Russian Journal of General Chemistry, Vol. 74, No. 6, 2004, pp. 954–956. Translated from Zhurnal Obshchei Khimii, Vol. 74, No. 6, 2004, pp. 1031–1034.

Macroheterocyclic Compounds with 2,3-Pyridino(pyrazino)pyrrole and 1,3,4-Thiadiazole Residues

M. A. Kulikov, Yu. G. Vorob'ev, G. R. Berezina, and V. A. Stepanenko

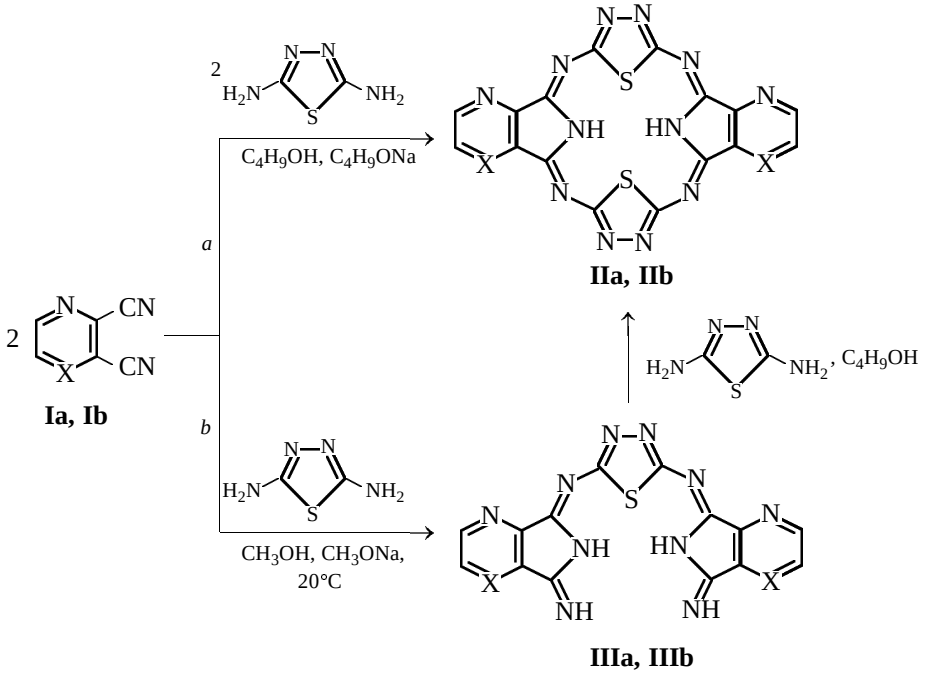
Ivanovo State University of Chemistry and Technology, Ivanovo, Russia

Received June 4, 2002

Abstract—Novel symmetrical macroheterocyclic compounds were prepared by the reactions of 2,3-dicyanopyridine and 2,3-dicyanopyraine with 2,5-diamino-1,3,4-thiadiazole in butanol in the presence of sodium butylate. Physicochemical properties and biological activity of the products were studied.

Macroheterocyclic compounds represent an abundant class of presently synthesized complex organic compounds. They have found application as dyes and pigments [1–3], catalysts in various redox reactions [4], etc. Compounds containing 1,3,4-thiadiazol fragments possess biological activity [5] and thus can be used as models in studying various biological processes. The present work is a continuation of our research into the effect of th replacement of isoindole fragments in macroheterocycles by pyridino-(pyrazino)pyrrole ones.

Macroheterocycles **IIa**, **IIb** were prepared by the reactions of 2,3-dicyanopyridine (**Ia**) and 2,3-dicyanopyrazine (**Ib**) with 2,5-diamino-1,3,4-thiadiazole in butanol in the presence of sodium butylate by procedure *a*.



X = CH (**Ia, IIa, IIIa**), N (**Ib, IIb, IIIb**).

1070-3632/04/7406-0954

Yields and properties of compounds **IIa, IIb, IIIa**, and **IIIb**

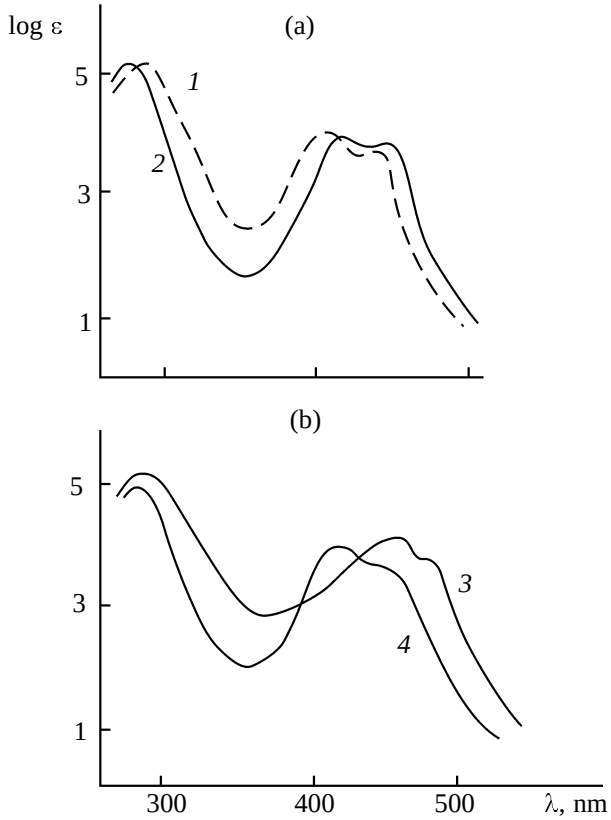
Comp. no.	Yield, % (method)	R_f	λ_{max}, nm (log ε) (DMF)	Found, %				Formula	Calculated, %			
				C	H	N	S		C	H	N	S
IIa	79 (*a*) 74 (*b*)	0.6	285 (5.0), 410 (4.0), 447 (3.6)	40.5	3.8	31.0	12.0	$C_{18}H_8N_{12}S_2$	41.1	3.0	31.9	12.2
IIb	79 (*a*) 73 (*b*)	0.61	290 (5.12), 454 (4.15), 481 (3.8)	35.5	3.2	36.5	11.8	$C_{16}H_6N_{14}S_2$	36.2	2.6	37.0	12.1
IIIa	77	0.68	280 (5.2), 421 (3.95), 448 (3.77)	50.9	3.0	37.0	9.1	$C_{16}H_{10}N_{10}S$	51.3	2.7	37.4	8.6
IIIb	81	0.7	286 (5.0), 422 (3.92), 451 (3.72)	44.3	2.6	44.0	9.1	$C_{14}H_8N_{12}S$	44.7	2.1	44.7	8.5

This method of synthesis we proposed previously [6] for aza derivatives with *m*-phenylene and 2,6-pyridine fragments. Compounds **IIa**, **IIb** were purified by reprecipitation from alcoholic alkali with glacial acetic acid followed by extraction of admixtures with acetone in a Soxhlet apparatus. Macroheterocycles **IIa**, **IIb** are bright red powders. They have no well-defined melting points and decompose above 350°C. The elemental analyses show that the compounds contain water of crystallization (see table).

The structure of compounds **IIa**, **IIb** was proved by their independent synthesis via arylenediamines **IIIa**, **IIIb** prepared from dinitriles **Ia**, **Ib** and 2,5-diamino-1,3,4-thiadiazole in methanol in the presence of sodium methylate by procedure *b*. Arylenediamines **IIIa**, **IIIb** are dark red powders. They decompose without melting above 350°C.

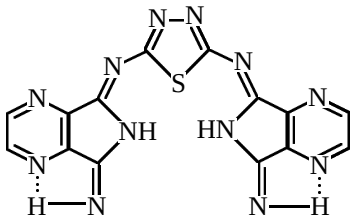
The electronic absorption spectra of compounds **IIa**, **IIb** contain three absorption bands each: 285, 410, and 447 nm for compound **IIa** and 290, 454, and 481 nm for compound **IIb** (see figure). The absorption bands at 285 and 290 nm relate to electronic transitions in pyridine and pyrazine fragments. The bands at 410 (compound **IIa**) and 454 nm (for compound **IIb**) we assigned to electronic transitions in the conjugation system including the pyridino(pyrazino)pyrrole and 1,3,4- thiadiazole fragments. In heterocycles with isoindole fragments, the same band appears at 392 nm [7]. In going from isoindole to pyridino(pyrazino)-pyrrole derivatives, this band shifts bathochromically by 18 and 62 nm for compounds **IIa** and **IIb**, respectively. This shift is explained by the fact that the strong electron-acceptor effect of the pyridine and pyrazine fragments enhances polarization of the conjugation system. The observation in the spectra of compounds **IIa** and **IIb** of long-wave bands (447 and 481 nm, respectively) that are lacking in the spectra of *m*-phenylene and 2,6-pyridino derivatives suggests that these macrocycles have a common conjugation system.

The electronic absorption spectra show that arylenediamines **IIIa**, **IIIb** are structurally similar to macroheterocycles **IIa**, **IIb**. At the same time, a bathochromic shift of the second maximum is observed in the spectra of 2,3-pyridinopyrrole derivatives (Δλ 10 nm), whereas in the spectra of pyrazinopyrrole derivatives both the first and second maxima are shifted hypsochromically ($\Delta\lambda_1$ 32, ($\Delta\lambda_2$ 30 nm).



Electronic absorption spectra of compounds (*1*) **IIa**, (*2* **IIIa**, (*3*) **IIb**, and (*4*) **IIIb**.

The bathochromic shift of the second maximum is explained by the presence in molecule **IIIa** of terminal imino groups that possecc auxochromic properties. In the case of compound **IIIb**, the auxochromic properties of terminal imino groups are strongly attenuated by intramolecular hydrogen bonding.



Comparison of the IR spectra of macroheterocycles **IIa**, **IIb** and arylenediamines **IIIa**, **IIIb** points to similarity of these structures. The IR spectra contain a number of bands characteristic of both arylenediamines and macroheterocycles. Therewith, the transition **IIIa**, **IIIb** → **IIa**, **IIb** is accompanied by enhancement of bands at 1200–1300 and 1500–1700 cm^{-1}, belonging to heterocyclic fragments [8]. In going from arylenediamines to macroheterocycles, the intensity of the C–N stretching vibration band of the endocyclic imino group at 1300–1400 cm^{-1} changes, which we explain in terms of enhanced rigidity of macroheterocycles. The broad band at 3500 cm^{-1} relate to N–H stretching vibrations of endocyclic imino groups. Nuclear vibrations of 1,3,4-thiadiazole appear at 1500–1550 cm^{-1}.

The ^1H NMR spectrum of compound **IIb** contains two groups of signals: a singlet at 6.67 ppm and a multiplet at 8.48–8.70 ppm. The splitting of the signal corresponding to four formally equivalent pyrazine ring protons to a multiplet implies a low symmetry of the macroheterocyclic molecule. Otherwise, a singlet signal would be observed. The singlet at 6.67 ppm belongs to endocyclic imino groups. The lack of signals at 4–5 ppm, corresponding to amino protons, provides evidence for a cyclic structure of compound **IIb**.

Since 2,5-diamino-1,3,4-thiadiazole and its derivatives are biologically active compounds, we have studied their activity against the following mold fungi: *Aspergillus niger van Thieghem, Chaetomium globosum Kunze, Cladosporium gossipicola Pidopl et Deniak, Cladosporium resinae Albida, Penicillium chrisogenum Thom, Penicillium ochro-cloron Biorge, Trichoderma koningii Oudemans, Trichoderma viride Pers.ex.Fr, Torula convoluta Harz, and Cenhalosporium acremonium Corda.* It was found that compound **IIa** acts as fungicide, and we recommend it for a more detailed study in this respect.

EXPERIMENTAL

The electronic absorption spectra were measured on a Specord M-400 instrument in DMF in quartz cells (*l* 1 cm) at 20–25°C. The IR spectra were obtained on an Avatar-360FT-IR-TSP instrument at 400–4000 cm^{-1} in KBr.

Arylenediamines IIIa and IIIb. Metallic sodium, 1.3 mmol, was dissolved in 15 ml of methanol. 2,3-Dicyanopyridine (**Ia**) or 2,3-dicyanopyrazine (**Ib**), 2.6 mmol, and 1.3 mmol of 2,5-diamino-1,3,4-thiadiazole were added to the resulting mixture, and it was stirred for 24 h. The precipitate that formed was filtered off and dried at 80°C. The reaction products were purified by reprecipitation from alcoholic alkali with glacial acetic acid followed by extraction of admixtures with acetone in a Soxhlet apparatus.

Macroheterocyclic compounds IIa and IIb. *a*. Metallic sodium, 0.8 mmol, was dissolved in 10 ml of absolute butanol. Diamine **Ia** or **Ib**, 3 mmol, and 3 mmol of 2,5-diamino-1,3,4-thiadiazole were added to the resulting solution of sodium butylate. The reaction mixture was vigorously stirred for 4 h at 50°C and then for 10 h at 90°C and then refluxed until ammonia no longer evolved. After cooling, the precipitate was filtered off, washed with water, and reprecipitated from alcoholic NaOH.

b. Arylenediamine **IIIa** or **IIIb**, 0.44 mmol, and 0.44 mmol of 2,5-diamino-1,3,4-thiadiazole were introduced into 10 ml of butanol, and the resulting mixture was refluxed with vigorous stirring for 15 h. After cooling, the precipitate was filtered off and washed with water. Further workup was similar to that described in procedure *a*.

REFERENCES

1. Gnedina, V.A., Smirnov, R.P., and Matyushkin, G.A., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 1973, vol. 16, no. 4, p. 589.
2. Borodkin, V.F., *Zh. Obshch. Khim.*, 1960, vol. 30, no. 5, p. 1547.
3. Gema de la Tore and Torres, T., *J. Org. Chem.*, 1996, vol. 61, no. 18, p. 6446.
4. Kudrik, E.V., *Cand. Sci. (Chem.) Dissertation*, Ivanovo, 1995.
5. Danilova, E.A. and Islyaikin, M.K., *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 1994, vol. 37, no. 2, p. 77.
6. Neustroeva, N.R., Kulikov, M.A., Vorob'ev, Yu.G., and Smirnov, R.P., *Zh. Obshch. Khim.*, 1999, vol. 69, no. 11, p. 1919.
7. Kolesnikov, N.A., *Cand. Sci. (Tech.) Dissertation*, Ivanovo, 1971.
8. Nakanishi, K., *Infrared Absorption Spectroscopy. Practical*, San Francisco: Holden-Day, 1962.