One-pot Synthesis of Substituted 2,5-Dihydrofurans from \( \beta \)-Oxo Amides and Cinnamaldehydes

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Electronic Supplementary Material (ESI)

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I . General

All reagents and substrates 1 and 2 were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. $^1$H NMR and $^{13}$C NMR spectra were recorded at 25 °C at 300 MHz and 100 MHz, respectively, with TMS as internal standard. IR spectra (KBr) were recorded on FTIR-spectrophotometer in the range of 400-4000 cm$^{-1}$.

II. Synthesis of substrates 1

Substrates 1a-1k were purchased from commercial sources and used without treatment. For the preparation of 1l, see: Z. Zhang, Y. Liu, L. Ling, Y. Li, Y. Dong, M. Gong, X. Zhao, Y. Zhang, J. Wang, J. Am. Chem. Soc. 2011, 133, 4330. For the preparation of 1m and 1p, see: M. Sechi, U. Azzena, M. P. Delussu, R. Dallocchio, A. Dessì, A. Cosseddu, N. Pala, N. Neamati, Molecules 2008, 13, 2442. For the preparation of 1n and 1o, see: M. Habash, M. O. Taha, Bioorg. Med. Chem. 2011, 19, 4746.

III. Synthesis and analytical data of substrate 3

1. Preparation of substrate 3aa.

Typical procedure for the synthesis of substituted Knoevenagel condensation adducts 3 (3aa as an example): To a 100 mL round-bottomed flask was added 3-oxo-N-(p-tolyl)butanamide 1a (10.0 mmol), 3-(4-methoxyphenyl)acrylaldehyde 2a (10.0 mmol), piperidine (5 % mmol 0.5 mmol) and ethyl acetate (30 mL). Then the mixture was heated under reflux for 3.5 h, and cooled to room temperature. The resulting mixture was slowly poured into saturated aqueous NaCl (100 mL), and extracted with dichloromethane (3 × 20 mL). The combined organic phase was washed with water and dried over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate 10:1, v/v) to give 84% yield of 3aa as yellow solid.

2. Analytical data of substrate 3aa

[Chemical structure diagram]

2-Acetyl-5-(4-methoxyphenyl)-N-phenylpenta-2,4-dienamide (3aa)

Yellow solid: m.p. 127-128 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.55 (s, 3H), 3.86 (s, 3H), 6.92 (d, $J = 8.7$ Hz, 2H), 7.11 (d, $J = 6.0$ Hz, 1H), 7.15 (s, 1H), 7.36 (t, $J = 8.7$ Hz, 2H), 7.59 (d, $J = 8.7$ Hz, 2H), 7.64-7.68 (m, 3H), 8.25-8.34 (dd, $J_1 = 15.3$ Hz, $J_2 = 3.9$ Hz, 1H), 10.41 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 27.6, 55.4, 114.4, 120.6, 123.56, 124.2, 128.6, 128.9, 130.2, 138.1, 148.0, 153.2, 161.6, 162.8, 200.4; Anal. Calcd for C$_{20}$H$_{19}$NO$_3$: C, 74.75; H, 5.96; N, 4.36; Found: C, 74.43; H, 5.77; N, 4.75.
. Synthesis and analytical data of products 4

1. Preparation of products 4aa-fe.

Typical procedure for the synthesis of substituted dihydrofurans 4 (4aa as an example): To a 100 mL round-bottomed flask was added 3-oxo-N-(p-tolyl)butanamide 1a (1.0 mmol), 3-(4-methoxyphenyl)acrylaldehyde 2a (1.0 mmol), piperidine (5 % mmol 0.05 mmol) and 1,3-dichloropropane (10 mL). Then the mixture was heated under reflux for 3.5 h, and cooled to room temperature. To a solution of mixture was added dropwise a solution of PIDA (0.386 g, 1.2 mmol) and BF$_3$·Et$_2$O (0.32 ml, 3.0 mmol) in dry CH$_2$ClCH$_2$Cl (10.0 mL) at 0 ºC under stirring. Then the mixture was stirred at room temperature for 5.0 h when 3aa was consumed (monitored by TLC). The reaction mixture was then poured into aqueous NaHCO$_3$ (50 mL), and extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic phase was washed with water (3 × 20 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, petroleum ether: diethyl ether = 8:1) to give 4aa (0.236 g, 74 %).


1-(5-(4-Methoxybenzylidene)-2-(phenylimino)-2,5-dihydrofuran-3-yl)ethanone (4aa)
Orange solid: m.p. 133-134 ; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.74 (s, 3H), 3.84 (s, 3H), 6.03 (s, 1H), 6.85 (d, $J$ = 9.0 Hz, 2H), 7.17-7.22 (m, 1H), 7.42 (m, 4H), 7.64 (d, $J$ = 9.0 Hz, 2H), 7.73 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 29.7, 55.3, 113.8, 114.4, 123.5, 124.8, 126.4, 128.7, 131.9, 132.1, 141.6, 145.8, 148.5, 154.7, 160.5, 193.3; IR (KBr, cm$^{-1}$): 2924, 2854, 1668, 1543, 1290, 1166, 769, 606; Anal. Calcd for C$_{20}$H$_{17}$NO$_3$: C, 75.22; H, 5.37; N, 4.39; Found: C, 75.43; H, 5.29; N, 4.26.

1-(5-(4-Methoxybenzylidene)-2-(p-tolylimino)-2,5-dihydrofuran-3-yl)ethanone (4ba)
Orange solid: m.p. 155-156 ; $^1$H NMR (400 MHz, DMSO): $\delta$ 2.35 (s, 3H), 2.62 (s, 3H), 3.81 (s, 3H), 6.41 (s, 1H), 6.98 (d, $J$ = 8.8 Hz, 2H), 7.25-7.30 (m, 4H), 7.69 (d, $J$ = 8.8 Hz, 2H), 8.10 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 21.1, 29.9, 55.4, 113.4, 114.5, 123.8, 126.5, 129.4, 131.8, 132.4, 134.7, 141.3, 142.9, 148.7, 154.1, 160.4, 193.6; IR (KBr, cm$^{-1}$): 2923, 2854, 1677, 1658, 1600, 1542, 1257, 1165, 821; Anal. Calcd for C$_{21}$H$_{19}$NO$_3$: C, 75.66; H, 5.74; N, 4.20; Found: C, 76.31; H, 5.83; N, 4.35.
1-(5-(4-Methoxybenzylidene)-2-(o-tolylimino)-2,5-dihydrofuran-3-yl)ethanone (4ca)
Orange solid: m.p. 129-130 ; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.35 (s, 3H), 2.77 (s, 3H), 3.82 (s, 3H), 6.02 (s, 1H), 6.83 (d, $J$ = 9.0 Hz, 2H), 7.08-7.13 (m, 1H), 7.21-7.27 (m, 2H), 7.42 (d, $J$ = 9.0 Hz, 1H), 7.60 (d, $J$ = 9.0 Hz, 2H), 7.74 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 18.5, 29.7, 30.0, 55.3, 113.8, 114.4, 124.7, 125.9, 126.4, 130.4, 131.9, 132.0, 141.7, 144.6, 148.5, 154.1, 160.4, 193.4; IR (KBr, cm$^{-1}$): 2924, 2854, 1660, 1542, 1253, 1167, 830; Anal. Calcd for C$_{21}$H$_{19}$NO$_3$: C, 75.66; H, 5.74; N, 4.20; Found: C, 75.01; H, 5.63; N, 4.07.

1-(2-(2,4-Dimethylphenylimino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4da)
Orange solid: m.p. 112-113 ; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.33 (s, 3H), 2.37 (s, 3H), 2.76 (s, 3H), 3.83 (s, 3H), 6.00 (s, 1H), 6.86 (d, $J$ = 9.0 Hz, 2H), 7.08 (t, $J$ = 8.1Hz, 2H), 7.43 (d, $J$ = 8.1 Hz, 1H), 7.65 (d, $J$ = 9.0 Hz, 2H), 7.72 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 18.5, 21.0, 30.00, 55.3, 113.4, 114.4, 121.4, 126.5, 131.2, 131.8, 132.2, 132.7, 134.4, 141.3, 141.6, 148.6, 153.6, 160.3, 193.6; IR (KBr, cm$^{-1}$): 2922, 2854, 1663, 1540, 1249, 1165, 972, 815; Anal. Calcd for C$_{22}$H$_{21}$NO$_3$: C, 76.06; H, 6.09; N, 4.03; Found: C, 75.55; H, 6.15; N, 4.16.

1-(2-(4-Chlorophenylimino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4ea)
Orange solid: m.p. 152-153 ; $^1$H NMR (400 MHz, DMSO): $\delta$ 2.61 (s, 3H), 3.81 (s, 3H), 6.46 (s, 1H), 6.99 (d, $J$ = 8.8 Hz, 2H), 7.36 (d, $J$ = 8.8 Hz, 2H), 7.51 (d, $J$ = 8.8 Hz, 2H), 7.65 (d, $J$ = 8.8 Hz, 2H), 8.14 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 29.8, 55.4, 114.4, 114.5, 124.9, 126.2, 128.8, 130.0, 131.9, 141.9, 144.3, 148.3, 155.0, 160.7, 193.1; IR (KBr, cm$^{-1}$): 2924, 2853, 1662, 1584, 1257, 1169, 998, 806; Anal. Calcd for C$_{20}$H$_{16}$ClNO$_3$: C, 67.90; H, 4.56; N, 3.96; Found: C, 68.54; H, 4.48; N, 4.21.
1-(2-(2-Chlorophenylimino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4fa)
Orange solid: m.p. 169-170; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 2.79 (s, 3H), 3.83 (s, 3H), 6.08 (s, 1H), 6.83 (d, \(J = 9.0\) Hz, 2H), 7.09-7.15 (m, 1H), 7.28-7.31 (m, 1H), 7.43-7.47 (m, 2H), 7.57 (d, \(J = 9.0\) Hz, 2H), 7.77 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 29.7, 30.0, 55.3, 114.4, 114.9, 123.1, 125.4, 126.2, 126.9, 129.9, 131.6, 132.1, 142.3, 143.4, 148.3, 160.6, 193.3; IR (KBr, cm\(^{-1}\)): 2924, 2854, 1660, 1540, 1254, 1166, 869, 756; Anal. Calcd for C\(_{20}\)H\(_{11}\)ClNO\(_3\): C, 67.90; H, 4.56; N, 3.96; Found: C, 67.03; H, 4.42; N, 4.01.

Crystal data for 4fa: C\(_{20}\)H\(_{16}\)ClNO\(_3\), Red crystal, \(M = 353.08\), Orthorhombic, Pca21, \(a =13.1628(8)\) Å, \(b =11.5556(7)\) Å, \(c =22.0722(13)\) Å, \(\alpha = 90.00^{\circ}\), \(\beta = 90.00^{\circ}\), \(\gamma = 90.00^{\circ}\), \(V = 3357.3(3)\) Å\(^3\), \(Z = 8\), \(T = 293(2)\) K, F000 = 1569. CCDC deposition number: 794625. These data can be obtained free of charge via www.ccdc.cam.ac.uk/contents/retrieving.html (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

1-(5-(4-Methoxybenzylidene)-2-((4-methoxyphenyl)imino)-2,5-dihydrofuran-3-yl)ethanone (4ga)
Red solid: m.p. 126-128; \(^1\)H NMR (300 MHz, DMSO): \(\delta\) 2.62 (s, 3H), 3.81 (s, 3H), 3.82 (s, 3H), 6.36 (s, 1H), 7.01 (d, \(J = 4.8\) Hz, 2H), 7.04 (d, \(J = 4.8\) Hz, 2H), 7.41 (d, \(J = 9.0\) Hz, 2H), 7.72 (d, \(J = 9.0\) Hz, 2H), 8.07 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 29.5, 55.3, 55.4, 113.2, 114.1, 114.6, 125.1, 126.2, 131.2, 131.5, 138.1, 141.9, 148.4, 153.2, 156.7, 160.0, 192.5; Anal. Calcd for C\(_{21}\)H\(_{19}\)NO\(_4\): C, 72.19; H, 5.48; N, 4.01; Found: C, 73.01; H, 5.32; N, 4.11.

1-(5-(4-Methoxybenzylidene)-2-((2-methoxyphenyl)imino)-2,5-dihydrofuran-3-yl)ethanone (4ha)
Red solid: m.p. 155-157; \(^1\)H NMR (300 MHz, DMSO): \(\delta\) 2.62 (s, 3H), 3.76 (s, 3H), 3.78 (s, 3H),
6.38 (s, 1H), 6.89 (d, \( J = 8.7 \) Hz, 2H), 6.98–7.03 (m, 1H), 7.11–7.20 (m, 3H), 7.54 (d, \( J = 8.7 \) Hz, 2H), 8.11 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 29.4, 55.3, 55.4, 111.9, 113.7, 114.4, 120.4, 122.4, 125.2, 126.1, 130.0, 131.7, 135.3, 143.0, 148.0, 150.9, 154.8, 160.0, 192.2; Anal. Calcd for C\(_{21}\)H\(_{19}\)NO\(_4\): C, 72.19; H, 5.48; N, 4.01; Found: C, 72.77; H, 5.36; N, 4.17.

1-(5-(4-Methoxybenzylidene)-2-((4-(trifluoromethyl)phenyl)imino)-2,5-dihydrofuran-3-yl)ethanone (4ia)

Red solid: m.p. 120–122; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 2.72 (s, 3H), 3.84 (s, 3H), 6.09 (s, 1H), 6.85 (d, \( J = 9.0 \) Hz, 2H), 7.42 (d, \( J = 9.0 \) Hz, 2H), 7.58 (d, \( J = 9.0 \) Hz, 2H), 7.67 (d, \( J = 9.0 \) Hz, 2H), 7.78 (s, 1H); \(^{13}\)C NMR (100 MHz, DMSO): \( \delta \) 29.4, 55.3, 114.6, 115.2, 123.3, 124.5 (q, \( J_{CF} = 31 \) Hz), 124.7 (q, \( J_{CF} = 270 \) Hz), 126.0 (d, \(^3\)J\(_{CF} = 3 \) Hz), 130.2, 131.9, 143.7, 147.9, 149.6, 155.8, 160.3, 191.9; Anal. Calcd for C\(_{21}\)H\(_{16}\)F\(_3\)NO\(_3\): C, 65.12; H, 4.16; N, 3.62; Found: C, 64.82; H, 4.09; N, 3.30.

1-(2-(Benzylimino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4ja)

Orange solid: m.p. 76–78; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 2.68 (s, 3H), 3.87 (s, 3H), 4.90 (s, 2H), 6.20 (s, 1H), 6.97 (d, \( J = 9.0 \) Hz, 2H), 7.30 (s, 1H), 7.37 (t, \( J = 7.5 \) Hz, 2H), 7.49 (d, \( J = 7.5 \) Hz, 2H), 7.70 (d, \( J = 9.0 \) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 29.6, 51.9, 55.0, 112.4, 113.7, 114.2, 126.4, 127.2, 128.1, 128.3, 131.6, 141.5, 159.9, 193.2; Anal. Calcd for C\(_{21}\)H\(_{19}\)NO\(_3\): C, 75.66; H, 5.74; N, 4.20; Found: C, 75.87; H, 5.68; N, 4.15.

(5-(4-Methoxybenzylidene)-2-(phenylimino)-2,5-dihydrofuran-3-yl)(phenyl)methanone (4ka)

Red solid: m.p. 133–134; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 3.84 (s, 3H), 5.99 (s, 1H), 6.86 (d, \( J = 8.0 \) Hz, 2H), 7.17 (q, \( J = 4.0 \) Hz, 1H), 7.38 (d, \( J = 4.0 \) Hz, 4H), 7.45 (s, 1H), 7.51 (t, \( J = 8.0 \) Hz, 2H), 7.61–7.66 (m, 3H), 7.99 (d, \( J = 8.0 \) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 55.3, 112.6, 114.4, 123.6, 124.8, 126.4, 128.4, 128.6, 129.8, 131.6, 132.0, 133.5, 137.0, 141.0, 145.8, 148.7, 154.9, 160.3, 188.8; Anal. Calcd for C\(_{25}\)H\(_{19}\)NO\(_3\): C, 78.72; H, 5.02; N, 3.67; Found: C,
87.53; H, 5.11; N, 3.49.

**Ethyl 5-(4-methoxybenzylidene)-2-((4-methoxyphenyl)imino)-2,5-dihydrofuran-3-carboxylate (4la)**

Orange solid: m.p. 140-142; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.40 (t, $J = 7.2$ Hz, 3H), 3.84 (s, 3H), 3.86 (s, 3H), 4.39 (q, $J = 7.2$ Hz, 2H), 5.96 (s, 1H), 6.88 (d, $J = 8.8$ Hz, 2H), 7.34 (d, $J = 8.8$ Hz, 2H), 7.47 (d, $J = 8.8$ Hz, 2H), 7.73 (d, $J = 8.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.2, 55.4(1), 55.4(2), 61.3, 112.6, 113.8, 114.4, 125.0, 125.4, 126.4, 131.6, 139.0, 142.4, 148.4, 157.0, 160.3, 161.0; Anal. Calcd for C$_{22}$H$_{21}$NO$_5$: C, 69.64; H, 5.58; N, 3.69; Found: C, 70.07; H, 5.61; N, 3.53.

**5-(4-Methoxybenzylidene)-N-phenyl-2-(phenylimino)-2,5-dihydrofuran-3-carboxamide (4ma)**

Orange solid: m.p. 214-215; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 3.78 (s, 3H), 6.10 (s, 1H), 6.83 (d, $J = 8.8$ Hz, 2H), 7.08 (t, $J = 8.0$ Hz, 1H), 7.19-7.22 (m, 1H), 7.31 (t, $J = 8.0$ Hz, 2H), 7.40 (t, $J = 8.0$ Hz, 2H), 7.48 (d, $J = 8.0$ Hz, 2H), 7.64 (d, $J = 8.8$ Hz, 2H), 7.68 (d, $J = 8.0$ Hz, 2H), 7.94 (s, 1H), 11.17 (s, 1H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 55.4, 114.4, 114.5, 119.9, 124.0, 124.5, 125.7, 126.1, 127.0, 129.0, 132.0, 138.0, 141.3, 144.1, 148.4, 156.0, 157.9, 160.7; IR (KBr, cm$^{-1}$): 3482, 1784, 1677, 1600, 1510, 1498, 1255, 754; Anal. Calcd for C$_{25}$H$_{20}$N$_2$O$_3$: C, 75.74; H, 5.08; N, 7.07. Found: C, 75.46; H, 4.89; N, 6.91.

Crystal data for **4ma**: C$_{25}$H$_{20}$N$_2$O$_3$, Red crystal, $M = 396.43$, triclinic, P-1, $a = 5.4633(7)$ Å, $b = 11.7064(14)$ Å, $c = 15.7002(19)$ Å, $\alpha = 86.485(2)$ $^\circ$, $\beta = 85.610(2)$ $^\circ$, $\gamma = 81.447(2)$ $^\circ$, $V = 988.8(2)$ Å$^3$, $Z = 2$, $T = 293(2)$ K, F000 = 296. CCDC deposition number: 884905. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).
N-(2-chlorophenyl)-2-((2-chlorophenyl)imino)-5-(4-methoxybenzylidene)-2,5-dihydrofuran-3-carboxamide (4na)
Orange solid: m.p. 203-204; $^1$H NMR (400 MHz, DMSO): $\delta$ 3.79 (s, 3H), 6.62 (s, 1H), 6.94 (d, $J = 8.0$ Hz, 2H), 7.19 (t, $J = 7.2$ Hz, 1H), 7.27 (t, $J = 7.2$ Hz, 1H), 7.41 (t, $J = 7.2$ Hz, 1H), 7.47 (t, $J = 7.2$ Hz, 1H), 7.53-7.62 (m, 5H), 8.37 (s, 1H), 8.45 (d, $J = 8.0$ Hz, 1H), 11.08 (s, 1H); $^{13}$C NMR (100 MHz, DMSO): $\delta$ 55.4, 114.7, 116.2, 122.1, 123.0, 123.7, 124.9, 125.5, 126.3, 127.7, 127.8, 129.5, 129.8, 132.2, 134.5, 144.2, 150.7, 157.1, 157.5, 160.6; Anal. Calcd for C$_{25}$H$_{18}$Cl$_{2}$N$_{2}$O$_{3}$: C, 64.53; H, 3.90; N, 6.02; Found: C, 64.81; H, 3.75; N, 5.86.

5-(4-Methoxybenzylidene)-N-(p-tolyl)-2-(p-tolylimino)-2,5-dihydrofuran-3-carboxamide (4oa)
Orange solid: m.p. 191-193; $^1$H NMR (300 MHz, DMSO): $\delta$ 2.30 (s, 3H), 2.38 (s, 3H), 3.83 (s, 3H), 6.55 (s, 1H), 7.06 (d, $J = 9.0$ Hz, 2H), 7.20 (d, $J = 9.0$ Hz, 2H), 7.34 (d, $J = 9.0$ Hz, 2H), 7.52 (d, $J = 9.0$ Hz, 2H), 7.63 (d, $J = 9.0$ Hz, 2H), 7.75 (d, $J = 9.0$ Hz, 2H), 8.20 (s, 1H), 11.08 (s, 1H); $^{13}$C NMR (100 MHz, DMSO): $\delta$ 19.5, 19.7, 54.8, 113.2, 114.2, 119.1, 123.0, 125.4, 126.2, 128.6, 128.7, 130.9, 132.8, 134.3, 134.8, 140.5, 140.8, 147.8, 154.6, 156.5, 159.9; Anal. Calcd for C$_{27}$H$_{24}$N$_{2}$O$_{3}$: C, 76.39; H, 5.70; N, 6.60; Found: C, 76.25; H, 5.79; N, 6.77.

5-(4-Methoxybenzylidene)-2-((2-methoxyphenyl)imino)-N-phenyl-2,5-dihydrofuran-3-carboxamide (4pa)
Orange solid: m.p. 209-210; $^1$H NMR (400 MHz, DMSO): $\delta$ 3.83 (s, 3H), 3.92 (s, 3H), 6.57 (s, 1H), 7.04 (d, $J = 8.0$ Hz, 2H), 7.11-7.21 (m, 3H), 7.27-7.31 (m, 1H), 7.43 (t, $J = 8.0$ Hz, 2H), 7.73-7.75 (m, 5H), 8.22 (s, 1H), 11.60 (s, 1H); $^{13}$C NMR (100 MHz, DMSO): $\delta$ 55.0, 55.5, 112.2, 113.9, 114.3, 119.0, 120.2, 122.5, 123.6, 125.5, 125.9, 126.2, 128.5, 131.3, 137.7, 141.0, 148.0, 152.8, 154.8, 156.9, 160.0; Anal. Calcd for C$_{26}$H$_{22}$N$_{2}$O$_{4}$: C, 73.23; H, 5.20; N, 6.57; Found: C,
72.59; H, 5.12; N, 6.73.

1-(2-((2-Chlorophenyl)imino)-5-(2-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4fb)
Red solid: m.p. 147-149 ; \( ^1H \) NMR (400 MHz, DMSO): \( \delta \) 2.65 (s, 3H), 3.85 (s, 3H), 6.79 (s, 1H), 6.82 (t, \( J = 8.0 \) Hz, 1H), 7.07(d, \( J = 8.0 \) Hz, 1H), 7.18-7.22 (m, 1H), 7.31-7.35 (m, 1H), 7.39-7.44 (m, 2H), 7.55 (d, \( J = 8.0 \) Hz, 1H), 7.71 (d, \( J = 8.0 \) Hz, 1H), 8.33 (s, 1H); \( ^{13}C \) NMR (100 MHz, CDCl3): \( \delta \) 29.7, 30.0, 55.6, 108.6, 110.6, 121.0, 122.4, 123.1, 125.4, 126.9, 129.8, 130.7, 130.9, 132.1, 142.7, 143.3, 149.5, 157.6, 193.3; IR (KBr, cm\(^{-1}\)): 2924, 2853, 1668, 1555, 1248, 1021, 750; Anal. Calcd for C\(_{20}\)H\(_{16}\)ClNO\(_3\): C, 67.90; H, 4.56; N, 3.96. Found: C, 69.77; H, 4.62; N, 3.82.

1-(2-((2-Chlorophenyl)imino)-5-(4-methylbenzylidene)-2,5-dihydrofuran-3-yl)ethanone (4fc)
Red solid: m.p. 111-113 ; \( ^1H \) NMR (300 MHz, CDCl3): \( \delta \) 2.35 (s, 3H), 2.80 (s, 3H), 6.10 (s, 1H), 7.11-7.16(m, 3H), 7.28-7.34(m, 1H), 7.44-7.50(m, 3H), 7.53(s, 1H), 7.79(s, 1H); \( ^{13}C \) NMR (100 MHz, CDCl3): \( \delta \) 21.5, 30.0, 114.9, 123.1, 125.5, 126.9, 129.6, 129.9, 130.3, 132.4, 140.0, 142.3, 143.4, 149.7, 155.6, 193.2; Anal. Calcd for C\(_{20}\)H\(_{16}\)ClNO\(_2\): C, 71.11; H, 4.77; N, 4.15. Found: C, 70.81; H, 4.85; N, 4.29.

1-(5-(4-Chlorobenzylidene)-2-((2-chlorophenyl)imino)-2,5-dihydrofuran-3-yl)ethanone (4fd)
Orange solid: m.p. 127-129 ; \( ^1H \) NMR (300 MHz, CDCl3): \( \delta \) 2.79 (s, 3H), 6.05 (s, 1H), 7.11-7.17 (m, 1H), 7.25-7.28 (m, 2H), 7.31-7.34 (m, 1H), 7.38-7.42 (m, 1H), 7.46-7.49 (m, 2H), 7.52 (s, 1H), 7.78 (s, 1H); \( ^{13}C \) NMR (100 MHz, CDCl3): \( \delta \) 30.1, 113.0, 122.9, 125.8, 127.0, 129.1, 130.0, 131.3, 131.7, 133.1, 135.2, 142.0, 143.2, 149.9, 155.2, 193.0; Anal. Calcd for C\(_{19}\)H\(_{13}\)Cl\(_2\)NO\(_2\): C, 63.71; H, 3.66; N, 3.91; Found: C, 63.06; H, 3.41; N, 4.14.
1-(5-Benzylidene-2-(2-chlorophenylimino)-2,5-dihydrofuran-3-yl)ethanone (4fe)
Orange solid: m.p. 109-110°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.80 (s, 3H), 6.11 (s, 1H), 7.11-7.16 (m, 1H), 7.30 (d, $J$ = 3.0 Hz, 2H), 7.31-7.34 (m, 2H), 7.45-7.51 (m, 2H), 7.61 (d, $J$ = 3.0 Hz, 1H), 7.63 (d, $J$ = 3.0 Hz, 1H), 7.80 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 30.1, 114.6, 123.1, 125.6, 126.9, 128.2, 128.8, 129.3, 129.9, 130.3, 132.8, 133.2, 142.3, 143.2, 149.6, 155.3, 193.2; IR (KBr, cm$^{-1}$): 2924, 2854, 1660, 1555, 1177, 971, 748, 680; Anal. Calcd for C$_{22}$H$_{23}$NO$_3$: C, 75.62; H, 6.63; N, 4.01. Found: C, 75.47; H, 6.75; N, 4.55.

V. Synthesis and analytical data of products 5

1. Preparation of products 5fa-pa.

Typical procedure for the synthesis of substituted furan-2(5H)-ones 5 (5fa as an example): To a 50 mLL round-bottomed flask was added 1-(2-((2-chlorophenyl)imino)-5-(2-methoxybenzylidene)-2,5-dihydrofuran-3-yl)ethanone 4fa (1.0 mmol), tetrahydrofuran (5 ml), HCl (aq, 37.5 %, 2.5 mmol). Then the mixture was stirred at room temperature for 2.0 h. The resulting mixture was slowly poured into saturated aqueous NaCl (100 mL), and extracted with dichloromethane (3 × 20 mL). The combined organic phase was washed with water and dried over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate10:1, v/v) to give 89% yield of 5fa as yellow solid.

3. Analytical data of products 5fa-pa

3-Acetyl-5-(4-methoxybenzylidene)furan-2(5H)-one (5fa)
Yellow solid: m.p. 164-166°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.60 (s, 3H), 3.88 (s, 3H), 6.30 (s, 1H), 6.96 (d, $J$ = 8.7 Hz, 2H), 7.84 (d, $J$ = 8.7 Hz, 2H), 8.04 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 29.0, 55.5, 114.8, 121.1, 125.4, 131.4, 133.9, 144.8, 148.1, 161.9, 167.2, 192.0; Anal. Calcd for C$_{14}$H$_{12}$O$_4$: C, 68.85; H, 4.95; Found: C, 69.01; H, 4.87.
3-Acetyl-5-(2-methoxybenzylidene)furan-2(5H)-one (5fb)
Yellow solid: m.p. 172-175 °C; ¹H NMR (300 MHz, CDCl₃): δ 2.60 (s, 3H), 3.91 (s, 3H), 6.92 (t, J = 6.0 Hz, 2H), 7.05 (t, J = 6.0 Hz, 1H), 7.36-7.42 (m, 1H), 8.07 (s, 1H), 8.24-8.27 (dd, J₁ = 6.0 Hz, J₂ = 3.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 29.0, 55.7, 110.7, 114.81, 121.3, 121.5, 126.1, 132.5, 145.9, 148.6, 158.34, 167.1, 191.9; IR (KBr, cm⁻¹): 1783, 1594, 1673, 1484, 1367, 1251, 1185, 923, 760; Anal. Calcd for C₁₄H₁₂O₄: C, 68.85; H, 4.95; Found: C, 68.70; H, 5.03.

3-Acetyl-5-(4-methylbenzylidene)furan-2(5H)-one (5fc)
Yellow solid: m.p. 145-147 °C; ¹H NMR (300 MHz, CDCl₃): δ 2.40 (s, 3H), 2.60 (s, 3H), 6.32 (s, 1H), 7.25 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 8.1 Hz, 2H), 8.05 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 21.7, 29.0, 121.0, 126.5, 129.8, 129.9, 131.8, 141.7, 145.6, 148.3, 167.0, 191.9; IR (KBr, cm⁻¹): 1759, 1686, 1568, 1366, 1178, 1092, 810; Anal. Calcd for C₁₄H₁₂O₃: C, 73.67; H, 5.30; Found: C, 73.41; H, 5.24.

3-Acetyl-5-(4-chlorobenzylidene)furan-2(5H)-one (5fd)
Yellow solid: m.p. 132-135 °C; ¹H NMR (400 MHz, CDCl₃): δ 2.61 (s, 3H), 6.28 (s, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.4 Hz, 2H), 8.05 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 29.0, 119.0, 127.3, 129.4, 130.7, 132.7, 136.9, 146.3, 148.1, 166.6, 191.7; Anal. Calcd for C₁₃H₉ClO₃: C, 62.79; H, 3.65; Found: C, 63.01; H, 3.59.

3-Acetyl-5-benzylidenefuran-2(5H)-one (5fe)
Yellow solid: m.p. 157-159 °C; ¹H NMR (300 MHz, CDCl₃): δ 2.60 (s, 3H), 6.33 (s, 1H), 7.44 (d, J = 6.0 Hz, 3H), 7.84-7.86 (m, 2H), 8.07 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 29.1,
120.6, 127.1, 129.1, 130.8, 131.7, 132.4, 146.1, 148.3, 166.9, 191.8; Anal. Calcd for C_{13}H_{10}O_{3}: C, 72.89; H, 4.71; Found: C, 72.74; H, 4.66.

5-(4-methoxybenzylidene)-2-oxo-N-phenyl-2,5-dihydrofuran-3-carboxamide (5pa)
Yellow solid: m.p. 194-196; ¹H NMR (400 MHz, DMSO): δ 3.84 (s, 3H), 6.75 (s, 1H), 7.11 (d, J = 8.8 Hz, 2H), 7.14 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.70 (d, J = 7.6 Hz, 2H), 7.82 (d, J = 8.8 Hz, 2H), 8.47 (s, 1H), 9.81 (s, 1H); ¹³C NMR (100 MHz, DMSO): δ 55.4, 114.9, 119.5, 119.8, 121.6, 124.3, 125.2, 128.9, 133.2, 137.8, 144.5, 147.7, 157.6, 161.1, 167.6; IR (KBr, cm⁻¹): 1784, 1776, 1601, 1498, 1252, 960, 764; Anal. Calcd for C_{19}H_{15}NO_{4}: C, 71.02; H, 4.71; N, 4.36; Found: C, 70.80; H, 4.64; N, 4.51.
VI. Copies of NMR spectra of substrate 3 and products 4, 5

3aa
4ba
4da
4fa
4ga
4ia
4ka
4na
4pa
4fe
5fb
5fd
5pa