

Synthesis of 5-R-3-Diphenylmethylene-2,3-dihydro-2-furanones from 5-Substituted 2,3-Dihydro-2,3-furandiones and Phenylbenzoyldiazomethane*

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Received March 11, 2001

Abstract—3-Reactions of 5-aryl, 5-hetaryl, and 5-styryl-2,3-dihydro-2,3-furandiones with phenylbenzoyldiazomethane gave rise to 5-substituted 3-dipenylmethylene-2,3-dihydro-2-furanones. The possible intermediates and reaction products were investigated by semiempirical SCF MO LCAO method in AM1 approximation.

The direction of reaction between substituted 2,3-dihydro-2,3-furandiones with diazo compounds depend to a large extent on the structure of the initial compounds and experimental conditions. For instance, in reaction of 4-unsubstituted and 5-aryl-4-methyl-2,3-dihydro-2,3-furandione with diazomethane spiro[furan-2,2'-oxiran]-3-ones formed in a low yield [1]. The use in the reaction of diazoethane resulted in substituted 3(5)-hydroxy-4H-pyranone [1]. The diphenyldiazomethane in reactions with 5-aryl-2,3-dihydro-2,3-furandiones (benzene, 50°C, 1 h) yielded substituted 3,4-dihydro-2H-2,4-pyranones [2] or furo[2,3-c]pyrazoles [2]. Under more stringent conditions (benzene, 80°C, 1 h) 5-aryl- and 5-aryl-4-halo-2,3-dihydro-2,3-furandiones are converted into substituted 2,3-dihydro-2-furanones [2], and 5-aryl-4-methyl-2,3-dihydro-2,3-furandiones (benzene, 80°C, 7 h) furnish spiro[furan-3,2'-oxiran]-2-ones [1]. In reaction of 5-aryl-2,3-dihydro-2,3-furandiones with benzoyldiazomethane (benzene, 80°C, 3 h) substituted 2-diazo-1,3,5-pentanetriones were obtained [3]. Substituted 4-hydroxy-2H-pyran-2-ones originated from the reaction of 5-aryl-2,3-dihydro-2,3-furandiones (benzene, 80°C, 6 h) with dibenzoyldiazomethane [4]. The other diazocarbonyl compounds were not investigated in reactions with substituted 2,3-dihydro-2,3-furandiones.

The goal of the present research was investigation of 5-aryl, 5-(2-furyl)-, 5-(2-thienyl)-, and 5-styryl-2,3-dihydro-2,3-furandiones **Ia-h** with phenylbenzo-

ylidiazomethane (**II**). It was established that heating of equimolar amounts of reagents in carbon tetrachloride (76°C) or benzene (80°C) resulted in formation of 5-substituted 3-methylene-2,3-dihydro-2-furanones **IIIa-g** (Table 1) disregarding the character of substituent in the furandione (Scheme 1).

Furanones **IIIa-g** synthesized are orange or orange-red crystalline substances (Table 1).

Their structure is confirmed by spectral data. For instance, in the mass spectrum of furanone **IIIa** appear the peaks with the following values of m/z (I_{rel}): 360, 358 (6.4, 18.9) $[M]^+$, 332, 330 (2.0, 5.8) $[M-CO]^+$, 191 (20.2) $[Ph_2CH=C=CH]^+$, 167 (17.6) $[Ph_2CH]^+$, 166, 164 (6.3, 20.0) $[ClC_6H_4COC\equiv CH]^+$, 141, 139 (33.4, 100.0) $[ClC_6H_4CO]^+$, 113, 111 (10.4, 30.9) $[ClC_6H_4]^+$.

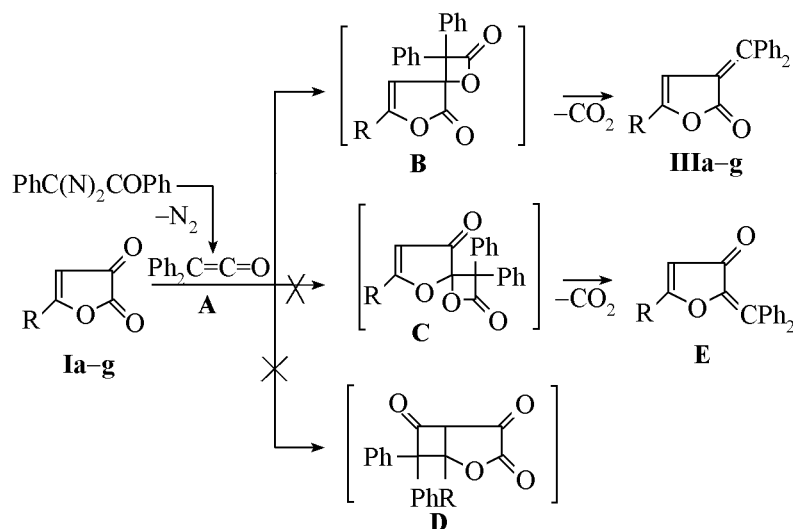
In the IR spectra (Table 2) were observed the absorption bands belonging to stretching vibrations of a lactone carbonyl in the region 1749-1780 and of a bond $C^3=C$ in the region 1605-1640 cm^{-1} that was in agreement with the published data on the similar in structure to compounds **IIIa-g** 5-aryl-3-benzylidene-2,3-dihydro-2-furanones [5]. These data permit rejection for the reaction products of regioisomeric structure of 5-substituted 2-diphenylmethylene-2,3-dihydro-3-furanones E.

In the ¹H NMR spectra alongside the proton signals of substituents attached to C⁵ atom of the dihydrofuran ring appears the singlet from vinyl proton C⁴H in the region 6.14-6.65 ppm (Table 2).

The scheme of compounds **IIIa-g** formation apparently includes preliminary thermolysis of the

* The study was carried out under financial support from the Russian Foundation for Basic Research (grant no. 98-03-32888).

Scheme 1.



R = Ph (a), *p*-CH₃C₆H₄ (b), *p*-BrC₆H₄ (c), *p*-ClC₆H₄ (d), 2-furyl (e), 2-thienyl (f), PhCH=CH (g).

Table 1. Yields, melting points, and elemental analyses of 5-R-3-diphenylmethylene-2,3-dihydro-2-furanones IIIa-g

Compd. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	Hlg		C	H	Hlg
IIIa	42	170–172	85.08	5.01		C ₂₃ H ₁₆ O ₂	85.16	4.97	
IIIb	46	156–158	85.27	5.43		C ₂₄ H ₁₈ O ₂	85.18	5.36	
IIIc	53	183–184	68.68	3.60	19.99	C ₂₃ H ₁₅ BrO ₂	68.50	3.74	19.81
IIId	49	174–175	77.10	4.12	10.01	C ₂₃ H ₁₅ ClO ₂	76.98	4.21	9.88
IIIe	60	139–140	80.51	4.63		C ₂₁ H ₁₄ O ₃	80.24	4.49	
IIIf	55	142–143	76.31	4.52	9.54	C ₂₁ H ₁₄ O ₂ S	76.34	4.27	9.70
IIIg	37	175–177	85.59	5.19		C ₂₅ H ₁₈ O ₂	85.69	5.18	

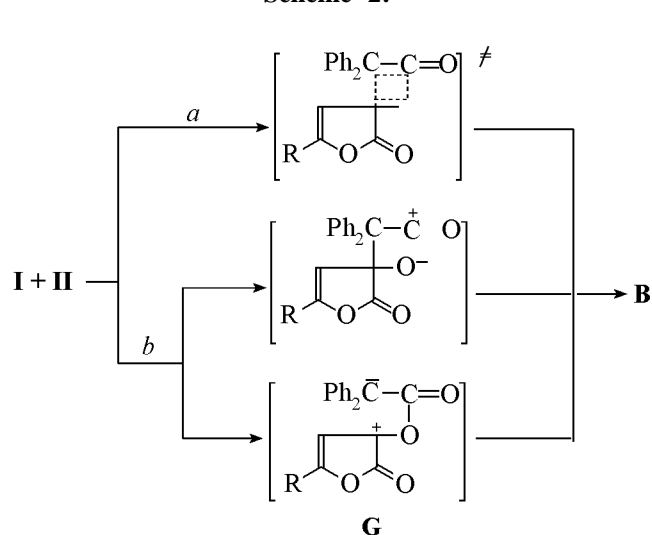
Table 2. Spectral characteristics of 5-R-3-diphenylmethylene-2,3-dihydro-2-furanones IIIa-g

Compd. no.	IR spectrum, ν, cm ⁻¹		¹ H NMR spectrum, δ, ppm
	C ² =O	C=C	
IIIa	1770	1624	6.47 s (1H, C ⁴ H), 7.33 m (15H, 3Ph)
IIIb	1768	1623	2.28 s (3H, CH ₃), 6.65 s (1H, C ⁴ H), 7.25 m (14H, 2Ph+C ₆ H ₄)
IIIc	1769	1624	6.63 s (1H, C ⁴ H), 7.30 m (14H, 2Ph+C ₆ H ₄)
IIId	1749	1605	6.64 s (1H, C ⁴ H), 7.28 m (14H, 2Ph+C ₆ H ₄)
IIIe	1756	1632	6.40 s (1H, C ⁴ H), 7.31 m (10H, 2Ph), 6.68 d (3H, furyl),
IIIf	1760	1636	6.32 s (1H, C ⁴ H), 7.30 m (10H, 2Ph), 7.01 m (3H, thienyl)
IIIg	1780	1640	6.14 s (1H, C ⁴ H), 5.63 d (1H, PhH=C ³ H, <i>J</i> 16.4 Hz), 7.30 m (16H, 3Ph+PhCH=CH)

phenylbenzoyldiazomethane accompanied by Wolf rearrangement [6]. The optimum temperature for the rearrangement according to published data [7] is 110°C. But we found that the conversion of phenyl-

benzoyldiazomethane into diphenylketene **A** can occur also at lower temperature. Heating of diazoketone **II** in carbon tetrachloride to 76°C for 30 mn results in its complete decomposition: The absorp-

Scheme 2.



tion bands of stretching vibrations of carbonyl (1640 cm^{-1}) and diazo group (2080 cm^{-1}) disappear, and an absorption band from the cumulated system of ketene **A** is observed at 2110 cm^{-1} .

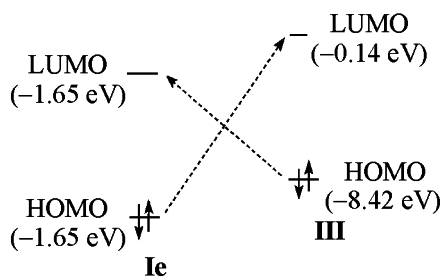
The diphenylketene formed enters into [2+2]-cycloaddition with a carbonyl group $\text{C}^3=\text{O}$ of furandione. However under the reaction conditions the spiroadduct **B** decomposes into furanone **III** and carbon dioxide. The presumable addition of ketene **A** to the $\text{C}^2=\text{O}$ bond of furandione **I** that would result in an alternative spiroadduct **C** and further in 3-furanone **E** does not occur.

Among publications, except [1, 8], no reactions of substituted 2,3-dihydro-2,3-furandiones were described with participation of carbonyl group $\text{C}^3=\text{O}$.

The spiroadducts of **B** or **C** type may presumably arise both from concerted (path *a*) or stepwise (path *b*) process (Scheme 2). The latter path should involve formation of one of zwitter-ions **F** or **G**. But in non-polar benzene and carbon tetrachloride *b* path seems less probable.

We failed to determine the structure of **F** and **G** species: In optimization their geometry by semiempirical SCF MO LCAO procedure in AM1 approximation [9] either closed an oxetane ring or occurred decomposition into the initial compounds **Ie** and **A**. The path *a* seems more probable, but taking into account the polarity of the reagents the formation of C-C and C-O bonds would not occur in concerted mode.

If the above assumption is correct then the formation of intermediates of **B** or **C** type may be reckoned by the perturbation theory of molecular orbitals [10]



Levels of frontier orbitals calculated for molecules of furandione **Ie** and ketene **A**.

as an exchange process related to reciprocal transfer of electrons from one reagent to another where an important role belongs to the energies of the highest occupied molecular orbitals (HOMO) and of the lowest unoccupied molecular orbitals (LUMO). The HOMO and LUMO energies obtained from calculation of molecules **Ie** and **A** in AM1 approximation are shown on the figure.

As follows from calculations, the energy gap between the HOMO of ketene and LUMO of furandione (6.77 eV) is narrower than an alternative one (9.43 eV). It means that in this reaction ketene **A** behaves as a donor, and furandione **Ie** as acceptor [11], and the electron transfer from HOMO of the former to the LUMO of the latter determines the regiodirection of the process. **If** is presumable that C^2 atom of ketene molecule with a charge of -0.211 a.u. and the factor at the 2_{pz} atomic orbital in HOMO ($c\ -0.502$) would interact with the carbon in the heterocyclic fragment that bears the largest positive charge or has the greatest 2_{pz} value of the orbital factor in LUMO. On the other hand the electron-deficient C^1 atom of ketene molecule [$q\ 0.281$, $c\ (\text{HOMO})\ -0.460$] may, although with less probability in keeping with the energies of frontier orbitals, be subject to attack of an electron-excessive atom of the furandione molecule. We tried to elucidate whether the atoms of the $\text{C}^3=\text{O}$ in the 2,3-dihydrofuran fragment of molecule **Ie** fit to these requirements. To this end we calculated their electron indices (q and c), and also π -electron charges (Table 3) with the use of various semiempirical SCF MO LCAO methods.

As seen from the data in Table 2, the atomic charges are not suitable as indices of reactivity governing the regiodirection of interaction between furandione **Ie** and diphenylketene. Actually, the relative values of charges essentially depend on the chosen approximation. Only in approximations AM1 and MNDO-PM3 [13] atom C^3 is the most electron-deficient. According to calculations in the approxi-

Table 3. Total π -electron charges of atoms and factors 2_{pz} of atomic orbitals in the frontier orbital of 2,3-dihydrofuran fragment of **Ie** molecule calculated by various semiempirical approximations of SCF MO LCAO method

Approximation	Charges of atoms q (a.u.)					AO factors 2_{pz} AO of atoms in HOMO/LUMO				
	C ²	C ³	C ⁵	C ² =O	C ³ =O	C ²	C ³	C ⁵	C ² =O	C ³ =O
CNDO/2	0.318	0.211	0.207	-0.227	-0.219	0.003	-0.052	-0.225	-0.048	0.356
	0.165	0.133	0.120	-0.235	-0.215	-0.207	-0.312	0.433	0.264	0.407
MINDO/3	0.684	0.492	0.457	-0.457	-0.446	0.007	-0.060	-0.148	0.002	0.204
	0.419	0.343	0.230	-0.502	-0.446	0.302	0.401	-0.52	-0.339	-0.241
MNDO	0.273	0.264	0.214	-0.226	-0.214	-0.015	0.031	0.223	0.029	-0.175
	0.229	0.225	0.089	-0.312	-0.280	0.236	0.349	-0.500	-0.242	-0.353
AM1	0.236	0.258	0.188	-0.203	-0.201	0.014	-0.042	-0.213	-0.018	0.200
	0.256	0.243	0.105	-0.343	-0.316	0.248	0.369	-0.489	-0.249	-0.364
MNDO	0.287	0.317	0.207	-0.240	-0.235	-0.013	0.032	0.218	0.025	-0.193
PM3 [12]	0.244	0.240	0.108	-0.332	-0.302	0.235	0.356	-0.488	-0.240	-0.357

ations CNDO/2 [14], MNDO/3 [15], and MNDO [16] the electron deficiency of carbon atoms grows in the series $C^5 < C^3 < C^2$. The same sequence was obtained by *ab initio* calculations of **Ie** molecule in basises STO 3G and STO 3-21G. The values of π -electron charges of atoms disregarding the approximation used change alike: $C^5 < C^3 < C^2$.

The most electron-excessive in furandione **Ie** molecule is the oxygen of the lactone carbonyl as show all the methods of calculation applied.

The most contribution to LUMO of furandione **Ie**, the orbital that should receive the electrons from HOMO of ketene **A**, provides the 2_{pz} atomic orbital of C⁵ atom as seen from the comparison of orbital factors values. This means that in the case of orbital control of the interaction the attack of this atom should be the most efficient.

Thus the static indices of reactivity often successfully used for prediction of regioselectivity of cycloaddition reaction in the case of reaction we describe have no forecasting effect. Apparently the electron density distribution in molecules of furandiones **Ia-g** is not the cause governing their reactivity. The other possible explanation of the reaction at the C³=O group may be dynamic factors: higher stability of the corresponding intermediates and activated complexes preceding them.

We calculated formation enthalpy (ΔH_f) and total energies (E_t) for possible intermediates **B** and **C**, reaction products **IIIa-g**, and their isomers 2-furanones **Ea-g** using the semiempirical SCF MO LCAO procedure

in AM1 approximation. The results of calculations are presented in Table 4.

As seen from Table 3, in each pair of isomeric compounds **B** and **C** the former are characterized by smaller values of formation enthalpy and total energy. This fact can be regarded as indication of the higher stability of compounds **B**. It is presumable that the activated complex, precursor of intermediates of **B**

Table 4. Formation enthalpy (ΔH_f) and total energy (E_t) of compounds **B**, **C**, **E**, **III** according to quantum-chemical calculations by SCF MO LCAO procedure in AM1 approximation

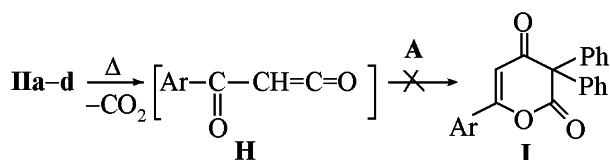
Compd no.	ΔH_f , kJ mol ⁻¹	E_t , eV	Compd. no.	ΔH_f , kJ mol ⁻¹	E_t , eV
Ba	31.85	-4570.32	Ca	39.47	-4570.24
Bb	-1.17	-4726.20	Cb	6.32	-4726.12
Bc	57.75	-4909.90	Cc	62.99	-4909.81
Bd	3.77	-4930.41	Cd	11.80	-4930.33
Be	-31.85	-4605.90	Ce	-23.77	-4605.81
Bf	54.62	-4480.93	Cf	61.23	-4880.86
Bg	85.68	-4853.52	Cg	93.21	-4853.45
IIIa	216.37	-3802.82	Ea	266.20	-3802.30
IIIb	183.74	-3958.69	Eb	233.30	-3958.18
IIIc	237.95	-4142.41	Ec	288.93	-4141.88
IIId	187.32	-4162.92	Ed	237.95	-4162.39
IIIe	151.18	-3838.41	Ee	202.41	-3837.88
IIIf	239.37	-3713.43	Ef	287.92	-3712.92
IIIg	270.42	-4886.02	Ng	320.32	-4885.50

type, also has a lower energy and forms with less energy consumption. The intermediate of **B** type decomposes further into 2-furanone **III** and carbon dioxide. According to calculations furanones **III**, the products of the reaction under study, are considerably more stable than their regioisomers of **C** type.

It turned out unexpectedly that a hypothetical addition product of diphenylketene to the $C^4=C^5$ bond of furandione **Ie**, bicyclic compound **D**, possessed smaller values of ΔH_f and E_t ($-91.32 \text{ kJ mol}^{-1}$ and -4606.51 eV respectively), and thus it should be more stable than spiro compound **B**. However the smaller values of formation enthalpy and total energy for **D** are apparently an artefact of AM1 approximation due to either overestimation of cyclobutane stability or underestimation of that of oxetanes. *Ab initio* calculations in STO 3-21G basis of molecules of model products originating from ketene addition to the $C^3=O$, $C^2=O$ and $C^4=C^5$ bonds of unsubstituted 2,3-dihydro-2,3-furandione confirmed the higher stability of the spiro[furan-3,2'-oxetane], analog of intermediate **B**, as followed from the comparison of E_t values.

It is possible that formation of [2+2]-cycloadducts of **B** and **D** type is reversible, but the spiro[furan-3,2'-oxetanes] **B** in contrast to **D** are capable further of elimination of stable carbon dioxide.

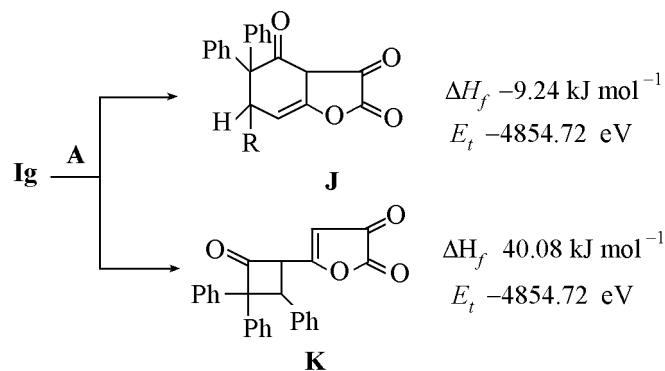
Note that furandiones **Ia-d** at temperature close to 80°C undergo thermal decarbonylation [17] affording reactive aroylketenes **H** [18]. Therefore [4+2]-cycloaddition might be expected to occur with participation of ketenes **H** and **A** where the former would play the role of diene and the latter of dienophile.



Along this scheme, i.e., with formation of [4+2]-cycloadducts furandiones **Ia-d** react with trimethylsilylketene [19]. But in reaction of compounds **I** and **A** no pyranones **I** were obtained. Apparently the decomposition of phenylbenzoyldiazomethane and its transformation into diphenylketene occurs under experimental conditions sufficiently fast and ends earlier than the possibility of furandione decarbonylation arises.

With 5-styryl-2,3-dihydro-2,3-furandione **Ig** two more reaction paths are possible: [4+2]-cycloaddition

at the diene fragment $\text{Ph}-\text{CH}=\text{CH}-\text{C}^5=\text{C}^4$, and [2+2]-cycloaddition to the $\text{C}=\text{C}$ bond of the substituent.



However these processes are not actually operating, although according to calculations the substituted 2,3,3a,4,5,6-hexahydrobenzo[*b*]furan-2,3,4-trione **J** is sufficiently stable. For efficient concerted [4+2]-cycloaddition the diene fragment of furandione **Ig** must be in *s-cis*-form. But it was shown formerly [20] that this form is less stable than *s-trans*-form, and the transition of the latter into the *s-cis*-conformation requires additional energy consumption. Apparently the activation barrier of the reaction $\text{Ig} + \text{A} \rightarrow \text{B}$ is sufficiently lower than that of reaction $\text{Ig} + \text{A} \rightarrow \text{J}$ for the latter reaction not to occur.

Low polarity of the $\text{C}=\text{C}$ bond in the styryl moiety of compound **Ig**, and also probably a high activation barrier prevent the formation of compound **K**.

EXPERIMENTAL

IR spectra were recorded on spectrophotometer UR-20 from mulls in mineral oil. ^1H NMR spectra were registered on spectrometer Tesla BS-487 (80 MHz), internal reference HMDS. Mass spectrum was measured on Varian Mat-311A instrument, ionizing electrons energy 70 eV. The monitoring of reaction progress and the purity of products was checked by TLC on Silufol UV-254 plates, eluent benzene-ethyl ether, 3:2, development in iodine vapor.

Quantum-chemical calculations were performed with the use of MOPAC 7.00 software [21].

3-Diphenylmethylene-5-phenyl-2,3-dihydro-2-furanone (IIIa). (a) A mixture of 0.55 g (32 mmol) of 5-phenyl-2,3-dihydro-2,3-furandione and 0.65 g (32 mmol) of phenylbenzoyldiazomethane in 15 ml of anhydrous carbon tetrachloride or benzene was boiled for 30 min. The solution was evaporated, the

residue was recrystallized from carbon tetrachloride. Yield 0.4 g.

(b) A solution of 1.11 g (50 mmol) of phenylbenzoyldiazomethane in 25 ml of anhydrous benzene was boiled for 30 mi, and then was added 0.087 g (50 mmol) of 5-phenyl-2,3-dihydro-2,3-furandione, and boiling was continued for 30 min. The solvent was evaporated, the residue was recrystallized from carbon tetrachloride. Yield 0.6 g.

Compounds **IIIb-g** were obtained in a similar way by procedure (b). The compounds were recrystallized from ethanol (compound **IIIb**), ethyl acetate (compound **IIIc**), acetonitrile (compounds **III d-g**).

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