Furan Ring Opening – Isocoumarine Ring Closure: A Recyclization Reaction of 2-Carboxyaryldifurylmethanes

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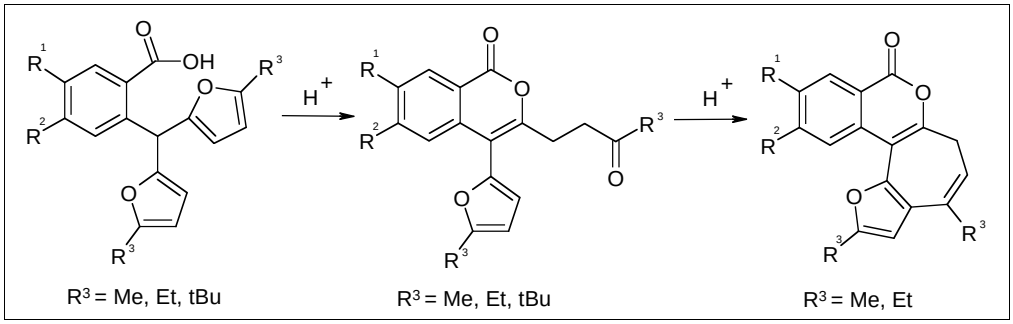

A general method for the synthesis of isocoumarine derivatives has been developed. Bis(5-R-2-furyl)methylbenzoic acids (R = methyl, ethyl) underwent recyclization and subsequent cyclization into tetracyclic isochromene-1-one derivatives under treatment with hydrogen chloride in methanol. It has been shown that intermediate 4-(5-R-furan-2-yl)-3-(3-oxo-3-R-propyl)-isochromene-1-ones can be obtained selectively by varying a concentration of the hydrogen chloride and reaction times. In the case of R = *tert*-butyl only corresponding 4-[5-(*tert*-butyl)-2-furyl]-3-(4,4-dimethyl-3-oxopentyl)-1-isochromenones were isolated regardless of the reaction conditions.

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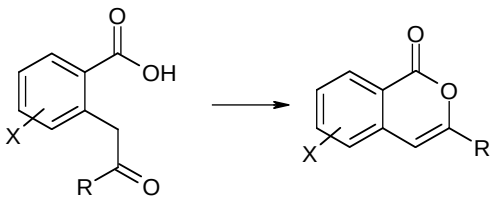
Introduction.

Isocoumarine derivatives are an important class of natural lactones possessing many kinds of biological activity [1]. A whole number of synthetic isocoumarines are of great interest as pharmaceuticals with antifungal [2], antibacterial [2b], anticoagulant activity [3], human leukocyte elastase inhibitors [4].

The highly reactive heterocyclic ring of isocoumarine makes it an attractive synthon for the synthesis of other types of hetero- and carbocyclic compounds. For example, total syntheses of some natural products like nitidine [5], tetracycline antibiotic pretetramide [6], antraquinone anticancer agents of angucyclines (±)-PD 116740 series [7], natural antibiotics (±)-Cervinomycins A_1 and A_2 [8], and cannabinoids [9] include isocoumarine ring transformation as an intermediate step.

Altogether it stimulates the development of new syntheses of isocoumarine core and their applications for practical needs. Although many synthetic approaches have been elaborated, the intramolecular cyclization of *ortho*-(ethan-2-one)benzoic acids remains the main among them (Scheme 1). There are at least three known ways to synthesize these compounds. The first one is based on building up the phenyl ring with simultaneous formation of the required configuration for carbonyl and carboxyl substituents [10]. The second way provides the introduction of a carboxy group into the *ortho*-position of benzylcarbonyl compounds [11]. The third approach, most popular, results from the attachment the of methylenecarbonyl group to the *ortho*-position of benzoic acids, and the function can exist both in explicit [2b,7,12] and in latent form (acetylenes [13], vinyl bromides [14], preoxidized ethylenes [5,15], enol ethers [16] etc.).

Scheme 1



It is well-known that alkylfurans can easily undergo protolytic furan ring cleavage to form 1,4-dicarbonyl compounds, and this property is often used in practice [17]. Therefore the furan could be considered as a masked equivalent of a carbonyl group (Scheme 2). From this

point of view, *ortho*-substituted benzylfurans are in fact latent equivalents of *ortho*-substituted benzylcarbonyl compounds.

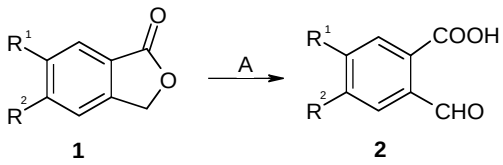
Such recyclization of *ortho*-substituted benzylfurans is prerequisite to our new successful method of building up numerous benzannelated heterocycles [18]. In the preliminary communication on two examples it was reported that the treatment of 2-carboxyaryldifuryl-methanes with boiling methanol saturated with hydrogen chloride don't stop on the stage of furan ring recyclization but accompanies with secondary cyclization into tetracyclic isocoumarine derivatives [19]. In the present work we showed applicability of this reaction for the synthesis of wide range of these compounds. Moreover the reaction conditions were found for the selective synthesis of the isocoumarine ketones which were postulated as intermediates in the preliminary communication [19].

Results and Discussion.

To realize the methodology of isocoumarine synthesis we had to prepare benzylfurans with carboxy group in *ortho*-position (Scheme 3). The easiest way to prepare *ortho*-functionalized benzylfurans is the acid-catalyzed condensation of alkylfurans with corresponding *ortho*-substituted benzaldehydes [19, 20].

Thus, the first step in the reaction sequence involved the synthesis of 2-formylbenzoic acid derivatives, which is a well developed area [21]. We used radical bromination of phthalides **1** with subsequent hydrolysis of 3-bromophthalides [22] to obtain a number of 2-formylbenzoic acids **2** (Scheme 4, Table 1).

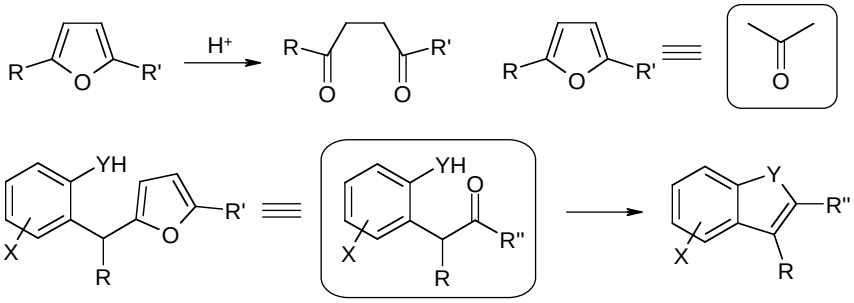
Scheme 4



A: 1) Br_2, *hv*, 2) H_2O

The synthesis of 2-carboxyaryldifurylmethanes **4** was carried out by keeping dioxane solutions of 2-formylbenzoic acids **2** and 2-alkylfurans **3** at 60 °C in the presence of $HClO_4$ (Scheme 5, Table 2). The elevated

Scheme 2



Scheme 3

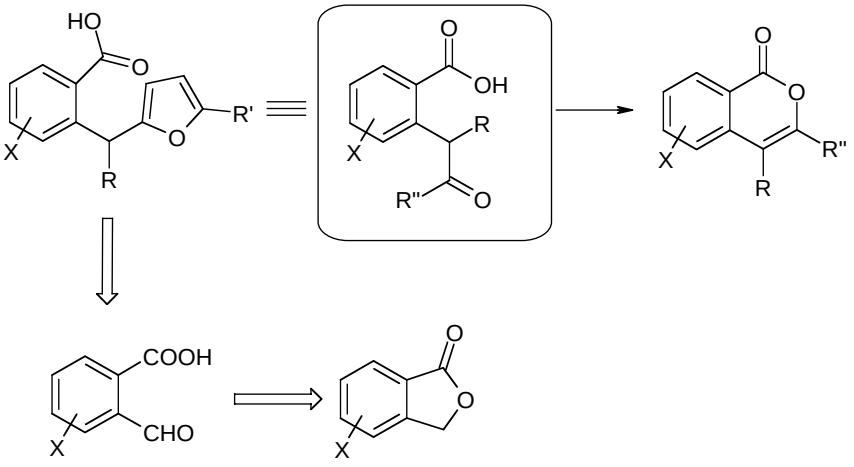


Table 1
Yields of 2-formylbenzoic acids **2a-i**

Entry	R^1	R^2	Product	Yield (%)
a	H	H	**2a**	70
b	NO_2	H	**2b**	73
c	Cl	H	**2c**	70
d	Br	H	**2d**	72
e	H	Br	**2e**	72
f	H	Cl	**2f**	70
g	OMe	H	**2g**	75
h	OMe	OMe	**2h**	78
i	I	H	**2i**	73

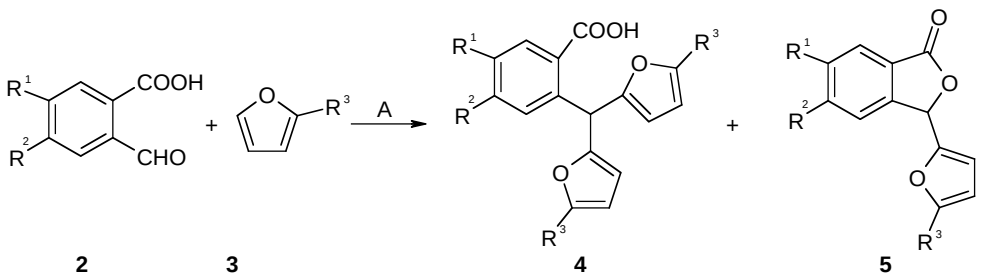
temperature allowed to reduce the reaction time to 20-30 minutes and to enhance the yields in comparison with the earlier reported procedure [19]. Noteworthy, the reaction with 2-*tert*-butylfuran was complicated by formation of reasonable amounts of 3-furylphthalides **5** as byproduct, and even longer reaction times did not change the products ratio but led to decomposition of participating compounds.

Keeping 2-carboxyaryldifurylmethanes **4a-j** under reflux in methanolic HCl solution (30 weight % of HCl) for 30 minutes led to formation of tetracyclic isocoumarines **7a-j** with only traces of the opened ketone **6** under TLC control (Scheme 6, Table 3). We observed similar secondary cyclizations in the reactions of N-benzyl-2-bis(5-methyl-2-furyl)-methylbenzamide [18f], 2-bis(5-methyl-2-furyl)-methylphenylmethanols [18g] and *N*-tosyl-2-bis(5-methyl-2-furyl)-methylanilines [23], where the reaction also did not come to stop on the stage of ketones. The facile intramolecular cyclization of such ketones was first demonstrated for 3-(5-methyl-2-furyl)-3-(3-oxobutyl)-benzo[*b*]furans [24], initial products of 2-bis(5-methyl-2-furyl)-methylphenols recyclization.

After some experimentation we were pleased to find that ketones **6** could be selectively obtained by treatment of 2-carboxyaryldifurylmethanes with more diluted methanolic HCl solution (8 % weight) for 40 minutes with 55-75% yield. Tetracyclic products **7** were also observed but in minor quantities (< 10%).

A completely different picture emerged after going from methyl and ethyl substituted benzylfurans **4a-j** to those with *tert*-butyl substituent in the position 5 of furans. Treatment of these compounds with highly concentrated HCl/MeOH solution for 5 minutes led

Scheme 5



A: $HClO_4$, 1,4-dioxane

Table 2
Yields of 2-Carboxyaryldifurylmethanes **4a-o** and 2-Furylphthalides **5k-o**

Entry	R^1	R^2	R^3	Product	Yield (%)	Product	Yield (%)
a	H	H	Me	**4a**	68		
b	NO_2	H	Me	**4b**	72		
c	Cl	H	Me	**4c**	64		
d	Br	H	Me	**4d**	67		
e	H	Br	Me	**4e**	69		
f	H	Cl	Me	**4f**	70		
g	OMe	H	Me	**4g**	60		
h	OMe	OMe	Me	**4h**	62		
i	H	H	Et	**4i**	68		
j	NO_2	H	Et	**4j**	70		
k	H	H	*t*Bu	**4k**	14	**5k**	21
l	NO_2	H	*t*Bu	**4l**	16	**5l**	29
m	Cl	H	*t*Bu	**4m**	18	**5m**	31
n	Br	H	*t*Bu	**4n**	19	**5n**	32
o	I	H	*t*Bu	**4o**	22	**5o**	36

Scheme 6

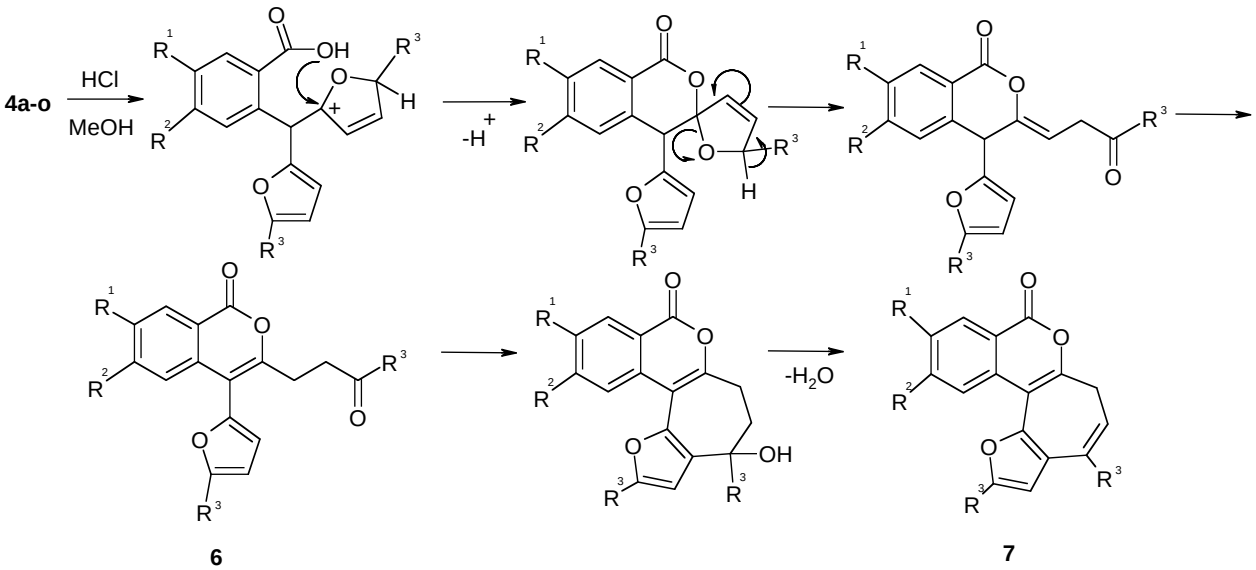


Table 3

Yields of Isocoumarine Derivatives **6** and **7**

Entry	R^1	R^2	R^3	Product	Yield (%)	Product	Yield (%)
a	H	H	Me	**6a**	55	**7a**	66
b	NO_2	H	Me	**6b**	72	**7b**	70
c	Cl	H	Me	**6c**	68	**7c**	72
d	Br	H	Me	**6d**	70	**7d**	75
e	H	Br	Me	**6e**	75	**7e**	65
f	H	Cl	Me			**7f**	63
g	MeO	H	Me			**7g**	68
h	MeO	MeO	Me			**7h**	65
i	H	H	Et			**7i**	69
j	NO_2	H	Et			**7j**	71
k	H	H	*t*Bu	**6k**	80		
l	NO_2	H	*t*Bu	**6l**	75		
m	Cl	H	*t*Bu	**6m**	82		
n	Br	H	*t*Bu	**6n**	81		
o	I	H	*t*Bu	**6o**	79		

exclusively to ketones **6k-o**. Even longer reaction times did not help in the formation of tetracyclic isocoumarines, as only strong decomposition was observed in this case. Such inability for secondary cyclizations can be attributed to lowered activity of the carbonyl group of ketones **6k-o** due to sterical hindrance caused by bulky *tert*-butyl substituent.

In conclusion, a general and easy method for preparation of biologically relevant isocoumarine derivatives was developed. Highly complex tetracyclic heterocyclic molecules were constructed in only two steps starting from as simple substances as 2-formylbenzoic acids **2** and 2-alkylfurans **3**.

EXPERIMENTAL

^{1}H nmr spectra were recorded on a Bruker AC200 spectrometer (200 MHz) and Bruker AM300 spectrometer (300 MHz) at ambient temperature in $CDC1_3$, DMSO-d_6 using $CHC1_3$, (δ = 7.26) or tetramethylsilane (δ = 0.00) as internal standards. Chemical shifts (δ) are quoted in ppm and coupling constants (J) are given in absolute values in Hz to the nearest 0.1 Hz. ^{13}C nmr spectra were recorded with a Bruker AM300 (75.5 MHz) at ambient temperature in $CDC1_3$ with δ ($CDC1_3$) = 77.0 as internal standard. Infrared spectra were recorded with an InfraLUM FT-02 spectrometer. Mass spectra were recorded on a Kratos MS-30 instrument with 70 eV electron impact ionization at 200 ºC. All solvents were distilled prior to use. Melting points are uncorrected.

6-Nitro-3H-isobenzofuran-1-one **1b** was synthesized by nitration of phthalide **1a** [25] under known conditions (KNO_3 /H_2SO_4) [26].

6-Halogenated isobenzofuran-1-ones **1c**, **1d**, **1i** were obtained by Sandmeyer reaction [27] from 6-amino-3H-isobenzofuran-1-one (see below).

6-Amino-3*H*-isobenzofuran-1-one.

A mixture of phthalide **1b** 70 g (0.391 mol), 60 g of Fe powder, 70 mL of acetic acid, 210 mL of ethyl acetate and 210 mL of water was stirred under reflux for 1 hour. The mixture was cooled, carefully treated with 100 g of solid $NaHCO_3$, and additionally refluxed for 10 minutes. The suspension was extracted three times with 300 mL of boiling dioxane. Combined organic extracts were treated with active charcoal, filtered and evaporated. The residue was recrystallized from EtOH/acetone to give 50 g (86%) of the title compound with mp 186-187°C.

5-Halogenated isobenzofuran-1-ones **1e** and **1f** were obtained by Sandmeyer reaction [28] from 5-amino-3H-isobenzofuran-1-one [29].

6-Methoxy-3H-isobenzofuran-1-one **1g** [30] and 5,6-dimethoxy-3H-isobenzofuran-1-one **1h** [31] were obtained by *ortho*-chloromethylation of corresponding methoxybenzoic acids.

2-Formylbenzoic acids **2a-i** were synthesized from isobenzofuran-1-one **1a-i** through the bromination followed by hydrolysis under slightly modified conditions [22c].

General Procedure for the Preparation of 2-Formylbenzoic acids **2a-i**.

A mixture of isobenzofuran-1-ones **1a-i** (0.14 mol) and Br_2 (0.14 mol) in 500 mL of CCl_4 was stirred under reflux and irradiation with a 200 W lamp. After the reaction is completed (TLC control), the solvent was evaporated, and the oily residue was dissolved in hot water. The solution was treated with active charcoal, filtered and left to crystallize.

General Procedure for the Preparation of 2-Carboxybenzylfurans **4a-o** and 3-Furylphthalides **5k-o**.

To a solution of 2-formylbenzoic acid (0.1 mol) and alkylfuran (0.4 mol) in 200 mL of dioxane 3 mL of $HClO_4$ (conc. 70%) was added in one portion. The mixture was thermostated at 60 ºC for 25 minutes, and then poured into water. The precipitated solid was collected by filtration and recrystallized.

In the case of 2-*tert*-butylfuran the mixture of compounds **4k-o** and phthalides **5k-o** was separated by column chromatography on silica gel (Sorbpolymer, 50-160 mkm) using hexane – CH_2Cl_2 (2:1) as an eluent.

Compounds **4a**, **4i** was described [19].

2-Bis(5-methyl-2-furyl)methyl-5-nitrobenzoic acid (**4b**).

This compound was obtained according to the general method in 72% yield as pale yellow prisms (dichloromethane-hexane), mp 189-190°; ir (Nujol): 1682 (O=C-O) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 2.24 (s, 6H, CH_3), 5.89 (d, ^3J = 3.2 Hz, 2H, 4-H_{Fur}), 5.97 (d, ^3J = 3.2 Hz, 2H, 3-H_{Fur}), 6.72 (s, 1H, CH), 7.58 (d, ^3J = 8.2 Hz, 1H, H_{Ar}), 8.32 (dd, ^4J = 2.0, ^3J = 8.2 Hz, 1 H, H_{Ar}), 8.91 (d, ^4J = 2.0 Hz, 1 H, H_{Ar}).

Anal. Calcd. for $C_{18}H_{15}NO_6$: C, 63.34, H, 4.43. Found: C, 63.22, H, 4.40.

5-Chloro-2-bis(5-methyl-2-furyl)methylbenzoic acid (**4c**).

This compound was obtained according to the general method in 64% yield as colorless prisms (ethanol-acetone), mp 222-223°; ir (Nujol): 1686 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.25 (s, 6H, CH_3), 5.89 (s, 4H, H_{Fur}), 6.60 (s, 1H, CH), 7.31 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 7.48 (dd, ^4J = 2.3, ^3J = 8.3 Hz, 1H, H_{Ar}), 8.04 (d, ^4J = 2.3 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{18}H_{15}ClO_4$: C, 65.36; H, 4.57. Found: C, 65.25; H, 4.61.

5-Bromo-2-bis(5-methyl-2-furyl)methylbenzoic acid (**4d**).

This compound was obtained according to the general method in 67% yield as colorless prisms (dichloromethane-hexane), mp 226-227°; ir (Nujol): 1685 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.25 (s, 6H, CH_3), 5.88 (s, 4H, H_{Fur}), 6.58 (s, 1H, CH), 7.24 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 7.63 (dd, ^4J = 2.0, ^3J = 8.3 Hz, 1H, H_{Ar}), 8.19 (d, ^4J = 2.0 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{18}H_{15}BrO_4$: C, 57.62; H, 4.03. Found: C, 57.70; H, 4.09.

4-Bromo-2-bis(5-methyl-2-furyl)methylbenzoic acid (**4e**).

This compound was obtained according to the general method in 69% yield as colorless prisms (dichloromethane-hexane), mp 153-154°; ir (Nujol): 1688 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.26 (s, 6H, CH_3), 5.90 (s, 4H, H_{Fur}), 6.66 (s, 1H, CH), 7.48 (dd, ^4J = 2.1, ^3J = 8.9 Hz, 1H, H_{Ar}), 7.52 (d, ^4J = 2.1 Hz, 1H, H_{Ar}), 7.93 (d, ^3J = 8.9 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{18}H_{15}BrO_4$: C, 57.62; H, 4.03. Found: C, 57.53; H, 3.96.

4-Chloro-2-bis(5-methyl-2-furyl)methylbenzoic acid (**4f**).

This compound was obtained according to the general method in 70% yield as colorless prisms (dichloromethane-hexane), mp 166-165°; ir (Nujol): 1684 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.26 (s, 6H, CH_3), 5.90 (s, 4H, H_{Fur}), 6.68 (s, 1H, CH), 7.33 (dd, ^4J = 2.1, ^3J = 9.0 Hz, 1H, H_{Ar}), 7.35 (d, ^4J = 2.1 Hz, 1H, H_{Ar}), 8.03 (d, ^3J = 9.0 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{18}H_{15}ClO_4$: C, 65.36; H, 4.57. Found: C, 65.23; H, 4.50.

2-Bis(5-methyl-2-furyl)methyl-5-methoxybenzoic acid (**4g**).

This compound was obtained according to the general method in 60% yield as colorless prisms (dichloromethane-hexane), mp 191-192°; ir (Nujol): 1668 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, DMSO-d_6): δ 2.19 (s, 6H, CH_3), 3.79 (s, 3H, OCH_3), 5.80 (d, ^4J = 3.2 Hz, 2H, 3-H_{Fur}), 5.96 (d, ^4J = 3.2 Hz, 2H, 4-H_{Fur}), 6.49 (s, 1H, CH), 7.09 (dd, ^4J = 2.6, ^3J = 8.6 Hz, 1H, H_{Ar}), 7.17 (d, ^3J = 8.6 Hz, 1H, H_{Ar}), 7.35 (d, ^4J = 2.6 Hz, 1H, H_{Ar}), 13.09 (bs, 1H, OH).

Anal. Calcd. for $C_{19}H_{18}O_5$: C, 69.93; H, 5.56. Found: C, 69.99; H, 5.51.

2-Bis(5-methyl-2-furyl)methyl-4,5-dimethoxybenzoic acid (**4h**).

This compound was obtained according to the general method in 62% yield as colorless prisms (dichloromethane-hexane), mp 138-139°; ir (Nujol): 1670 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.56 (s, 6H, CH_3), 3.83 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 5.88 (s, 4H, H_{Fur}), 6.77 (s, 1H, CH), 6.89 (s, 1H, H_{Ar}), 7.64 (s, 1H, H_{Ar}).

Anal. Calcd. for $C_{20}H_{20}O_6$: C, 67.41; H, 5.66. Found: C, 67.50; H, 5.72.

2-Bis(5-ethyl-2-furyl)methyl-5-nitrobenzoic acid (**4j**).

This compound was obtained according to the general method in 70% yield as pale yellow prisms (dichloromethane-hexane), mp 131-132°; ir (Nujol): 1685 (O=C-O) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 1.19 (t, ^3J = 7.5 Hz, 6H, CH_2CH_3), 2.58 (q, ^3J = 7.5 Hz, 4H, CH_2CH_3), 5.89 (d, ^3J = 3.2 Hz, 2H, 4-H_{Fur}), 5.97 (d, ^3J = 3.2 Hz, 2H, 3-H_{Fur}), 6.73 (s, 1H, CH), 7.58 (d, ^3J = 8.2 Hz, 1H, H_{Ar}), 8.33 (dd, ^4J = 2.0, ^3J = 8.2 Hz, 1H, H_{Ar}), 8.92 (d, ^4J = 2.0 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24. Found: C, 70.88; H, 6.29.

2-Bis[5-(*tert*-butyl)-2-furyl]methylbenzoic acid (**4k**).

This compound was obtained according to the general method in 14% yield as colorless prisms (dichloromethane-hexane), mp 118-119°; ir (Nujol): 1684 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.24 (s, 18 H, *t*Bu), 5.82 (d, ^3J = 3.1 Hz, 2H, 4-H_{Fur}), 5.86 (d, ^3J = 3.1 Hz, 2H, 3-H_{Fur}), 6.66 (s, 1H, CH), 7.28-7.36 (m, 2H, H_{Ar}), 7.45-7.52 (m, 1H, H_{Ar}), 8.04-8.07 (m, 1H, H_{Ar}).

Anal. Calcd. for $C_{24}H_{28}O_4$: C, 75.76; H, 7.42. Found: C, 75.88; H, 7.38.

2-Bis[5-(*tert*-butyl)-2-furyl]methyl-5-nitrobenzoic acid (**4l**).

This compound was obtained according to the general method in 16% yield as oil; ir (Nujol): 1687 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.18 (s, 18 H, *t*Bu), 5.81 (d, ^3J = 3.1 Hz, 2H, 3-H_{Fur}), 5.87 (d, ^3J = 3.1 Hz, 2H, 4-H_{Fur}), 6.77 (s, 1H, CH), 7.49 (d, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.22 (dd, ^4J = 2.0, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.79 (d, ^4J = 2.0 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{24}H_{27}NO_6$: C, 67.75; H, 6.40. Found: C, 67.69; H, 6.43.

5-Chloro-2-bis[5-(*tert*-butyl)-2-furyl]methylbenzoic acid (**4m**).

This compound was obtained according to the general method in 18% yield as colorless prisms (hexane), mp 144-145°; ir (Nujol): 1682 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.24 (s, 18 H, *t*Bu), 5.86 (s, 4H, H_{Fur}), 6.60 (s, 1H, CH), 7.26 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 7.46 (dd, ^4J = 2.2, ^3J = 8.0 Hz, 1H, H_{Ar}), 8.04 (d, ^4J = 2.2 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{24}H_{27}ClO_4$: C, 69.47; H, 6.56. Found: C, 69.38; H, 6.59.

5-Bromo-2-bis[5-(*tert*-butyl)-2-furyl]methylbenzoic acid (**4n**).

This compound was obtained according to the general method in 19% yield as colorless prisms (benzene), mp 59-60°; ir (Nujol): 1681 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.19 (s, 18 H, *t*Bu), 5.80 (s, 4H, H_{Fur}), 6.59 (s, 1H, CH), 7.15 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 7.53 (dd, ^4J = 2.0, ^3J = 8.3 Hz, 1H, H_{Ar}), 8.10 (d, ^4J = 2.0 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{24}H_{27}BrO_4$: C, 62.75; H, 5.92. Found: C, 62.65; H, 5.93.

2-Bis[5-(*tert*-butyl)-2-furyl]methyl-5-iodobenzoic acid (**4o**).

This compound was obtained according to the general method in 22% yield as colorless prisms (hexane), mp 114-116°; ir (Nujol): 1687 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.19 (s, 18 H, *t*Bu), 5.79 (s, 4H, H_{Fur}), 6.57 (s, 1H, CH), 7.02 (d, ^3J = 8.3 Hz, 1H, H_{Ar}), 7.73 (dd, ^4J = 2.0, ^3J = 8.3 Hz, 1H, H_{Ar}), 8.29 (d, ^4J = 2.0 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{24}H_{27}IO_4$: C, 56.93; H, 5.37. Found: C, 56.99; H, 5.34.

3-[5-(*tert*-Butyl)-2-furyl]-1,3-dihydro-1-isobenzofuranone (**5k**).

This compound was obtained according to the general method in 21% yield as colorless prisms (dichloromethane-hexane), mp 73-74°; ir (Nujol): 1768 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.26 (s, 9 H, *t*Bu), 5.94 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.16 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 6.45 (s, 1H, CH), 7.47-7.72 (m, 3H, H_{Ar}), 7.95-7.99 (m, 1H, H_{Ar}).

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.89; H, 6.23.

3-[5-(*tert*-Butyl)-2-furyl]-6-nitro-1,3-dihydro-1-isobenzofuranone (**5l**).

This compound was obtained according to the general method in 29% yield as pale yellow prisms (dichloromethane-hexane), mp 117-118°; ir (Nujol): 1766 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.24 (s, 9 H, *t*Bu), 5.99 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.28 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 6.55 (s, 1H, CH), 7.68 (d, ^3J = 8.4 Hz, 1H, H_{Ar}), 8.57 (d.d, ^4J = 1.9, ^3J = 8.4 Hz, 1H, H_{Ar}), 8.79 (d, ^4J = 1.9 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{16}H_{15}NO_5$: C, 63.78; H, 5.02. Found: C, 63.89; H, 5.06.

3-[5-(*tert*-Butyl)-2-furyl]-6-chloro-1,3-dihydro-1-isobenzofuranone (**5m**).

This compound was obtained according to the general method in 31% yield as colorless prisms (dichloromethane-hexane), mp 109-110°; ir (Nujol): 1766 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.25 (s, 9 H, *t*Bu), 5.95 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.19 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 6.43 (s, 1H, CH), 7.43 (d, ^3J = 8.2 Hz, 1H, H_{Ar}), 7.67 (d.d, ^4J = 1.4, ^3J = 8.2 Hz, 1H, H_{Ar}), 7.93 (d, ^4J = 1.4 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{16}H_{15}ClO_3$: C, 66.10; H, 5.20. Found: C, 66.18; H, 5.18.

6-Bromo-3-[5-(*tert*-butyl)-2-furyl]-1,3-dihydro-1-isobenzofuranone (**5n**).

This compound was obtained according to the general method in 32% yield as colorless prisms, mp 112-113° (dichloromethane-hexane); ir (Nujol): 1765 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.25 (s, 9 H, *t*Bu), 5.95 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.19 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 6.40 (s, 1H, CH), 7.38 (d, ^3J = 8.1 Hz, 1H, H_{Ar}), 7.82 (d.d, ^4J = 1.4, ^3J = 8.1 Hz, 1H, H_{Ar}), 8.09 (d, ^4J = 1.4 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{16}H_{15}BrO_3$: C, 57.33; H, 4.51. Found: C, 57.41; H, 4.55.

3-[5-(*tert*-Butyl)-2-furyl]-6-iodo-1,3-dihydro-1-isobenzofuranone (**5o**).

This compound was obtained according to the general method in 36% yield as colorless prisms (dichloromethane-hexane), mp 111-112°; ir (Nujol): 1769 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.25 (s, 9 H, *t*Bu), 5.95 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.19 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 6.39 (s, 1H, CH), 7.25 (d, ^3J = 8.0 Hz, 1H, H_{Ar}), 8.01 (d.d, ^4J = 1.4, ^3J = 8.0 Hz, 1H, H_{Ar}), 8.30 (d, ^4J = 1.4 Hz, 1H, H_{Ar}).

Anal. Calcd. for $C_{16}H_{15}IO_3$: C, 50.28; H, 3.96. Found: C, 50.14; H, 3.91.

General Procedure for the Preparation of 3-(3-Oxobutyl)-1-isochromenones (**6a-e**).

2-Carboxybenzylfurans **4a-e** (0.025 mol) were stirred under reflux in 130 mL of HCl/methanol solution (8 weight % HCl) for 40 minutes, and then poured into cold water. The mixture was extracted with CH_2Cl_2, washed with water. The organic layer was diluted with hexane and filtered through a short pad of silica gel. The solvent was evaporated, and the solid residue was recrystallized.

4-(5-Methyl-2-furyl)-3-(3-oxobutyl)-1-isochromenone (**6a**).

This compound was obtained according to the general method in 55% yield as colorless prisms (dichloromethane-hexane), mp 77-78°; ir (Nujol): 1747 (O=C-O), 1703 (C=O) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 2.17 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.81–2.89 (m, 4H, CH_2CH_2), 6.13 (d, ^3J = 3.1 Hz, 1H, 4-H_{Fur}), 6.37 (d, ^3J = 3.1 Hz, 1H, 3-H_{Fur}), 7.28-7.31 (m, 1H, H_{Ar}), 7.45-7.50 (m, 1H, H_{Ar}), 7.64-7.69 (m, 1H, H_{Ar}), 8.28-8.30 (m, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.68, 26.04, 29.80, 40.79, 106.00, 108.09, 112.65, 119.76, 124.51, 127.85, 129.39, 134.83, 137.89, 144.28, 152.95, 156.65, 161.75, 206.25; ms: m/z 297 (19) [M^+ + 1], 296 (100) [M^+], 254 (12), 253 (61), 235 (12), 211 (16), 197 (36), 43 (18).

Anal. Calcd. for $C_{18}H_{16}O_4$: C, 72.96, H; 5.44. Found: C, 72.87; H, 5.50.

4-(5-Methyl-2-furyl)-7-nitro-3-(3-oxobutyl)-1-isochromenone (**6b**).

This compound was obtained according to the general method in 72% yield as pale yellow prisms, mp 128-130° (dichloromethane-hexane); ir (Nujol): 1744 (O=C-O), 1705 (C=O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.19 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 2.89 (s, 4H, CH_2CH_2), 6.17 (d, ^3J = 3.1 Hz, 1H, 4-H_{Fur}), 6.44 (d, ^3J = 3.1 Hz, 1H, 3-H_{Fur}), 7.46 (d, ^3J = 8.9 Hz, 1H, H_{Ar}), 8.44 (d.d, ^4J = 2.4, ^3J = 8.9 Hz, 1H, H_{Ar}), 9.12 (d, ^4J = 2.4 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.68, 26.26, 29.78, 40.23, 107.28, 107.73, 113.41, 120.13, 125.29, 126.24, 128.78, 142.78, 142.92, 146.68, 153.68, 159.86, 160.68, 205.80; ms: m/z 342 (19) [M^+ + 1], 341 (100) [M^+], 326 (17), 298 (32), 280 (13), 252 (11), 196 (12), 43 (37), 28 (15).

Anal. Calcd. for $C_{18}H_{15}NO_6$: C, 63.34; H, 4.43. Found: C, 63.40; H, 4.38.

7-Chloro-4-(5-methyl-2-furyl)-3-(3-oxobutyl)-1-isochromenone (**6c**).

This compound was obtained according to the general method in 68% yield as colorless prisms (hexane), mp 82-83°; ir (Nujol): 1748 (O=C-O), 1699 (C=O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.17 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.85 (s, 4H, CH_2CH_2), 6.14 (d, ^3J = 3.1 Hz, 1H, 4-H_{Fur}), 6.37 (d, ^3J = 3.1 Hz, 1H, 3-H_{Fur}), 7.25 (d, ^3J = 8.6 Hz, 1H, H_{Ar}), 7.60 (d.d, ^4J = 2.0, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.25 (d, ^4J = 2.0 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.66, 25.96, 29.79, 40.60, 107.12, 107.64, 112.89, 120.99, 126.32, 128.73, 133.75, 135.10, 136.30, 143.78, 153.22, 157.00, 160.61, 206.16; ms: m/z 333/331 (7/20) [M^+ + 1], 332/330 (34/100) [M^+], 317/315 (5/14), 289/287 (19/54), 269 (13), 245 (15), 233 (17), 231 (42), 139 (11), 43 (21).

Anal. Calcd. for $C_{18}H_{15}ClO_4$: C, 65.36; H, 4.57. Found: C, 65.41; H, 4.50.

7-Bromo-4-(5-methyl-2-furyl)-3-(3-oxobutyl)-1-isochromenone (**6d**).

This compound was obtained according to the general method in 70% yield as colorless prisms (hexane), mp 88-90°; ir (Nujol): 1747 (O=C-O), 1703 (C=O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.18 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.82-2.87 (m, 4H, CH_2CH_2), 6.14 (d, ^3J = 3.1 Hz, 1H, 4-H_{Fur}), 6.37 (d, ^3J = 3.1 Hz, 1H, 3-H_{Fur}), 7.18 (d, ^3J = 8.6 Hz, 1H, H_{Ar}), 7.75 (d.d, ^4J = 2.1, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.43 (d, ^4J = 2.1 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.68, 26.03, 29.80, 40.57, 107.09, 107.70, 112.90, 121.21, 121.48, 126.39, 131.84, 136.67, 137.88, 143.72, 153.19, 157.14, 160.44, 206.05; ms: m/z 377/375 (19/21) [M^+ + 1], 376/374 (99/100) [M^+], 333/331 (46/48), 289 (11), 277 (34), 275 (33), 139 (15), 43 (42).

Anal. Calcd. for $C_{18}H_{15}BrO_4$: C, 57.62; H, 4.03. Found: C, 57.71; H, 3.99.

6-Bromo-4-(5-methyl-2-furyl)-3-(3-oxobutyl)-1-isochromenone (**6e**).

This compound was obtained according to the general method in 75% yield as colorless prisms (hexane), mp 113-115°; ir (Nujol): 1747 (O=C-O), 1700 (C=O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.18 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.79-2.90 (m, 4H, CH_2CH_2), 6.16 (d, ^3J = 3.1 Hz, 1H, 4-H_{Fur}), 6.39 (d, ^3J = 3.1 Hz, 1H, 3-H_{Fur}), 7.45 (d, ^4J = 1.8 Hz, 1H, H_{Ar}), 7.60 (d.d, ^4J = 1.8, ^3J = 8.4 Hz, 1H, H_{Ar}), 8.13 (d, ^3J = 8.4 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.71, 26.12, 29.80, 40.58, 107.17, 113.02, 118.43, 127.31, 130.63, 131.01, 131.12, 131.24, 139.33, 143.47, 153.29, 158.13, 161.06, 206.02; ms: m/z 377/375 (20/21) [M^+ + 1], 376/374 (99/100) [M^+], 334/332 (13/14), 333/331 (65/66), 291 (13), 289 (15), 277 (26), 275 (24), 139 (16), 43 (27).

Anal. Calcd. for $C_{18}H_{15}BrO_4$: C, 57.62; H, 4.03. Found: C, 57.70; H, 4.11.

General Procedure for the Preparation of 3-(4,4-Dimethyl-3-oxopentyl)-1-isochromenones (**6k-o**).

2-Carboxybenzylfurans **4k-o** (0.025 mol) were stirred under reflux in 130 mL of HCl/methanol solution (30 weight % HCl) for 5 minutes, and then poured into cold water. The mixture was extracted with CH_2Cl_2, washed with water. The organic layer was diluted with hexane and filtered through a short pad of silica gel. The solvent was evaporated, and the solid residue was recrystallized.

4-[5-(*tert*-Butyl)-2-furyl]-3-(4,4-dimethyl-3-oxopentyl)-1-isochromenone (**6k**).

This compound was obtained according to the general method in 80% yield as oil; ir (Nujol): 1746 (O=C-O), 1701 (C=O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.16 (s, 9 H, *t*Bu), 1.33 (s, 9 H, *t*Bu), 2.76-2.85 (m, 2H, CH_2), 2.92-3.00 (m, 2H, CH_2), 6.12 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.37 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 7.31-7.35 (m, 1H, H_{Ar}), 7.46-7.53 (m, 1H, H_{Ar}), 7.65-7.72 (m, 1H, H_{Ar}), 8.29-8.33 (m, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 26.54(4C), 29.06(3C), 32.76, 34.56, 44.08, 103.37, 108.19, 112.01, 119.85, 124.46, 127.83, 128.34, 129.49, 134.89, 137.93, 144.13, 157.21, 164.96, 213.80; ms: m/z 381 (6) [M^+ + 1], 380 (23) [M^+], 324 (21), 323 (100), 57 (66), 55 (21), 43 (43).

Anal. Calcd. for $C_{24}H_{28}O_4$: C, 75.76; H, 7.42. Found: C, 75.88; H, 7.37.

4-[5-(*tert*-Butyl)-2-furyl]-3-(4,4-dimethyl-3-oxopentyl)-7-nitro-1-isochromenone (**6l**).

This compound was obtained according to the general method in 75% yield as colorless prisms (hexane), mp 115-116°; ir (Nujol): 1749 (O=C-O), 1708 (C=O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.17 (s, 9 H, *t*Bu), 1.33 (s, 9 H, *t*Bu), 2.81-2.89 (m, 2H, CH_2), 2.93-3.01 (m, 2H, CH_2), 6.16 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.44 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 7.48 (d, ^3J = 8.9 Hz, 1H, H_{Ar}), 8.45 (d.d, ^4J = 2.4, ^3J = 8.9 Hz, 1H, H_{Ar}), 9.13 (d, ^4J = 2.4 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 26.50(3C), 26.77, 29.01(3C), 32.83, 34.00, 44.07, 103.63, 107.79, 112.75, 120.20, 125.35, 126.07, 128.76, 142.71, 142.78, 146.63, 159.97, 161.14, 165.61, 213.25; ms: m/z 426 (5) [M^+ + 1], 425 (18) [M^+], 369 (21), 368 (100), 57 (12).

Anal. Calcd. for $C_{24}H_{27}NO_6$: C, 67.75; H, 6.40. Found: C, 67.83; H, 6.45.

4-[5-(*tert*-Butyl)-2-furyl]-7-chloro-3-(4,4-dimethyl-3-oxopentyl)-1-isochromenone (**6m**).

This compound was obtained according to the general method in 82% yield as colorless prisms (hexane), mp 94-95°; ir (Nujol): 1745 (O=C-O), 1702 (C=O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 1.15 (s, 9 H, *t*Bu), 1.32 (s, 9 H, *t*Bu), 2.72-2.84 (m, 2H, CH_2), 2.90-3.02 (m, 2H, CH_2), 6.11 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.37 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 7.28 (d, J = 8.6 Hz, 1H, H_{Ar}), 7.61 (d.d, ^4J = 2.2, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.26 (d, ^4J = 2.2 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 26.51(4C), 29.02(3C), 32.77, 34.31, 44.06, 103.42, 107.67, 112.20, 121.05, 126.16, 128.75, 133.64, 135.05, 136.32, 143.58, 157.45, 160.70, 165.12, 213.44; ms: m/z 416/414 (8/23) [M^+], 359/357 (33/100), 57 (18).

Anal. Calcd. for $C_{24}H_{27}ClO_4$: C, 69.47; H, 6.56. Found: C, 69.38; H, 6.49.

7-Bromo-4-[5-(*tert*-butyl)-2-furyl]-3-(4,4-dimethyl-3-oxopentyl)-1-isochromenone (**6n**).

This compound was obtained according to the general method in 81% yield as colorless prisms (hexane), mp 87-88°; ir (Nujol): 1749 (O=C-O), 1699 (C=O) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 1.16 (s, 9 H, *t*Bu), 1.32 (s, 9 H, *t*Bu), 2.77-2.83 (m, 2H, CH_2), 2.90-2.96 (m, 2H, CH_2), 6.11 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.37 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 7.20 (d, ^3J = 8.6 Hz, 1H, H_{Ar}), 7.75 (d.d, ^4J = 2.0, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.43 (d, ^4J = 2.0 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 26.51(3C), 26.57, 29.04(3C), 32.77, 34.28, 44.07, 103.42, 107.74, 112.21, 121.27, 121.36, 126.29, 131.85, 136.70, 137.85, 143.54, 157.61, 160.56, 165.15, 213.45; ms: m/z 460/458 (26/26) [M^+], 404/402 (22/22), 403/401 (100/97), 57 (28).

Anal. Calcd. for $C_{24}H_{27}BrO_4$: C, 62.75; H, 5.92. Found: C, 62.67; H, 5.88.

4-[5-(*tert*-Butyl)-2-furyl]-3-(4,4-dimethyl-3-oxopentyl)-7-iodo-1-isochromenone (**6o**).

This compound was obtained according to the general method in 79% yield as colorless prisms (hexane), mp 104-105°; ir (Nujol): 1750 (O=C-O), 1703 (C=O) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 1.15 (s, 9 H, *t*Bu), 1.31 (s, 9 H, *t*Bu), 2.77-2.82 (m, 2H, CH_2), 2.90-2.95 (m, 2H, CH_2), 6.11 (d, ^3J = 3.2 Hz, 1H, 4-H_{Fur}), 6.36 (d, ^3J = 3.2 Hz, 1H, 3-H_{Fur}), 7.05 (d, ^3J = 8.6 Hz, 1H, H_{Ar}), 7.94 (d.d, ^4J = 1.8, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.63 (d, ^4J = 1.8 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 26.51(3C), 26.62, 29.05(3C), 32.77, 34.26, 44.07, 92.13, 103.42, 107.81, 112.20, 121.31, 126.21, 137.16, 137.97, 143.49, 157.84, 160.30, 165.13, 165.21, 213.41; ms: m/z 507 (10) [M^+ + 1], 506 (37) [M^+], 450 (23), 449 (100), 57 (14).

Anal. Calcd. for $C_{24}H_{27}IO_4$: C, 56.93; H, 5.37. Found: C, 56.83; H, 5.32.

General Procedure for the Preparation of Tetracyclic Isochromenones (**7a-j**).

2-Carboxybenzylfurans **4a-j** (0.025 mol) were stirred under reflux in 130 mL of HCl/methanol solution (30 weight % HCl) for 30 minutes, and then poured into cold water. The mixture was extracted with CH_2Cl_2, washed with water. The organic layer was diluted with hexane and filtered through a short pad of silica gel. The solvent was evaporated, and the solid residue was recrystallized.

Compounds **7a** and **7i** was described [19].

2,4-Dimethyl-10-nitrofuro[2',3':3,4]cyclohepta[1,2-c]isochromen-8(6*H*)-one (**7b**).

This compound was obtained according to the general method in 70% yield as yellow prisms (ethanol), mp 237-238°; ir (Nujol): 1741 (O=C-O) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 2.04 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 3.02 (d, ^3J = 6.7 Hz, 2H, CH_2), 5.40 (t, ^3J = 6.7 Hz, 1H, =CH), 6.32 (s, 1H, H_{Fur}), 8.53 (s, 2H, H_{Ar}), 9.17 (s, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.85, 20.31, 32.01, 105.08, 106.07, 115.31, 120.43, 125.76, 126.25, 127.99, 128.80, 132.29, 140.58, 144.35, 146.38, 149.94, 152.11, 160.53; ms: m/z 324 (21) [M^+ + 1], 323 (100) [M^+], 309 (12), 308 (59), 262 (17).

Anal. Calcd. for $C_{18}H_{13}NO_5$: C, 66.87; H, 4.05. Found: C, 66.78; H, 4.10.

10-Chloro-2,4-dimethylfuro[2',3':3,4]cyclohepta[1,2-*c*]isochromen-8(6*H*)-one (**7c**).

This compound was obtained according to the general method in 72% yield as colorless powder (ethanol), mp 185-186°; ir (Nujol): 1733 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.04 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 2.97 (d, ^3J = 6.6 Hz, 2H, CH_2), 5.38 (t, ^3J = 6.6 Hz, 1H, =CH), 6.30 (s, 1H, H_{Fur}), 7.70 (d.d, ^4J = 2.2, ^3J = 8.8 Hz, 1H, H_{Ar}), 8.30 (d, ^3J = 2.2 Hz, 1H, H_{Ar}), 8.32 (d, ^4J = 8.8 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.81, 20.32, 31.66, 104.99, 105.89, 115.483, 121.20, 126.27, 127.33, 129.14, 131.73, 133.27, 133.93, 134.99, 145.10, 146.90, 151.54, 161.09; ms: m/z 314/312 (34/100) [M^+], 313 (27), 311 (24), 299/297 (28/83).

Anal. Calcd. for $C_{18}H_{13}ClO_3$: C, 69.13; H, 4.19. Found: C, 69.22; H, 4.11.

10-Bromo-2,4-dimethylfuro[2',3':3,4]cyclohepta[1,2-*c*]isochromen-8(6*H*)-one (**7d**).

This compound was obtained according to the general method in 75% yield as colorless powder (ethanol), mp 176-177°; ir (Nujol): 1734 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.04 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 2.97 (d, ^3J = 6.7 Hz, 2H, CH_2), 5.38 (t, ^3J = 6.7 Hz, 1H, =CH), 6.30 (s, 1H, H_{Fur}), 7.84 (d.d, ^4J = 2.2, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.24 (d, ^3J = 8.6 Hz, 1H, H_{Ar}), 8.47 (d, ^4J = 2.2 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.83, 20.33, 31.73, 105.07, 105.89, 115.47, 121.01, 121.42, 126.39, 127.37, 131.76, 132.27, 134.33, 137.82, 145.10, 147.08, 151.54, 160.96; ms: m/z 359 (20) [M^+ + 1], 358/356 (100/100) [M^+], 357 (41), 355 (22), 344/342 (15/15), 343/341 (73/74), 178 (13).

Anal. Calcd. for $C_{18}H_{13}BrO_3$: C, 60.53; H, 3.67. Found: C, 60.43; H, 3.60.

11-Bromo-2,4-dimethylfuro[2',3':3,4]cyclohepta[1,2-*c*]isochromen-8(6*H*)-one (**7e**).

This compound was obtained according to the general method in 65% yield as colorless powder (ethanol), mp 188-189°; ir (Nujol): 1742 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.05 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 2.97 (d, ^3J = 6.6 Hz, 2H, CH_2), 5.38 (t, ^3J = 6.6 Hz, 1H, =CH), 6.31 (s, 1H, H_{Fur}), 7.61 (d.d, ^4J = 1.8, ^3J = 8.5 Hz, 1H, H_{Ar}), 8.18 (d, ^3J = 8.5 Hz, 1H, H_{Ar}), 8.53 (d, ^4J = 1.8 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.99, 20.43, 31.88, 104.68, 105.94, 115.61, 118.63, 127.44, 127.58, 130.72, 130.92, 131.54, 131.87, 137.06, 145.01, 151.76, 161.85; ms: m/z 359 (19) [M^+ + 1], 358/356 (99/100) [M^+], 357 (41), 355 (22), 344/342 (14/15), 343/341 (75/75), 178 (13).

Anal. Calcd. for $C_{18}H_{13}BrO_3$: C, 60.53; H, 3.67. Found: C, 60.61; H, 3.61.

11-Chloro-2,4-dimethylfuro[2',3':3,4]cyclohepta[1,2-*c*]isochromen-8(6*H*)-one (**7f**).

This compound was obtained according to the general method in 63% yield as colorless powder (ethanol), mp 177-178°; ir (Nujol): 1735 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.05 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 2.98 (d, ^3J = 6.6 Hz, 2H, CH_2), 5.39 (t, ^3J = 6.6 Hz, 1H, =CH), 6.31 (s, 1H, H_{Fur}), 7.45 (d.d, ^4J = 1.7, ^3J = 8.5 Hz, 1H, H_{Ar}), 8.26 (d, ^3J = 8.5 Hz, 1H, H_{Ar}), 8.35 (d, ^4J = 1.7 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.83, 20.30, 31.79, 104.72, 105.85, 115.50, 118.21, 124.37, 127.35, 127.90, 131.46, 131.79, 136.90, 141.67, 145.00, 147.96, 151.66, 161.46; ms: m/z 314/312 (33/100) [M^+], 313 (29), 311 (27), 299/297 (31/89), 298 (18).

Anal. Calcd. for $C_{18}H_{13}ClO_3$: C, 69.13; H, 4.19. Found: C, 69.21; H, 4.12.

10-Methoxy-2,4-dimethylfuro[2',3':3,4]cyclohepta[1,2-*c*]-isochromen-8(6*H*)-one (**7g**).

This compound was obtained according to the general method in 68% yield as colorless powder (ethanol), mp 205-206°; ir (Nujol): 1731 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, DMSO-d_6): δ 2.00 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 2.90 (d, ^3J = 6.6 Hz, 2H, CH_2), 3.89 (s, 3H, OCH_3), 5.44 (t, ^3J = 6.6 Hz, 1H, =CH), 6.51 (s, 1H, H_{Fur}), 7.50 (d.d, ^4J = 2.8, ^3J = 8.3 Hz, 1H, H_{Ar}), 7.63 (d, ^4J = 2.8 Hz, 1H, H_{Ar}), 8.26 (d, ^3J = 8.3 Hz, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.80, 20.34, 31.47, 55.65, 105.44, 105.80, 110.36, 115.76, 121.13, 124.31, 126.24, 126.93, 129.22, 131.44, 144.99, 145.77, 151.23, 158.79, 162.46; ms: m/z 309 (21) [M^+ + 1], 308 (100) [M^+], 307 (22), 294 (18), 293 (86).

Anal. Calcd. for $C_{19}H_{16}O_4$: C, 74.01; H, 5.23. Found: C, 74.11; H, 5.18.

10,11-Dimethoxy-2,4-dimethylfuro[2',3':3,4]cyclohepta[1,2-c]-isochromen-8(6*H*)-one (**7h**).

This compound was obtained according to the general method in 65% yield as colorless powder (ethanol)s, mp 230-231°; ir (Nujol): 1732 (O=C-O) cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$): δ 2.04 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.97 (d, ^3J = 6.6 Hz, 2H, CH_2), 3.99 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 5.38 (t, ^3J = 6.6 Hz, 1H, =CH), 6.31 (s, 1H, H_{Fur}), 7.70 (s, 1H, H_{Ar}), 7.85 (s, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 13.74, 20.30, 31.60, 55.86, 56.10, 105.29, 105.66, 105.88, 109.76, 113.13, 115.70, 126.88, 131.12, 131.32, 145.82 146.10, 148.91, 150.89, 154.88, 162.10; ms: m/z 339 (22) [M^+ + 1], 338 (100) [M^+], 337 (16), 224 (14), 223 (67).

Anal. Calcd. for $C_{20}H_{18}O_5$: C, 71.00; H, 5.36. Found: C, 71.09; H, 5.30.

2,4-Diethyl-10-nitrofuro[2',3':3,4]cyclohepta[1,2-*c*]isochromen-8(6*H*)-one (**7j**).

This compound was obtained according to the general method in 71% yield as yellow powder (ethanol), mp 193-194°; ir (Nujol): 1739 (O=C-O) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 1.08 (t, ^3J = 7.5 Hz, 3H, CH_2CH_3), 1.39 (t, ^3J = 7.5 Hz, 3H, CH_2CH_3), 2.42 (q, ^3J = 7.5 Hz, 2H, CH_2CH_3), 2.84 (q, ^3J = 7.5 Hz, 2H, CH_2CH_3), 3.03 (d, ^3J = 6.7 Hz, 2H, CH_2), 5.40 (t, ^3J = 6.7 Hz, 1H, =CH), 6.32 (s, 1H, H_{Fur}), 8.52 (s, 2H, H_{Ar}), 9.17 (s, 1H, H_{Ar}); ^{13}C nmr (75.5 MHz, $CDCl_3$): δ 12.11, 13.27, 21.58, 27.25, 31.89, 104.18, 105.10, 113.77, 120.43, 125.71, 126.18, 127.16, 128.75, 138.29, 140.64, 144.62, 146.32, 150.28, 157.56, 160.47; ms: m/z 352 (14) [M^+ + 1], 351 (64) [M^+], 336 (26), 323 (21), 322 (100), 276 (17).

Anal. Calcd. for $C_{20}H_{17}NO_5$: C, 68.37; H, 4.88. Found: C, 68.32; H, 4.82.

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