Chemistry of Heterocyclic Compounds, Vol. 48, No. 9, December, 2012 (Russian Original Vol. 48, No. 9, September, 2012)

THERMOLYTIC TRANSFORMATIONS OF 5-ARYL-4-QUINOXALIN-2-YLFURAN-2,3-DIONES IN THE PRESENCE OF *N*-CYANO COMPOUNDS

N. Yu. Lisovenko[1]*, D. D. Nekrasov[1], and V. I. Karmanov[2]

6-Aryl-5-quinoxalinyl-1,3-oxazin-4-ones were obtained by thermolysis of 5-aryl-4-quinoxalinylfuran-2,3-diones in the presence of tert-butylcyanamide, 4-morpholinecarbonitrile, and N-cyanobenzamide.

Keywords: aroyl(imidoyl)ketenes, *N*-cyano compounds, 1,3-oxazin-4-ones, [4+2] cycloaddition.

Aroylketenes, generated from 4-unsubstituted 5-arylfuran-2,3-diones, enter into a Diels–Alder reaction with *N*-cyano compounds [1-3], where the aroylketene fragment acts as diene, while the C≡N bond of the *N*-cyano compound acts as dienophile.

The presence of the quinoxaline fragment at the position 4 of the 5-arylfuran-2,3-dione molecule in thermolytic reactions leads to the corresponding aroyl(imidoyl)ketenes, which have alternative paths for cycloaddition at the aroylketene or imidoylketene fragment. In the absence of reaction partners they undergo intermolecular dimerization, where one molecule of the ketene acts as diene through the conjugated imidoylketene bond system while another acts as dienophile through the C=C bond of the aroylketene fragment [4]. In the presence of active dienophiles, cycloaddition takes place at the aroylketene fragment of the aroyl(imidoyl)ketene [5, 6].

The possibility of aroyl(imidoyl)ketenes generated from 5-aryl-4-quinoxalinylfuran-2,3-diones undergoing cycloaddition in both directions was investigated by us for the case of *N*-cyano compounds containing substituents with various electronic effects at the cyano group.

Substituted 6-aryl-5-quinoxalinyl-1,3-oxazin-4-ones **2a-f** (Tables 1, 2) were obtained by the thermolysis of furandiones **1a**,**b** with commercially available *tert*-butylcyanamide, 4-morpholinecarbonitrile, and *N*-cyanobenzamide.

Compounds **2a-f** are evidently formed as a result of [4+2] cycloaddition of the aroylketene fragment of the aroyl(imidoyl)ketenes **A**, generated from the furandiones **1a**,**b**, at the C≡N bond of the *N*-cyanoamide reagent.

In the IR spectra of the obtained compounds, the absence of absorption bands characteristic of the ketone carbonyl in the aroyl fragment makes it possible to rule out the formation of the isomeric structure **3**.

---

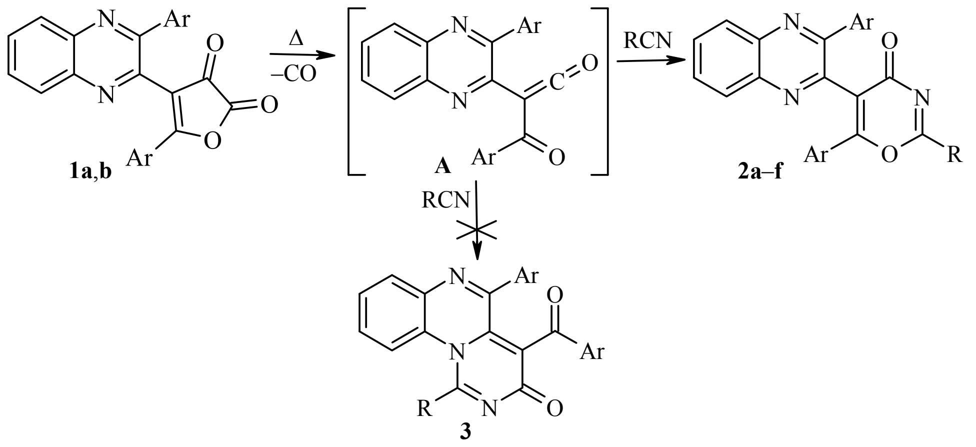
*To whom correspondence should be addressed, e-mail: lisovn@mail.ru.

[1] Perm State National Research University, 15 Bukireva St., Perm 614990, Russia.

[2] Institute of Technical Chemistry, Ural Branch, Russian Academy of Sciences, 3 Acad. Koroleva St., Perm 614013, Russia e-mail: info@itch.perm.ru.

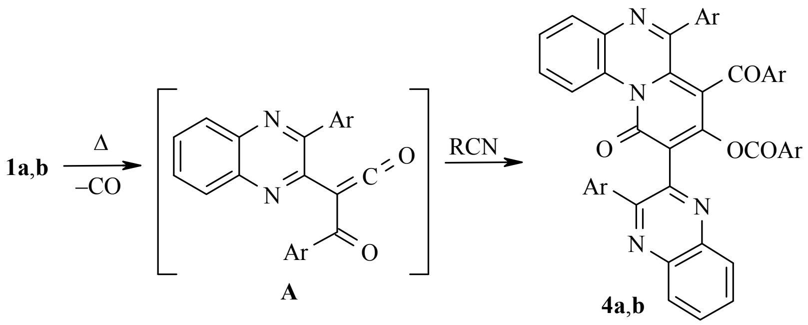
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1456-1459, September, 2012. Original article submitted May 29, 2011.

The reaction of benzoylketene, generated from 5-phenylfuran-2,3-diones, with compounds containing a C≡N bond has been modelled by the semiempirical SCF-MO-LCAO method in the MNDO-PM3 approximation, indicating that the reaction proceeds by a pseudopericyclic mechanism [7]. It can be supposed that compounds **2a-f** will be formed by a similar mechanism.



1 a Ar = Ph, **b** Ar = 4-MeC$_6$H$_4$; **2 a** Ar = Ph, R = *t*-BuNH; **b** Ar = 4-MeC$_6$H$_4$, R = *t*-BuNH; **c** Ar = Ph, R = morpholin-4-yl; **d** Ar = 4-MeC$_6$H$_4$, R = morpholin-4-yl; **e** Ar = Ph, R = PhCONH; **f** Ar = 4-MeC$_6$H$_4$, R = PhCONH

Unlike *tert*-butylcyanamide, 4-morpholinecarbonitrile, and *N*-cyanobenzamide, aliphatic and aromatic nitriles do not react with aroyl(imidoyl)ketenes **A**. In the course of the reaction only the dimers **4a**,**b** were isolated, with physicochemical characteristics matching those of previously obtained samples [4].



R = Me, 4-EtOC$_6$H$_4$, 2,4-(EtO)$_2$C$_6$H$_3$, 4-Me$_2$NC$_6$H$_4$

This is probably explained by the fact that the reaction of aroyl(imidoyl)ketenes with unsaturated compounds is a [4+2] cycloaddition with inverse electron demands in comparison with usual Diels–Alder reactions. Therefore, only cyanides in which the C≡N bond is activated by strong electron-donating groups enter into reactions with aroyl(imidoyl)ketenes.

Thus, investigation of the thermolytic transformations of furan-2,3-diones in the presence of *N*-cyano compounds has demonstrated the regiospecific nature of such reactions. In the course of the reaction only the products from dienophile cycloaddition at the aroylketene fragment of the aroyl(imidoyl)ketenes (substituted 1,3-oxazin-4-ones) are formed. Estimation of the reactivity of compounds containing C≡N bonds in intermolecular cycloaddition with ketenes showed that the reaction only occurs with cyano compounds activated by strong electron-donating groups.

TABLE 1. The Physicochemical Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % Calculated, %			Mp, °C (solvent)	Yield, %
		C	H	N		
2a	$C_{28}H_{24}N_4O_2$	74.99 74.98	5.34 5.39	12.47 12.49	275-276 (MeCN)	76
2b	$C_{30}H_{28}N_4O_2$	75.66 75.61	5.95 5.92	11.70 11.76	277-279 (MeCN)	87
2c	$C_{28}H_{22}N_4O_3$	72.68 72.71	4.77 4.79	12.16 12.11	180-181 (PhMe)	78
2d	$C_{30}H_{26}N_4O_3$	73.51 73.45	5.38 5.34	11.49 11.42	231-233 (PhMe)	75
2e	$C_{31}H_{20}N_4O_3$	74.91 74.99	4.11 4.06	11.31 11.28	243-245 (PhMe)	60
2f	$C_{33}H_{24}N_4O_3$	75.52 75.56	4.60 4.61	10.61 10.68	194-196 (PhMe)	67

EXPERIMENTAL

The IR spectra were recorded in vaseline oil on an FSM-1201 spectrometer. The ^{1}H NMR spectra were obtained in $CDCl_3$ on a Mercury 300 Plus instrument (300 MHz) with HMDS as internal standard (δ 0.05 ppm). Elemental analysis was performed on an automatic LECO CHNS-932 analyzer. The melting points were determined on a PTP-2 instrument. The chemical purity of the compounds and the progress of the reactions were monitored by TLC on Silufol UV-254 plates with 5:2 hexane–EtOAc as eluent and with detection by iodine vapor.

2-*tert*-Butylamino-6-phenyl-5-(3-phenylquinoxalin-2-yl)-4*H*-1,3-oxazin-4-one (2a). A solution of furandione **1a** (378 mg, 1 mmol) and *tert*-butylcyanoamide (98 mg, 1 mmol) in absolute *p*-xylene (15 ml) was refluxed for 30 min, the solvent was evaporated, and the residue was recrystallized.

Compounds **2b-f** were synthesized similarly to compound **2a**.

2-*tert*-Butylamino-6-(4-methylphenyl)-5-[3-(4-methylphenyl)quinoxalin-2-yl]-4*H*-1,3-oxazin-4-one (2b). This compound was obtained from the furandione **1b** and *tert*-butylcyanoamide.

2-(Morpholin-4-yl)-6-phenyl-5-(3-phenylquinoxalin-2-yl)-4*H*-1,3-oxazin-4-one (2c). This compound was obtained from the furandione **1a** and 4-morpholinecarbonitrile.

6-(4-Methylphenyl)-5-[3-(4-methylphenyl)quinoxalin-2-yl]-2-(morpholin-4-yl)-4H-1,3-oxazin-4-one (2d). This compound was obtained from the furandione **1b** and 4-morpholinecarbonitrile.

TABLE 2. The Spectral Characteristics of the Synthesized Compounds

Compound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm
2a	1668 (CON), 3220 (br., NH)	1.40 (9H, s, $C(CH_3)_3$); 6.99–8.18 (14H, m, H Ar); 8.32 (1H, s, NH)
2b	1664 (CON), 3219 (br., NH)	1.44 (9H, s, $C(CH_3)_3$); 2.26 (3H, s, CH_3); 2.37 (3H, s, CH_3); 7.00-8.20 (12H, m, H Ar); 8.33 (1H, s, NH)
2c	1668 (CON)	3.74 (8H, br. s, 4CH_2 morpholine); 7.11–8.21 (14H, m, H Ar)
2d	1674 (CON)	2.26 (3H, s, CH_3); 2.37 (3H, s, CH_3); 3.74 (8H, br. s, 4CH_2 morpholine); 7.06-8.20 (12H, m, H Ar)
2e	1662 (CON), 3228 (br., NH)	7.49-8.23 (19H, m, H Ar); 11.88 (1H, s, NH)
2f	1666 (CON), 3231 (br., NH)	2.45 (3H, s, CH_3); 2.52 (3H, s, CH_3); 7.25–8.02 (17H, m, H Ar); 11.63 (1H, s, NH)

***N*-[4-Oxo-6-phenyl-5-(3-phenylquinoxalin-2-yl)-4*H*-[1,3]oxazin-2-yl]benzamide (2e)**. This compound was obtained from the furandione **1a** and *N*-cyanobenzamide.

N-{6-(4-Methylphenyl)-4-oxo-5-[3-(4-methylphenyl)quinoxalin-2-yl]-4H-[1,3]oxazin-2-yl}benzamide (2f). This compound was obtained from the furandione **1b** and *N*-cyanobenzamide.

The work was carried out with financial support from the Ministry of Education of Perm Region (project MIG).

REFERENCES

1. Yu. S. Andreichikov and D. D. Nekrasov, *Khim. Geterotsikl. Soedin.*, 166 (1985). [*Chem. Heterocycl. Compd.*, **21**, 132 (1985).]
2. D. D. Nekrasov, S. V. Kol'tsova, and Yu. S. Andreichikov, *Zh. Org. Khim.*, **31**, 591 (1995).
3. Yu. S. Andreichikov and D. D. Nekrasov, *Zh. Org. Khim.*, **20**, 1755 (1984).
4. A. N. Maslivets, N. Yu. Lisovenko, O. P. Krasnykh, O. P. Tarasova, Z. G. Aliev, and L. O. Atovmyan, *Izv. Akad. Nauk*, *Ser. Khim.*, 785 (2002).
5. N. Yu. Lisovenko, A. N. Maslivets, and Z. G. Aliev, *Zh.. Org. Khim.*, **40**, 1094 (2004).
6. N. Yu. Lisovenko, A. N. Maslivets, and Z. G. Aliev, *Zh. Org. Khim.*, **43**, 111 (2007).
7. D. D. Nekrasov and S. N. Shurov, in: *Prospects for the Development of Natural Sciences in High School*, *Proceedings of International Conference* [in Russian], Vol. 1, Perm (2001), p. 56.