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Synthesis of 1,3-Oxazines and Furo[2,3-*b*]pyrans by Reaction of 2-Amino-4,5-dihydro-3-furancarbonitriles with Dibenzoyldiazomethanes

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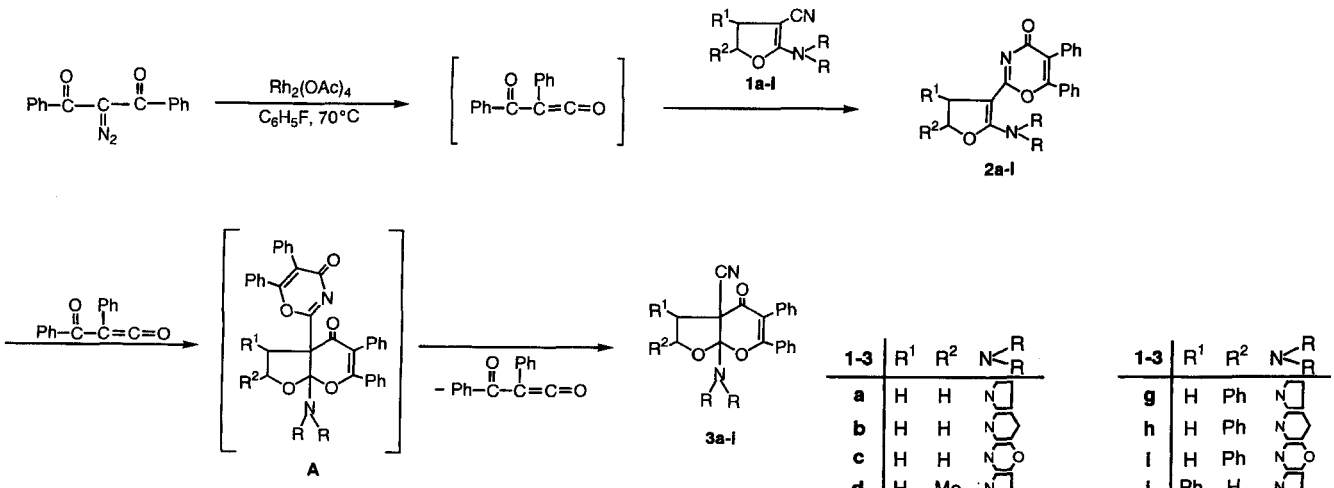
Abstract. 2-Amino-4,5-dihydro-3-furancarbonitriles (**1**) react with a slight excess of dibenzoyldiazomethane in the presence of rhodium(II) acetate to give 1,3-oxazin-4-ones (**2**). With three equivalents of dibenzoyldiazomethane compounds **1** react to afford furo[2,3-*b*]pyran-3a-carbonitriles (**3**). Compound **3a** was also obtained by treatment of **2a** with two equivalents of dibenzoyldiazomethane.

Diacyldiazomethanes are suitable precursors for the generation of acylketenes via thermal, photolytic, or catalytic elimination of nitrogen accompanied by Wolff rearrangement [1, 2]. Several examples of [2+4] cycloaddition of heterodienophiles [3–5] as well as of electron-rich alkenes such as enamines [6] to benzoylphenylketene have been reported. Recently, we showed that 4,5-dihydro-3-thiophenecarbonitriles react with dibenzoyldiazomethane [7] in the presence of rhodium(II) acetate to form 1,3-oxazin-4-ones [8]. In continuation of this study, we investigated the reactions of 4,5-dihydro-2-pyrrolidino-, as well as of 2-piperidino- and 2-morpholino-3-furancarbonitriles **1a–l** [9] with dibenzoyldiazomethane. The starting compounds **1b,e,h,k** were prepared by reaction of the corresponding 2-amino derivatives [10] with piperidine in the presence of trimethylamine hydrochloride in dioxane.

When a mixture of 4,5-dihydro-3-furancarbonitrile **1a**, dibenzoyldiazomethane (1.2 equiv.), and rhodium(II) acetate in fluorobenzene was heated at 70 °C, the 1,3-oxazin-4-one **2a** was obtained in 87% yield (Scheme 1).

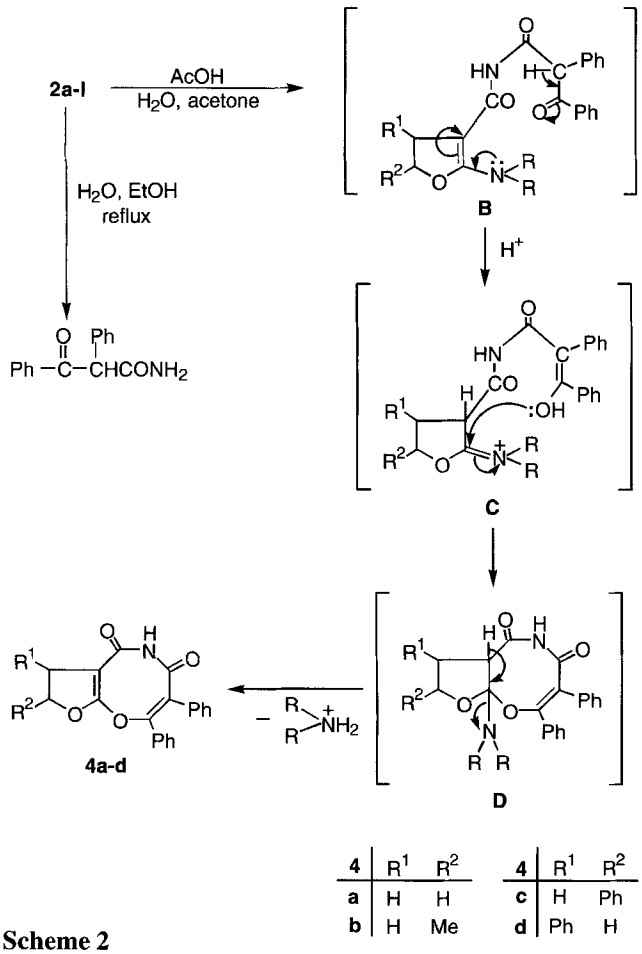


1-3	R^1	R^2	N<R R
a	H	H	
b	H	H	
c	H	H	
d	H	Me	
e	H	Me	
f	H	Me	

1-3	R^1	R^2	N<R R
g	H	Ph	
h	H	Ph	
i	H	Ph	
j	Ph	H	
k	Ph	H	
l	Ph	H	

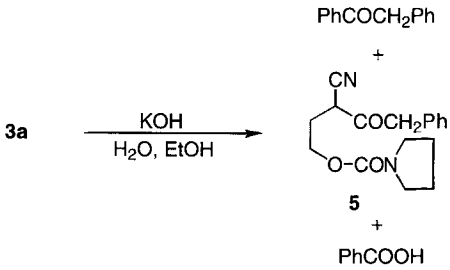
Scheme 1

Hydrolysis of **2a** with aqueous acetic acid afforded the furo[2,3-*b*][1,5]oxazocine **4a**. Probably, this reaction proceeds by initial 1,3-oxazine ring opening to form an imide **B**, which is converted into an enol **C**. The ring closure of the enol **C** affords an intermediate **D**, which undergoes elimination of pyrrolidine to form **4a**. In this reaction the imide **B** seems to behave as an enamine. The analogous intramolecular cyclization was also observed by Hünig *et al.* in their study dealing with the reaction of morpholine enamine and diketene [11]. Hydrolysis of **2a** in refluxing aqueous ethanol yielded 3-oxo-2-phenylbenzenepropanamide [12], presumably again via the imide **B**. The corresponding 3-furancarboxylic acid was not isolated (Scheme 2). Similarly, the reaction of the 4,5-dihydro-3-furancarbonitriles **1b–l** with dibenzoyldiazomethane (1.2 equiv.) furnished the 1,3-oxazin-4-ones **2b–l**. Treatment of compounds **2b–l** with aqueous acetic acid provided the furo[2,3-*b*][1,5] oxazocines **4a–d**.



Scheme 2

However, if a 1:3 molar ratio of **1a** to dibenzoyldiazomethane was used, instead of **2a** the furo[2,3-*b*]pyran-3a-carbonitrile **3a** was obtained in 85% yield. The same compound **3a** was also obtained by treatment of **2a** with dibenzoyldiazomethane (2 equiv.). Compound **2a** was not transformed into **3a** after 10 h of heating at 70 °C in fluorobenzene, and **2a** was recovered unchanged. When heated to near its melting point, **2a** decomposed to tarry matter. These findings suggest that **3a** was formed from **A** (Scheme 1). The structure of **3a** was determined by elemental analysis and the spectral data. Hydrolysis of **3a** with potassium hydroxide in aqueous ethanol furnished 1,2-diphenylethanone, pentyl 1-pyrrolidinecarboxylate **5**, and benzoic acid (Scheme 3).



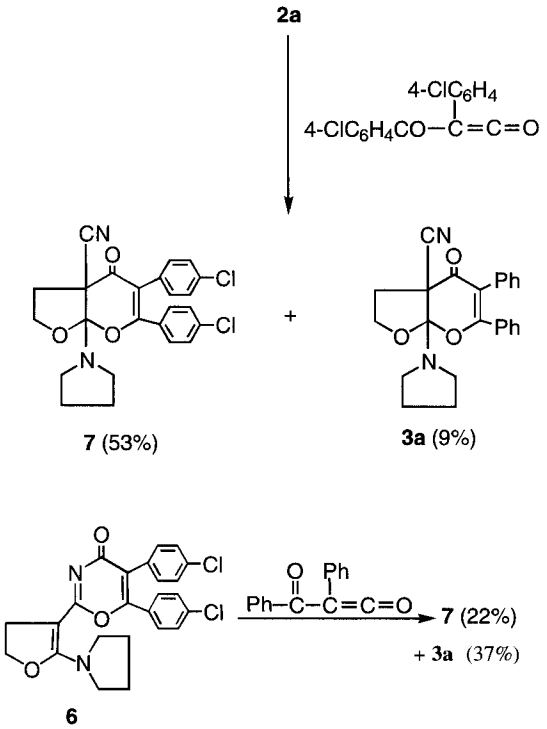
Scheme 3

Subsequently, reactions of the 2-amino-4,5-dihydro-3-furancarbonitriles **1b–l** with excess of dibenzoyldiazomethane (3 equiv.) were examined. From compounds **1b–e,h** only the furo[2,3-*b*]pyrans **3b–e,h** were obtained in good yields, while **1f,g,i** furnished mixtures of furo[2,3-*b*]pyrans **3f,g,i** and 1,3-oxazin-4-ones **2f,g,i**. From the 4,5-dihydro-4-phenyl-3-furancarbonitriles **1j–l** only the 1,3-oxazin-4-ones **2j–l** were formed. In a similar manner, **1a** reacted with 1.2 equivalents of bis(4-chlorobenzoyl)diazomethane [13] to afford 5,6-bis(4-chlorophenyl)-1,3-oxazin-4-one **6** in 75% yield, while with three equivalents of bis(4-chlorobenzoyl)diazomethane, 5,6-bis(4-chlorophenyl)furo[2,3-*b*]pyran-3a-carbonitrile **7** was formed in 68% yield.

In order to get insight into the formation of the furo [2,3-*b*]pyrans **3**, cross-over experiments were carried out. Thus, the rhodium(II) acetate catalyzed decomposition of bis(4-chlorobenzoyl)diazomethane (2 equiv.) in the presence of **2a** gave **3a** and **7** in 9, respectively 53% yield. Similarly, compound **6** reacted with dibenzoyldiazomethane to form **3a** and **7** in 37, respectively 22% yield (Scheme 4).

Although the IR spectra of compounds **3a–i**, **7** did not show nitrile bands around 2240–2260 cm^{-1}, the nitrile carbon could be found in the ^{13}C NMR spectra (~120 ppm).

On the basis of the above observations, the reaction pathway for the formation of furo[2,3-*b*]pyran-3a-carbonitrile **3a** can be illustrated as shown in Scheme 1. Wolff rearrangement of the dibenzoylcarbenoid results



Scheme 4

in the formation of benzoylphenylketene, which undergoes cycloaddition to the cyano group of **1a** to yield **2a**. Addition of another molecule of benzoylphenylketene to the olefinic moiety of the dihydrofuran ring of **2a** gives the bicyclic intermediate **A**, which eliminates the first molecule of benzoylphenylketene to produce **3a**.

Experimental

All melting points are uncorrected. IR spectra (KBr) were taken with a Jasco IRA-2. ^1H and ^{13}C NMR spectra were measured on a Hitachi R22 (90 MHz) and Jeol JNM-A500 (500 MHz) in $CDCl_3$ with TMS as internal standard, δ scale; couplings in Hz. Mass spectra were recorded with a Jeol JMS-D300, 70 eV.

4,5-Dihydro-2-piperidino-3-furancarbonitriles (1) (General Procedure)

A mixture of the 2-amino-4,5-dihydro-3-furancarbonitrile (50 mmol), piperidine (8.50 g, 100 mmol), and trimethylamine hydrochloride (1.00 g) in dioxane (20 ml) was refluxed for 1 h (**1b,e,h**) or 2.5 h (**1k**). The solvent was removed and H_2O was added to the residue. The mixture was acidified with 10% HCl (4 ml) and then extracted with CH_2Cl_2. The extract was washed with H_2O, dried with Na_2SO_4. Evaporation of the solvent and purification of the residue by column chromatography on alumina with CH_2Cl_2 as eluent, afforded **1** (NR_2 = piperidino).

4,5-Dihydro-2-piperidino-3-furancarbonitrile (**1b**)

From 2-amino-4,5-dihydro-3-furancarbonitrile [10] (5.50 g, 50 mmol). Yield 5.84 g (66%); colorless columns; *m.p.* 50–52 °C (Et_2O/petroleum ether). – IR: 2180 cm^{-1} (C≡N).– ^1H NMR: 1.43–1.80 [m, 6 H, 3×CH_2 (piperidine)], 2.90 (t, J = 9, 2H, 4-H), 3.30–3.66 [m, 4 H, 2×CH_2 (piperidine)], 4.33 (t, J = 9, 2 H, 5-H).

$C_{10}H_{14}N_2O$	Calcd.:	C 67.39	H 7.92	N 15.72
(178.2)	Found:	C 67.57	H 7.93	N 15.61.

4,5-Dihydro-5-methyl-2-piperidino-3-furancarbonitrile (**1e**)

From 2-amino-4,5-dihydro-5-methyl-3-furancarbonitrile [10] (6.20 g, 50 mmol). Yield 7.32 g (76%); pale yellow oil. – IR (neat): 2185 cm^{-1} (C≡N). – ^1H NMR: 1.35 (d, J = 6.5, 3H, CH_3), 1.40–1.78 [m, 6 H, 3×CH_2 (piperidine)], 2.50 (dd, J = 7.5/11.5, 1 H, 4-H), 3.00 (dd, J = 9/11.5, 1 H, 4-H), 3.27–3.60 [m, 4H, 2CH_2 (piperidine)], 4.48–4.88 (m, 1 H, 5-H).

$C_{11}H_{16}N_2O$	Calcd.:	C 68.72	H 8.39	N 14.57
(192.3)	Found:	C 68.25	H 8.39	N 14.19.

4,5-Dihydro-5-phenyl-2-piperidino-3-furancarbonitrile (**1h**)

From 2-amino-4,5-dihydro-5-phenyl-3-furancarbonitrile [10] (9.30 g, 50 mmol). Yield 10.62 g (84%); colorless columns; *m.p.* 39–40 °C (CH_2Cl_2/petroleum ether). – IR: 2170 cm^{-1} (C≡N). –^1H NMR: 1.30–1.77 [m, 6 H, 3×CH_2 (piperidine)], 2.90 (dd, J = 9/13.5, 1H, 4-H), 3.30 (dd, J = 9/13.5, 1H, 4-H), 3.33–3.67 [m, 4H, 2×CH_2 (piperidine)], 5.49 (t, J = 9, 1H, 5-H), 7.37 (s, 5H, aryl).

$C_{16}H_{18}N_2O$	Calcd.:	C 75.56	H 7.13	N 11.01
(254.3)	Found:	C 75.38	H 7.13	N 10.89.

4,5-Dihydro-4-phenyl-2-piperidino-3-furancarbonitrile (**1k**)

From 2-amino-4,5-dihydro-4-phenyl-3-furancarbonitrile [10] (9.30 g, 50 mmol). Yield 9.93 g (78%); colorless prisms; *m.p.* 71–72 °C (Et_2O/petroleum ether). – IR: 2180 cm^{-1} (C≡N). – ^1H NMR: 1.45–1.80 [m, 6H, 3×CH_2 (piperidine)], 3.40–3.70 [m, 4H, 2×CH_2 (piperidine)], 4.06–4.40 (m, 2H, 5-H), 4.46–4.75 (m, 1H, 4-H), 7.31 (s, 5H, aryl).

$C_{16}H_{18}N_2O$	Calcd.:	C 75.56	H 7.13	N 11.01
(254.3)	Found:	C 75.59	H 7.12	N 11.01.

General Procedures for Reactions of 2-Amino-4,5-dihydro-3-furancarbonitriles (1) with Dibenzoyldiazomethane

Procedure a: A mixture of **1** (5 mmol), dibenzoyldiazomethane [7] (1.50 g, 6 mmol), and $Rh_2(OAc)_4$ (0.05 g) in C_6H_5F (10 ml) was heated at 70 with stirring for 4 h. The solvent was removed, and the residue was chromatographed on alumina with CH_2Cl_2 as eluent. Yields: **3b** (0.42 g, 21%), **3h** (0.16 g, 7%). Further elution with CH_2Cl_2/acetone (4 : 1) gave **2a** (1.68 g, 87%), **2b** (0.86 g, 43%), **2c** (1.41 g, 70%), **2d** (1.74 g, 87%), **2e** (1.25 g, 60%), **2f** (1.37 g, 66%), **2g** (2.08 g, 90%), **2h** (1.54 g, 65%), **2i** (2.20 g, 92%), **2j** (2.17 g, 94%), **2k** (1.85 g, 66%), and **2l** (2.05 g, 73%).

Procedure b: From **1** (5 mmol) and dibenzoyldiazomethane (3.75 g, 15 mmol) as described for *procedure a*. Yields: **3a** (1.63 g, 85%), **3b** (1.97 g, 99%), **3c** (1.43 g, 71%), **3d** (1.51 g, 76%), **3e** (1.71 g, 83%), **3f** (0.43 g, 21%), **3g** (1.32 g, 57%), **3h** (1.75 g, 72%), and **3i** (0.44 g, 18%). Further elution with CH_2Cl_2/acetone (4:1) gave **2f** (0.63 g, 30%), **2g** (0.76 g, 33%),

2i (0.89 g, 37%), **2j** (2.08 g, 90%), **2k** (2.20 g, 78%), and **2l** (2.68 g, 95%).

2-(4,5-Dihydro-2-pyrrolidino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2a**)

From **1a** [9] (0.82 g, 5 mmol). Pale yellow columns; *m.p.* 173 °C (dec.) (acetone/petroleum ether). –MS, *m/z* (%): 386 (23) [M^+].

2-(4,5-Dihydro-2-piperidino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2b**)

From **1b** (0.89 g, 5 mmol). Pale yellow prisms; *m.p.* 177 °C (dec.) (CH_2Cl_2/Et_2O).

2-(4,5-Dihydro-2-morpholino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2c**)

From **1c** [9] (0.90 g, 5 mmol). Pale yellow columns; *m.p.* 205 °C (dec.) (acetone).

2-(4,5-Dihydro-5-methyl-2-pyrrolidino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2d**)

From **1d** [9] (0.89 g, 5 mmol). Pale yellow needles; *m.p.* 163 °C (dec.) (acetone/petroleum ether).

2-(4,5-Dihydro-5-methyl-2-piperidino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2e**)

From **1e** (0.96 g, 5 mmol). Pale yellow prisms; *m.p.* 143–145 °C (CH_2Cl_2/ Et_2O).

2-(4,5-Dihydro-5-methyl-2-morpholino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2f**)

From **1f** [9] (0.97 g, 5 mmol). Pale yellow needles; *m.p.* 189 °C (dec.) (acetone/petroleum ether).

2-(4,5-Dihydro-5-phenyl-2-pyrrolidino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2g**)

From **1g** [9] (1.20 g, 5 mmol). Pale yellow columns; *m.p.* 195 °C (dec.) (acetone).

2-(4,5-Dihydro-5-phenyl-2-piperidino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2h**)

From **1h** (1.27 g, 5 mmol). Colorless needles; *m.p.* 176 °C (dec.) (CH_2Cl_2/Et_2O).

2-(4,5-Dihydro-2-morpholino-5-phenyl-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2i**)

From **1i** [9] (1.28 g, 5 mmol). Pale yellow columns; *m.p.* 179–181 °C (CH_2Cl_2/ petroleum ether).

2-(4,5-Dihydro-4-phenyl-2-pyrrolidino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2j**)

From **1j** [9] (1.20 g, 5 mmol). Pale yellow scales; *m.p.* 208 °C (dec.) (acetone).

2-(4,5-Dihydro-4-phenyl-2-piperidino-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2k**)

From **1k** (1.27 g, 5 mmol). Pale yellow prisms; *m.p.* 108 °C (dec.) (CH_2Cl_2/ petroleum ether).

2-(4,5-Dihydro-2-morpholino-4-phenyl-3-furanyl)-5,6-diphenyl-4H-1,3-oxazin-4-one (**2l**)

From **1l** [9] (1.28 g, 5 mmol). Colorless prisms; *m.p.* 185–187 °C (CH_2Cl_2/ petroleum ether).

2,3,3a,7a-Tetrahydro-4-oxo-5,6-diphenyl-7a-pyrrolidino-4H-furo[2,3-b]pyran-3a-carbonitrile (**3a**)

From **1a** [9] (0.82 g, 5 mmol). Colorless prisms; *m.p.* 211–212 °C (acetone/ petroleum ether). – MS, *m/z* (%): 386 (75) [M^+]. – ^{13}C NMR: 24.9, 25.6, 25.8, 46.7, 48.3, 70.8, 109.1, 122.6 (C≡N), 127.0, 127.7, 127.9, 129.1, 129.3, 131.1, 133.5, 133.7, 155.0, 158.2, 159.5, 178.3 (C=O).

2,3,3a,7a-Tetrahydro-4-oxo-5,6-diphenyl-7a-piperidino-4H-furo[2,3-b]pyran-3a-carbonitrile (**3b**)

From **1b** (0.89 g, 5 mmol). Colorless needles; *m.p.* 201–202 °C (CH_2Cl_2/Et_2O). – ^{13}C NMR: 24.3, 25.8, 26.1, 46.2, 70.4, 109.4, 122.6 (C≡N), 127.1, 127.8, 127.9, 129.1, 129.3, 131.1, 133.5, 133.7, 155.9, 158.3, 159.6, 178.4 (C=O).

2,3,3a,7a-Tetrahydro-7a-morpholino-4-oxo-5,6-diphenyl-4H-furo[2,3-b]pyran-3a-carbonitrile (**3c**)

From **1c** [9] (0.90 g, 5 mmol). Colorless needles; *m.p.* 232–233 °C (CH_2Cl_2/ petroleum ether). – ^{13}C NMR: 25.9, 45.3, 66.4, 70.8, 110.1, 122.7 (C≡N), 127.2, 127.8, 128.0, 129.2, 129.3, 131.1, 133.3, 133.5, 155.5, 158.5, 159.1, 178.4 (C= O).

2,3,3a,7a-Tetrahydro-2-methyl-4-oxo-5,6-diphenyl-7a-pyrrolidino-4H-furo[2,3-b]pyran-3a-carbonitrile (**3d**)

From **1d** [9] (0.89 g, 5 mmol). Colorless needles; *m.p.* 202–203 °C (acetone). – ^{13}C NMR: 21.4, 25.0, 25.6, 31.6, 46.8, 48.1, 78.8, 107.3, 122.6 (C≡N), 127.0, 127.7, 127.9, 129.1, 129.3, 131.1, 133.5, 133.8, 154.2, 158.2, 159.9, 178.4 (C=O).

2,3,3a,7a-Tetrahydro-2-methyl-4-oxo-5,6-diphenyl-7a-piperidino-4H-furo[2,3-b]pyran-3a-carbonitrile (**3e**)

From **1e** (0.96 g, 5 mmol). Colorless needles; *m.p.* 203–204 °C (acetone). – ^{13}C NMR: 21.2, 24.3, 25.8, 31.9, 46.3, 78.7, 107.6, 122.6 (C≡N), 127.0, 127.8, 127.9, 129.1, 129.3, 131.1, 133.5, 133.8, 155.0, 158.3, 160.1, 178.5 (C=O).

2,3,3a,7a-Tetrahydro-2-methyl-7a-morpholino-4-oxo-5,6-diphenyl-4H-furo[2,3-b]pyran-3a-carbonitrile (**3f**)

From **1f** [9] (0.97 g, 5 mmol). Colorless needles; *m.p.* 205–206 °C (acetone/ petroleum ether). – ^{13}C NMR: 21.2, 31.7, 45.4, 66.4, 79.0, 108.3, 122.8 (C≡N), 127.2, 127.8, 128.0, 129.2, 129.3, 131.1, 133.4, 133.6, 154.6, 158.5, 159.4, 178.5 (C=O).

2,3,3a,7a-Tetrahydro-4-oxo-2,5,6-triphenyl-7a-pyrrolidino-4H-furo[2,3-b]pyran-3a-carbonitrile (**3g**)

From **1g** [9] (1.20 g, 5 mmol). Colorless needles; *m.p.* 222–223 °C (CH_2Cl_2/petroleum ether). – ^{13}C NMR: 25.0, 25.6, 32.7, 47.1, 48.3, 83.1, 107.8, 122.7 (C≡N), 125.7, 127.1, 127.8, 127.9, 128.2, 128.6, 129.1, 129.4, 131.1, 133.5, 133.7, 139.8, 154.1, 158.3, 159.8, 178.3 (C=O).

2,3,3a,7a-Tetrahydro-4-oxo-2,5,6-triphenyl-7a-piperidino-4H-furo[2,3-b]pyran-3a-carbonitrile (**3h**)

From **1h** (1.27 g, 5 mmol). Colorless prisms; *m.p.* 217 °C (dec.) (CH_2Cl_2/Et_2O). – ^{13}C NMR: 24.3, 25.7, 32.9, 46.6, 83.2, 108.1, 122.7 (C≡N), 125.9, 127.1, 127.8, 127.9, 128.4, 128.7, 129.2, 129.4, 131.1, 133.5, 133.7, 139.6, 155.1, 158.4, 159.9, 178.4 (C=O).

2,3,3a,7a-Tetrahydro-7a-morpholino-4-oxo-2,5,6-triphenyl-4H-furo[2,3-b]pyran-3a-carbonitrile (**3i**)

From **1i** [9] (1.28 g, 5 mmol). Colorless columns; *m.p.* 225–226 °C (CH_2Cl_2/petroleum ether). – ^{13}C NMR: 32.6, 45.5, 66.4, 83.6, 108.8, 122.9 (C≡N), 125.9, 127.2, 127.9, 128.0, 128.6, 128.8, 129.29, 129.32, 131.1, 133.3, 133.5, 139.2, 154.8, 158.6, 159.3, 178.4 (C=O).

Tab. 1 Analytical and spectral data of **2a–l**, **3a–i**

	Formula	Analysis Calcd./Found C	H	N	IR (cm^{-1}) C=O	^1H NMR, δ (ppm), J (Hz)
2a	$C_{24}H_{22}N_2O_3$ (386.5)	74.59 74.53	5.74 5.76	7.25 7.23	1640	1.80–2.00 [m, 4H, $2CH_2$ (pyrrolidine)], 3.12 (t, J = 8, 2H, 4-H), 3.56–3.85 [m, 4H, $2CH_2$ (pyrrolidine)], 4.36 (t, J = 8, 2H,5-H), 7.24 (s, 10H, aryl)
2b	$C_{25}H_{24}N_2O_30.5H_2O$ (409.5)	73.33 73.46	6.15 6.00	6.84 6.99	1640	1.50–1.80 [m, 6H, $3CH_2$ (piperidine)], 3.12 (t, J = 8, 2H, 4-H), 3.40–3.70 [m, 4H, $2CH_2$ (piperidine)], 4.33 (t, J = 8, 2H, 5-H), 7.26 (s, 10H, aryl)
2c	$C_{24}H_{22}N_2O_4$ (402.4)	71.63 71.72	5.51 5.63	6.96 6.95	1636	3.15 (t, J = 8.5, 2H, 4-H), 3.55–3.97 [m, 8H, $4CH_2$ (morpholine)], 4.37 (t, J = 8.5, 2H, 5-H), 7.23 (s, 5H, aryl), 7.25 (s, 5H, aryl)
2d	$C_{25}H_{24}N_2O_3$ (400.5)	74.98 74.98	6.04 6.09	7.00 6.99	1655	1.43 (d, J = 7, 3H, CH_3), 1.75–2.05 [m, 4H, $2CH_2$ (pyrrolidine)], 2.75 (dd, J = 7.5/13, 1H, 4-H), 3.25 (dd, J = 8/13, 1H, 4-H), 3.40–3.90 [m, 4H, $2CH_2$ (pyrrolidine)], 4.60–4.90 (m, 1H,5-H), 7.26 (s, 10H, aryl)
2e	$C_{26}H_{26}N_2O_3$ (414.5)	75.34 75.11	6.32 6.31	6.76 6.94	1642	1.42 (d, J = 6.5, 3H, CH_3), 1.50–1.80 [m, 6H, $3CH_2$ (piperidine)], 2.73 (dd, J = 7/13, 1H, 4-H), 3.25 (dd, J = 8/13, 1H, 4-H), 3.40–3.70 [m, 4H, $2CH_2$ (piperidine)], 4,60–4.80 (m, 1H, 5-H), 7.26 (s, 10H, aryl)
2f	$C_{25}H_{24}N_2O_4$ (416.5)	72.10 72.22	5.81 5.85	6.73 6.76	1640	1.45 (d, J = 6, 3H, CH_3), 2.77 (dd, J = 7/13, 1H, 4-H), 3.20 (dd, J = 8.5/13, 1H, 4-H), 3.54–3.96 [m, 8H, $4CH_2$ (morpholine)], 4.55–4.95 (m, 1H, 5-H), 7.23 (s, 5H, aryl), 7.25 (s, 5H, aryl)
2g	$C_{30}H_{26}N_2O_3$ (462.5)	77.90 77.94	5.670 5.89	6.06 6.08	1655	1.80–2.05 [m, 4H, $2CH_2$ (pyrrolidine)], 3.15 (dd, J = 9/12, 1H, 4-H), 3.56 (dd, J = 9/ 12, 1H, 4-H), 3.50–4.10 [m, 4H, $2CH_2$ (pyrrolidine)], 5.56 (t, J = 9, 1H, 5-H), 7.22 (s, 5H, aryl), 7.24 (s, 5H, aryl), 7.38 (s, 5H, aryl)
2h	$C_{31}H_{28}N_2O_3$ (476.6)	78.13 78.33	5.92 6.04	5.88 5.99	1644	1.45–1.80 [m, 6H, $3CH_2$ (piperidine)], 3.14 (dd, J = 9/13, 1H, 4-H), 3.40–3.80 [m, 5H, 4-H/$2CH_2$ (piperidine)], 5.51 (t, J= 9, 1 H, 5-H), 7.24 (s, 10H, aryl), 7.38 (s, 5H, aryl)
2i	$C_{30}H_{26}N_2O_4$ (478.5)	75.30 75.28	5.48 5.39	5.85 5.86	1654	3.16 (dd, J = 9/13.5, 1H, 4-H), 3.58 (dd, J = 9/ 13.5, 1H, 4-H), 3.70–3.90 [m, 8H, $4CH_2$ (morpholine)], 5.55 (t, J = 9, 1H, 5-H), 7.23 (s, 10H, aryl), 7.39 (s, 5H, aryl)
2j	$C_{30}H_{26}N_2O_3$ (462.5)	77.90 78.00	5.67 5.71	6.06 6.15	1637	1.85–2.15 [m, 4H, $2CH_2$ (pyrrolidine)], 3.38–3.70 [m, 2H, CH_2(pyrrolidine)], 3.90–4.20 [m, 2H, CH_2 (pyrrolidine)], 4.20–4.80 (m, 3 H, 4-H/5-H), 6.70–7.10 (m, 5 H, aryl), 7.19 (s, 5H, aryl), 7.31 (s, 5H, aryl)
2k	$C_{31}H_{28}N_2O_3CH_2Cl_2$ (561.5)	68.45 68.65	5.39 5.36	4.99 5.01	1642	1.50–2.05 [m, 6H, $3CH_2$ (piperidine)], 3.40–3.95 [m, 4H, $2CH_2$(piperidine)], 4.20–4.70 (m, 3H, 4-H/5-H), 6.80–7.15 (m, 5H, aryl), 7.20 (s, 5H, aryl), 7.32 (s, 5H, aryl)
2l	$C_{30}H_{26}N_2O_4CH_2Cl_2$ (563.5)	66.08 66.13	5.01 5.13	4.97 5.02	1640	3.50–4.10 [m, 8H, $4CH_2$ (morpholine)], 4.25–4.80 (m, 3H, 4-H/5-H), 6.76–7.50 (m, 10H, aryl), 7.20 (s, 5H, aryl)
3a	$C_{24}H_{22}N_2O_3$ (386.5)	74.59 74.50	5.74 5.81	7.25 7.22	1620	1.75–2.05 [m, 4H, $2CH_2$ (pyrrolidine)], 3.06 (t, J = 5, 2H, 3-H), 3.20–3.75 [m, 4H, $2CH_2$ (pyrrolidine)], 4.52 (t, J = 5, 2 H, 2-H), 7.10–7.50 (m, 10H, aryl)
3b	$C_{25}H_{24}N_2O_3$ (400.5)	74.98 74.98	6.04 6.13	7.00 7.00	1620	1.44–1.80 [m, 6H, $3CH_2$ (piperidine)], 3.05 (t, J = 5, 2 H, 3-H), 3.45–3.80 [m, 4H, $2CH_2$ (piperidine)], 4.50 (t, J = 5, 2H, 2-H), 7.10–7.42 (m, 10H, aryl)
3c	$C_{24}H_{22}N_2O_4$ (402.4)	71.63 71.41	5.51 5.50	6.96 6.76	1630	3.07 (t, J = 5, 2 H, 3-H), 3.55–3.80 [m, 8H, $4CH_2$ (morpholine)], 4.52 (t, J = 5, 2H, 2-H), 7.00–7.50 (m, 10H, aryl)
3d	$C_{25}H_{24}N_2O_3$ (400.5)	74.98 75.15	6.04 6.12	7.00 7.06	1630	1.47 (d, J = 6.5, 3H, CH_3), 1.80–2.05 [m, 4H, $2CH_2$ (pyrrolidine)], 2.62 (dd, J = 8/16, 1H, 3-H), 3.35 (dd, J = 1.5/16, 1H, 3-H), 3.20–3.80 [m, 4H, $2CH_2$ (pyrrolidine)], 4.55–4.85 (m, 1H, 2-H), 7.05–7.50 (m, 10H, aryl)
3e	$C_{26}H_{26}N_2O_3$ (414.5)	75.34 75.39	6.32 6.23	6.76 6.72	1620	1.44 (d, J = 6, 3H, CH_3), 1.40–1.80 [m, 6H, $3CH_2$ (piperidine)], 2.58 (dd, J = 9/17, 1H, 3-H), 3.25 (dd, J = 1.5/17, 1H, 3-H), 3.45–3.75 [m, 4H, $2CH_2$ (piperidine)], 4,55–4.80 (m, 1H, 2-H), 7.10–7.44 (m, 10H, aryl)
3f	$C_{25}H_{24}N_2O_4$ (416.5)	72.10 72.20	5.81 6.01	6.73 6.46	1625	1.50 (d, J = 6, 3H, CH_3), 2.65 (dd, J = 8.5/17.5, 1H, 3-H), 3.36 (dd, J = 1.5/17.5, 1H, 3-H), 3.60–3.85 [m, 8H, $4CH_2$ (morpholine)], 4.55–4.90 (m, 1H, 2-H), 7.05–7.50 (m, 10H, aryl)
3g	$C_{30}H_{26}N_2O_3$ (462.5)	77.90 77.72	5.67 5.55	6.06 6.05	1625	1.80–2.10 [m, 4H, $2CH_2$ (pyrrolidine)], 2.95 (dd, J = 9/17, 1H, 3-H), 3.35–3.80 [m, 4H, $2CH_2$ (pyrrolidine)], 3.65 (dd, J = 2/17, 1H, 3-H), 5.53 (dd, J = 2/9, 1H, 2-H), 7.15–7.60 (m, 15H, aryl)
3h	$C_{31}H_{28}N_2O_30.5H_2O$ (485.6)	76.68 76.82	6.02 5.89	5.77 5.78	1630	1.40–1.80 [m, 6H, $3CH_2$ (piperidine)], 2.99 (dd, J = 9/17, 1H, 3-H), 3.40–3.80 [m, 4H, $2CH_2$ (piperidine)], 3.58 (dd, J = 1.5/17, 1H, 3-H), 5.48 (dd, J = 1.5/9, 1H, 2-H), 7.10–7.35 (m, 10H, aryl), 7.40 (s, 5H, aryl)
3i	$C_{30}H_{26}N_2O_40.5H_2O$ (487.6)	73.91 73.76	5.58 5.59	5.75 5.81	1625	3.00 (dd, J = 9/17, 1H, 3-H), 3.50–3.80 [m, 9H, 3-H/$4CH_2$ (morpholine)], 5.51 (dd, J = 1.5/9, 1H, 2-H), 7.10–7.35 (m, 10H, aryl), 7.40 (s, 5H, aryl)

Reaction of 2-(4,5-Dihydro-2-pyrrolidino-3-furanyl)-5,6-diphenyl-4*H*-1,3-oxazin-4-one(2a) with Dibenzoyldiazomethane: Synthesis of 2,3,3a,7a-Tetrahydro-4-oxo-5,6-diphenyl-7a-pyrrolidino-4*H*-furo[2,3-*b*]pyran-3a-carbonitrile (3a)

A mixture of **2a** (1.29 g, 3.3 mmol), dibenzoyldiazomethane (1.67 g, 6.7 mmol), and $Rh_2(OAc)_4$ (0.04 g) in C_6H_5F (10 ml) was heated at 70 °C with stirring for 4 h. The solvent was removed, and the residue was purified by column chromatography on alumina with CH_2Cl_2 as eluent to give **3a** (1.12 g, 87%).

General Procedures for Reactions of 2a–l with Aqueous Acetic Acid

A mixture of **2a–l** (2.5 mmol), acetic acid (0.5 ml), and water (1 ml)(**2a–i**) or (2 ml) (**2j–l**) in acetone (15 ml)(**2a–i**) or (30 ml) (**2j–l**) was heated at 50 °C with stirring for 4 h (**2a–i**) or 30 h (**2j–l**). The solvent was removed, and H_2O was added to the residue. The mixture was extracted with CH_2Cl_2. The extract was washed with H_2O, and dried with Na_2SO_4. Evaporation of the solvent and purification of the residue by column chromatography on silica gel with CH_2Cl_2/acetone (4:1) as eluent afforded **4a** [from **2a** (0.97 g, 2.5 mmol): yield 0.65 g (78%), from **2b** (1.03 g, 2.5 mmol): yield 0.79 g (95%), from **2c** (1.01 g, 2.5 mmol): yield 0.67 g (80%)], **4b** [from **2d** (1.00 g, 2.5 mmol): yield 0.66 g (77%), from **2e** (1.04 g, 2.5 mmol): yield 0.80 g (93%), from **2f** (1.04 g, 2.5 mmol): yield 0.77 g (90%)], **4c** [from **2g** (1.16 g, 2.5 mmol): yield 0.85 g (83%), from **2h** (1.19 g, 2.5 mmol): yield 0.90 g (88%), from **2i** (1.20 g, 2.5 mmol): yield 0.89 g (87%)] or **4d** [from **2j** (1.16 g, 2.5 mmol): yield 0.47 g (46%), from **2k** (1.40 g, 2.5 mmol): yield 0.89 g (87%), from **2l** (1.41 g, 2.5 mmol): yield 0.87 g (85%)].

7,8-Dihydro-2,3-diphenyl-4H-furo[2,3-b][1,5]oxazocin-4,6(5H)-dione (**4a**)

Pale yellow needles; *m.p.* 232–233 °C (acetone). – IR: 3240 cm^{-1} (NH), 1717, 1680 (C = O). – ^1H NMR: 3.03 (t, J = 7.5, 2 H, 7-H), 4.43 (t, J = 7.5, 2 H, 8-H), 7.05–7.40 (m, 10 H, aryl), 10.56 (br. s, 1 H, NH). – MS, *m/z* (%): 333 (50) [M^+].

$C_{20}H_{15}NO_4$	Calcd.:	C 72.06	H 4.54	N 4.20
(333.3)	Found:	C 72.17	H 4.57	N 4.34.

7,8-Dihydro-8-methyl-2,3-diphenyl-4H-furo[2,3-b][1,5]oxazocin-4,6(5H)-dione (**4b**)

Pale yellow needles; *m.p.* 224–226 °C (CH_2Cl_2/Et_2O). – IR: 3210 cm^{-1} (NH), 1720, 1685 (C = O). – ^1H NMR: 1.44 (d, J = 7, 3 H, CH_3), 2.57 (dd, J = 6.5/15.5, 1 H, 7-H), 3.17 (dd, J = 9/15.5, 1 H, 7-H), 4.58–4.90 (m, 1 H, 8-H), 7.05–7.43 (m, 10 H, aryl), 10.58 (br. s, 1 H, NH).

$C_{21}H_{17}NO_4$	Calcd.:	C 72.61	H 4.93	N 4.03
(347.4)	Found:	C 72.47	H 4.87	N 4.10.

7,8-Dihydro-2,3,8-triphenyl-4H-furo[2,3-b][1,5]oxazocin-4,6(5H)-dione (**4c**)

Pale yellow needles; *m.p.* 211–212 °C (CH_2Cl_2/Et_2O). – IR: 3250 cm^{-1} (NH), 1716, 1690 (C = O). – ^1H NMR: 2.93 (dd, J = 7/14, 1 H, 7-H), 3.48 (dd, J = 9/14, 1 H, 7-H), 5.60 (dd, J = 7/9, 1 H, 8-H), 7.05–7.35 (m, 10 H, aryl), 7.37 (s, 5 H, aryl), 10.61 (br. s, 1 H, NH).

$C_{26}H_{19}NO_4$	Calcd.:	C 76.27	H 4.68	N 3.42
(409.4)	Found:	C 76.02	H 4.79	N 3.61.

7,8-Dihydro-2,3,7-triphenyl-4H-furo[2,3-b][1,5]oxazocin-4,6(5H)-dione (**4d**)

Pale yellow needles; *m.p.* 202–204 °C (CH_2Cl_2/Et_2O). – IR: 3200 cm^{-1} (NH), 1715, 1694 (C = O). – ^1H NMR: 4.05–4.80 (m, 3 H, 7-H/8-H), 6.45–7.35 (m, 15 H, aryl), 10.73 (br. s, 1 H, NH).

$C_{26}H_{19}NO_4$	Calcd.:	C 76.27	H 4.68	N 3.42
(409.4)	Found:	C76.18	H 4.66	N 3.61.

Reaction of 2-(4,5-Dihydro-2-pyrrolidino-3-furanyl)-5,6-diphenyl-4*H*-1,3-oxazin-4-one (2a) with Aqueous Ethanol

A mixture of **2a** (0.97 g, 2.5 mmol) and water (5 ml) in ethanol (15 ml) was refluxed for 7 h. The solvent was removed, and Et_2O was added to the residue. The precipitate was collected by filtration and recrystallized from acetone/petroleum ether to give 3-oxo-2-phenylbenzenepropanamide (0.40 g, 67%) as colorless needles; *m.p.* 176–177 °C (lit. [12] a) 172–174 °C, [12] b) 174–176 °C).

Hydrolysis of 2,3,3a,7a-Tetrahydro-4-oxo-5,6-diphenyl-7a-pyrrolidino-4*H*-furo[2,3-*b*]pyran-3a-carbonitrile (3a): Synthesis of 3-Cyano-4-oxo-5-phenylpentyl1-pyrrolidinecarboxylate (5)

A mixture of **3a** (1.93 g, 5 mmol), KOH (1.12 g, 20 mmol), and H_2O (5 ml) in EtOH (20 ml) was refluxed for 1.5 h. The solvent was removed, and H_2O was added to the residue. The mixture was extracted with Et_2O. The extract was washed with H_2O and dried with Na_2SO_4, and concentrated. The residue was recrystallized from petroleum ether to afford 1,2-diphenylethanone [0.53 g (54%), *m.p.* 55–56 °C]. This compound was identical with an authentic sample [deoxybenzoin (Aldrich Chemical Company, Inc.)] on the basis of the IR spectra. The aqueous layer was acidified with 10% HCl and extracted with CH_2Cl_2. The extract was dried with Na_2SO_4. Evaporation of the solvent and purification of the residue by column chromatography on silica gel with CH_2Cl_2 as eluent, afforded benzoic acid (0.09 g, 15%). Further elution with CH_2Cl_2/acetone (4:1) gave **5** (0.58 g, 39%).

3-Cyano-4-oxo-5-phenylpentyl-pyrrolidinecarboxylate (**5**)

Pale yellow oil. – IR ($CHCl_3$): 2240 cm^{-1} (C≡N), 1730, 1690 (C = O). – ^1H NMR: 1.70–2.05 [m, 4 H, 2×CH_2(pyrrolidine)], 2.10–2.40 (m, 2 H, $OCH_2C\underline{H}_2$), 3.10–3.50 [m, 4 H, 2×CH_2 (pyrrolidine)], 3.67 (dd, J = 6/8, 1 H, CH–CN), 4.00 (s, 2H, $COCH_2$), 4.10–4.40 (m, 2 H, $OC\underline{H}_2CH_2$), 7.10–7.55 (m, 5H, aryl). – MS, *m/z* (%): 300 (9) [M^+].

$C_{17}H_{20}N_2O_3$	Calcd.:	C 67.98	H 6.71	N 9.33
(300.4)	Found:	C 68.18	H 6.71	N 9.34.

5,6-Bis(4-chlorophenyl)-2-(4,5-dihydro-2-pyrrolidino-3-furanyl)-4H-1,3-oxazin-4-one (**6**)

A mixture of **1a** (0.55 g, 3.3 mmol), bis(4-chlorobenzoyl)diazomethane [13] (1.28 g, 4 mmol), and $Rh_2(OAc)_4$ (0.05 g) in C_6H_5F (10 ml) was heated at 70 °C with stirring for 4 h.

The solvent was removed, and the residue was chromatographed on alumina with CH_2Cl_2/acetone (4:1) as eluent to yield **6** (1.14 g, 75%). Pale yellow needles; *m.p.* 191 °C (dec.) (CH_2Cl_2/Et_2O). – IR: 1640 cm^{-1} (C = O). – ^1H NMR: 1.75–2.10 [m, 4 H, 2×CH_2 (pyrrolidine)], 3.10 (t, J = 8, 2 H, 4-H), 3.55–3.85 [m, 4 H, 2×CH_2 (pyrrolidine)], 4.38 (t, J = 8, 2 H, 5-H), 7.05–7.35 (m, 8 H, aryl).

$C_{24}H_{20}N_2O_3Cl_2$	Calcd.:	C 63.31	H 4.43	N 6.15
(455.3)	Found:	C 63.20	H 4.38	N 6.14.

5,6-Bis(4-chlorophenyl)-2,3,3a,7a-tetrahydro-4-oxo-7a-pyrrolidino-4H-furo[2,3-b]pyran-3a-carbonitrile (**7**)

A mixture of **1a** (0.55 g, 3.3 mmol), bis(4-chlorobenzoyl)diazomethane (3.19 g, 10 mmol), $Rh_2(OAc)_4$ (0.05 g) in C_6H_5F (10 ml) was heated at 70 °C with stirring for 4 h. The solvent was removed, and the residue was chromatographed on alumina with CH_2Cl_2 as eluent to afford **7** (1.04 g, 68%). Colorless columns; *m.p.* 235–237 °C (acetone). – IR: 1620 cm^{-1} (C=O). – ^1H NMR: 1.80–2.10 [m, 4 H, 2×CH_2 (pyrrolidine)], 3.03(t, J = 5, 2 H, 3-H), 3.30–3.70 [m, 4 H, 2CH_2 (pyrrolidine)], 4.50 (t, J = 5, 2H, 2-H), 7.05–7.35 (m, 8 H, aryl). – ^{13}C NMR: 24.9, 25.6, 25.8, 46.7, 48.3, 70.7, 109.1, 121.6 (C≡N), 128.3, 128.4, 130.6, 131.7, 132.0, 132.4, 133.3, 135.5, 155.1, 157.2, 159.6, 177.7 (C=O).

$C_{24}H_{20}N_2O_3Cl_2$	Calcd.:	C 63.31	H 4.43	N 6.15
(455.3)	Found:	C 63.52	H 4.60	N 6.20.

Reaction of 2-(4,5-Dihydro-2-pyrrolidino-3-furanyl)-5,6-diphenyl-4*H*-1,3-oxazin-4-one (2a) with Bis(4-chlorobenzoyl)diazomethane

A mixture of **2a** (1.49 g, 3.3 mmol), bis(4-chlorobenzoyl)diazomethane (2.13 g, 6.7 mmol), and $Rh_2(OAc)_4$ (0.05 g) in C_6H_5F (10 ml) was heated at 70 °C with stirring for 4 h. The solvent was removed, and the residue was chromatographed on alumina with CH_2Cl_2 as eluent to give a mixture of **3a** and **7**. Fractional recrystallization from acetone/petroleum ether gave colorless prisms (**3a**, 0.12 g, 9%) and colorless columns (**7**, 0.80 g, 53%).

Reaction of 5,6-Bis(4-chlorophenyl)-2-(4,5-dihydro-2-pyrrolidino-3-furanyl)-4*H*-1,3-oxazin-4-one (6) with Dibenzoyldiazomethane

A mixture of **6** (1.51 g, 3.3 mmol), dibenzoyldiazomethane (1.67 g, 6.7 mmol), and $Rh_2(OAc)_4$ (0.05 g) in C_6H_5F (10 ml) was heated at 70 °C with stirring for 4 h. The solvent was removed, and the residue was chromatographed on alumina with CH_2Cl_2 as eluent to give a mixture of **3a** (0.48 g, 37%) and **7** (0.34 g, 22%).

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