

Five-Membered 2,3-Dioxo Heterocycles: XLVII.* Reaction of 5-Aryl-4-phenyl-2,3-dihydrofuran-2,3-diones with Compounds Containing C=N and C≡N Bonds

E. S. Vostrov, E. V. Leont'eva, O. P. Tarasova, and A. N. Maslivets

Perm State University, ul. Bukireva 15, Perm, 614990 Russia
e-mail: koh@psu.ru

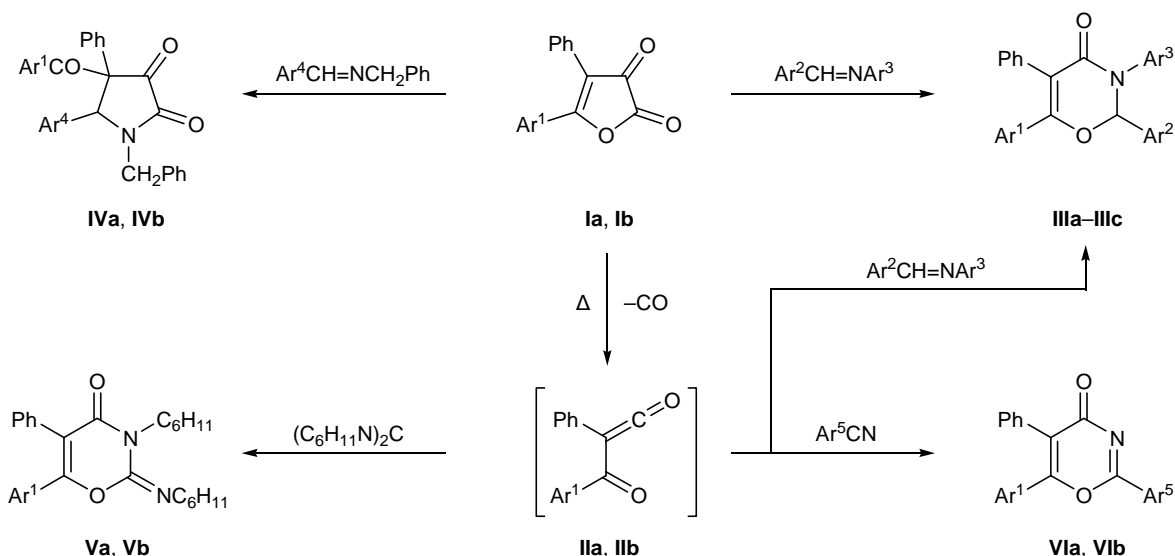
Received April 9, 2003

Abstract—Thermal decarbonylation of 5-aryl-4-phenyl-2,3-dihydrofuran-2,3-diones gives rise to intermediate aroyl(phenyl)ketenes which react with nonactivated Schiff bases, *N,N'*-dicyclohexylcarbodiimide, and *p*-dimethylaminobenzonitrile according to the [4+2]-cycloaddition pattern with formation of 6-aryl-5-phenyl-4*H*-1,3-oxazin-4-ones. Reactions of 5-aryl-4-phenyl-2,3-dihydrofuran-2,3-diones with activated Schiff bases at a temperature below the thermolysis temperature lead to 4-aryloxy-4-phenyltetrahydropyrrole-2,3-diones.

5-Aryl-4-halo-2,3-dihydrofuran-2,3-diones and their analogs containing no substituent at C⁴ undergo thermal decarbonylation (80–110°C) to generate aroylketenes which act as dienes (through the conjugated O=C–C=C bond system) in [4+2]-cycloadditions at the C=N bond of nonactivated Schiff bases [2–4] and carbodiimides [5] or at the C≡N bond of cyanamides [6].

As a result, the corresponding 1,3-oxazin-4-one derivatives are formed. Activated Schiff bases react with 5-aryl-4-phenyl-2,3-dihydrofuran-2,3-diones under milder conditions (at room temperature), and the reaction includes opening of the furan ring and subsequent recyclization to substituted 3-hydroxypyrrol-2-ones [4, 7].

Scheme 1.



I, II, Ar¹ = Ph (**a**), 2,5-Me₂C₆H₃ (**b**); **III**, Ar¹ = Ph, Ar² = *p*-BrC₆H₄, Ar³ = *p*-MeOC₆H₄ (**a**); Ar¹ = Ar² = Ph, Ar³ = 2,5-Me₂C₆H₃ (**b**); Ar¹ = 2,5-Me₂C₆H₃, Ar² = *p*-BrC₆H₄, Ar³ = *p*-MeOC₆H₄ (**c**); **IV**, Ar¹ = Ph, Ar⁴ = *p*-Me₂NC₆H₄ (**a**); Ar¹ = 2,5-Me₂C₆H₃, Ar⁴ = *p*-Et₂NC₆H₄ (**b**); **V**, Ar¹ = Ph (**a**), 2,5-Me₂C₆H₃ (**b**); **VI**, Ar⁵ = *p*-Me₂NC₆H₄, Ar¹ = Ph (**a**), 2,5-Me₂C₆H₃ (**b**).

* For communication XLVI, see [1].

In order to estimate the effect of a phenyl group in position 4 of the furan ring on the above process, we examined reactions of 5-aryl-4-phenyl-2,3-dihydrofuran-2,3-diones **Ia** and **Ib** with some activated and nonactivated Schiff bases, *N,N'*-dicyclohexylcarbodiimide, and *p*-dimethylaminobenzonitrile. Heating of mixtures of compound **Ia** or **Ib** and *N*-benzylideneanilines in dry boiling 1,2,4-trimethylbenzene at 160–165°C over a period of 30–40 min promoted thermal decarbonylation of the former with generation of aroyl (phenyl)ketenes **IIa** and **IIb** which reacted as dienes at the C=N bond of Schiff bases according to the [4+2]-cycloaddition pattern. As a result, the corresponding 2,3,6-triaryl-5-phenyl-3,4-dihydro-2*H*-1,3-oxazin-4-ones **IIIa–IIIc** were obtained (Scheme 1).

The IR spectra of products **IIIa–IIIc** contained a strong absorption band at 1655–1678 cm⁻¹ due to stretching vibrations of the lactam carbonyl group (C⁴=O). Its position is well consistent with the IR spectra of their analogs containing a halogen atom or no substituent at C⁵ [2–4]. In the ¹H NMR spectra of **IIIa–IIIc** we observed signals from aromatic protons, a singlet at δ 6.85–6.87 ppm from 2-H, singlets at δ 1.74–2.19 ppm from the methyl group protons (**IIIb**, **IIIc**), and a singlet at δ 3.78–3.79 ppm from the methoxy group proton (**IIIa**, **IIIc**). Compound **IIIb** showed in the ¹³C NMR spectrum signals from aromatic carbon atoms (δ_C 126.28–139.02 ppm), methyl groups attached to the aromatic rings (δ_C 18.34, 20.27 ppm), and signals at δ_C 89.20, 160.39, 114.87, and 162.16 ppm from the C², C⁴, C⁵, and C⁶ atoms of the 1,3-oxazine ring, respectively. These data are consistent with the assumed structure. The mass spectrum of **IIIa** contained the following ion peaks, *m/z* (*I*_{rel}, %): 289/291 (54/61) [*p*-BrC₆H₄CH=NC₆H₄-OMe-*p*]⁺, 222 (35) [PhCO(Ph)C=C=O]⁺. This fragmentation pattern corresponds to the retro-Diels–Alder decomposition.

By reaction of furandiones **Ia** and **Ib** with *N*-(benzylidene)benzylamines in dry boiling chloroform (63–64°C, 20–30 min) we obtained 4-aryloxy-5-aryl-1-benzyl-4-phenyl-2,3,4,5-tetrahydro-1*H*-pyrrole-2,3-diones **IVa** and **IVb**, respectively [8]. In the IR spectra of pyrrolediones **IVa** and **IVb**, stretching vibrations of the lactam carbonyl group (C²=O) appeared at 1770–1776 cm⁻¹, and absorption bands due to ketone carbonyl groups C³=O and 4-COAr were located at 1719–1725 and 1680–1695 cm⁻¹, respectively. The ¹H NMR spectra of pyrrolediones **IVa** and **IVb** contained signals from protons in the aromatic rings and

groups attached thereto, a doublet of doublets at δ 3.80–5.04 ppm (*AB* system) from the CH₂ protons of the benzyl group, and a singlet from 5-H at δ 5.78–5.98 ppm. Compound **IVa** showed the following signals in the ¹³C NMR spectrum, δ_C, ppm: 119.58–150.08 (C_{arom}), 39.53 (Me₂N), 45.84 (CH₂), 62.49 (C⁴), 67.74 (C⁵), 156.86 (C²=O), 192.15 (PhC=O), 192.31 (C³=O).

Presumably, in the first stage, opening of the furan ring in **Ia** and **Ib** as a result of nucleophilic attack by the nitrogen atom of activated Schiff base gives zwitterionic intermediate which then undergoes intramolecular cyclization to **IVa** and **IVb** [8].

Heating of furandiones **Ia** and **Ib** in boiling 1,2,4-trimethylbenzene (160–165°C, 30–40 min) in the presence of *N,N'*-dicyclohexylcarbodiimide afforded 6-aryl-5-phenyl-3-cyclohexyl-2-cyclohexylimino-3,4-dihydro-2*H*-1,3-oxazin-4-ones **Va** and **Vb** via [4+2]-cycloaddition of intermediate aroylketenes **IIa** and **IIb** at the C=N bond of carbodiimide. In the IR spectra of oxazinones **Va** and **Vb**, absorption bands at 1700–1702 and 1655–1660 cm⁻¹ were present due to stretching vibrations of the lactam carbonyl group (C⁴=O) and C=N bond, respectively. The ¹H NMR spectra of **Va** and **Vb** contained singlets from the methyl group protons at δ 2.12 and 2.14 ppm (**Vb**), a set of signals from ten CH₂ groups in the two cyclohexyl fragments in the regions δ 1.09–1.82 and 2.52–2.62 ppm, two quintets from the CH protons in the cyclohexyl fragments at 3.60–3.78 and 4.70–4.79 ppm, and a set of aromatic proton signals in the region δ 7.02–7.43 ppm. Compound **Va** showed the following signals in the ¹³C NMR spectrum, δ_C, ppm: 127.73–132.18 (C_{arom}); 24.35–34.14, 53.47, 55.41 (cyclohexyl); 138.87 (C²), 162.06 (C⁴), 112.21 (C⁵), 156.79 (C⁶).

The reaction of furandiones **Ia** and **Ib** with *p*-dimethylaminobenzonitrile in Dowtherm A [9] at 140–145°C (20–30 min) gave 6-aryl-2-(*p*-dimethylaminophenyl)-5-phenyl-4*H*-1,3-oxazin-4-ones **VIa** and **VIb**, respectively, as a result of [4+2]-cycloaddition of aroyl(phenyl)ketenes **IIa–IIc** (generated by thermal decarbonylation of **Ia** and **Ib**) at the C≡N bond of the nitrile. The IR spectra of **VIa** and **VIb** contained absorption bands belonging to stretching vibrations of the lactam carbonyl group (C⁴=O) at 1660–1680 cm⁻¹ and C=N bond in the oxazine ring at 1620–1621 cm⁻¹; their position is well consistent with the IR spectra of structural analogs having no substituent at C⁵ [5]. Compound **VIa** showed the following ion peaks in the mass spectrum, *m/z* (*I*_{rel}, %): 368 (5) [*M*]⁺, 146 (100) [*p*-Me₂NC₆H₄C≡N]⁺.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer from samples dispersed in mineral oil. The ^1H and ^{13}C NMR spectra** were obtained on a Bruker AM-400 instrument (400 MHz for ^1H) from solutions in $\text{DMSO}-d_6$ or CDCl_3 using tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were recorded on an MKh-1310 mass spectrometer. The purity of the products was checked by TLC on Silufol plates using ethyl acetate, ethyl acetate–benzene (1:5), or benzene as eluent; development with iodine vapor.

2-*p*-Bromophenyl-3-*p*-methoxyphenyl-5,6-diphenyl-3,4-dihydro-2*H*-1,3-oxazin-4-one (IIIa). A solution of 2.16 mmol of furandione **Ia** and 2.16 mmol of *N*-(*p*-bromobenzylidene)-*p*-methoxyaniline in 5 ml of dry 1,2,4-trimethylbenzene was heated for 30–40 min under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 0.55 g (50%), mp 144–146°C (decomp., from CCl_4 –hexane, 1:1). IR spectrum, ν , cm^{-1} : 1655 ($\text{C}^4=\text{O}$). ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 3.78 s (3H, OMe), 6.85 s (1H, 2-H), 6.89–7.65 m (18H, H_{arom}). Mass spectrum, m/z (I_{rel} , %): 289/291 (54/61) [*p*-BrC₆H₄CH=NC₆H₄OMe-*p*]⁺, 222 (35) [Ph(PhCO)C=C=O]⁺, 105 (100) [PhCO]⁺, 77 (88) [Ph]⁺. Found, %: C 67.99; H 4.31; Br 15.65; N 2.75. C₂₉H₂₂BrNO₃. Calculated, %: C 67.98; H 4.33; Br 15.59; N 2.73.

5-(2,5-Dimethylphenyl)-2,3,5-triphenyl-3,4-dihydro-2*H*-1,3-oxazin-4-one (IIIb) was synthesized in a similar way. Yield 48%, mp 174–176°C (decomp., from benzene). IR spectrum, ν , cm^{-1} : 1668 ($\text{C}^4=\text{O}$). ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 1.74 s (3H, Me), 2.12 s (3H, Me), 6.87 s (1H, 2-H), 6.92–7.60 m (18H, H_{arom}). ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$), δ_{C} , ppm: 18.34 (Me), 20.27 (Me), 89.20 (C^2), 114.87 (C^5), 126.28–139.02 (C_{arom}), 160.39 (C^4), 162.16 (C^6). Found, %: C 83.47; H 5.82; N 3.25. C₃₀H₂₅NO₂. Calculated, %: C 83.47; H 5.84; N 3.25.

2-*p*-Bromophenyl-6-(2,5-dimethylphenyl)-3-*p*-methoxyphenyl-5-phenyl-3,4-dihydro-2*H*-1,3-oxazin-4-one (IIIc) was synthesized in a similar way. Yield 47%, mp 195–197°C (decomp., from acetonitrile). IR spectrum, ν , cm^{-1} : 1678 ($\text{C}^4=\text{O}$). ^1H NMR spectrum (CDCl_3), δ , ppm: 1.85 s (3H, Me), 2.19 s (3H, Me), 3.79 s (3H, OMe), 6.68 s (1H, 2-H), 6.82–

7.60 m (16H, H_{arom}). Found, %: C 68.90; H 4.87; Br 14.80; N 2.63. C₃₁H₂₆BrNO₃. Calculated, %: C 68.89; H 4.85; Br 14.78; N 2.59.

4-Benzoyl-1-benzyl-5-*p*-dimethylaminophenyl-2,3,4,5-tetrahydro-1*H*-pyrrole-2,3-dione (IVa). A solution of 5 mmol of furandione **Ia** and 5 mmol of *N*-(*p*-dimethylaminobenzylidene)benzylamine in 15 ml of dry chloroform was heated for 20–30 min under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 1.95 g (80%), mp 197–198°C (from isopropyl alcohol). IR spectrum, ν , cm^{-1} : 1770 ($\text{C}^2=\text{O}$), 1725 ($\text{C}^3=\text{O}$), 1680 (PhC=O). ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 2.78 s (6H, Me₂N), 3.80 d (1H, CH₂, AB system, $J = 14.3$ Hz), 5.04 d (1H, CH₂, AB system, $J = 14.3$ Hz), 5.98 s (1H, 5-H), 6.44–7.47 m (19H, H_{arom}). ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$), δ_{C} , ppm: 39.53 (Me₂N), 45.84 (CH₂), 62.49 (C^4), 67.74 (C^5), 119.58–150.08 (C_{arom}), 156.86 (C^2), 192.15 (PhCO), 192.31 (C^3). Found, %: C 78.72; H 5.78; N 5.70. C₃₂H₂₈N₂O₃. Calculated, %: C 78.67; H 5.78; N 5.73.

1-Benzyl-5-*p*-diethylaminophenyl-4-(2,5-dimethylbenzoyl)-2,3,4,5-tetrahydro-1*H*-pyrrole-2,3-dione (IVb) was synthesized in a similar way. Yield 71%, mp 182–183°C (from isopropyl alcohol). IR spectrum, ν , cm^{-1} : 1776 ($\text{C}^2=\text{O}$), 1719 ($\text{C}^3=\text{O}$), 1695 ($\text{C}_6\text{H}_3\text{C}=\text{O}$). ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 1.01 t (6H, CH₃CH₂, $J = 7.0$ Hz), 1.92 s (3H, Me), 1.96 s (3H, Me), 3.24 q (4H, CH₃CH₂, $J = 7.0$ Hz), 3.94 d (1H, CH₂, AB system, $J = 14.5$ Hz), 4.93 d (1H, CH₂, AB system, $J = 14.5$ Hz), 5.78 s (1H, 5-H), 6.44–7.28 m (17H, H_{arom}). Found, %: C 79.42; H 6.70; N 5.20. C₃₆H₃₆N₂O₃. Calculated, %: C 79.38; H 6.66; N 5.14.

3-Cyclohexyl-2-cyclohexylimino-5,6-diphenyl-3,4-dihydro-2*H*-1,3-oxazin-4-one (Va). A solution of 2.16 mmol of furandione **Ia** and 2.16 mmol of *N,N'*-dicyclohexylcarbodiimide in 5 ml of dry 1,2,4-trimethylbenzene was heated for 30–40 min under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 0.88 g (95%), mp 166–168°C (from hexane). IR spectrum, ν , cm^{-1} : 1700 ($\text{C}^4=\text{O}$), 1655 ($\text{C}=\text{N}$). ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 1.17–1.82 m, 2.52–2.62 m, 3.78 m, and 4.79 m (22H, C₆H₁₁-cyclo); 7.18–7.43 m (10H, H_{arom}). ^{13}C NMR spectrum (100 MHz, CDCl_3), δ , ppm: 24.35–55.41 (C₆H₁₁-cyclo), 112.21 (C^5), 127.73–132.18 (C_{arom}), 138.87 (C^2), 156.79 (C^6), 162.06 (C^4). Found, %: C 78.45; H 7.55; N 6.58. C₂₈H₃₂N₂O₂. Calculated, %: C 78.47; H 7.53; N 6.54.

** NMR studies were performed at the *Ural-YaMR* Center under support by the Russian Foundation for Basic Research (project no. 00-03-40139).

3-Cyclohexyl-2-cyclohexylimino-6-(2,5-dimethylphenyl)-5-phenyl-3,4-dihydro-2H-1,3-oxazin-4-one (Vb) was synthesized in a similar way. Yield 87%, mp 133–135°C (from hexane). IR spectrum, ν , cm^{-1} : 1702 ($\text{C}^4=\text{O}$), 1660 ($\text{C}=\text{N}$). ^1H NMR spectrum ($\text{DMSO-}d_6$), δ , ppm: 2.12 s (3H, Me); 2.14 s (3H, Me); 1.09–1.81 m, 2.52–2.60 m, 3.60 m, and 4.70 m (22H, C_6H_{11} -*cyclo*); 7.02–7.19 m (8H, H_{arom}). Found, %: C 78.94; H 7.98; N 6.15. $\text{C}_{30}\text{H}_{36}\text{N}_2\text{O}_2$. Calculated, %: C 78.91; H 7.95; N 6.13.

2-*p*-Dimethylaminophenyl-5,6-diphenyl-4H-1,3-oxazin-4-one (VIa). A solution of 2 mmol of furandione **Ia** and 2.00 mmol of *p*-dimethylaminobenzonitrile in 3 ml of Dowtherm A was heated for 20–30 min at 140–145°C. The mixture was cooled, and the precipitate was filtered off. Yield 0.63 g (85%), mp 243–245°C (from isopropyl alcohol). IR spectrum, ν , cm^{-1} : 1660 ($\text{C}^4=\text{O}$), 1621 ($\text{C}=\text{N}$). ^1H NMR spectrum ($\text{DMSO-}d_6$), δ , ppm: 3.12 s (6H, Me_2N), 6.78–8.08 m (14H, H_{arom}). Mass spectrum, m/z (I_{rel} , %): 368 (5) [M] $^+$, 146 (100) [p - $\text{Me}_2\text{NC}_6\text{H}_4\text{C}\equiv\text{N}$] $^+$, 105 (25) [PhCO] $^+$, 77 (16) [Ph] $^+$. Found, %: C 78.26; H 5.50; N 7.63. $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_2$. Calculated, %: C 78.24; H 5.47; N 7.60.

2-*p*-Dimethylaminophenyl-6-(2,5-dimethylphenyl)-6-phenyl-4H-1,3-oxazin-4-one (VIb) was synthesized in a similar way. Yield 94%, mp 204–206°C (from isopropyl alcohol). IR spectrum, ν , cm^{-1} : 1665 ($\text{C}^4=\text{O}$), 1620 ($\text{C}=\text{N}$). ^1H NMR spectrum (CDCl_3), δ , ppm: 2.32 s (3H, Me), 2.42 s (3H, Me), 3.07 s (6H, Me_2N), 6.60–7.79 m (12H, H_{arom}). Found,

%: C 78.75; H 6.12; N 7.10. $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_2$. Calculated, %: C 78.76; H 6.10; N 7.06.

This study was performed under financial support by the Russian Foundation for Basic Research (project nos. 04-03-33024 and 04-03-96033) and by the Ministry of Education of the Russian Federation (project no. A03-2.11-55).

REFERENCES

1. Lisovenko, N.Yu., Maslivets, A.N., and Aliev, Z.G., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 1053.
2. Andreichikov, Yu.S., Koz'minykh, O.V., Ionov, Yu.V., and Saraeva, R.F., *Khim. Geterotsikl. Soedin.*, 1978, p. 271.
3. Andreichikov, Yu.S. and Ionov, Yu.V., *Zh. Org. Khim.*, 1982, vol. 18, p. 2430.
4. Karpova, L.N., Kolotova, N.V., Shurov, S.N., and Andreichikov, Yu.S., *Zh. Org. Khim.*, 1992, vol. 28, p. 779.
5. Andreichikov, Yu.S. and Shurov, S.N., *Zh. Org. Khim.*, 1983, vol. 19, p. 1983.
6. Andreichikov, Yu.S., Nekrasov, D.D., Rudenko, M.A., and Konovalov, A.Yu., *Khim. Geterotsikl. Soedin.*, 1987, p. 740.
7. Andreichikov, Yu.S., Maslivets, A.N., and Ivanenko, O.I., *Zh. Org. Khim.*, 1986, vol. 22, p. 1790.
8. Vostrov, E.S., Lisovenko, N.Yu., Tarasova, O.P., and Maslivets, A.N., *Khim. Geterotsikl. Soedin.*, 2001, p. 1282.
9. Fieser, L.F. and Fieser, M., *Reagents for Organic Synthesis*, New York: Wiley, 1968, vol. 1. Translated under the title *Reagenty dlya organicheskogo sinteza*, Moscow: Mir, 1970, vol. 1, p. 239.