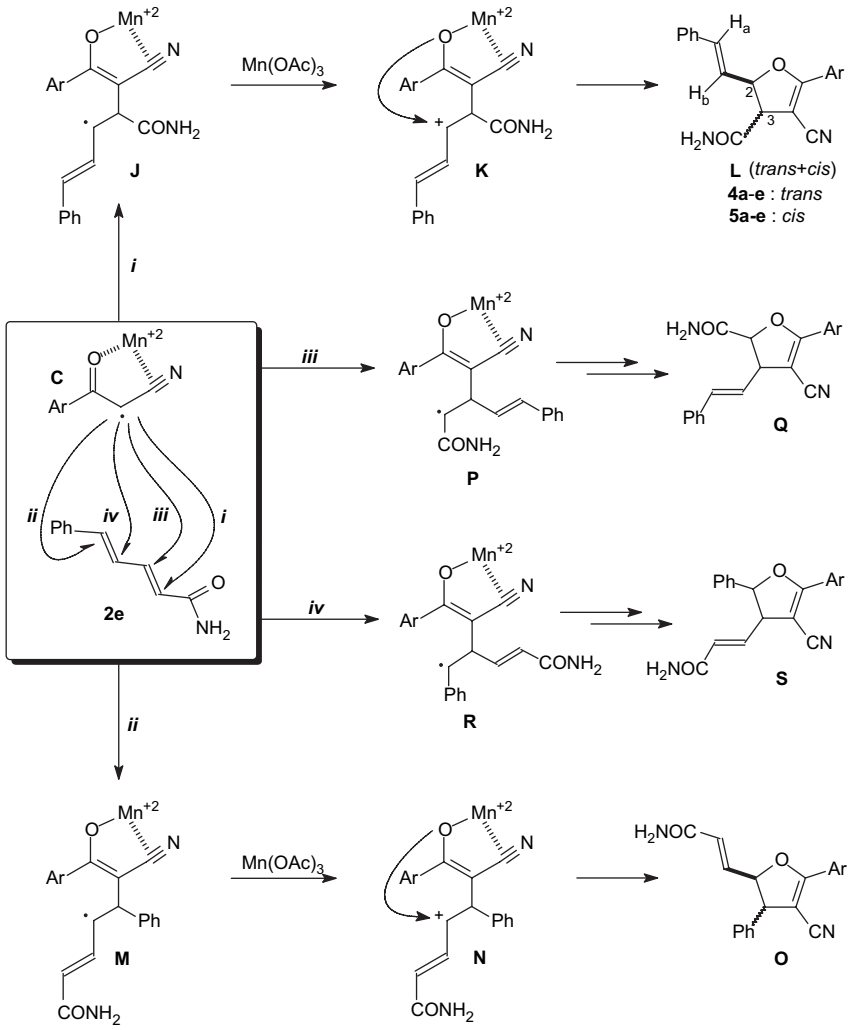
Entry	3-Oxopropanenitrile	α,β-Unsaturated amide	4-Cyano-2,3-dihydrofuran-3-carboxamide	Product and yield,[a] %
1	 **1a**	 **2c**		**3h**, 47
2	 **1c**	**2c**		**3i**, 49
3	 **1e**	**2c**		**3j**, 43
4	 **1h**	**2c**		**3k**, 34
5	 **1f**	**2c**		**3l**, 45
6	 **1g**	**2c**		**3m**, 36

[a] Yield of isolated product based on the alkene **2c**.

exactly using only their ^{1}H NMR spectra since the coupling constant and chemical shift values of H-2, H-3 and olefinic protons of compounds **L** and **O** are very close to each other. So, we differentiated these compounds using HMBC spectra. The amide carbonyl is coupled with H-2 and H-3, but not with olefinic protons in these spectra. As a result, we decided that the isolated compounds are 2-vinylphenyl substituted 2,3-dihydrofuran-3-carboxamides **L**, and they are formed via pathway ***i***. Although both intermediate products **J** and **M** are allylic radicals, only the cyclization product of **J** is produced. This shows that the α-carbon radical is added to **2e** in a way to form a more stable allylic radical intermediate product (by choosing the one which is conjugated with the phenyl group).

The oxidative cyclizations of 3-oxopropanenitriles with **2e** produced 2-vinylphenyl substituted 2,3-dihydrofuran-3-carboxamides **L** (**4** and **5**), as a mixture of two isomers, which cannot be isolated from each other by chromatographical methods, in moderate yields (Table 3). It is seen that both of these isomer protons give similar couples in HMBC spectra and have the same molecular weights in LC–MS. Moreover, it is obvious that they are not geometric isomers since both of the isomers have trans coupling (J=15.6–16.0 Hz) between Ha and Hb olefinic protons. However, ^{1}H NMR spectra show that H-2 and H-3 protons of major products have trans coupling (J=6.0–7.5 Hz) and that of minor products have cis coupling (J=9.6–10.0 Hz). Based on these data it is concluded that the obtained compounds are mixtures of trans and cis diastereomers of which we determined the ratio (approximately 75:25) by ^{1}H NMR spectra.

As a result, here we studied the oxidative cyclization of derivatives of phenyl, 2-thienyl, 2-furyl, 2-(5-methylfuryl), and vinylphenyl substituted α,β-unsaturated acrylamides with various 3-oxopropanenitriles via manganese(III) acetate. No product could be obtained in the radical reactions of 2-furyl (**2b**) and phenyl (**2d**) substituted acrylamides. However, we regio- and stereoselectively obtained polyfunctional 4-cyano-2,3-dihydrofuran-3-carboxamides as a result of the reactions of other unsaturated amides (**2a**, **2c** and **2e**). In the oxidative cyclizations of (2*E*,4*E*)-5-phenylpenta-2,4-dienamide **2e** with 3-oxopropanenitriles, we obtained



Scheme 2. Mechanism for the oxidative cyclization of 3-oxopropanenitrile with (2*E*,4*E*)-5-phenylpenta-2,4-dienamide **2e**.

2-vinylphenyl substituted 4-cyano-2,3-dihydrofuran-3-carboxamides as diastereomeric mixtures and we proposed a reaction mechanism for the formation of these compounds.

3. Experimental

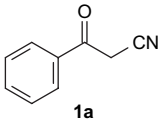
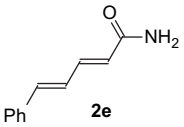
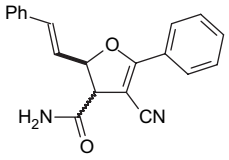
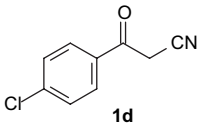
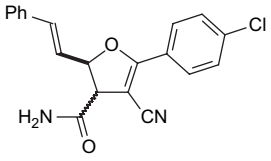
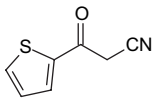
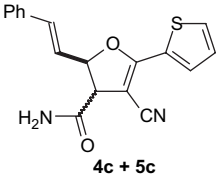
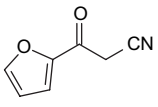
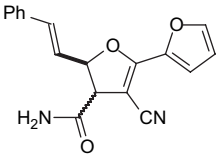
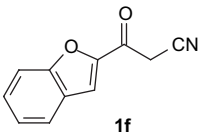
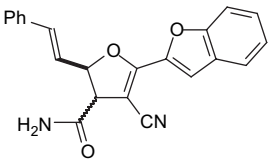
3.1. General

Melting points were determined on a Gallenkamp capillary melting point apparatus. IR spectra (KBr disc, $CHCl_3$) were obtained with a Matson 1000 FT-IR spectrometer in the 400–4000 cm^{-1} range with 4 cm^{-1} resolution. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker Avance DPX-400 MHz and Varian Mercury-400 High performance Digital FT-NMR spectrophotometers. The mass spectra were measured on a Waters 2695 Alliance HPLC, Waters micromass 2Q (ESI+) spectrophotometer. Elemental analyses were performed on a Leco 932 CHNS-O instrument. Thin layer chromatography (TLC) was performed on Merck aluminium-packed silica gel plates. Purification of products was performed by column chromatography on silica gel (Merck silica gel 60, 40–60 μm) or preparative TLC on silica gel of Merck ($PF_{254-366\ nm}$). All reagents, 3-(4-chlorophenyl)-3-oxopropanenitrile, 1-benzofuran-2-carboxylic acid and (2*E*)-3-phenylacrylamide were purchased from Sigma–Aldrich.

3.1.1. General procedure for unsaturated amides. α,β-Unsaturated amides **2a**, **2b** and **2e** are synthesized according to the method explained below. To a solution of carboxylic acid in 100 mL chloroform was added thionyl chloride (11 mL, 0.15 mol, freshly distilled) at room temperature. The mixture was allowed to stand for 12 h. Then the solution of acyl chloride in chloroform was added slowly into a solution of 100 mL ammonia (35%) containing sodium hydroxide (8 g, 0.2 mol), which was cooled in ice bath and stirred vigorously. Amide which was separated is filtered and washed with 50 mL water. Additional solids were obtained from chloroform solution.

3.1.1.1. Synthesis of (2*E*)-3-(5-methyl-2-furyl)acrylamide 2a.[13] (2*E*)-3-(5-Methyl-2-furyl)acrylic acid was prepared from the reaction of 5-methyl-furfural (5-methyl-2-furaldehyde) and malonic acid described in the literature.[13,14] Compound **2a** was produced from this acid, which is explained above. Yield (12.8 g) 85% as a white solid (**2a**), mp 130–132 °C from EtOH/H_2O (lit. mp 130–132 °C from

Table 3. Synthesis of 2-(2-vinylphenyl)-4-cyano-2,3-dihydrofuran-3-carboxamides **4** and **5**

Entry	3-Oxopropanenitrile	Unsaturated amide	4-Cyano-2,3-dihydrofuran-3-carboxamide	Yield,[a] % (trans:cis)[b]
1	 **1a**	 **2e**	 **4a + 5a**	30 (74:26)
2	 **1d**	**2e**	 **4b + 5b**	40 (76:24)
3	 **1e**	**2e**	 **4c + 5c**	31 (76:24)
4	 **1h**	**2e**	 **4d + 5d**	24 (76:24)
5	 **1f**	**2e**	 **4e + 5e**	30 (72:28)

[a] Yields of isolated product based on the alkene **2e**.
[b] Diastereomeric ratio is determined by ^{1}H NMR spectra.

acetone).[16] δ_H (400 MHz, $CDCl_3$) 7.15 (1H, d, J=15.2 Hz, H_{olefin}), 6.54 (1H, s, NH), 6.25 (1H, d, J=3.6 Hz, arom. CH), 6.20 (1H, d, J=15.2 Hz, H_{olefin}), 5.96 (1H, s, NH), 5.90 (1H, d, J=4.0 Hz, arom. CH), 2.18 (3H, s, CH_3).

3.1.1.2. Synthesis of (2*E*)-3-(2-furyl)acrylamide 2b.[15] (2*E*)-3-(2-Furyl)acrylic acid was prepared from the reaction of furfural (2-furaldehyde) and malonic acid described in the literature.[16] Compound **2b** was produced from this acid, which is explained above. Yield (12.6 g) 92% as a white solid (**2b**), mp 171–173 °C recrystallization from MeOH/H_2O (lit. mp 168 °C from H_2O).[15a] δ_H (400 MHz, $CDCl_3$) 7.47 (1H, d, J=2.0 Hz, arom.CH), 7.45 (1H, d, J=15.2 Hz, H_{olefin}), 6.61 (1H, d, J=3.6 Hz, arom.CH), 6.47 (1H, dd, J=3.6, 2.0 Hz, arom.CH), 6.37 (1H, d, J=15.2 Hz, H_{olefin}), 5.84 (2H, s, NH_2).

3.1.1.3. Synthesis of (2*E*,4*E*)-5-phenylpenta-2,4-dienamide 2e.[15a,17] (2*E*,4*E*)-5-Phenylpenta-2,4-dienoic acid was prepared from the reaction of (2*E*)-3-phenylacrylaldehyde and malonic acid in pyridine/piperidine described in the literature.[18] Compound **2e** was produced from this acid, which is explained above. Yield (12.3 g) 71% as a white solid (**2e**), mp 188–189 °C recrystallization from MeOH/H_2O (lit. mp 185 °C from ethanol).[17e] δ_H (400 MHz, $CDCl_3$) 7.49–7.45 (3H, m, arom. CH and NH overlap), 7.38–7.30 (3H, m, arom. CH), 7.14 (1H, s, NH), 6.93 (1H, d, J=15.2 Hz, H5), 6.89 (1H, d, J=15.2 Hz, H4), 6.04 (2H, d, J=14.8 Hz, H2 and H3).

3.1.2. Synthesis of 3-(4-methylphenyl)-3-oxopropanenitrile 1b.[19] A suspension of methyl 4-methylbenzoate (15 g, 0.1 mol) and NaH (8 g, 0.2 mol, 60 wt % in white oil) in 100 mL dry toluene is heated up to 90 °C. Then under vigorous stirring acetonitrile (10.4 mL, 0.2 mol) was added to the suspension within 2 h. Stirring was continued subsequently at this temperature until the evolution of hydrogen

ceased (6 h). After cooling to room temperature, it is filtered with suction and washed with 20 mL Et_2O. The solid material was dissolved in 100 mL of water and cooling ice/salt mixture. Then HCl 15% was added until pH value of the solution becomes 2 and in a manner that its temperature shall not exceed 5 °C. The precipitated solids were filtered off with suction and washed with water until they become neutral, then recrystallized from ethanol/H_2O to give **1b** (11.0 g, 69%), mp 106–108 °C (lit. mp 103–104 °C from ethanol).[19a]

3.1.3. Synthesis of 3-(2-benzofuroyl)-3-oxopropanenitrile 1f.[20] 3-(2-Benzofuroyl)-3-oxopropanenitrile (**1f**) was prepared by the method described above. Methyl 1-benzofuran-2-carboxylate was prepared from the reaction of 1-benzofuran-2-carboxylic acid and MeOH in HCl described in the literature.[21] Yield (17.2 g) 93% as a light brown solid (**1f**), mp 148 °C from acetone (lit. mp 148.5 °C from acetone).[20]

3.1.4. General procedure for the synthesis of 4-cyano-2,3-dihydrofuran-3-carboxamides. A solution of manganese(III) acetate dihydrate (0.83 g, 3 mmol) in 15 mL of glacial acetic acid was heated under nitrogen atmosphere at 80 °C until it dissolved. After the solution was cooled down to 70 °C, a solution of 3-oxopropanenitrile (2 mmol) and alkene (1 mmol) in acetic acid was added to this mixture. The reaction was completed when dark brown colour of the solution changed to red colour (in 30–60 min). Water (20 mL) was added to this solution and extracted with $CHCl_3$ (3×20 mL). The combined organic phases were neutralized with satd $NaHCO_3$ solution, and dried over anhydrous Na_2SO_4 and evaporated. Crude products were purified by column chromatography on silica gel or preparative TLC (20×20 cm plates, 2 mm thickness) using *n*-hexane/EtOAc (1:1) as eluent.

3.1.4.1. *trans*-4-Cyano-5′-methyl-5-phenyl-2,3-dihydro-2,2′-bifuran-3-carboxamide (3a). Yield 56% (170 mg) as a white solid, mp 164–166 °C (*n*-hexane/EtOAc). Found: C, 69.54; H, 4.91; N, 9.22. $C_{17}H_{14}N_2O_3$ requires C, 69.38; H, 4.79; N, 9.52%; ν_{max} (KBr disc) 3439 (NH), 3304 (NH), 2206 (CN), 1672 (C═O), 1608 (C═C), 1232 (C–O–C), 691; δ_H (400 MHz, $CDCl_3$) 7.97 (2H, d, *J*=6.8 Hz, arom.), 7.48 (3H, m, arom.), 6.43 (1H, d, *J*=2.0 Hz, arom.), 6.18 (1H, d, *J*=6.8 Hz, H2), 6.00 (2H, s, NH and Ar–H, overlap), 5.88 (1H, s, NH), 4.30 (1H, d, *J*=6.8 Hz, H3), 2.31 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 170.6 (C═O), 168.2 (C5), 154.5, 148.1, 132.3 (C4), 128.9, 127.8, 127.5, 117.3 (CN), 111.9, 107.0, 79.7, 79.1 (C2), 53.7 (C3), 13.9 (Me); *m/z* (ESI+) 295 (MH^+, %100).

3.1.4.2. *trans*-4-Cyano-5′-methyl-5-(4-methylphenyl)-2,3-dihydro-2,2′-bifuran-3-carboxamide (3b). Yield 42% (130 mg) as a white solid, mp 185–187 °C (*n*-hexane/EtOAc). Found: C, 70.44; H, 4.99; N, 9.22. $C_{18}H_{16}N_2O_3$ requires C, 70.12; H, 5.23; N, 9.09%; ν_{max} (KBr disc) 3378 (NH), 3194 (NH), 2208 (CN), 1660 (C═O), 1618 (C═C), 1564 (NH), 1254 (C–O–C), 920, 791; δ_H (400 MHz, $CDCl_3$) 7.85 (2H, d, *J*=8.0 Hz, arom.), 7.23 (2H, d, *J*=8.4 Hz, arom.), 6.40 (1H, d, *J*=3.2 Hz, arom.), 6.13 (1H, d, *J*=7.6 Hz, H2), 6.04 (1H, s, NH), 6.00 (1H, s, NH), 5.97 (1H, dq, *J*=3.2, 0.8 Hz, arom.), 4.27 (1H, d, *J*=7.6 Hz, H3), 2.39 (3H, s, Me), 2.29 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 170.9 (C═O), 168.4 (C5), 157.4, 148.3, 143.0, 129.6, 127.7, 124.8, 117.5 (CN), 111.7, 107.0, 79.7, 78.2 (C2), 53.7 (C3), 21.9 (Me), 13.9 (Me); *m/z* (ESI+) 309 (MH^+, %100).

3.1.4.3. *trans*-4-Cyano-5-(4-methoxyphenyl)-5′-methyl-2,3-dihydro-2,2′-bifuran-3-carboxamide (3c). Yield 64% (210 mg) as a light brown solid, mp 170–171 °C (*n*-hexane/EtOAc). Found: C, 66.79; H, 5.04; N, 8.42. $C_{18}H_{16}N_2O_4$ requires C, 66.66; H, 4.97; N, 8.64%; ν_{max} (KBr disc) 3389 (NH), 3194 (NH), 2198 (CN), 1664 (C═O), 1610 (NH), 1259 (C–O–C), 1178 (C–O–C), 831, 787; δ_H (400 MHz, $CDCl_3$) 7.87 (2H, d, *J*=8.8 Hz, arom.), 6.86 (2H, d, *J*=8.8 Hz, arom.), 6.66 (1H, s, NH), 6.34 (1H, d, *J*=3.2 Hz, arom.), 6.17 (1H, s, NH), 6.03 (1H, d, *J*=7.6 Hz, H2), 5.91 (1H, dq, *J*=3.2, 0.8 Hz, arom.), 4.24 (1H, d, *J*=7.6 Hz, H3), 3.79 (3H, s, OMe), 2.24 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 171.2 (C═O), 167.7 (C5), 162.5, 154.2, 148.4, 129.6, 120.1, 117.7 (CN), 114.2, 111.6, 110.0, 106.9 (C4), 79.7 (C2), 55.6 (OMe), 53.5 (C3), 13.9 (Me); *m/z* (ESI+) 325 (MH^+, %100).

3.1.4.4. *trans*-5-(4-Chlorophenyl)-4-cyano-5′-methyl-2,3-dihydro-2,2′-bifuran-3-carboxamide (3d). Yield 55% (180 mg) as a light brown solid, mp 200–202 °C (*n*-hexane/EtOAc). Found: C, 62.02; H, 4.19; N, 8.54. $C_{17}H_{13}ClN_2O_3$ requires C, 62.11; H, 3.99; N, 8.52%; ν_{max} (KBr disc) 3401 (NH), 3316 (NH), 2208 (CN), 1674 (C═O), 1616 (C═C), 1236 (C–O–C), 910; δ_H (400 MHz, $CDCl_3$) 7.55 (2H, d, *J*=8.8 Hz, arom.), 7.04 (2H, d, *J*=8.8 Hz, arom.), 6.97 (1H, s, NH), 6.12 (1H, s, NH), 6.06 (1H, d, *J*=3.2 Hz, arom.), 5.73 (1H, d, *J*=7.6 Hz, H2), 5.63 (1H, dq, *J*=3.2, 0.8 Hz, arom.), 4.02 (1H, d, *J*=7.6 Hz, H3), 1.95 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 175.6 (C═O), 171.1 (C5), 159.0, 152.8, 142.7, 133.8, 133.7, 130.9, 121.5, 116.6 (CN), 111.7, 85.7, 84.9 (C2), 58.2 (C3), 18.6 (Me); *m/z* (ESI+) 329 (MH^+, %100).

3.1.4.5. *trans*-4-Cyano-5′-methyl-5-(2-thienyl)-2,3-dihydro-2,2′-bifuran-3-carboxamide (3e). Yield 53% (160 mg) as a yellow solid, mp 210–211 °C (*n*-hexane/EtOAc). Found: C, 59.64; H, 3.75; N, 9.25; S, 10.82. $C_{15}H_{12}N_2O_3S$ requires C, 59.99; H, 4.03; N, 9.33; S, 10.68%; ν_{max} (KBr disc) 3399 (NH), 3314 (NH), 2208 (CN), 1674 (C═O), 1610 (C═C); δ_H (400 MHz, $CDCl_3$) 7.57 (1H, dd, *J*=4.0, 1.2 Hz, arom.), 7.30 (1H, dd, *J*=4.8, 1.2 Hz, arom.), 7.26 (1H, s, NH), 6.87 (1H, dd, *J*=5.2, 4.0 Hz, arom.), 6.38 (1H, s, NH), 6.15 (1H, d, *J*=3.2 Hz, arom.), 5.80 (1H, d, *J*=7.6 Hz, H2), 5.72 (1H, dq, *J*=3.2, 0.8 Hz, arom.), 4.10 (1H, d, *J*=7.6 Hz, H3), 2.02 (3H, s, Me); δ_C (100 MHz, DMSO-d_6) 170.7 (C═O), 162.9 (C5), 154.5, 148.5, 132.6 (C4), 131.2, 129.3, 129.3, 116.6 (CN), 113.0, 107.7, 81.1, 80.2 (C2), 53.0 (C3), 14.2 (Me); *m/z* (ESI+) 301 (MH^+, %100).

3.1.4.6. *trans*-4′-Cyano-5-methyl-2′,3′-dihydro-2,2′:5′,2″-terfuran-3′-carboxamide (3f). Yield 49% (160 mg) as a yellow solid, mp 180–182 °C (*n*-hexane/EtOAc). Found: C, 68.36; H, 4.20; N, 8.45. $C_{19}H_{14}N_2O_4$ requires C, 68.26; H, 4.22; N, 8.38%; ν_{max} (KBr disc) 3381 (NH), 3194 (NH), 2214 (CN), 1645 (C═O), 1180 (C–O–C); δ_H (400 MHz, $CDCl_3$) 7.56 (1H, dd, *J*=8.0, 0.8 Hz, arom.), 7.50 (1H, dd, *J*=8.4, 1.2 Hz, arom.), 7.34 (1H, td, *J*=8.4, 1.2 Hz, arom.), 7.30 (1H, s, arom.), 7.25 (1H, dd, *J*=8.8,

1.2 Hz, arom.), 6.95 (1H, s, NH), 6.38 (1H, d, J=3.2 Hz, arom.), 6.19 (1H, s, NH), 6.12 (1H, d, J=7.6 Hz, H2), 5.92 (1H, dq, J=3.2, 0.8 Hz, arom.), 4.32 (1H, d, J=7.6 Hz, H3), 2.23 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 170.4 (C=O), 158.7 (C5), 154.5, 154.5, 147.8, 144.3, 127.4, 127.3, 124.1, 122.6, 115.8 (CN), 112.3, 112.2, 111.3, 107.0, 81.7, 81.0 (C2), 53.0 (C3), 13.9 (Me); *m/z* (ESI+) 335 (MH^+, %100).

3.1.4.7. *trans*-5-*tert*-Butyl-4-cyano-5′-methyl-2,3-dihydro-2,2′-bifuran-3-carboxamide (3g). Yield 42% (240 mg) as a yellow oil. Found: C, 65.54; H, 6.57; N, 10.35. $C_{15}H_{18}N_2O_3$ requires C, 65.68; H, 6.61; N, 10.21%; ν_{max} (KBr disc) 3401 (NH), 3341 (NH), 2959, 2923, 2210 (CN), 1684 (C=O), 1616 (C=C), 1165 (C–O–C); δ_H (400 MHz, $CDCl_3$) 6.32 (1H, d, J=3.2 Hz, arom.), 5.97 (1H, d, J=6.4 Hz, H2), 5.95 (1H, dq, J=3.2, 0.4 Hz, arom.), 5.81 (1H, s, NH), 5.66 (1H, s, NH), 4.01 (1H, d, J=6.8 Hz, H3), 2.30 (3H, s, Me), 1.29 (9H, s, Me); δ_C (100 MHz, $CDCl_3$) 180.9 (C=O), 173.0 (C5), 170.7, 153.9, 148.4 (C4), 116.8 (CN), 110.8, 106.6, 79.2 (C2), 78.0, 53.5 (C3), 27.9 (Me), 13.6 (Me); *m/z* (ESI+) 275 (MH^+, %100).

3.1.4.8. *trans*-4-Cyano-5-phenyl-2-(2-thienyl)-2,3-dihydrofuran-3-carboxamide (3h). Yield 47% (140 mg) as a white solid, mp 163–164 °C (*n*-hexane/EtOAc). Found: C, 63.12; H, 4.34; N, 9.76; S, 10.70. $C_{16}H_{12}N_2O_2S$ requires C, 64.85; H, 4.08; N, 9.45; S, 10.82%; ν_{max} (KBr disc) 3395 (NH), 3196 (NH), 2208 (CN), 1666 (C=O), 1620 (C=C), 1234 (C–O–C), 750–691; δ_H (400 MHz, $CDCl_3$) 8.00 (2H, dd, J=7.2, 1.5 Hz, arom.), 7.53 (1H, tt, J=7.2, 1.3 Hz, arom.), 7.48 (2H, t, J=7.7 Hz, arom.), 7.37 (1H, dd, J=5.1, 1.1 Hz, arom.), 7.20 (1H, d, J=3.3 Hz, arom.), 7.04 (1H, dd, J=5.1, 3.6 Hz, arom.), 6.50 (1H, d, J=6.4 Hz, H2), 6.00 (1H, s, NH), 5.88 (1H, s, NH), 4.13 (1H, d, J=6.4 Hz, H3); δ_C (100 MHz, $CDCl_3$) 170.0 (C=O), 167.9 (C5), 141.3, 132.3, 128.8, 127.6, 127.2, 127.1, 126.7, 126.3, 116.8 (CN), 82.3 (C2), 78.6, 57.7 (C3); *m/z* (ESI+) 297 (MH^+, %100).

3.1.4.9. *trans*-4-Cyano-5-(4-methoxyphenyl)-2-(2-thienyl)-2,3-dihydrofuran-3-carboxamide (3i). Yield 49% (160 mg) as a white solid, mp 162–164 °C (*n*-hexane/EtOAc). Found: C, 62.12; H, 4.34; N, 8.76; S, 9.70. $C_{17}H_{14}N_2O_3S$ requires C, 62.56; H, 4.32; N, 8.58; S, 9.83%; ν_{max} (KBr disc) 3379 (NH), 3192 (NH), 2204 (CN), 1664 (C=O), 1610 (C=C), 1263 (C–O–C), 831; δ_H (400 MHz, $CDCl_3$) 7.95 (2H, d, J=9.2 Hz, arom.), 7.34 (1H, dd, J=5.2, 1.2 Hz, arom.), 7.16 (1H, d, J=3.6 Hz, arom.), 7.01 (1H, dd, J=5.2, 3.6 Hz, arom.), 6.95 (2H, d, J=8.8 Hz, arom.), 6.44 (1H, d, J=6.0 Hz, H2), 5.99 (1H, s, NH), 5.87 (1H, s, NH), 4.06 (1H, d, J=6.4 Hz, H3), 3.85 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 170.7 (C=O), 168.0 (C5), 162.9, 141.8, 129.8, 127.3, 126.8, 126.4, 119.8 (C4), 117.6 (CN), 114.4, 82.3 (C2), 57.8 (Me), 55.7 (C3); *m/z* (ESI+) 327 (MH^+, %100).

3.1.4.10. *trans*-4-Cyano-2,5-di-2-thienyl-2,3-dihydrofuran-3-carboxamide (3j). Yield 43% (130 mg) as a white solid, mp 194–196 °C (*n*-hexane/EtOAc). Found: C, 55.86; H, 3.34; N, 9.27; S, 20.91. $C_{14}H_{10}N_2O_2S_2$ requires C, 55.61; H, 3.33; N, 9.26; S, 21.21%; ν_{max} (KBr disc) 3412 (NH), 3314 (NH), 2206 (CN), 1672 (C=O), 1608 (C=C), 1217 (C–O–C); δ_H (400 MHz, $CDCl_3$) 7.94 (1H, dd, J=3.8, 0.9 Hz, arom.), 7.60 (1H, dd, J=5.0, 1.0 Hz, arom.), 7.38 (1H, dd, J=5.1, 1.1 Hz, arom.), 7.20–7.17 (2H, m, arom.), 7.05 (1H, dd, J=5.0, 3.6 Hz, arom.), 6.50 (1H, d, J=6.3 Hz, H2), 5.90 (1H, s, NH), 5.71 (1H, s, NH), 4.10 (1H, d, J=6.3 Hz, H3); δ_C (100 MHz, $CDCl_3$) 170.0 (C=O), 163.0 (C5), 141.2, 131.3, 131.2, 129.1, 128.3, 127.2, 126.8, 126.5, 116.4 (CN), 83.0 (C2), 57.4 (C3); *m/z* (ESI+) 303 (MH^+, %100).

3.1.4.11. *trans*-3-Cyano-5-(2-thienyl)-4,5-dihydro-2,2′-bifuran-4-carboxamide (3k). Yield 34% (100 mg) as a light yellow solid, mp 180–182 °C (*n*-hexane/EtOAc). Found: C, 58.80; H, 3.34; N, 9.82; S, 11.23. $C_{14}H_{10}N_2O_3S$ requires C, 58.73; H, 3.52; N, 9.78; S, 11.20%; ν_{max} (KBr disc) 3406 (NH), 3314 (NH), 2212 (CN), 1672 (C=O), 1618 (C=C), 1242 (C–O–C); δ_H (400 MHz, $CDCl_3$) 7.66 (1H, d, J=1.5 Hz, arom.), 7.38 (1H, dd, J=5.1, 1.0 Hz, arom.), 7.20 (1H, d, J=3.5 Hz, arom.), 7.07 (1H, d, J=3.6 Hz, arom.), 7.04 (1H, dd, J=5.0, 3.6 Hz, arom.), 6.57 (1H, dd, J=3.6, 1.8 Hz, arom.), 6.50 (1H, d, J=6.4 Hz, H5), 5.96 (1H, s, NH), 5.77 (1H, s, NH), 4.10 (1H, d, J=6.4 Hz, H4); δ_C (100 MHz, DMSO-d_6) 170.7 (C=O), 157.6 (C5), 147.9, 142.9, 141.3 (C4), 128.5, 128.4, 127.9, 115.9 (CN), 115.8, 113.3, 83.9, 80.4 (C2), 56.7 (C3); *m/z* (ESI+) 287 (MH^+, %100).

3.1.4.12. *trans*-5-(1-Benzofuran-2-yl)-4-cyano-2-(2-thienyl)-2,3-dihydrofuran-3-carboxamide (3l). Yield 45% (150 mg) as a white solid, mp 183–184 °C (*n*-hexane/EtOAc). Found: C, 63.92; H, 3.77; N, 8.18; S, 9.08. $C_{18}H_{12}N_2O_3S$ requires C, 64.27; H, 3.60; N, 8.33; S, 9.53%; ν_{max} (KBr disc) 3426 (NH), 3327 (NH), 2212 (CN), 1678 (C=O), 1643 (C=C), 1617 (N–H), 1177 (C–O–C), 752, 756; δ_H (400 MHz, $CDCl_3$) 7.66 (1H, d, J=7.8 Hz, arom.), 7.61 (1H, d, J=8.4 Hz, arom.), 7.45 (1H, t, J=7.3 Hz, arom.), 7.40 (1H, s, arom.), 7.38 (2H, d, J=5.1 Hz, arom.), 7.32 (1H, t, J=7.4 Hz, arom.), 7.22 (1H, d, J=3.4 Hz, arom.), 7.05 (1H, dd, J=5.0, 3.6 Hz, arom.), 6.56 (1H, d, J=6.6 Hz, H2), 6.07 (1H, s, NH), 5.91 (1H, s, NH), 4.17 (1H, d, J=6.6 Hz, H3); δ_C (100 MHz, $CDCl_3$) 169.9 (C=O), 158.9 (C5), 155.8, 143.9, 140.8, 127.6, 127.2, 127.0, 126.8, 124.0, 122.5, 115.5 (CN), 112.2 (C4), 111.7, 83.4 (C2), 80.2, 57.2 (C3); *m/z* (ESI+) 337 (MH^+, %100).

3.1.4.13. *trans*-5-*tert*-Butyl-4-cyano-2-(2-thienyl)-2,3-dihydrofuran-3-carboxamide (3m). Yield 36% (100 mg) as a yellow oil. Found: C, 61.12; H, 5.97; N, 10.03; S, 11.34. $C_{14}H_{16}N_2O_2S$ requires C, 60.85; H, 5.84; N, 10.14; S, 11.60%; ν_{max} (KBr disc, $CHCl_3$) 3414 (NH), 3335 (NH), 2210 (CN), 1683 (C=O), 1616 (C=C), 1246 (C–O–C); δ_H (400 MHz, $CDCl_3$) 7.36 (1H, d, J=5.1 Hz, arom.), 7.11 (1H, d, J=3.4 Hz, arom.), 7.02 (1H, dd, J=5.0, 3.6 Hz, arom.), 6.35 (1H, d, J=6.0 Hz, H2), 5.84 (2H, s, NH), 3.86 (1H, d, J=6.0 Hz, H3), 1.36 (9H, s, Me); *m/z* (ESI+) 277 (MH^+, %100).

3.1.4.14. *trans*-4-Cyano-5-phenyl-2-[(*E*)-2-phenylvinyl]-2,3-dihydrofuran-3-carboxamide (4a). Yield 29% (90 mg) as a yellow solid, mp 182–184 °C (*n*-hexane/EtOAc). Found: C, 75.72; H, 5.36; N, 8.68. $C_{20}H_{16}N_2O_2$ requires C, 75.93; H, 5.10; N, 8.86%; ν_{max} (KBr disc) 3403 (NH), 3310 (NH), 2206 (CN), 1674 (C=O), 1616

(C═C), 1234 (C–O–C), 752, 689; δ_H (400 MHz, $CDCl_3$) 7.94 (2H, d, J=7.6 Hz), 7.48–7.21 (8H, m, arom.), 6.86 (1H, s, NH), 6.70 (1H, d, J=15.6 Hz, Ha), 6.25 (1H, dd, J=15.6, 7.2 Hz, Hb), 6.14 (1H, s, NH), 5.75 (1H, t, J=7.2 Hz, H2), 3.87 (1H, d, J=7.2 Hz, H3); δ_C (100 MHz, $CDCl_3$) 171.4 (C═O), 167.4 (C5), 136.1, 134.1, 132.7, 129.8, 129.4, 129.1, 127.8, 127.6, 127.5, 126.7, 117.2 (CN), 87.5 (C2), 82.0 (C4), 55.5 (C3); m/z (ESI+) 317 (MH^+, %100).

3.1.4.15. *cis*-4-Cyano-5-phenyl-2-[(*E*)-2-phenylvinyl]-2,3-dihydrofuran-3-carboxamide (5a). δ_H (400 MHz, $CDCl_3$) 7.94 (2H, d, J=7.6 Hz), 7.48–7.21 (8H, m, arom.), 6.66 (1H, s, NH), 6.73 (1H, d, J=15.6 Hz, Ha), 6.39 (1H, dd, J=16.0, 7.4 Hz, Hb), 6.05 (1H, s, NH), 5.52 (1H, t, J=9.6 Hz, H2), 4.13 (1H, d, J=10.0 Hz, H3); δ_C (100 MHz, DMSO-d_6) 170.0 (C═O), 168.0 (C5), 136.3, 135.5, 132.6, 129.7, 129.4, 129.1, 128.0, 127.5, 127.4, 123.7, 117.7 (CN), 86.0 (C2), 82.6 (C4), 54.0 (C3).

3.1.4.16. *trans*-5-(4-Chlorophenyl)-4-cyano-2-[(*E*)-2-phenylvinyl]-2,3-dihydrofuran-3-carboxamide (4b). Yield 40% (140 mg) as a white solid, mp 211–213 °C (*n*-hexane/EtOAc). Found: C, 68.73; H, 4.25; N, 8.08. $C_{20}H_{15}ClN_2O_2$ requires C, 68.48; H, 4.31; N, 7.99%; ν_{max} (KBr disc) 3395 (NH), 3306 (NH), 3204, 2208 (CN), 1674 (C═O), 1616 (C═C), 1232 (C–O–C), 835, 754 (C–Cl); δ_H (400 MHz, $CDCl_3$) 7.96 (2H, d, J=8.4 Hz, arom.), 7.46–7.29 (7H, m, arom.), 6.78 (1H, d, J=15.6 Hz, Ha), 6.29 (1H, dd, J=15.6, 7.2 Hz, Hb), 5.90 (1H, s, NH), 5.87 (1H, t, J=7.2 Hz, H2), 5.71 (1H, s, NH), 3.85 (1H, d, J=7.2 Hz, H3); δ_C (100 MHz, DMSO-d_6) 171.2 (C═O), 168.4 (C5), 166.1, 137.3, 136.1, 134.2, 130.0, 129.4, 129.3, 129.2, 127.6, 126.6, 117.0 (CN), 87.7 (C2), 82.6 (C4), 55.6 (C3); m/z (ESI+) 351 (MH^+, %100).

3.1.4.17. *cis*-5-(4-Chlorophenyl)-4-cyano-2-[(*E*)-2-phenylvinyl]-2,3-dihydrofuran-3-carboxamide (5b). δ_H (400 MHz, $CDCl_3$) 7.96 (2H, d, J=8.4 Hz, arom.), 7.46–7.29 (7H, m, arom.), 6.80 (1H, d, J=15.6 Hz, Ha), 6.40 (1H, dd, J=15.6, 8.0 Hz, Hb), 5.75 (1H, s, NH), 5.68 (1H, s, NH), 5.61 (1H, t, J=9.6 Hz, H2), 4.12 (1H, d, J=10.0 Hz, H3); δ_C (100 MHz, DMSO-d_6) 69.8 (C═O), 168.4 (C5), 166.8, 137.2, 136.3, 135.6, 129.9, 129.5, 129.3, 129.1, 127.5, 126.7, 117.4 (CN), 86.1 (C2), 83.3 (C4), 54.1 (C3).

3.1.4.18. *trans*-4-Cyano-2-[(*E*)-2-phenylvinyl]-5-(2-thienyl)-2,3-dihydrofuran-3-carboxamide (4c). Yield 31% (200 mg) as a yellow solid, mp 235–237 °C (*n*-hexane/EtOAc). Found: C, 66.83; H, 4.06; N, 8.67; S, 9.88. $C_{18}H_{14}N_2O_2S$ requires C, 67.06; H, 4.38; N, 8.69; S, 9.95%; ν_{max} (KBr disc) 3412 (NH), 3310 (NH), 3208, 2208 (CN), 1674 (C═O), 1612 (C═C), 1213 (C–O–C), 962, 750, 712; δ_H (400 MHz, $CDCl_3$) 7.93 (1H, dd, J=3.6, 0.8 Hz, arom.), 7.58 (1H, dd, J=4.8, 0.8 Hz, arom.), 7.43–7.26 (5H, m, arom.), 7.17 (1H, dd, J=4.8, 3.6 Hz, arom.), 6.78 (1H, d, J=15.6 Hz, Ha), 6.29 (1H, dd, J=16.0, 7.6 Hz, Hb), 5.86 (2H, t, J=6.8 Hz, H2 and NH, overlap), 5.61 (1H, s, NH), 3.84 (1H, d, J=6.8 Hz, H3); δ_C (100 MHz, DMSO-d_6) 171.2 (C═O), 162.4 (C5), 136.1, 134.4, 132.4, 131.1, 129.6, 129.4, 129.3, 129.2, 127.6, 126.5, 116.9 (CN), 88.2 (C2), 80.3 (C4), 55.2 (C3); m/z (ESI+) 323 (MH^+, %100).

3.1.4.19. *cis*-4-Cyano-2-[(*E*)-2-phenylvinyl]-5-(2-thienyl)-2,3-dihydrofuran-3-carboxamide (5c). δ_H (400 MHz, $CDCl_3$) 7.98 (1H, dd, J=4.0, 0.4 Hz, arom.), 7.60 (1H, dd, J=4.8, 0.4 Hz, arom.), 7.43–7.26 (5H, m, arom.), 7.17 (1H, dd, J=4.8, 3.2 Hz, arom.), 6.81 (1H, d, J=15.2 Hz, Ha), 6.37 (1H, dd, J=16.0, 8.0 Hz, Hb), 5.78 (1H, s, NH), 5.65 (2H, m, H2 and NH, overlap), 4.12 (1H, d, J=10.0 Hz, H3); δ_C (100 MHz, DMSO-d_6) 170.5 (C═O), 160.1 (C5), 137.2, 134.9, 131.7, 131.1, 129.8, 129.1, 129.3, 129.2, 127.6, 126.6, 117.3 (CN), 87.5 (C2), 81.2 (C4), 53.6 (C3).

3.1.4.20. *trans*-3-Cyano-5-[(*E*)-2-phenylvinyl]-4,5-dihydro-2,2′-bifuran-4-carboxamide (4d). Yield 24% (140 mg) as a yellow solid, mp 231–233 °C (*n*-hexane/EtOAc). Found: C, 70.45; H, 4.32; N, 9.27. $C_{18}H_{14}N_2O_3$ requires C, 70.58; H, 4.61; N, 9.15%; ν_{max} (KBr disc) 3352 (NH), 3194 (NH), 2210 (CN), 1678 (C═O), 1649 (C═C), 1124 (C–O–C), 754, 691; δ_H (400 MHz, $CDCl_3$) 7.57 (1H, d, J=1.6 Hz, arom.), 7.35 (1H, d, J=6.8 Hz, arom.), 7.30–7.21 (4H, m, arom.), 7.01 (1H, d, J=3.2 Hz, arom.), 6.80 (1H, s, NH), 6.70 (1H, d, J=15.6 Hz, Ha), 6.50 (1H, dd, J=3.6, 1.6 Hz, arom.), 6.23 (1H, dd, J=16.0, 7.6 Hz, Hb), 6.06 (1H, s, NH), 5.75 (1H, t, J=7.0 Hz, H2), 3.82 (1H, d, J=6.8 Hz, H3); δ_C (100 MHz, $CDCl_3$) 170.8 (C═O), 159.0 (C5), 145.9, 135.4, 134.4, 128.7, 126.9, 124.8, 115.9, 115.2 (CN), 112.1, 87.3 (C2), 78.3 (C4), 54.9 (C3); m/z (ESI+) 307 (MH^+, %100).

3.1.4.21. *cis*-3-Cyano-5-[(*E*)-2-phenylvinyl]-4,5-dihydro-2,2′-bifuran-4-carboxamide (5d). δ_H (400 MHz, $CDCl_3$) 7.57 (1H, d, J=1.6 Hz, arom.), 7.35 (1H, d, J=6.8 Hz, arom.), 7.30–7.21 (4H, m, arom.), 7.02 (1H, d, J=3.6 Hz, arom.), 6.72 (1H, d, J=16.0 Hz, Ha), 6.63 (1H, s, NH), 6.50 (1H, dd, J=3.6, 1.2 Hz, arom.), 6.36 (1H, dd, J=16.0, 8.0 Hz, Hb), 5.98 (1H, s, NH), 5.52 (1H, t, J=9.6 Hz, H2), 4.10 (1H, d, J=10.0 Hz, H3); δ_C (100 MHz, $CDCl_3$) 169.8 (C═O), 160.1 (C5), 143.1, 136.4, 135.5, 128.7, 127.1, 121.6, 115.7, 115.4 (CN), 112.1, 86.9 (C2), 79.6 (C4), 53.7 (C3).

3.1.4.22. *trans*-5-(1-Benzofuran-2-yl)-4-cyano-2-[(*E*)-2-phenylvinyl]-2,3-dihydrofuran-3-carboxamide (4e). Yield 30% (110 mg) as a white solid, mp 227–229 °C (*n*-hexane/EtOAc). Found: C, 74.82; H, 4.26; N, 7.58. $C_{22}H_{16}N_2O_3$ requires C, 74.15; H, 4.53; N, 7.86%; ν_{max} (KBr disc) 3406 (NH), 3318 (NH), 2212 (CN), 1676 (C═O), 1618 (C═C), 1253 (C–O–C), 750, 691; δ_H (400 MHz, $CDCl_3$) 7.74 (1H, s, NH), 7.62 (3H, m, arom.), 7.49 (1H, d, J=8.33 Hz, arom.), 7.37–7.20 (6H, m, arom.), 6.89 (1H, s, NH), 6.68 (1H, d, J=15.8 Hz, Ha), 6.30 (1H, dd, J=15.8, 7.5 Hz, Hb), 5.68 (1H, t, J=7.5 Hz, H2), 3.97 (1H, d, J=7.5 Hz, H3); δ_C (100 MHz, $CDCl_3$) 171.0 (C═O), 158.2 (C5), 155.5, 144.5, 136.2, 134.7, 129.4, 129.3, 128.3, 127.6, 127.5, 126.2, 124.9, 123.6, 115.8 (CN), 112.4, 111.4, 88.7 (C2), 84.5 (C4), 55.2 (C3); m/z (ESI+) 357 (MH^+, %100).

3.1.4.23. *cis*-5-(1-Benzofuran-2-yl)-4-cyano-2-[(*E*)-2-phenylvinyl]-2,3-dihydrofuran-3-carboxamide (5e). δ_H (400 MHz, $CDCl_3$) 7.62 (3H, m, arom.), 7.49 (1H, d, J=8.33 Hz, arom.), 7.44 (1H, s, NH), 7.37–7.20 (7H, m, arom.), 6.75 (2H, m, Ha and NH, overlap), 6.38 (1H, dd,

J=16.0, 8.5 Hz, Hb), 5.58 (1H, t, J=10.3 Hz, H2), 4.22 (1H, d, J=10.3 Hz, H3); δ_C (100 MHz, $CDCl_3$) 169.7 (C=O), 158.9 (C5), 155.5, 144.5, 136.0, 135.2, 129.5, 129.1, 128.5, 127.7, 127.5, 126.4, 125.0, 123.2, 116.4 (CN), 112.4, 111.2, 87.2 (C2), 83.7 (C4), 53.7 (C3).

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