

Decyclization of 5-Aryl-4-methyl-2,3-dihydrofuran-2,3-diones by the Action of Nucleophiles*

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Received March 18, 2002

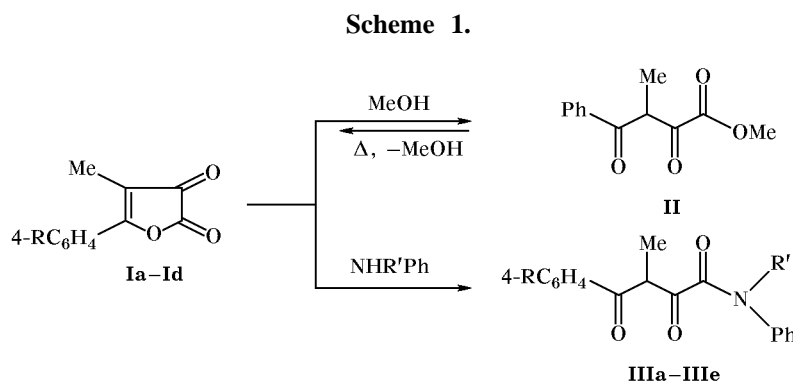
Abstract—Ring cleavage in 4-methyl-5-phenyl-2,3-dihydrofuran-2,3-dione by the action of methanol and in 5-aryl-4-methyl-2,3-dihydrofuran-2,3-diones by the action of aniline and *N*-methylaniline results in formation of, respectively, methyl 3-methyl-4-phenyl-2,4-dioxobutanoate and 4-aryl-3-methyl-2,4-dioxobutanilides. The reaction mechanism was studied by ¹H NMR spectroscopy.

The synthesis and chemical transformations of 5-aryl-4-methyl-2,3-dihydrofuran-2,3-diones **Ia–Id** were reported in a limited number of publications [1–10]. Nevertheless, the available data indicate essentially different chemical behavior of furandiones **Ia–Id** as compared to their analogs having no substituent in position 4, 5-aryl-2,3-dihydrofuran-2,3-diones, which were studied in much more detail [11].

We have found that the reaction of 4-methyl-5-phenyl-2,3-dihydrofuran-2,3-dione (**Ia**) with methanol results in opening of the furan ring with formation of methyl 3-methyl-2,4-dioxo-4-phenylbutanoate (**II**). Likewise, aniline and *N*-methylaniline react with 5-aryl-4-methyl-2,3-dihydrofuran-2,3-diones **Ia–Id** to

give 4-aryl-3-methyl-2,4-dioxobutanilides **IIIa–IIIe** (Scheme 1). The yields, physical properties, spectral data, and elemental analyses of compounds **II** and **IIIa–IIIe** are given in Tables 1 and 2. On heating under reduced pressure, ester **II** undergoes cyclization to initial furandione **Ia** with loss of methanol molecule. According to the spectral data, compounds **II** and **IIIa–IIIe** in crystal and in solution exist in the diketone form, in contrast to analogous esters and amides having no methyl group in the 3-position [11].

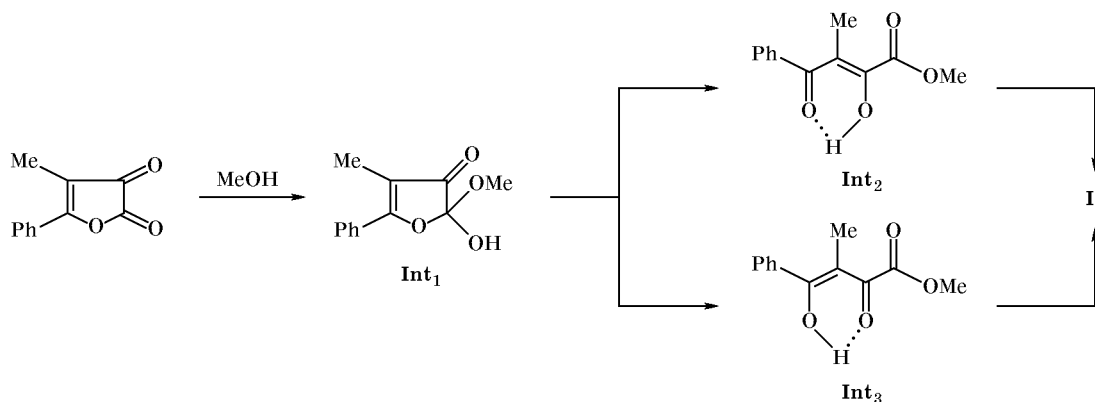
Obviously, ester **II** and amides **III** are formed via nucleophilic attack by the alcohol or amine on the C² atom of the furan ring, followed by ring opening in intermediate **Int₁**. In the reaction of furandione **Ia**



* This study was financially supported by the Russian Foundation for Basic Research (project no. 01-03-32641).

† Deceased.

Scheme 2.

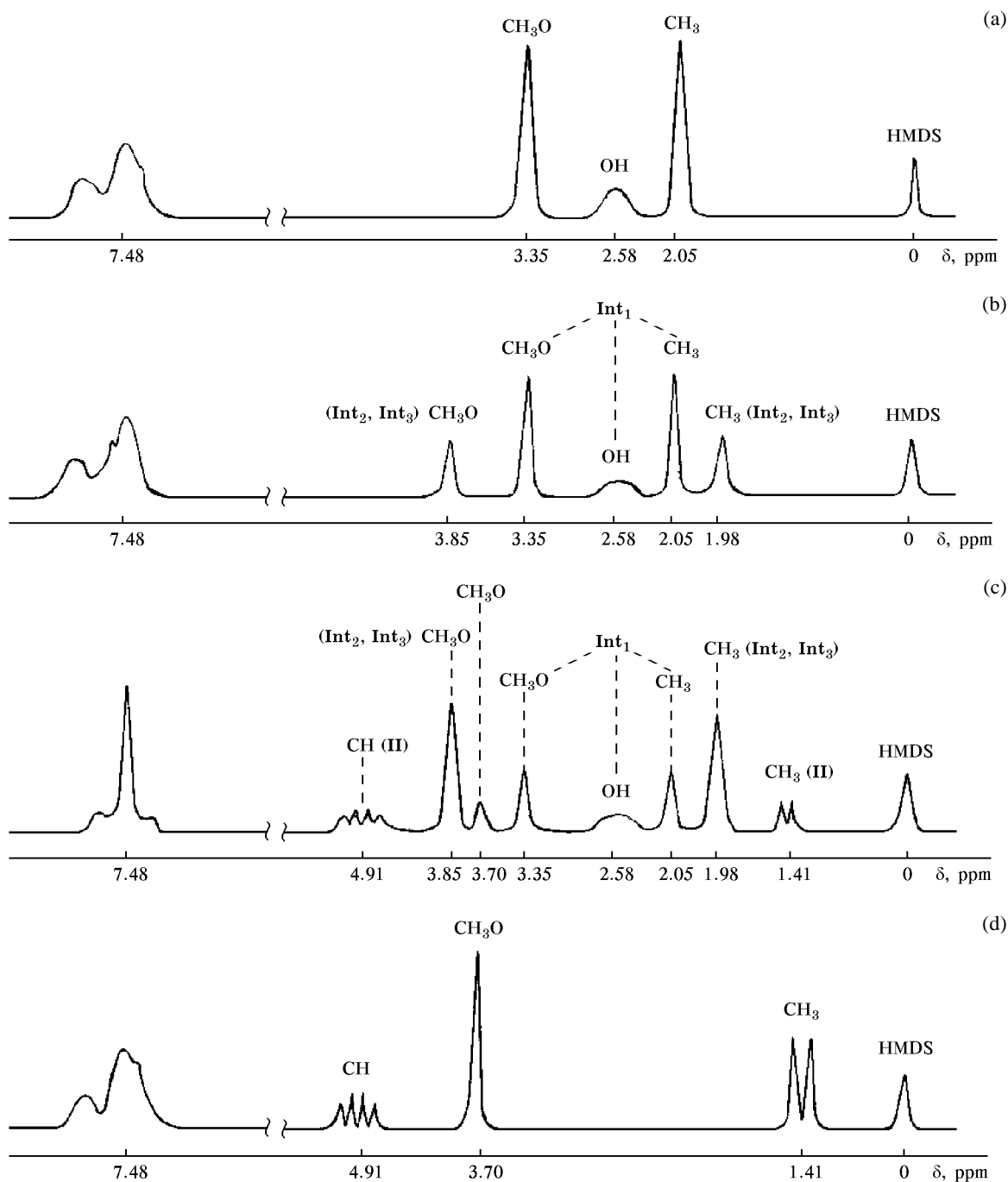
**Table 1.** Yields, melting points, and IR and ^1H NMR spectra of compounds **II** and **IIIa–IIIe**

Comp. no.	Yield, %	mp, °C	IR spectrum, ν , cm^{-1}	^1H NMR spectrum (CDCl_3), δ , ppm, (J , Hz)
II	51	Oily liquid	1743 (COOCH_3), 1712 ($\text{C}^2=\text{O}$), 1675 ($\text{C}^4=\text{O}$)	1.41 d (3H, CH_3 , 8), 3.70 s (3H, COOCH_3), 4.91 q (1H, CH, 8), 7.48 s (5H, C_6H_5)
IIIa	64	123–125	3305 (NH), 1696 br ($\text{C}^2=\text{O}$, CONH), 1658 ($\text{C}^4=\text{O}$)	1.40 d (3H, CH_3 , 6), 5.06 q (1H, CH, 6), 7.45 m (10H, C_6H_5), 8.98 s (1H, NH)
IIIb	71	150–151	3364 (NH), 1717 ($\text{C}^2=\text{O}$), 1690 (CONH), 1662 ($\text{C}^4=\text{O}$)	1.38 d (3H, CH_3 , 7), 2.36 s (3H, $\text{CH}_3\text{C}_6\text{H}_4$), 5.28 q (1H, CH, 7), 7.41 m (9H, H_{arom}), 8.59 s (1H, NH) [3]
IIIc^a	43	147–149	3309 (NH), 1699 ($\text{C}^2=\text{O}$), 1649 br (CONH, $\text{C}^4=\text{O}$)	1.37 d (3H, CH_3 , 7), 4.69 q (1H, CH, 7), 7.52 m (9H, H_{arom}), 10.33 s (1H, NH)
III^d	59	144–145	3346 (NH), 1731 ($\text{C}^2=\text{O}$), 1693 (CONH), 1678 ($\text{C}^4=\text{O}$)	1.43 d (3H, CH_3 , 6.5), 5.22 q (1H, CH, 6.5), 7.37 m (9H, H_{arom}), 8.68 s (1H, NH)
III^e	59	Oily liquid	3317 (NH), 1703 ($\text{C}^2=\text{O}$), 1691 (CONH), 1660 ($\text{C}^4=\text{O}$)	1.21 d (3H, CH_3 , 7), 3.18 s (3H, CH_3N), 5.05 q (1H, CH, 7), 7.25 m (10H, C_6H_5)

^a The ^1H NMR spectrum was recorded in $\text{DMSO}-d_6$.

Table 2. Elemental analyses of compounds **II** and **IIIa–IIIe**

Comp. no.	Found, %				Formula	Calculated, %			
	C	H	N	Hlg		C	H	N	Hlg
II	65.57	5.60			$\text{C}_{12}\text{H}_{12}\text{O}_4$	65.45	5.49		
IIIa	72.39	5.30	5.05		$\text{C}_{17}\text{H}_{15}\text{NO}_3$	72.58	5.38	4.98	
IIIb	73.03	5.99	4.60		$\text{C}_{18}\text{H}_{17}\text{NO}_3$	73.20	5.80	4.74	
IIIc	68.07	4.81	4.50	6.49	$\text{C}_{17}\text{H}_{14}\text{FNO}_3$	68.22	4.72	4.68	6.35
III^d	64.90	4.28	4.61	11.06	$\text{C}_{17}\text{H}_{14}\text{ClNO}_3$	64.67	4.47	4.44	11.23
III^e	73.35	6.00	4.63		$\text{C}_{18}\text{H}_{17}\text{NO}_3$	73.20	5.80	4.74	



^1H NMR spectra in chloroform-*d* at -50°C : (a) intermediate **Int**₁, (b) intermediates **Int**₁–**Int**₃ (5 min after the reaction started), (c) intermediates **Int**₁–**Int**₃ and ester **II** (10 min after the reaction started), and (d) ester **II** (30 min after the reaction started).

with methanol, ring opening in **Int**₁ is likely to give two enol intermediates **Int**₂ and **Int**₃ which are characterized by similar stabilities. Proton migration to the C³ atom in **Int**₂ or **Int**₃ leads to the final product, ester **II** (Scheme 2).

By ^1H NMR monitoring of the reaction of furandi-one **Ia** with methanol we succeeded in detecting inter-

mediates **Int**₁–**Int**₃ (see figure). Immediately after the reaction started, we observed in the ^1H NMR spectrum signals from the methyl (δ 2.05 ppm, s), methoxy (δ 3.35 ppm, s), and hydroxy protons (δ 2.58 ppm) of intermediate **Int**₁ (see figure, a). After 5 min, signals from the methyl and methoxy protons (δ 1.98 and 3.85 ppm) of enol intermediates **Int**₂ and **Int**₃

appeared (b). Their intensity increased in parallel with disappearance of the signals belonging to **Int**₁. When the fraction of **Int**₁ was 27.5%, the spectrum contained a doublet from methyl protons at δ 1.41 ppm, a singlet from methoxy group at δ 3.70 ppm, and a quartet from CH proton at δ 4.91 ppm, which correspond to the final product, ester **II** (c). The reaction was complete in 30 min (d).

An analogous spectral pattern was observed in the reaction of furandione **Ia** with *N*-methylaniline with the only difference that signals from the resulting 3,*N*-dimethyl-4-phenyl-2,4-dioxobutanilide (**IIIe**) and the corresponding enol forms appeared in the ¹H NMR spectrum immediately after the reaction started.

EXPERIMENTAL

The IR spectra were recorded on Specord-80M and UR-20 instruments from samples dispersed in mineral oil. The ¹H NMR spectra were obtained on RYa-2310 (60 MHz) and Bruker WR-80SY spectrometers in CDCl₃ or DMSO-*d*₆ with HMDS as internal reference. The progress of reactions was monitored, and the purity of the products was checked, by TLC on Silufol UV-254 plates using diethyl ether–benzene–acetone (10:9:1) as eluent.

Methyl 3-methyl-2,4-dioxo-4-phenylbutanoate (II). A solution of 1.74 g (0.01 mol) of furandione **Ia** in 20 ml of methanol was heated to the boiling point, the solvent was evaporated, the residue was refluxed in 10 ml of methanol with addition of charcoal, the mixture was filtered, and the filtrate was evaporated to obtain 1.05 g (51%) of ester **II** as an oily liquid.

3-Methyl-4-phenyl-2,4-dioxobutanilide (IIIa). A solution of 1.74 g (0.01 mol) of furandione **Ia** and 0.93 g (0.01 mol) of aniline in 20 ml of dry chloroform was stirred for 1 h at 20–25°C. The solvent was removed, and the residue was recrystallized from cyclohexane. Yield 1.72 g (64%), mp 123–125°C. Anilides **IIIc–IIIe** were synthesized in a similar way. Compounds **IIIa** and **IIIb** were recrystallized from cyclohexane, and **IIIb** and **IIIc**, from methanol.

Anilide **IIIb** was obtained by the procedure reported in [3].

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