Isocyanide-Based Three-Component Synthesis of Functionalized 5-Alkylimino-2,5-dihydrofuran-3,4-dicarboxylate and Their Conversion to Substituted Furanones

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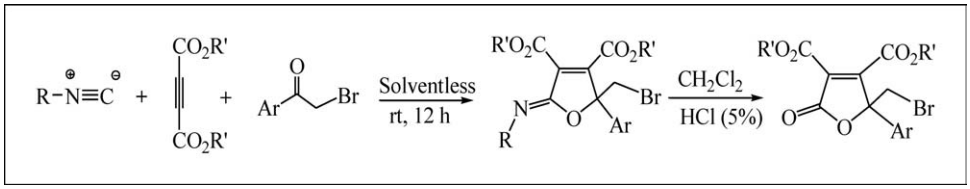

The zwitterionic 1:1 intermediates formed from alkyl isocyanides and acetylenic esters are trapped by alkyl bromides to form 5-alkylimino-2,5-dihydrofuran-3,4-dicarboxylate in relatively good yields at room temperature under solventless conditions. Hydrolysis of these compounds by HCl (5%) produced substituted furanones.

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INTRODUCTION

Furans and their derivatives play an important role in organic chemistry because of their presence as key structural units in many natural products and pharmaceuticals, and as essential building blocks for the total synthesis of complex naturally occurring compounds. Furthermore, polyfunctionalized furans are versatile synthetic starting materials for the preparation of a variety of heterocyclic and acyclic compounds [1–9]. Especially, 2,5-disubstituted furan-3,4-dicarboxylates are very important starting materials in the synthesis of natural products containing tetrahydrofuran rings [10]. So far, many synthetic protocols for the synthesis of iminolactones have been reported. The most widely used approach to iminolactones synthesis is the isocyanide-based reactions [11–18].

Furanones, a unit occurring in a large number of natural products [19], have caught the attention of both organic and bioorganic chemists because many of the butenolide-containing compounds may be considered as potential insecticides, bactericides, fungicides, phospholiphase A_2 inhibitors, etc [20,21]. Furanones are also versatile building blocks for the synthesis of a wide variety of biologically active compounds and complex natural products [22]. Despite these achievements, the development of efficient synthetic methods leading to the formation of this class of compounds with a new structural feature readily for further elaboration is still of current interest. Not surprisingly, a great degree of synthetic efforts have been devoted for developing versatile and efficient route to furanones [23].

As part of an ongoing development of efficient protocols for the preparation of biologically active heterocycles from common intermediates [24–26], we report the synthesis of iminolactones **4** *via* the three-component condensation of isocyanides **1**, dialkyl acetylenedicarboxylates **2**, and phenacyl bromide or its derivatives **3** in solvent-free conditions at ambient temperature (Scheme 1). Hydrolysis of 5-alkylimino-2,5-dihydrofuran-3,4-dicarboxylates **4** with aqueous HCl (5%) in dichloromethane afforded butenolides **5** (see Table 1).

RESULT AND DISCUSSION

As indicated in Scheme 1, the 1:1:1 addition reaction of isocyanides **1** with dialkyl acetylenedicarboxylates **2** and alkyl bromide or its derivatives **3** occurs smoothly at room temperature to produce 5-alkylimino-2,5-dihydrofuran-3,4-dicarboxylate **4**. Hydrolysis of **4** with aqueous HCl (5%) in dichloromethane afforded furanones **5**.

The structures of the products were deduced from their Infrared (IR), mass, ^{1}H-NMR, and ^{13}C-NMR spectra. The mass spectra of these compounds displayed molecular ion peaks at the appropriate *m*/*z* values. The ^{1}H-

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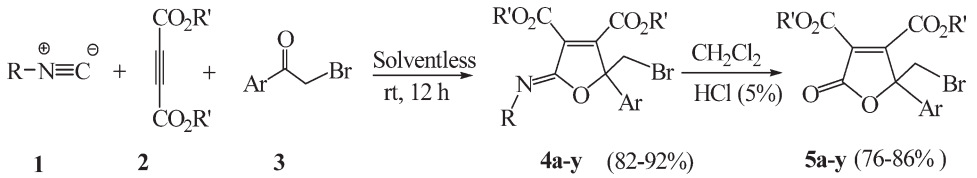
Scheme 1



1 **2** **3** **4a-y** (82-92%) **5a-y** (76-86%)

NMR spectrum of **4a** in $CDCl_3$ showed a singlet at $\delta = 1.39$ for *tert*-butyl group and a singlet at 2.36 for the methyl group. The methylene protons of CH_2Br are diastereotopic and showed two doublet at $\delta = 4.12$ (d, $^2J = 11.0$ Hz) and 4.52 (d, $^2J = 11.0$ Hz). Two peaks at $\delta = 160.9$ and 162.3 are observed in the ^{13}C-NMR spectrum of **4a**, which are attributed to the carbonyl groups. The ^{1}H- and ^{13}C-NMR spectra of **4b**–**4x** are similar to those for **4a** except for the imino or aromatic moieties and the substituents in position 4, which show characteristic resonances in appropriate regions of the spectrum.

To explore the scope of this reaction further, we extended our studies to the reaction of various dialkyl acetylenedicarboxylates and isocyanides with alkyl bromide. As indicated in Table 1, the reactions proceeded very efficiently in excellent yields. Although the mechanism of this reaction has not been established, a plausible rationalization can be advanced to explain product formation (Scheme 2).

On the basis of the well-established chemistry of isocyanides [27–31], it is reasonable to assume that zwitterionic intermediate **6** produced by reaction between the isocyanide and the dialkyl acetylenedicarboxylate adds to phenacyl bromide **3** resulting in the formation of **7**, which undergoes cyclization to give the 5-alkylimino-2,5-dihydrofuran-3,4-dicarboxylate **4**. Hydrolysis of 5-alkylimino-2,5-dihydrofuran-3,4-dicarboxylate **4** with aqueous HCl (5%) in dichloromethane afforded butenolides **5**.

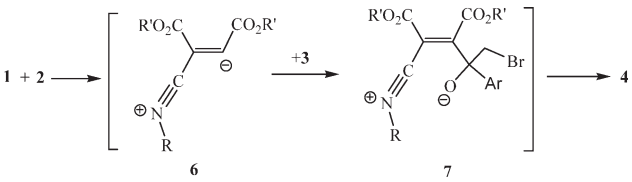
In conclusion, a facile one-pot method for the synthesis of 5-alkylimino-2,5-dihydrofuran-3,4-dicarboxylate derivatives from readily accessible precursors has been proceed. These compounds are important starting materials in the synthesis of natural products containing tetrahydrofuran rings [10]. Hydrolysis of these compounds with HCl (5%) produced furanones in dichloromethane as the solvent. The advantages of our work are as follows: (1) the reaction is performed under neutral and mild conditions, (2) no catalyst is required for this reaction, and (3) the simplicity of the present procedure makes it an interesting alternative to the complex multistep approaches.

Table 1

Synthesis of 5-alkylimino-2,5-dihydro-3,4-furandicarboxylates and furanones.

Entry	R	R′	Ar	Compound **4**	Yield of **4** (%)	Compound **5**	Yield of **5** (%)
1	*tert*-Butyl	Me	4-Me—C_6H_4	**4a**	85	**5a**	82
2	*tert*-Butyl	Et	4-Me—C_6H_4	**4b**	84	**5b**	80
3	*tert*-Butyl	Me	4-NO_2—C_6H_4	**4c**	85	**5c**	82
4	*tert*-Butyl	Et	4-NO_2—C_6H_4	**4d**	87	**5d**	85
5	*tert*-Butyl	Me	4-Ph—C_6H_4	**4e**	83	**5e**	80
6	*tert*-Butyl	Et	4-Ph—C_6H_4	**4f**	80	**5f**	76
7	*tert*-Butyl	Me	4-Cl—C_6H_4	**4g**	84	**5g**	82
8	*tert*-Butyl	Et	4-Cl—C_6H_4	**4h**	82	**5h**	80
9	*tert*-Butyl	Me	4-OMe—C_6H_4	**4i**	87	**5i**	85
10	*tert*-Butyl	Et	4-OMe—C_6H_4	**4j**	83	**5j**	78
11	Cyclohexyl	Me	4-OMe—C_6H_4	**4k**	90	**5k**	86
12	Cyclohexyl	Et	4-OMe—C_6H_4	**4l**	92	**5l**	80
13	Cyclohexyl	Me	4-Me—C_6H_4	**4m**	85	**5m**	83
14	Cyclohexyl	Et	4-Me—C_6H_4	**4n**	92	**5n**	82
15	Cyclohexyl	Me	4-NO_2—C_6H_4	**4o**	87	**5o**	80
16	Cyclohexyl	Et	4-NO_2—C_6H_4	**4p**	90	**5p**	85
17	Cyclohexyl	Me	4-Ph—C_6H_4	**4q**	85	**5q**	82
18	Cyclohexyl	Et	4-Ph—C_6H_4	**4r**	86	**5r**	78
19	Cyclohexyl	Me	4-Cl—C_6H_4	**4s**	87	**5s**	84
20	Cyclohexyl	Et	4-Cl—C_6H_4	**4t**	85	**5t**	80
21	Cyclohexyl	Me	Naphthyl	**4u**	85	**5u**	83
22	Cyclohexyl	Et	Naphthyl	**4v**	87	**5v**	85
23	*tert*-Butyl	Me	Naphthyl	**4w**	84	**5w**	82
24	*tert*-Butyl	Et	Naphthyl	**4x**	85	**5x**	84

Scheme 2



EXPERIMENTAL

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were obtained with a Bruker FT-500 spectrometer in $CDCl_3$, and tetramethylsilane was used as an internal standard. Mass spectra were recorded with a Finnigan Mat TSQ-70 spectrometer. IR spectra were acquired on a Nicollet Magna 550-FT spectrometer. Elemental analyses were carried out with a Perkin-Elmer model 240-C apparatus. The results of elemental analyses (C, H, and N) were within $\pm$0.4% of the calculated values. Acetylenic ester, phenacyl bromide, or its derivatives and isocyanides were obtained from Fluka and were used without further purification.

General procedure for the preparation of compounds 4a–4x. A mixture of alkyl bromides (2 mmol) and dialkyl acetylenedicarboxylate (2 mmol) was stirred at room temperature. To this mixture, isocyanides (2 mmol) was added slowly. The reaction mixture was stirred for 12 h at room temperature and purified by short column chromatography (silica gel) using petroleum ether-ethyl acetate as eluent. The product was then crystallized from hexane to give the desired compound.

Dimethyl 2-bromomethyl-5-(tert-butylimino)-2-(p-tolyl)-2,5-dihydrofuran-3,4-dicarboxylate (4a). Yellow crystals, yield: 0.74 g (85%), m.p. 121–123°C. IR (KBr) (ν_{max}/cm^{-1}): 1726, 1680, 1652, 1583, 1263 cm^{-1}. ^{1}H-NMR: δ = 1.39 (9 H, s, Me_3C), 2.36 (3 H, s, Me), 3.78 (3 H, s, MeO), 3.90 (3 H, s, MeO), 4.12 (1 H, d, ^2J = 11.0 Hz, CH), 4.52 (1 H, d, ^2J = 11.0 Hz, CH), 7.16 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.33 (2 H, d, ^3J = 7.5 Hz, 2 CH). ^{13}C-NMR: δ = 20.9 (Me), 29.5 (Me_3C), 36.8 (CH_2Br), 52.7 (MeO), 52.8 (MeO), 54.8 (Me_3C), 90.5 (C), 125.6 (2 CH), 129.4 (2 CH), 133.8 (C), 138.6 (C), 138.9 (C), 141.9 (C), 152.2 (C=N), 161.0 (C=O), 162.3 (C=O). Anal Calcd for $C_{20}H_{24}BrNO_5$: C, 54.80; H, 5.52; N, 3.20; found: C, 54.97; H, 5.74; N, 3.02.

Diethyl 2-bromomethyl-5-(tert-butylimino)-2-(p-tolyl)-2,5-dihydrofuran-3,4-dicarboxylate (4b). Yellow crystals, yield: 0.78 g (84%), m.p. 126–128°C. IR (KBr) (ν_{max}/cm^{-1}): 1725, 1678, 1662, 1580, 1260 cm^{-1}. ^{1}H-NMR: δ = 1.15 (3 H, t, ^3J = 7.3 Hz, Me), 1.27 (3 H, t, ^3J = 7.2 Hz, Me), 1.35 (9 H, s, Me_3C), 2.34 (3 H, s, Me), 4.10 (1 H, d, ^2J = 11.2 Hz, CH), 4.25–4.30 (2 H, m, OCH_2), 4.32–4.40 (2 H, q, OCH_2), 4.45 (1 H, d, ^2J = 11.2 Hz, CH), 7.15 (2 H, d, ^3J = 7.5 Hz, 2 CH), 7.37 (2 H, d, ^3J = 7.8 Hz, 2 CH). ^{13}C-NMR: δ = 13.5 (Me), 14.0 (Me), 21.2 (Me), 29.5 (Me_3C), 37.4 (CH_2Br), 56.2 (Me_3C), 60.37 (OCH_2), 61.5 (OCH_2), 87.5 (C), 125.2 (2 CH), 128.9 (2 CH), 133.7 (C), 139.0 (C), 139.5 (C), 142.0 (C), 154.2 (C=N), 162.0 (C=O), 162.8 (C=O). Anal Calcd for $C_{22}H_{28}BrNO_5$: C, 56.66; H, 6.05; N, 3.00; found: C, 56.38; H, 5.74; N, 3.30.

Dimethyl 2-bromomethyl-5-(tert-butylimino)-2-(4-nitrophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4c). Yellow powder, yield: 0.80 g (85%), m.p. 157–159°C. IR (KBr) (ν_{max}/cm^{-1}): 1740, 1681, 1658, 1587, 1254 cm^{-1}. ^{1}H-NMR: δ = 1.39 (9 H, s, Me_3C), 3.79 (3 H, s, MeO), 3.90 (3 H, s, MeO), 4.16 (1 H, d, ^2J = 11.2 Hz, CH), 4.44 (1 H, d, ^2J = 11.2 Hz, CH), 7.68 (2 H, d, ^3J = 8.5 Hz, 2 CH), 8.23 (2 H, d, ^3J = 8.5 Hz, 2 CH). ^{13}C-NMR: δ = 29.5 (Me_3C), 35.8 (CH_2Br), 53.1 (MeO), 53.4 (MeO), 55.2 (Me_3C), 89.9 (C), 123.8 (2 CH), 127.4 (2 CH), 139.5 (C), 140.6 (C), 143.7 (C), 148.0 (C), 151.0 (C=N), 160.7 (C=O), 161.9 (C=O). Anal Calcd for $C_{19}H_{21}BrN_2O_5$ (469.29): C, 48.63; H, 4.51; N, 5.97; found: C, 48.80; H, 4.32; N, 5.75.

Diethyl 2-bromomethyl-5-(tert-butylimino)-2-(4-nitrophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4d). Orange powder, yield: 0.86 g (87%), m.p. 158–160°C. IR (KBr) (ν_{max}/cm^{-1}): 1743, 1695, 1664, 1586, 1249 cm^{-1}. ^{1}H-NMR: δ = 1.23 (3 H, t, ^3J = 7.2 Hz, Me), 1.34 (3 H, t, ^3J = 7.4 Hz, Me), 1.37 (9 H, s, Me_3C), 4.15 (1 H, d, ^2J = 11.5 Hz, CH), 4.23–4.30 (2 H, m, OCH_2), 4.34 (1 H, d, ^2J = 11.5 Hz, CH), 4.38 (2 H, q, ^3J = 7.5 Hz, OCH_2), 7.67 (2 H, d, ^3J = 8.4 Hz, 2 CH), 8.22 (2 H, d, ^3J = 8.4 Hz, 2 CH). ^{13}C-NMR: δ = 14.0 (Me), 14.5 (Me), 30.2 (Me_3C), 36.8 (CH_2Br), 56.8 (Me_3C), 61.4 (OCH_2), 62.0 (OCH_2), 90.0 (C), 124.8 (2 CH), 128.2 (2 CH), 140.0 (C), 141.4 (C), 143.5 (C), 148.4 (C), 151.9 (C=N), 160.5 (C=O), 161.9 (C=O). Anal Calcd for $C_{21}H_{25}BrN_2O_7$: C, 50.72; H, 5.07; N, 5.63; found: C, 50.54; H, 4.86; N, 5.37.

Dimethyl 2-bromomethyl-5-(tert-butylimino)-2-(p-biphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4e). Yellow powder, yield: 0.83 g (83%), m.p. 138–140°C. IR (KBr) (ν_{max}/cm^{-1}): 1720, 1675, 1642, 1583, 1270 cm^{-1}. ^{1}H-NMR: δ = 1.34 (9 H, s, Me_3C), 3.82 (3 H, s, MeO), 3.90 (3H, s, MeO), 4.23 (1 H, d, ^2J = 11.2 Hz, CH), 4.54 (1 H, d, ^2J = 11.2 Hz, CH), 7.34 (1 H, t, ^3J = 7.6 Hz, CH), 7.42 (2 H, t, ^3J = 7.6 Hz, 2 CH), 7.65 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.67 (2 H, d, ^3J = 8.2 Hz, 2 CH), 7.74 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 29.8 (Me_3C), 38.5 (CH_2Br), 52.8 (MeO), 53.0 (MeO), 55.8 (Me_3C), 89.0 (C), 127.2 (2 CH), 127.8 (2 CH), 128.0 (2 CH), 128.2 (CH), 129.0 (2 CH), 136.5 (C), 138.0 (C), 141.2 (C), 142.6 (C), 143.2 (C), 159.4 (C=N), 162.0 (C=O), 162.6 (C=O). Anal Calcd for $C_{25}H_{26}BrNO_5$: C, 60.01; H, 5.24; N, 2.80; found: C, 60.32; H, 5.42; N, 3.00.

Diethyl 2-bromomethyl-5-(tert-butylimino)-2-(p-biphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4f). Yellow powder, yield: 0.84 g (80%), m.p. 165–167°C. IR (KBr) (ν_{max}/cm^{-1}): 1725, 1674, 1650, 1585, 1272 cm^{-1}. ^{1}H-NMR: δ = 1.28 (3 H, t, ^3J = 7.5 Hz, Me), 1.35 (3 H, t, ^3J = 7.4 Hz, Me), 1.38 (9 H, s, Me_3C), 4.14 (1 H, d, ^2J = 11.0 Hz, CH), 4.38–4.42 (2 H, m, OCH_2), 4.45 (2 H, q, ^3J = 7.3 Hz, OCH_2), 4.57 (1 H, d, ^2J = 11.0 Hz, CH), 7.37 (1 H, t, ^3J = 7.6 Hz, CH), 7.45 (2 H, t, ^3J = 7.5 Hz, 2 CH), 7.50 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.57 (2 H, d, ^3J = 8.4 Hz, 2 CH), 7.61 (2 H, d, ^3J = 8.4 Hz, 2 CH). ^{13}C-NMR: δ = 14.0 (Me), 14.2 (Me), 30.4 (Me_3C), 36.7 (CH_2Br), 56.9 (C—N), 60.2 (OCH_2), 61.8 (OCH_2), 89.5 (C), 127.0 (2 CH), 127.5 (2 CH), 127.8 (2 CH), 128.0 (CH), 128.9 (2 CH), 136.6 (C), 137.7 (C), 140.4 (C), 142.7 (C), 143.0 (C), 158.6 (C=N), 161.5 (C=O), 162.7 (C=O). MS: *m/z* (%) = 529 (M^+ + 2, 15), 527 (M^+, 15), 514 (94), 468 (78), 314 (36), 181 (100), 152 (48), 57 (72). Anal Calcd for $C_{27}H_{30}BrNO_5$: C, 61.37; H, 5.72; N, 2.65; found: C, 61.24; H, 5.68; N, 2.53.

Dimethyl 2-bromomethyl-5-(tert-butylimino)-2-(4-chlorophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4g). Pale yellow powder, yield: 0.77 g (84%), m.p. 148–150°C. IR (KBr) (ν_{max}/cm^{-1}): 1730, 1682, 1638, 1590, 1257 cm^{-1}. ^{1}H-NMR: δ = 1.38 (9 H, s, Me_3C), 3.75 (3 H, s, MeO), 3.92 (3 H, s, MeO),

4.12 (1 H, d, ^2J = 11.0 Hz, CH), 4.45 (1 H, d, ^2J = 11.0 Hz, CH), 7.35 (2 H, d, ^3J = 8.0 Hz, 2 CH), 7.42 (2 H, d, ^3J = 7.9 Hz, 2 CH). ^{13}C-NMR: δ = 29.8 (Me_3C), 38.4 (CH_2Br), 52.4 (MeO), 53.4 (MeO), 58.4 (C—N), 90.4 (C), 127.8 (2 CH), 128.4 (2 CH), 136.0 (C), 137.7 (C), 142.8 (C), 148.7 (C), 154.0 (C=N), 161.9 (C=O), 162.4 (C=O). Anal Calcd for $C_{19}H_{21}BrClNO_5$: C, 49.75; H, 4.61; N, 3.05; found: C, 49.57; H, 4.40; N, 2.82.

Diethyl 2-bromomethyl-5-(tert-butylimino)-2-(4-chlorophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4h). Yellow powder, yield: 0.80 g (82%), m.p. 158–160°C. IR (KBr) (ν_{max}/cm^{-1}): 1727, 1684, 1664, 1584, 1270 cm^{-1}. ^{1}H-NMR: δ = 1.25 (3 H, t, ^3J = 7.3 Hz, Me), 1.32 (3 H, t, ^3J = 7.3 Hz, Me), 1.39 (9 H, s, Me_3C), 4.18 (1 H, d, ^2J = 11.3 Hz, CH), 4.22–4.28 (2 H, m, OCH_2), 4.38 (2 H, q, ^3J = 7.5 Hz, OCH_2), 4.42 (1 H, d, ^2J = 11.3 Hz, CH), 7.35 (2 H, d, ^3J = 8.0 Hz, 2 CH), 7.43 (2 H, d, ^3J = 8.0 Hz, 2 CH). ^{13}C-NMR: δ = 13.5 (Me), 14.2 (Me), 29.8 (Me_3C), 37.7 (CH_2Br), 58.0 (C—N), 62.7 (OCH_2), 62.5 (OCH_2), 90.2 (C), 128.3 (2 CH), 129.0 (2 CH), 134.0 (C), 139.2 (C), 140.8 (C), 143.6 (C), 148.9 (C), 158.5 (C=N), 161.5 (C=O), 162.5 (C=O). Anal Calcd for $C_{21}H_{25}BrClNO_5$: C, 51.82; H, 5.18; N, 2.88; found: C, 51.64; H, 5.29; N, 2.58.

Dimethyl 2-bromomethyl-5-(tert-butylimino)-2-(4-methoxyphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4i). Yellow crystals, yield: 0.79 g (87%), m.p. 135–137°C. IR (KBr) (ν_{max}/cm^{-1}): 1725, 1684, 1657, 1580, 1267 cm^{-1}. ^{1}H-NMR: δ = 1.39 (9 H, s, Me_3C), 3.75 (3 H, s, MeO), 3.80 (3 H, s, MeO), 3.95 (3 H, s, MeO), 4.15 (1 H, d, ^2J = 11.5 Hz, CH), 4.55 (1 H, d, ^2J = 11.5 Hz, CH), 7.00 (2 H, d, ^3J = 8.5 Hz, 2 CH), 7.35 (2 H, d, ^3J = 8.5 Hz, 2 CH). ^{13}C-NMR: δ = 29.7 (Me_3C), 37.0 (CH_2Br), 52.5 (MeO), 52.8 (MeO), 53.4 (MeO), 57.2 (C—N), 89.4 (C), 113.2 (2 CH), 128.5 (2 CH), 135.6 (C), 138.7 (C), 141.3 (C), 148.7 (C), 156.5 (C=N), 161.0 (C=O), 162.4 (C=O). Anal Calcd for $C_{20}H_{24}BrNO_6$: C, 52.88; H, 5.32; N, 3.08; found: C, 52.97; H, 5.53; N, 3.04.

Diethyl 2-bromomethyl-5-(tert-butylimino)-2-(4-methoxyphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4j). Pale yellow crystals, yield: 0.80 g (83%), m.p. 143–145°C. IR (KBr) (ν_{max}/cm^{-1}): 1734, 1678, 1648, 1576, 1258 cm^{-1}. ^{1}H-NMR: δ = 1.24 (3 H, t, ^3J = 7.2 Hz, Me), 1.35 (3 H, t, ^3J = 7.3 Hz, Me), 1.38 (9 H, s, Me_3C), 4.15 (1 H, d, ^2J = 11.0 Hz, CH), 4.25–4.32 (2 H, m, OCH_2), 4.35 (2 H, q, ^3J = 7.3 Hz, OCH_2), 4.54 (1 H, d, ^2J = 11.0 Hz, CH), 6.85 (2 H, d, ^3J = 8.4 Hz, 2 CH), 7.30 (2 H, d, ^3J = 8.5 Hz, 2 CH). ^{13}C-NMR: δ = 13.2 (Me), 14.5 (Me), 29.9 (Me_3C), 37.3 (CH_2Br), 53.4 (MeO), 57.5 (C—N), 62.5 (OCH_2), 62.8 (OCH_2), 90.7 (C), 114.5 (2 CH), 127.4 (2 CH), 135.6 (C), 138.6 (C), 141.3 (C), 148.8 (C), 156.3 (C=N), 161.9 (C=O), 162.2 (C=O). Anal Calcd for $C_{22}H_{28}BrNO_6$: C, 54.78; H, 5.85; N, 2.90; found: C, 54.55; H, 5.60; N, 2.73.

Dimethyl 2-bromomethyl-5-(cyclohexylimino)-2-(4-methoxyphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4k). Pale yellow crystals, yield: 0.86 g (90%), m.p. 137–139°C. IR (KBr) (ν_{max}/cm^{-1}): 1726, 1680, 1652, 1583, 1263 cm^{-1}. ^{1}H-NMR: δ = 1.22–1.88 (10 H, m, 5 CH_2), 2.35 (3 H, s, Me), 3.72 (1 H, m, CH), 3.79 (3 H, s, MeO), 3.81 (3 H, s, MeO), 3.92 (3 H, s, MeO), 4.10 (1 H, d, ^2J = 11.0 Hz, CH), 4.51 (1 H, d, ^2J = 11.0 Hz, CH), 6.90 (2 H, d, ^3J = 8.7 Hz, 2 CH), 7.34 (2 H, d, ^3J = 8.7 Hz, 2 CH). ^{13}C-NMR: δ = 24.8 (2 CH_2), 25.6 (CH_2), 32.8 (2 CH_2), 36.7 (CH_2Br), 52.7 (MeO), 52.9 (MeO), 53.1 (MeO), 56.8 (C—N), 86.5 (C), 114.2 (2 CH), 127.0 (2 CH), 134.6 (C), 138.2 (C), 140.3 (C), 148.9 (C), 156.0 (C=N), 160.9 (C=O), 162.0 (C=O). Anal Calcd for $C_{22}H_{26}BrNO_6$: C, 55.01; H, 5.46; N, 2.92; found: C, 54.72; H, 5.24; N, 2.70.

Diethyl 2-bromomethyl-5-(cyclohexylimino)-2-(4-methoxyphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4l). Yellow crystals, yield: 0.93 g (92%), m.p. 152–154°C. IR (KBr) (ν_{max}/cm^{-1}): 1734, 1678, 1664, 1580, 1272 cm^{-1}. ^{1}H-NMR: δ = 1.25 (3 H, t, ^3J = 7.4 Hz, Me), 1.35 (3 H, t, ^3J = 7.3 Hz, Me), 1.45–1.95 (10 H, m, 5 CH_2), 3.77 (1 H, m, CH), 3.85 (3 H, s, MeO), 4.14 (1 H, d, ^2J = 11.2 Hz, CH), 4.25–4.30 (2 H, m, OCH_2), 4.34 (2 H, q, ^3J = 7.4 Hz, OCH_2), 4.55 (1 H, d, ^2J = 11.2 Hz, CH), 7.12 (2 H, d, ^3J = 8.5 Hz, 2 CH), 7.32 (2 H, d, ^3J = 8.5 Hz, 2 CH). ^{13}C-NMR: δ = 13.0 (Me), 14.2 (Me), 24.5 (2 CH_2), 25.4 (CH_2), 33.0 (2 CH_2), 37.3 (CH_2Br), 53.4 (MeO), 57.8 (C—N), 62.4 (OCH_2), 62.9 (OCH_2), 90.4 (C), 113.2 (2 CH), 127.3 (2 CH), 135.2 (C), 137.8 (C), 141.3 (C), 149.0 (C), 156.4 (C=N), 161.6 (C=O), 162.4 (C=O). Anal Calcd for $C_{24}H_{30}BrNO_6$: C, 56.70; H, 5.95; N, 2.76; found: C, 56.85; H, 6.12; N, 2.93.

Dimethyl 2-bromomethyl-5-(cyclohexylimino)-2-(p-tolyl)-2,5-dihydrofuran-3,4-dicarboxylate (4m). Pale yellow powder, yield: 0.78 g (85%), m.p. 134–136°C. IR (KBr) (ν_{max}/cm^{-1}): 1735, 1684, 1631, 1587, 1281 cm^{-1}. ^{1}H-NMR: δ = 1.38–1.57 (10 H, m, 5 CH_2), 2.35 (3 H, s, Me), 3.71 (1 H, m, CH), 3.77 (3 H, s, MeO), 3.91 (3H, s, MeO), 4.09 (1 H, d, ^2J = 11.0 Hz, CH), 4.52 (1 H, d, ^2J = 11.0 Hz, CH), 7.17 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.28 (2 H, d, ^3J = 7.6 Hz, 2 CH). ^{13}C-NMR: δ = 20.9 (Me), 24.7 (2 CH_2), 25.6 (CH_2), 32.8 (2 CH_2), 36.6 (CH_2Br), 52.7 (MeO), 52.9 (MeO), 56.7 (C—N), 89.7 (C), 125.5 (2 CH), 129.4 (2 CH), 133.6 (C), 137.2 (C), 139.0 (C), 142.9 (C), 154.2 (C=N), 160.9 (C=O), 162.0 (C=O). Anal Calcd for $C_{22}H_{26}BrNO_5$: C, 56.90; H, 5.64; N, 3.02; found: C, 56.65; H, 5.82; N, 3.32.

Diethyl 2-bromomethyl-5-(cyclohexylimino)-2-(p-tolyl)-2,5-dihydrofuran-3,4-dicarboxylate (4n). Pale yellow crystals, yield: 0.91g (92%), m.p. 135–137°C. IR (KBr) (ν_{max}/cm^{-1}): 1754, 1689 1655, 1585, 1269 cm^{-1}. ^{1}H-NMR: δ = 1.23 (3 H, t, ^3J = 7.3 Hz, Me), 1.34 (3 H, t, ^3J = 7.3 Hz, Me), 1.40–1.92 (10 H, m, 5 CH_2), 2.34 (3 H, s, Me), 3.82 (1 H, m, CH), 4.15 (1 H, d, ^2J = 11.0 Hz, CH), 4.24–4.36 (2 H, m, OCH_2), 4.38 (2 H, q, ^3J = 7.3 Hz, OCH_2), 4.52 (1 H, d, ^2J = 11.0 Hz, CH), 7.65 (2 H, d, ^3J = 8.0 Hz, 2 CH), 8.27 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 13.6 (Me), 13.9 (Me), 20.9 (Me), 24.6 (2 CH_2), 25.6 (CH_2), 32.8 (2 CH_2), 36.7 (CH_2Br), 56.5 (C—N), 61.8 (OCH_2), 61.9 (OCH_2), 89.6 (C), 125.6 (2 CH), 129.3 (2 CH), 133.8 (C), 137.2 (C), 138.9 (C), 142.7 (C), 154.3 (C=N), 160.6 (C=O), 161.6 (C=O). Anal Calcd for $C_{24}H_{30}BrNO_5$: C, 58.54; H, 6.14; N, 2.84; found: C, 58.33; H, 5.92; N, 2.58.

Dimethyl 2-bromomethyl-5-(cyclohexylimino)-2-(4-nitrophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4o). Yellow powder, yield: 0.86 g (87%), m.p. 150–152°C. IR (KBr) (ν_{max}/cm^{-1}): 1739, 1697, 1661, 1508, 1262 cm^{-1}. ^{1}H-NMR: δ = 1.42–1.85 (10 H, m, 5 CH_2), 3.72 (1 H, m, CH), 3.79 (3 H, s, MeO), 3.91 (3 H, s, MeO), 4.11 (1 H, d, ^2J = 11.0 Hz, CH), 4.47 (1 H, d, ^2J = 11.0 Hz, CH), 7.66 (2 H, d, ^3J = 9.0 Hz, 2 CH), 8.24 (2 H, d, ^3J = 9.0 Hz, 2 CH). ^{13}C-NMR: δ = 24.6 (2 CH_2), 25.2 (CH_2), 32.8 (2 CH_2), 35.8 (CH_2Br), 52.7 (MeO), 53.2 (MeO), 57.0 (C—N), 89.2 (C), 123.9 (2 CH), 127.1 (2 CH), 138.2 (C), 141.7 (C), 143.5 (C), 148.1 (C), 153.3 (C=N), 160.7 (C=O), 161.6 (C=O). MS: *m/z* (%) = 497 (M^+

+ 2, 35), 495 (M^+, 35), 415 (78), 383 (46), 318 (100), 123 (38). Anal Calcd for $C_{21}H_{23}BrN_2O_7$: C, 50.92; H, 4.68; N, 5.66; found: C, 50.74; H, 4.83; N, 5.85.

Diethyl 2-bromomethyl-5-(cyclohexylimino)-2-(4-nitrophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4p). Yellow crystals, yield: 0.94 g (90%), m.p. 168–170°C. IR (KBr) (ν_{max}/cm^{-1}): 1735, 1675, 1655, 1582, 1260 cm^{-1}. ^{1}H-NMR: δ = 1.27 (3 H, t, ^3J = 7.2 Hz, Me), 1.37 (3 H, t, ^3J = 7.2 Hz, Me), 1.46–1.91 (10 H, m, 5 CH_2), 3.78 (1 H, m, CH), 4.17 (1 H, d, ^2J = 11.0 Hz, CH), 4.21–4.30 (2 H, m, OCH_2), 4.39 (2 H, q, ^3J = 7.3 Hz, OCH_2), 4.57 (1 H, d, ^2J = 11.0 Hz, CH), 7.53 (2 H, d, ^3J = 8.5 Hz, 2 CH), 7.63 (2 H, d, ^3J = 8.5 Hz, 2 CH). ^{13}C-NMR: δ = 13.7 (Me), 14.0 (Me), 24.7 (2 CH_2), 25.7 (CH_2), 32.9 (2 CH_2), 36.7 (CH_2Br), 56.7 (C—N), 62.3 (OCH_2), 62.4 (OCH_2), 89.7 (C), 127.0 (2 CH), 128.9 (2 CH), 137.5 (C), 140.0 (C), 141.8 (C), 142.5 (C), 154.2 (C=N), 160.7 (C=O), 161.6 (C=O). Anal Calcd for $C_{23}H_{27}BrN_2O_7$: C, 52.78; H, 5.20; N, 5.35; found: C, 52.57; H, 5.02; N, 5.13.

Dimethyl 2-bromomethyl-5-(cyclohexylimino)-2-biphenyl-2,5-dihydrofuran-3,4-dicarboxylate (4q). Pale yellow powder, yield: 0.72 g (85%), m.p. 141–143°C. IR (KBr) (ν_{max}/cm^{-1}): 1725, 1679, 1645, 1585, 1274 cm^{-1}. ^{1}H-NMR: δ = 1.26–1.89 (10 H, m, 5 CH_2), 3.72 (1 H, m, CH), 3.80 (3 H, s, MeO), 3.92 (3H, s, MeO), 4.14 (1 H, d, ^2J = 11.0 Hz, CH), 4.57 (1 H, d, ^2J = 11.0 Hz, CH), 7.37 (1 H, t, ^3J = 7.6 Hz, CH), 7.45 (2 H, t, ^3J = 7.5 Hz, 2 CH), 7.50 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.57 (2 H, d, ^3J = 8.3 Hz, 2 CH), 7.61 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 24.8 (2 CH_2), 25.3 (CH_2), 32.9 (2 CH_2), 36.7 (CH_2Br), 52.9 (MeO), 53.1 (MeO), 56.9 (C—N), 89.5 (C), 126.2 (2 CH), 127.1 (2 CH), 127.5 (2 CH), 127.8 (CH), 128.9 (2 CH), 135.6 (C), 137.5 (C), 140.0 (C), 142.0 (C), 142.9 (C), 158.7 (C=N), 161.1 (C=O), 162.1 (C=O). Anal Calcd for $C_{27}H_{28}BrNO_5$: C, 61.60; H, 5.36; N, 2.66; found: C, 61.45; H, 5.18; N, 2.47.

Diethyl 2-bromomethyl-5-(cyclohexylimino)-2-biphenyl-2,5-dihydrofuran-3,4-dicarboxylate (4r). Orange powder, yield: 0.95 g (86%), m.p. 168–170°C. IR (KBr) (ν_{max}/cm^{-1}): 1735, 1675, 1667, 1582, 1279 cm^{-1}. ^{1}H-NMR: δ = 1.28 (3 H, t, ^3J = 7.3 Hz, Me), 1.35 (3 H, t, ^3J = 7.4 Hz, Me), 1.27–1.86 (10 H, m, 5 CH_2), 3.75 (1 H, m, CH), 4.23 (1 H, d, ^2J = 11.0 Hz, CH), 4.25–4.32 (2 H, m, OCH_2), 4.38 (2 H, q, ^3J = 7.4 Hz, OCH_2), 4.56 (1 H, d, ^2J = 11.2 Hz, CH), 7.35 (1 H, t, ^3J = 7.5 Hz, CH), 7.42 (2 H, t, ^3J = 7.6 Hz, 2 CH), 7.53 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.58 (2 H, d, ^3J = 8.4 Hz, 2 CH), 7.65 (2 H, d, ^3J = 8.4 Hz, 2 CH). ^{13}C-NMR: δ = 13.5 (Me), 13.8 (Me), 24.7 (2 CH_2), 25.2 (CH_2), 33.0 (2 CH_2), 37.5 (CH_2Br), 57.6 (C—N), 62.0 (OCH_2), 62.8 (OCH_2), 89.3 (C), 127.2 (2 CH), 127.8 (2 CH), 128.2 (2 CH), 128.7 (CH), 129.2 (2 CH), 136.3 (C), 137.7 (C), 141.3 (C), 142.5 (C), 142.9 (C), 158.4 (C=N), 161.51 (C=O), 162.9 (C=O). Anal Calcd for $C_{29}H_{32}BrNO_5$: C, 62.82; H, 5.82; N, 2.53; found: C, 62.64; H, 5.68; N, 2.36.

Dimethyl 2-bromomethyl-5-(cyclohexylimino)-2-(4-chlorophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4s). Yellow powder, yield: 0.84g (87%), m.p. 158–160°C. IR (KBr) (ν_{max}/cm^{-1}): 1735, 1684, 1631, 1587, 1281 cm^{-1}. ^{1}H-NMR: δ = 1.22–1.89 (10 H, m, 5 CH_2), 3.71 (1 H, m, CH), 3.79 (3 H, s, MeO), 3.93 (3 H, s, MeO), 4.08 (1 H, d, ^2J = 11.1 Hz, CH), 4.48 (1 H, d, ^2J = 11.1 Hz, CH), 7.37 (2 H, d, ^3J = 8.2 Hz, 2 CH), 7.39 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 24.8 (2 CH_2), 25.7 (CH_2), 32.9 (2 CH_2), 36.4 (CH_2Br), 52.9 (MeO), 53.1 (MeO), 56.9 (C—N), 89.5 (C), 127.3 (2 CH), 129.0 (2 CH), 135.3 (C), 137.6 (C), 142.5 (C), 148.4 (C), 153.9 (C=N), 160.9 (C=O), 161.9 (C=O). Anal Calcd for $C_{21}H_{23}BrClNO_5$: C, 52.03; H, 4.78; N, 2.89; found: C, 52.25; H, 4.60; N, 2.62.

Diethyl 2-bromomethyl-5-(cyclohexylimino)-2-(4-chlorophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (4t). Yellow powder, yield: 0.87 g (85%), m.p. 147–149°C. IR (KBr) (ν_{max}/cm^{-1}): 1732, 1672, 1654, 1578, 1275 cm^{-1}. ^{1}H-NMR: δ = 1.27 (3 H, t, ^3J = 7.5 Hz, Me), 1.35 (3 H, t, ^3J = 7.5 Hz, Me), 1.45–1.87 (10 H, m, 5 CH_2), 3.74 (1 H, m, CH), 4.10 (1 H, d, ^2J = 11.3 Hz, CH), 4.09–4.29 (2 H, m, OCH_2), 4.40 (2 H, q, ^3J = 7.5 Hz, OCH_2), 4.46 (1 H, d, ^2J = 11.3 Hz, CH), 7.33 (2 H, d, ^3J = 8.0 Hz, 2 CH), 7.40 (2 H, d, ^3J = 8.0 Hz, 2 CH). ^{13}C-NMR: δ = 13.7 (Me), 14.0 (Me), 24.5 (2 CH_2), 25.7 (CH_2), 32.8 (2 CH_2), 36.3 (CH_2Br), 56.8 (C—N), 62.3 (OCH_2), 62.4(OCH_2), 89.8 (C), 127.3 (2 CH), 128.5 (2 CH), 134.2 (C), 138.8 (C), 140 (C), 143.4 (C), 148.5 (C), 158.2 (C=N), 160.5 (C=O), 161.4 (C=O). Anal Calcd for $C_{23}H_{27}BrClNO_5$: C, 53.87; H, 5.31; N, 2.73; found: C, 54.05; H, 5.53; N, 2.94.

Dimethyl 2-bromomethyl-5-(cyclohexylimino)-2-(2-naphthyl)-2,5-dihydrofuran-3,4-dicarboxylate (9u). Yellow powder, yield: 0.85 g (85%), m.p. 129–131°C. IR (KBr) (ν_{max}/cm^{-1}): 1742, 1694, 1658, 1595, 1276 cm^{-1}. ^{1}H-NMR: δ = 1.36–1.90 (10 H, m, 5 CH_2), 3.72 (1 H, m, CH), 3.76 (3 H, s, MeO), 3.92 (3 H, s, MeO), 4.24 (1 H, d, ^2J = 11.0 Hz, CH), 4.67 (1 H, d, ^2J = 11.0 Hz, CH), 7.49–7.91 (7 H, m, 7 CH). ^{13}C-NMR: δ = 24.8 (2 CH_2), 25.7 (CH_2), 32.9 (2 CH_2), 36.6 (CH_2Br), 52.9 (MeO), 53.1 (MeO), 56.9 (C—N), 90.7 (C), 123.0 (CH), 125.5 (CH), 126.7 (CH), 127.1 (CH), 127.6 (CH), 128.5 (CH), 128.8 (CH), 132.9 (C), 133.2 (C), 133.9 (C), 146.7 (C), 148.5 (C), 156.4 (C=N), 161.0 (C=O), 162.1 (C=O). MS: *m/z* (%) = 501 (M^+ + 2, 25), 499 (M^+, 25), 420 (100), 388 (48), 323 (70), 127 (58). Anal Calcd for $C_{25}H_{26}BrNO_5$: C, 60.01; H, 5.24; N, 2.80; found: C, 60.22; H, 5.50; N, 2.97.

Diethyl 2-bromomethyl-5-(cyclohexylimino)-2-(2-naphthyl)-2,5-dihydrofuran-3,4-dicarboxylate (9v). Yellow powder, yield: 0.92 g (87%), m.p. 150–152°C. IR (KBr) (ν_{max}/cm^{-1}): 1754, 1684, 1625, 1580, 1280 cm^{-1}. ^{1}H-NMR: δ = 1.23 (3 H, t, ^3J = 7.4 Hz, Me), 1.36 (3 H, t, ^3J = 7.5 Hz, Me), 1.43–1.90 (10 H, m, 5 CH_2), 3.79 (1 H, m, CH), 4.17–4.23 (2 H, m, OCH_2), 4.25 (1 H, d, ^2J = 11.0 Hz, CH), 4.38 (2 H, q, ^3J = 7.5 Hz, OCH_2), 4.64 (1 H, d, ^2J = 11.0 Hz, CH), 7.50–7.92 (7 H, m, 7 CH). ^{13}C-NMR: δ = 13.8 (Me), 14.1 (Me), 24.7 (2 CH_2), 25.8 (CH_2), 32.9 (2 CH_2), 36.8 (CH_2Br), 56.8 (C—N), 62.1 (OCH_2), 62.2 (OCH_2), 90.2 (C), 123.1 (CH), 125.5 (CH), 126.7 (CH), 127.0 (CH), 127.6 (CH), 128.5 (CH), 128.7 (CH), 132.9 (C), 133.2 (C), 134.2 (C), 145.7 (C), 148.5 (C), 156.6 (C=N), 161.3 (C=O), 162.0 (C=O). Anal Calcd for $C_{27}H_{30}BrNO_5$: C, 61.37; H, 5.72; N, 2.65; found: C, 61.13; H, 5.60; N, 2.41.

Dimethyl 2-bromomethyl-5-(tert-butylimino)-2-(2-naphthyl)-2,5-dihydrofuran-3,4-dicarboxylate (9w). Yellow powder, yield: 0.79 g (84%), m.p. 145–147°C. IR (KBr) (ν_{max}/cm^{-1}): 1745, 1697, 1668, 1590, 1278 cm^{-1}. ^{1}H-NMR: δ = 1.37 (9 H, s, Me_3C), 3.75 (3 H, s, MeO), 3.89 (3 H, s, MeO), 4.27 (1 H, d, ^2J = 11.3 Hz, CH), 4.65 (1 H, d, ^2J = 11.3 Hz, CH), 7.45–7.92 (7 H, m, 7 CH). ^{13}C-NMR: δ = 29.8 (Me_3C), 37.8 (CH_2Br), 52.5 (MeO), 52.9 (MeO), 57.8 (C—N), 90.5

(C), 123.2 (CH), 125.6 (CH), 126.8 (CH), 127.5 (CH), 127.8 (CH), 128.4 (CH), 128.9 (CH), 132.8 (C), 133.5 (C), 134.0 (C), 146.5 (C), 148.8 (C), 156.6 (C=N), 161.7 (C=O), 162.8 (C=O). Anal Calcd for $C_{23}H_{24}BrNO_5$: C, 58.24; H, 5.10; N, 2.95; found: C, 58.42; H, 5.28; N, 3.16.

Diethyl 2-bromomethyl-5-(tert-butylimino)-2-(2-naphthyl)-2,5-dihydrofuran-3,4-dicarboxylate (9x). Yellow powder, yield: 0.85 g (85%), m.p. 153–155°C. IR (KBr) (ν_{max}/cm^{-1}): 1752, 1687, 1637, 1595, 1278 cm^{-1}. ^{1}H-NMR: δ = 1.27 (3 H, t, ^3J = 7.2 Hz, Me), 1.32 (3 H, t, ^3J = 7.3 Hz, Me), 1.38 (9 H, s, *Me*$_3$C), 4.17–4.23 (2 H, m, OCH_2), 4.25 (1 H, d, ^2J = 11.2 Hz, CH), 4.38 (2 H, q, ^3J = 7.5 Hz, OCH_2), 4.64 (1 H, d, ^2J = 11.2 Hz, CH), 7.50–7.92 (7 H, m, 7 CH). ^{13}C-NMR: δ = 13.8 (Me), 14.1 (Me), 1.38 (9 H, s, *Me*$_3$C), 37.8 (CH_2Br), 57.4 (C—N), 62.4 (OCH_2), 62.8 (OCH_2), 89.6 (C), 123.5 (CH), 125.8 (CH), 127.0 (CH), 127.5 (CH), 127.8 (CH), 128.7 (CH), 129.1 (CH), 133.2 (C), 133.8 (C), 134.6 (C), 146.2 (C), 148.2 (C), 157.6 (C=N), 162.3 (C=O), 162.8 (C=O). Anal Calcd for $C_{25}H_{28}BrNO_5$: C, 59.77; H, 5.62; N, 2.79; found: C, 59.58; H, 5.83; N, 2.55.

General procedure for the preparation of compounds 5a–5j and 5u–5v. To a stirred solution of 5-alkylimino-2,5-dihydrofuran-3,4-dicarboxylate **4** (2 mmol) in 5 mL of CH_2Cl_2 was added aqueous HCl (5%, 5 mL) slowly at room temperature. After stirring the reaction mixture for 5 h, it was diluted by adding CH_2Cl_2 (2 mL) and H_2O (3 mL). The mixture was stirred for additional 30 min and two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (SiO_2; *n*-hexanes/EtOAc 8:1) to afford pure desired products.

Dimethyl 2-bromomethyl-5-oxo-2-(p-tolyl)-2,5-dihydrofuran-3,4-dicarboxylate (5a). White crystals yield: 0.63 g (82%), m.p. 125–127°C. IR (KBr) (ν_{max}/cm^{-1}): 1720, 1675, 1648, 1582, 1265 cm^{-1}. ^{1}H-NMR: δ = 2.29 (3 H, s, Me), 3.75 (3 H, s, MeO), 3.82 (3 H, s, MeO), 4.15 (1 H, d, ^2J = 11.2 Hz, CH), 4.50 (1 H, d, ^2J = 11.2 Hz, CH), 7.12 (2 H, d, ^3J = 7.5 Hz, 2 CH), 7.28 (2 H, d, ^3J = 7.5 Hz, 2 CH). ^{13}C-NMR: δ = 21.4 (Me), 36.5 (CH_2Br), 51.8 (MeO), 52.3 (MeO), 92.4 (C), 125.2 (2 CH), 129.0 (2 CH), 133.6 (C), 138.4 (C), 139.0 (C), 141.7 (C), 158.7 (C=O), 161.7 (C=O), 162.4 (C=O). Anal Calcd for $C_{16}H_{15}BrNO_6$: C, 50.15; H, 3.95; found: C, 49.95; H, 3.87.

Diethyl 2-bromomethyl-5-oxo-2-(p-tolyl)-2,5-dihydrofuran-3,4-dicarboxylate (5b). White powder, yield: 0.66 g (80%), m.p. 116–118°C. IR (KBr) (ν_{max}/cm^{-1}): 1725, 1715, 1700, 1210 cm^{-1}. ^{1}H-NMR: δ = 1.26 (3 H, t, ^3J = 7.2 Hz, Me), 1.35 (3 H, t, ^3J = 7.2 Hz, Me), 2.35 (3 H, s, Me), 4.09 (1 H, d, ^2J = 11.1 Hz, CH), 4.26–4.32 (2 H, m, OCH_2), 4.33–4.39 (2 H, q, OCH_2), 4.45 (1 H, d, ^2J = 11.1 Hz, CH), 7.18 (2 H, d, ^3J = 7.6 Hz, 2 CH), 7.29 (2 H, d, ^3J = 7.5 Hz, 2 CH). ^{13}C-NMR: δ = 13.6 (Me), 14.0 (Me), 21.0 (Me), 35.4 (CH_2Br), 62.5 (OCH_2), 62.8 (OCH_2), 87.4 (C), 125.5 (2 CH), 129.5 (C), 129.6 (2 CH), 130.9 (C), 139.9 (C), 155.1 (C), 159.9 (C=O), 160.2 (C=O), 165.4 (C=O). Anal Calcd for $C_{18}H_{19}BrO_6$: C, 52.57; H, 4.66; found: C, 52.40; H, 4.38.

Dimethyl 2-bromomethyl-5-oxo-2-(4-nitrophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (5c). Yellow powder, yield: 0.68 g (82%), m.p. 148–150°C. IR (KBr) (ν_{max}/cm^{-1}): 1737, 1683, 1652, 1574, 1225, 1154 cm^{-1}. ^{1}H-NMR: δ = 3.82 (3 H, s, MeO), 3.87 (3 H, s, MeO), 4.20 (1 H, d, ^2J = 11.5 Hz, CH), 4.45 (1 H, d, ^2J = 11.5 Hz, CH), 7.55 (2 H, d, ^3J = 8.4 Hz, 2 CH), 8.27 (2 H, d, ^3J = 8.4 Hz, 2 CH). ^{13}C-NMR: δ = 34.5 (CH_2Br), 52.6 (MeO), 53.2 (MeO), 90.2 (C), 122.7 (2 CH), 128.4 (2 CH), 138.7 (C), 141.0 (C), 142.7 (C), 147.8 (C), 158.4 (C=O), 161.2 (C=O), 162.0 (C=O). Anal Calcd for $C_{15}H_{12}BrNO_8$: C, 43.50; H, 2.92; N, 3.38; found: C, 43.38; H, 2.84; N, 3.25.

Diethyl 2-bromomethyl-5-oxo-2-(4-nitrophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (5d). Pale yellow powder, yield: 0.75 g (85%), m.p. 162–164°C. IR (KBr) (ν_{max}/cm^{-1}): 1757, 1687, 1667, 1592, 1248, 1147 cm^{-1}. ^{1}H-NMR: δ = 1.25 (3 H, t, ^3J = 7.3 Hz, Me), 1.35 (3 H, t, ^3J = 7.3 Hz, Me), 4.12 (1 H, d, ^2J = 10.8 Hz, CH), 4.25–4.31 (2 H, m, OCH_2), 4.37 (1 H, d, ^2J = 10.8 Hz, CH), 4.42 (2 H, q, ^3J = 7.3 Hz, OCH_2), 7.65 (2 H, d, ^3J = 8.2 Hz, 2 CH), 8.25 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 13.8 (Me), 14.0 (Me), 37.2 (CH_2Br), 61.8 (OCH_2), 62.4 (OCH_2), 91.4 (C), 123.7 (2 CH), 128.7 (2 CH), 141.3 (C), 141.7 (C), 142.8 (C), 147.6 (C), 159.4 (C=O), 161.0 (C=O), 162.3 (C=O). Anal Calcd for $C_{17}H_{16}BrNO_8$: C, 46.17; H, 3.65; N, 3.17; found: C, 46.22; H, 3.41; N, 3.05.

Dimethyl 2-bromomethyl-5-oxo-2-(p-biphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (5e). Pale yellow powder, yield: 0.71 g (80%), m.p. 145–147°C. IR (KBr) (ν_{max}/cm^{-1}): 1735, 1668, 1654, 1572, 1275, 1124 cm^{-1}. ^{1}H-NMR: δ = 3.80 (3 H, s, MeO), 3.87 (3H, s, MeO), 4.18 (1 H, d, ^2J = 11.0 Hz, CH), 4.38 (1 H, d, ^2J = 11.0 Hz, CH), 7.35 (1 H, t, ^3J = 7.5 Hz, CH), 7.38 (2 H, t, ^3J = 7.4 Hz, 2 CH), 7.52 (2 H, d, ^3J = 7.5 Hz, 2 CH), 7.58 (2 H, d, ^3J = 8.0 Hz, 2 CH), 7.67 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 38.4 (CH_2Br), 51.7 (MeO), 52.6 (MeO), 90.8 (C), 127.5 (2 CH), 128.2 (2 CH), 128.6 (2 CH), 129.2 (CH), 129.8 (2 CH), 135.8 (C), 138.4 (C), 141.5 (C), 142.4 (C), 143.7 (C), 159.4 (C=O), 162.3 (C=O), 162.7 (C=O). Anal Calcd for $C_{21}H_{17}BrO_6$: C, 56.65; H, 3.85; found: C, 56.88; H, 3.69.

Diethyl 2-bromomethyl-5-oxo-2-(p-biphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (5f). White powder, yield: 0.72 g (76%), m.p. 158–160°C. IR (KBr) (ν_{max}/cm^{-1}): 1728, 1664, 1648, 1594, 1268, 1157 cm^{-1}. ^{1}H-NMR: δ = 1.24 (3 H, t, ^3J = 7.3 Hz, Me), 1.32 (3 H, t, ^3J = 7.4 Hz, Me), 4.16 (1 H, d, ^2J = 11.5 Hz, CH), 4.25–4.32 (2 H, m, OCH_2), 4.38 (2 H, q, ^3J = 7.3 Hz, OCH_2), 4.47 (1 H, d, ^2J = 11.5 Hz, CH), 7.27 (1 H, t, ^3J = 7.4 Hz, CH), 7.36 (1 H, t, ^3J = 7.5 Hz, CH), 7.42 (2 H, d, ^3J = 7.5 Hz, 2 CH), 7.52 (2 H, d, ^3J = 8.2 Hz, 2 CH), 7.58 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 13.9 (Me), 14.0 (Me), 37.2 (CH_2Br), 61.4 (OCH_2), 62.4 (OCH_2), 91.4 (C), 127.6 (2 CH), 127.8 (2 CH), 128.3 (2 CH), 128.7 (CH), 129.2 (2 CH), 137.4 (C), 138.0 (C), 141.3 (C), 142.7 (C), 143.5 (C), 159.3 (C=O), 161.8 (C=O), 163.2 (C=O). MS: *m/z* (%) = 474 (M^+ + 2, 10), 472 (M^+, 10), 428 (58), 321 (78), 154 (100), 152 (48), 45 (68). Anal Calcd for $C_{23}H_{21}BrO_6$: C, 58.36; H, 4.47; found: C, 58.50; H, 4.25.

Dimethyl 2-bromomethyl-5-oxo-2-(4-chlorophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (5g). Pale yellow powder, yield: 0.66 g (82%), m.p. 135–137°C. IR (KBr) (ν_{max}/cm^{-1}): 1736, 1678, 1643, 1567, 1248, 1157 cm^{-1}. ^{1}H-NMR: δ = 3.78 (3 H, s, MeO), 3.86 (3 H, s, MeO), 4.15 (1 H, d, ^2J = 10.5 Hz, CH), 4.45 (1 H, d, ^2J = 10.5 Hz, CH), 7.32 (2 H, d, ^3J = 8.2 Hz, 2 CH), 7.38 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 38.6 (CH_2Br), 51.7 (MeO), 52.6 (MeO), 90.8 (C), 128.4 (2 CH), 128.8 (2 CH), 136.4 (C), 138.2 (C), 143.3 (C), 148.6 (C),

158.9 (C=O), 162.3 (C=O), 163.4 (C=O). Anal Calcd for $C_{15}H_{12}BrClO_6$: C, 44.64; H, 3.00; found: C, 44.49; H, 3.23.

Diethyl 2-bromomethyl-5-oxo-2-(4-chlorophenyl)-2,5-dihydrofuran-3,4-dicarboxylate (5h). White powder, yield: 0.69 g (80%), m.p. 147–149°C. IR (KBr) (ν_{max}/cm^{-1}): 1725, 1675, 1660, 1574, 1265, 1148 cm^{-1}. ^{1}H-NMR: δ = 1.23 (3 H, t, ^3J = 7.3 Hz, Me), 1.30 (3 H, t, ^3J = 7.3 Hz, Me), 4.25 (1 H, d, ^2J = 11.0 Hz, CH), 4.25–4.30 (2 H, m, OCH_2), 4.36 (2 H, q, ^3J = 7.4 Hz, OCH_2), 4.43 (1 H, d, ^2J = 11.0 Hz, CH), 7.28 (2 H, d, ^3J = 7.8 Hz, 2 CH), 7.37 (2 H, d, ^3J = 7.8 Hz, 2 CH). ^{13}C-NMR: δ = 13.8 (Me), 14.0 (Me), 37.5 (CH_2Br), 61.6 (OCH_2), 62.3 (OCH_2), 91.5 (C), 127.8 (2 CH), 128.7 (2 CH), 133.8 (C), 139.3 (C), 141.4 (C), 143.5 (C), 148.7 (C), 159.4 (C=O), 161.9 (C=O), 162.7 (C=O). Anal Calcd for $C_{17}H_{16}BrClO_6$: C, 47.30; H, 3.75; found: C, 47.57; H, 3.99.

Dimethyl 2-bromomethyl-5-oxo-2-(4-methoxyphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (5i). Yellow powder, yield: 0.68 g (85%), m.p. 142–144°C. IR (KBr) (ν_{max}/cm^{-1}): 1738, 1680, 1648, 1567, 1257, 1124 cm^{-1}. ^{1}H-NMR: δ = 3.78 (3 H, s, MeO), 3.82 (3 H, s, MeO), 3.94 (3 H, s, MeO), 4.12 (1 H, d, ^2J = 11.3 Hz, CH), 4.38 (1 H, d, ^2J = 11.3 Hz, CH), 7.14 (2 H, d, ^3J = 8.2 Hz, 2 CH), 7.38 (2 H, d, ^3J = 8.2 Hz, 2 CH). ^{13}C-NMR: δ = 37.6 (CH_2Br), 51.3 (MeO), 52.2 (MeO), 53.6 (MeO), 92.0 (C), 114.0 (2 CH), 128.7 (2 CH), 136.2 (C), 138.5 (C), 142.3 (C), 147.8 (C), 158.9 (C=O), 161.4 (C=O), 162.5 (C=O). Anal Calcd for $C_{16}H_{15}BrO_7$: C, 48.14; H, 3.79; found: C, 48.37; H, 3.92.

Diethyl 2-bromomethyl-5-oxo-2-(4-methoxyphenyl)-2,5-dihydrofuran-3,4-dicarboxylate (5j). Yellow crystals, yield: 0.67 g (78%), m.p. 146–148°C. IR (KBr) (ν_{max}/cm^{-1}): 1745, 1700, 1684, 1625, 1485, 1378 cm^{-1}. ^{1}H-NMR: δ = 1.25 (3 H, t, ^3J = 7.2 Hz, Me), 1.32 (3 H, t, ^3J = 7.3 Hz, Me), 4.08 (1 H, d, ^2J = 11.2 Hz, CH), 4.20–4.26 (2 H, m, OCH_2), 4.34 (2 H, q, ^3J = 7.3 Hz, OCH_2), 4.38 (1 H, d, ^2J = 11.2 Hz, CH), 6.74 (2 H, d, ^3J = 8.4 Hz, 2 CH), 7.36 (2 H, d, ^3J = 8.4 Hz, 2 CH). ^{13}C-NMR: δ = 13.6 (Me), 14.2 (Me), 38.2 (CH_2Br), 52.8 (MeO), 61.8 (OCH_2), 62.3 (OCH_2), 91.3 (C), 113.8 (2 CH), 127.8 (2 CH), 136.3 (C), 138.5 (C), 142.4 (C), 148.5 (C), 158.8 (C=O), 162.4 (C=O), 163.2 (C=O). Anal Calcd for $C_{18}H_{19}BrO_7$: C, 50.60; H, 4.48; found: C, 50.37; H, 4.71.

Dimethyl 2-bromomethyl-5-oxo-(2-naphthyl)-2,5-dihydrofuran-3,4-dicarboxylate (5u). Yellow powder, yield: 0.70 g (83%), m.p. 134–136°C. IR (KBr) (ν_{max}/cm^{-1}): 1745, 1715, 1682, 1597, 1452, 1354, 1245 cm^{-1}. ^{1}H-NMR: δ = 3.75 (3 H, s, MeO), 3.87 (3 H, s, MeO), 4.18 (1 H, d, ^2J = 10.8 Hz, CH), 4.47 (1 H, d, ^2J = 10.8 Hz, CH), 7.35–7.42 (7 H, m, 7 CH). ^{13}C-NMR: δ = 37.4 (CH_2Br), 51.7 (MeO), 52.8 (MeO), 92.2 (C), 122.8 (CH), 124.5 (CH), 125.7 (CH), 127.8 (CH), 128.2 (CH), 128.6 (CH), 129.3 (CH), 133.4 (C), 133.8 (C), 134.5 (C), 145.8 (C), 147.6 (C), 159.7 (C=O), 161.8 (C=O), 162.5 (C=O). Anal Calcd for $C_{19}H_{15}BrO_6$: C, 54.43; H, 3.61; found: C, 54.64; H, 3.37.

Diethyl 2-bromomethyl-5-oxo-2-(2-naphthyl)-2,5-dihydrofuran-3,4-dicarboxylate (5v). Yellow powder, yield: 0.76 g (85%), m.p. 125–127°C. IR (KBr) (ν_{max}/cm^{-1}): 1752, 1735, 1725, 1234 cm^{-1}. ^{1}H-NMR: δ = 1.26 (3 H, t, ^3J = 7.2 Hz, Me), 1.36 (3 H, t, ^3J = 7.4 Hz, Me), 4.22 (1 H, d, ^2J = 11.1 Hz, CH), 4.27–4.31 (2 H, m, OCH_2), 4.34 (2 H, q, ^3J = 7.4 Hz, OCH_2), 4.60 (1 H, d, ^2J = 11.1 Hz, CH), 7.45–7.94 (7 H, m, 7 CH). ^{13}C-NMR: δ = 13.6 (Me), 13.9 (Me), 35.3 (CH_2Br), 62.6 (OCH_2), 62.9 (OCH_2), 87.4 (C), 122.1 (CH), 125.4 (CH), 126.9 (CH), 127.3 (CH), 127.5 (CH), 128.3 (CH), 129.1 (CH), 129.5 (C), 130.9 (C), 132.8 (C), 133.3 (C), 155.1 (C), 159.7 (C=O), 160.2 (C=O), 165.4 (C=O). Anal Calcd for $C_{21}H_{19}BrO_6$: C, 56.39; H, 4.28; found: C, 56.62; H, 4.09.

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