# Preparation of 5,6′-diaryl-2,2′-bipyridines using a 1,2,4-triazine methodology

*D. S. Kopchuk,[a,b] N. V. Chepchugov,[a] G. A. Kim,[a,b] G. V. Zyryanov,[a,b]* I. S. Kovalev,[a] V. L. Rusinov,[a,b] and O. N. Chupakhin[a,b]*

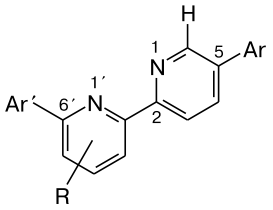
[a] *Ural Federal University named after the first President of Russia B. N. Eltsin, 19 ul. Mira, 620002 Ekaterinburg, Russian Federation. Phone: +7 (343) 375 4501. E-mail: gvzyryanov@gmail.com*

[b] *I. Ya. Postovsky Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences, 20 ul. S. Kovalevskoi, 620219 Ekaterinburg, Russian Federation. Phone: +7 (343) 374 1189. E-mail: chupakhin@ios.uran.ru*

New unsymmetric 5,6′-diaryl-2,2′-bipyridines were synthesized in high yields using a 1,2,4-triazine methodology. Their photophysical properties were studied.

**Key words:** 1,2,4-triazine, Diels—Alder reaction, 5,6′-diaryl-2,2′-bipyridines.

2,2′-Bipyridines and 1,10-phenanthrolines bearing aromatic substituents at positions 5 and 6′ are of interest as ligand fragments for transition metal cations,[1—5] for preparation of promising photoluminescent materials,[6] as well as catalysts.[7] In supramolecular chemistry, the fragments of the aryl-substituted 2,2′-bipyridines and 1,10-phenanthrolines are used for the design of some cyclophanes.[8] In this case, the absence of a substituent at position 6 usually has a positive effect on the coordination properties of the compound.

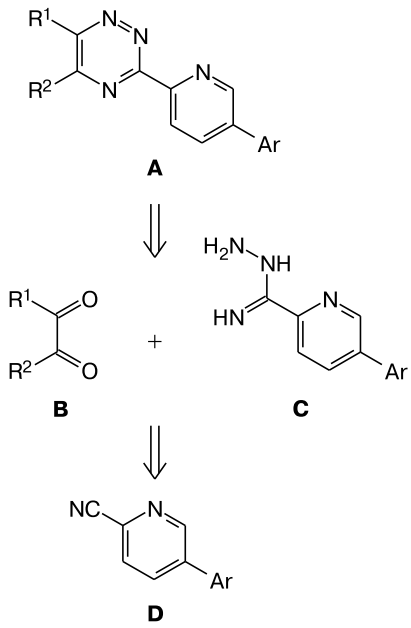


As for the approaches to the synthesis of such compounds, there are only few literature examples of their preparation using, for example, cross-coupling reactions[1,4,6,8] or sequential nucleophilic substitution of hydrogen and cross-coupling reactions.[5,7]

In the present work, we suggest a synthetic approach to unsymmetric 2,2′-bipyridines bearing aromatic substituents at positions 5 and 6′ and having no substituents at position 6. To accomplish the task, we applied twice a methodology for the preparation of substituted pyridines *via* their 1,2,4-triazine analogs, which at present are very successfully used in the synthesis of various substituted pyridines.[9,10]

It is obvious that the preparation of the target compounds required the development of a convenient method for the synthesis of their 1,2,4-triazine analogs **A** (Scheme 1). The most acceptable approach to their synthesis was a heterocyclization of 1,2-diketones **B** with amidrazone **C** described earlier[11,12] (Scheme 1). Therefore, first it is necessary to synthesize 5-aryl-2-cyanopyridine **D** to further convert it to amidrazone **C**.

**Scheme 1**

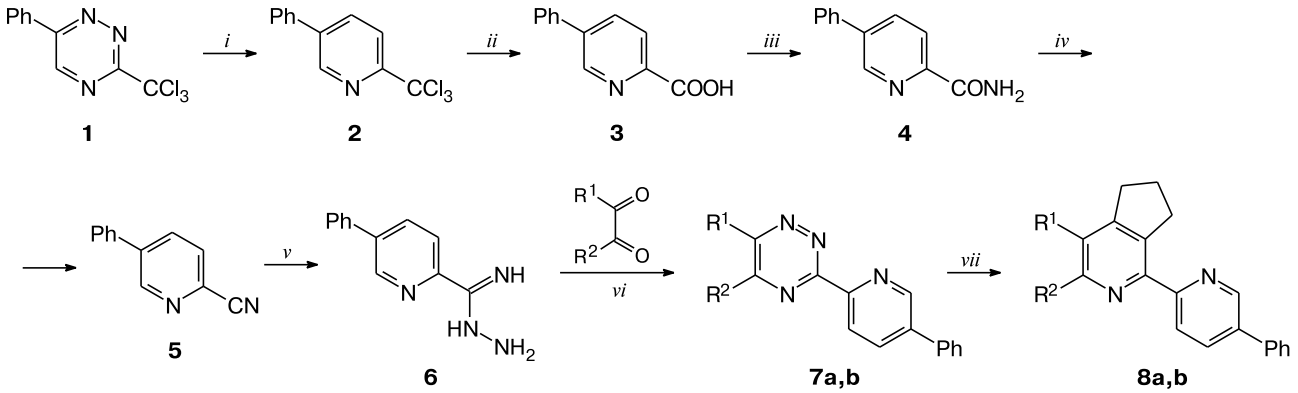


Analysis of literature data showed that 5-aryl-2-cyanopyridines can be prepared, for example, by the introduction of aromatic fragments in pyridines using cross-coupling reactions,[13,14] a direct cyanation of 3-arylpyridine *N*-oxides[15] (however, 2-cyano-substituted compounds are frequent side products[16]), a nucleophilic

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 4, pp. 0897—0900, April, 2015.

1066-5285/15/6404-0897 © 2015 Springer Science+Business Media, Inc.

**Scheme 2**



$R^1$, $R^2$ = biphenyl-2,2′-diyl (**a**), $R^1 = R^2$ = Ph (**b**)

**Reagents and conditions:** *i*. 2,5-norbornadiene, *o*-xylene, 143 °C, 10 h; *ii*. 85% formic acid, reflux, 20 h; *iii*. $SOCl_2$, reflux, 3 h, then aqueous ammonia, 5—10 °C, 1 h; *iv*. $POCl_3$, reflux, 1.5 h; *v*. hydrazine hydrate, ethanol—THF (1 : 1), 3 days; *vi*. ethanol—THF (7 : 3), reflux, 10 h; *vii*. 1-morpholinocyclopentene, 200 °C, 3 h.

substitution for the halogen atom with the cyano group,[17] as well as by a sequence of transformations acid—amide—nitrile.[18]

In our opinion, the preparation of 5-aryl-2-cyanopyridines *via* 5-arylpyridine-2-carboxylic acids is the most convenient method of all the approaches considered. In the framework of this work, we developed a new approach to the synthesis of these compounds, which also uses a 1,2,4-triazine methodology. Thus, earlier authors[19,20] described an efficient method for the preparation of 6-aryl-3-trichloromethyl-1,2,4-triazines having no substituents at position 5 by the reaction of isonitrosoacetophenone hydrazones with trichloroacetonitrile iminoester obtained *in situ*. It is known that a trichloromethyl group can undergo a number of transformations interesting from the point of view of further functionalization of pyridine.[21,22] Following a procedure described earlier, we obtained 3-trichloromethyl-6-phenyl-1,2,4-triazine (**1**), which was converted to the corresponding pyridine **2** by the aza-Diels—Alder reaction with 2,5-norbornadiene (Scheme 2). It should be noted that earlier the preparation of 2-trichloromethylpyridine derivatives by this method was not described. Further, carboxylic acid **3** was obtained by the hydrolysis of the trichloromethyl group, then it was converted to amide **4** (using a simplified version of the method suggested in the work[18]), which was dehydrated upon treatment with $POCl_3$ (carried out according to the described procedure[18]) to yield 2-cyano-5-phenylpyridine (**5**). The latter was converted to amidrazone **6**, which reacted with 1,2-diketones to give 1,2,4-triazine analogs of the target compounds **7** in good yields. Finally, the aza-Diels—Alder reaction with 1-morpholinocyclopentene as a dieneophile according to an efficient procedure suggested earlier in the literature[23] resulted in the required ligands **8**. It is also necessary to note that the annulation of the fused cycloalkene fragment to the pyridine ring usually leads to the increase in the solubility of compounds in organic solvents.[24]

In the course of the work, we studied photophysical properties of new ligands **8a** and **8b**, the results are given in Table 1, the luminescence spectra are shown in Fig. 1.

In particular, the data obtained show that the presence of an additional phenyl ring in the pyridine fragment of pyridylmonoazatriphenylene significantly shifts both the luminescence and absorption maxima to the longer wavelength region as compared to the unsubstituted compound.[26] Besides, the replacement of the monoazatriphenylene fragment with the pyridyl one with two separate phenyl rings led to a considerable increase in the emission intensity and a hypsochromic shift of the luminescence and absorption maxima.

In conclusion, in the present work we suggested an efficient synthetic approach to the preparation of 5,6′-diaryl-6*H*-2,2′-bipyridines, which are poorly available by

**Table 1.** Quantum yield of luminescence (Φ), absorption ($A_{max}$) and luminescence ($I_{max}$) maxima in acetonitrile for compounds **8a**,**b**

| Compound | λ/nm | | Φ* |
|---|---|---|---|
| | $A_{max}$ | $I_{max}$ | |
| **8a** | 206, 223 sh, 253, 271, 292 sh, 312 sh, 326, 380 | 473 | 0.174 |
| **8b** | 211, 236 sh, 283, 350 | 425 | 0.699 |

* Quantum yields for all the compounds were measured relative to quinine sulfate (Φ = 0.546 in 0.1 *N* aqueous solution of $H_2SO_4$).[25]

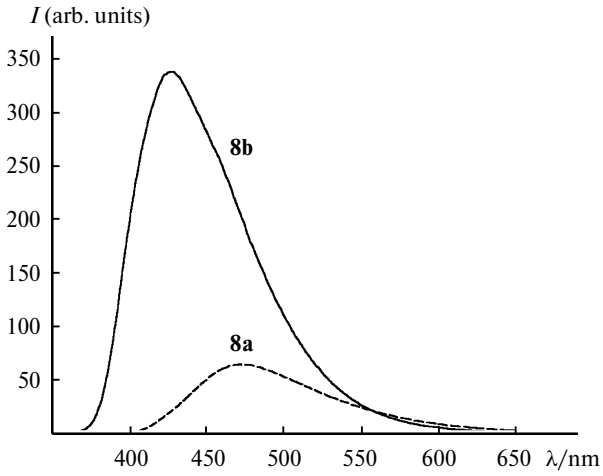



**Fig. 1.** Luminescence spectra of bipyridines **8**.

other methods, and studied photophysical properties of new compounds.

## Experimental

$^1$H and $^{13}$C NMR spectra were recorded on a Bruker Avance-400 spectrometer (400 MHz and 100 MHz, respectively), using $SiMe_4$ as an internal standard. Melting points were measured on a Boetius apparatus. Electrospray ionization mass spectra were recorded on a Bruker Daltonics Series MicrOTOF-Q II (Bremen, Germany). Elemental analysis was performed on a Perkin Elmer Model PE 2400, Series II CHN analyzer. Absorption spectra were recorded on a Shimadzu UV-2401PC spectrophotometer. Luminescence spectra were recorded on a Varian Cary Eclipse fluorimeter. 3-Trichloromethyl-5-phenyl-1,2,4-triazine (**1**)[19] and 2-cyano-5-phenylpyridine (**5**)[18] were obtained according to the described procedures.

**5-Phenyl-2-trichloromethylpyridine (2).** Triazine **1** (3 g, 10.93 mmol) was suspended in *o*-xylene (40 mL), followed by the addition of 2,5-norbornadiene (3.3 mL, 32.79 mmol) and reflux of the mixture for 10 h. The solvent was evaporated at reduced pressure, the residue was purified by column chromatography (silica gel, eluent chloroform). The yield was 2.23 g (75%), m.p. 198—200 °C. Found (%): C, 52.73; H, 2.81; N, 4.93. $C_{12}H_8ClN$. Calculated (%): C, 52.88; H, 2.96; N, 5.14. $^1$H NMR (DMSO-$d_6$), δ: 7.42—7.48 (m, 1 H, Ph); 7.49—7.55 (m, 2 H, Ph); 7.72—7.77 (m, 2 H, Ph); 8.12 (d, 1 H, H(3), $J$ = 7.9 Hz); 8.23 (dd, 1 H, H(4), $J$ = 7.9 Hz, $J$ = 2.5 Hz); 8.95 (d, 1 H, H(6), $J$ = 2.5 Hz). MS (ESI), $m/z$: 271.98 $[M + H]^+$.

**5-Phenylpyridine-2-carboxylic acid (3).** Trichloromethylpyridine **2** (1 g, 3.67 mmol) was suspended in 85% aqueous formic acid (25 mL), and the mixture was refluxed for 20 h. The solvent was evaporated at reduced pressure, the residue was treated with hexane, a precipitate formed was filtered off, washed with hexane, and dried. The product was used in the next step without additional purification. The yield was 0.62 g (85%). $^1$H NMR (DMSO-$d_6$), δ: 7.43—7.49 (m, 1 H, Ph); 7.49—7.55 (m, 2 H, Ph); 7.74—7.79 (m, 2 H, Ph); 8.18 (d, 1 H, H(3), $J$ = 7.9 Hz); 8.28 (dd, 1 H, H(4), $J$ = 7.9 Hz, $J$ = 2.5 Hz); 8.97 (d, 1 H, H(6), $J$ = 2.5 Hz). MS (ESI), $m/z$: 198.06 $[M - H]^-$.

**5-Phenylpyridine-2-carboxamide (4).** Acid **3** (0.62 g, 3.12 mmol) was suspended in thionyl chloride (40 mL), and the mixture was refluxed for 3 h. The solvent was evaporated at reduced pressure, aqueous ammonia (30 mL) was added to the residue, and the mixture obtained was stirred for 1 h with cooling in an ice bath. A precipitate formed was filtered off, washed with water, and dried *in vacuo*. The product was used in the next step without additional purification. The yield was 0.53 g (85%). $^1$H NMR (DMSO-$d_6$), δ: 7.39—7.46 (m, 1 H, Ph); 7.46—7.58 (m, 3 H, Ph, NH); 7.67—7.75 (m, 2 H, Ph); 7.85 (br.s, 1 H, NH); 8.10—8.19 (m, 2 H, H(3) and H(4)); 8.84 (d, 1 H, H(6), $J$ = 2.5 Hz). MS (ESI), $m/z$: 199.09 $[M + H]^+$.

**5-Phenylpyridine-2-carboxamide hydrazone (6).** Cyanopyridine **5** (0.5 g, 2.77 mmol) was dissolved in a mixture of ethanol—THF (1 : 1, 50 mL), followed by the addition of hydrazine hydrate (190 μL, 3.9 mmol). The mixture obtained was allowed to stand at room temperature for 3 days. The solvents were evaporated at reduced pressure, the residue was treated with diethyl ether, a precipitate formed was filtered off and dried. The product was used in the next step without additional purification. The yield was 440 mg (75%). $^1$H NMR (DMSO-$d_6$), δ: 5.65 (br.s, 2 H, $NH_2$); 7.35—7.40 (m, 1 H, Ph); 7.44—7.50 (m, 2 H, Ph); 7.63—7.68 (m, 2 H, Ph); 7.93 (dd, 1 H, H(4), $J$ = 7.9 Hz, $J$ = 2.5 Hz); 8.00 (d, 1 H, H(3), $J$ = 7.9 Hz); 8.71 (d, 1 H, H(6), $J$ = 2.5 Hz). MS (ESI), $m/z$: 213.11 $[M + H]^+$.

**Synthesis of 1,2,4-triazines 7 (general procedure).** Amidrazone **6** (250 mg, 1.18 mmol) was dissolved in ethanol (30 mL), followed by the addition of a solution of the corresponding 1,2-dione (1.18 mmol) in a mixture of ethanol—THF (1 : 1, 50 mL). The resulting mixture was refluxed for 10 h and cooled to room temperature. A precipitate formed was filtered off, washed with ethanol, and dried. An analytical sample was obtained by recrystallization from ethanol.

**3-(5-Phenylpyridin-2-yl)phenanthro[9,10-*e*]-1,2,4-triazine (7a).** The yield was 270 mg (60%), m.p. > 250 °C. Found (%): C, 81.14; H, 4.02; N, 14.39. $C_{26}H_{16}N_4$. Calculated (%): C, 81.23; H, 4.20; N, 14.57. $^1$H NMR (DMSO-$d_6$), δ: 7.44—7.50 (m, 1 H, Ph); 7.53—7.59 (m, 2 H, Ph); 7.80—7.91 (m, 4 H); 7.92—7.98 (m, 1 H); 7.98—8.04 (m, 1 H); 8.32 (d, 1 H, $H_{Py}$(3), $J$ = 8.1 Hz); 8.78—8.85 (m, 2 H); 8.89 (dd, 1 H, $H_{Py}$(4), $J$ = 8.1 Hz, $J$ = 2.3 Hz); 9.17 (d, 1 H, $H_{Py}$(6), $J$ = 2.3 Hz); 9.43—9.50 (m, 2 H, H(5) and H(12)). MS (ESI), $m/z$: 385.15 $[M + H]^+$.

**5,6-Diphenyl-3-(5-phenylpyridin-2-yl)-1,2,4-triazine (7b).** The yield was 230 mg (50%), m.p. 189—191 °C. Found (%): C, 80.71; H, 4.56; N, 14.57. $C_{26}H_{16}N_4$. Calculated (%): C, 80.81; H, 4.69; N, 14.50. $^1$H NMR (DMSO-$d_6$), δ: 7.37—7.51 (m, 7 H, Ph); 7.51—7.57 (m, 2 H, Ph); 7.58—7.63 (m, 2 H, Ph); 7.64—7.70 (m, 2 H, Ph); 7.78—7.84 (m, 2 H, Ph); 8.27 (dd, 1 H, $H_{Py}$(4), $J$ = 8.3 Hz, $J$ = 2.3 Hz); 8.68 (d, 1 H, $H_{Py}$(3), $J$ = 8.3 Hz); 9.12 (d, 1 H, $H_{Py}$(6), $J$ = 2.3 Hz). MS (ESI), $m/z$: 387.16 $[M + H]^+$.

**Synthesis of bipyridines 8 (general procedure).** A mixture of the corresponding triazine **7** (0.25 mmol) and 1-morpholinocyclopentene (0.2 mL, 1.25 mmol) was stirred for 2 h at 200 °C under argon. Then, 1-morpholinocyclopentene (0.1 mL, 0.625 mmol) was added and the stirring was continued for another 1 h in the same regime. Afterwards, the reaction mixture was cooled to room temperature and diluted with acetonitrile, the resulting mixture was heated to boiling, then cooled to room temperature. A precipitate formed was filtered off, washed with acetonitrile, and dried. An analytical sample was obtained by recrystallization from acetonitrile.

**10-(5-Phenylpyridin-2-yl)-12,13-dihydro-11*H*-dibenzo[*f,h*]-cyclopenta[*c*]quinoline (8a).** The yield was 90 mg (84%), m.p. 170—172 °C. Found (%): C, 87.94; H, 5.11; N, 6.48. $C_{31}H_{22}N_2$. Calculated (%): C, 88.12; H, 5.25; N, 6.63. $^1$H NMR ($CDCl_3$), δ: 2.27 (m, 2 H, $CH_2$(12)); 3.68 (t, 2 H, $CH_2$(11), $J$ = 7.6 Hz); 3.74 (t, 2 H, $CH_2$(13), $J$ = 7.6 Hz); 7.41—7.47 (m, 1 H, Ph); 7.49—7.56 (m, 2 H, Ph); 7.62—7.76 (m, 6 H); 8.12 (dd, 1 H, $H_{Py}$(4), $J$ = 8.3 Hz, $J$ = 2.3 Hz); 8.58—8.63 (m, 1 H); 8.63—8.68 (m, 1 H); 8.69—8.73 (m, 1 H); 8.78 (d, 1 H, $H_{Py}$(3), $J$ = 8.3 Hz); 8.99 (d, 1 H, $H_{Py}$(6), $J$ = 2.3 Hz); 9.53 (m, 1 H, H(8)). $^{13}$C NMR ($CDCl_3$), δ: 26.1, 33.3, 37.4, 122.4, 123.1, 123.3, 123.5, 126.1, 126.6, 127.2, 127.3, 127.8, 128.1, 128.3, 129.1, 130.1, 130.7, 131.1, 131.8, 134.7, 135.5, 138.0, 138.9, 144.9, 146.9, 149.9, 152.0, 157.6. MS (ESI), $m/z$: 423.19 $[M + H]^+$.

**3,4-Diphenyl-1-(5-phenylpyridin-2-yl)-6,7-dihydro-5*H*-cyclopenta[*c*]pyridine (8b).** The yield was 80 mg (74%), m.p. 138—140 °C. Found (%): C, 87.62; H, 5.57; N, 6.44. $C_{31}H_{24}N_2$. Calculated (%): C, 87.70; H, 5.70; N, 6.60. $^1$H NMR ($CDCl_3$), δ: 2.12 (m, 2 H, $CH_2$(6)); 2.85 (t, 2 H, $CH_2$(7), $J$ = 7.6 Hz); 3.59 (t, 2 H, $CH_2$(5), $J$ = 7.6 Hz); 7.15—7.23 (m, 5 H, Ph); 7.25—7.33 (m, 3 H, Ph); 7.38—7.45 (m, 3 H, Ph); 7.47—7.53 (m, 2 H, Ph); 7.65—7.70 (m, 2 H, Ph); 8.01 (dd, 1 H, $H_{Py}$(4), $J$ = 8.3 Hz, $J$ = 2.3 Hz); 8.50 (d, 1 H, $H_{Py}$(3), $J$ = 8.3 Hz); 8.94 (d, 1 H, $H_{Py}$(6), $J$ = 2.3 Hz). $^{13}$C NMR ($CDCl_3$), δ: 25.4, 32.9, 33.7, 123.2, 127.0, 127.1, 127.3, 127.6, 128.0, 128.2, 129.1, 129.9, 130.2, 132.6, 134.7, 135.3, 138.0, 138.8, 140.7, 147.0, 150.0, 154.5, 155.8, 157.4. MS (ESI), $m/z$: 425.20 $[M + H]^+$.

This work was financially supported by the Ministry of Education and Science of the Russian Federation (State Contract 8430), the President of the Russian Federation Council for Grants (Program for State Support of Young Scientists of the Russian Federation, Grant MK-3079.2015.3), as well as by the Government of the Russian Federation (Program 211, Agreement No. 02.A03.21.0006).

## References

1. P. N. W. Baxter, *J. Org. Chem.*, 2000, ***65,*** 1257.
2. M. Linke, J.-C. Chambron, V. Heitz, J.-P. Sauvage, *Chem. Commun.*, 1999, 2419.
3. S. Bonnet, J.-P. Collin, J.-P. Sauvage, *Chem. Commun.*, 2005, 3195.
4. C. R. Woods, M. Benaglia, S. Toyota, K. Hardcastle, J. S. Siegel, *Angew. Chem., Int. Ed.*, 2001, **40**, 749.
5. S. Bonnet, J.-P. Collin, J.-P. Sauvage, *Inorg. Chem.*, 2007, **46**, 10520.
6. J. C. Loren, J. S. Siegel, *Angew. Chem., Int. Ed.*, 2001, **40**, 754.
7. Y. Nishikawa, H. Yamamoto, *J. Am. Chem. Soc.*, 2011, **133**, 8432.
8. K. I. Arias, E. Zysman-Colman, J. C. Loren, A. Lindena, J. S. Siegel, *Chem. Commun.*, 2011, **47**, 9588.
9. A. M. Prokhorov, D. N. Kozhevnikov, *Chem. Heterocycl. Compd.* (*Engl. Transl.*), 2012, **48**, 1153 [*Khim. Geterotsikl. Soedin.*, 2012, 1237].
10. G. R. Pabst, O. C. Pfüller, J. Sauer, *Tetrahedron*, 1999, **55**, 8045.
11. R. Metze, *Chem. Ber.*, 1956, **89**, 2056.
12. F. H. Case, *J. Org. Chem.*, 1965, **30**, 931.
13. Pat. US/0149510 A1, 2009.
14. L. Hu, R. K. Arafa, M. A. Ismail, A. Patel, M. Munde, W. D. Wilson, T. Wenzler, R. Brun, D. W. Boykin, *Bioorg. Med. Chem.*, 2009, **17**, 6651.
15. A. C. Benniston, *Tetrahedron Lett.*, 1997, **38**, 8279.
16. T. Sakamoto, S. Kaneda, S. Nishimura, H. Yamanaka, *Chem. Pharm. Bull.*, 1985, **33**, 565.
17. A. Breteche, P. Marchand, M.-R. Nourrisson, P. Hautefaye, G. De Nanteuil, M. Duflos, *Tetrahedron*, 2011, **67**, 4767.
18. A. I. Pavlyuchenko, V. V. Titov, N. I. Smirnova, V. T. Grachev, *Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1980, **16**, 681 [*Khim. Geterotsikl. Soedin.*, 1980, 888].
19. D. N. Kozhevnikov, N. N. Kataeva, V. L. Rusinov, O. N. Chupakhin, *Russ. Chem. Bull.* (*Int. Ed.*), 2004, **53**, 1243 [*Izv. Akad. Nauk, Ser. Khim.*, 2004, 1243].
20. D. N. Kozhevnikov, V. N. Kozhevnikov, V. L. Rusinov, O. N. Chupakhin. *Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1999, **35**, 1377 [*Khim. Geterotsikl. Soedin.*, 1999, 1574].
21. L. J. Allen, S. H. Lee, Y. Cheng, P. S. Hanley, J. M. Muhuhi, E. Kane, S. L. Powers, J. E. Anderson, B. M. Bell, G. A. Roth, M. S. Sanford, D. C. Bland, *Org. Process Res. Dev.*, 2014, **18**, 1045.
22. J. Coates, P. G. Sammes, R. M. West, *J. Chem. Soc.*, *Perkin Trans. 2*, 1996, **7**, 1275.
23. V. N. Kozhevnikov, M. M. Ustinova, P. A. Slepukhin, A. Santoro, D. W. Bruce, D. N. Kozhevnikov, *Tetrahedron Lett.*, 2008, **49**, 4096.
24. D. S. Kopchuk, Ph.D. Thesis (Chem.), UGTU-UPI, Ekaterinburg, 2010, 122 pp. (in Russian).
25. W. H. Melhuish, *J. Phys. Chem.*, 1961, **65**, 229.
26. D. S. Kopchuk, A. F. Khasanov, I. S. Kovalev, G. A. Kim, I. L. Nikonov, G. V. Zyryanov, V. L. Rusinov, O. N. Chupakhin, *Chem. Heterocycl. Compd.* (*Engl. Transl.*), 2014, **50**, 864 [*Khim. Geterotsikl. Soedin.,* 2014, 936].

*Received January 27, 2015;*
*in revised form March 10, 2015*