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Bromination of Tetraazaporphine and Its β-Substituted Derivatives Using Pyridine as Solvent and Catalyst

N. V. Chizhova, O. G. Khelevina, N. Yu. Nikitina, and B. D. Berezin

Institute of Solution Chemistry, Russian Academy of Sciences, Ivanovo, Russia
Ivanovo State University of Chemical Technology, Ivanovo, Russia

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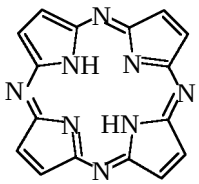
Abstract — The selectivity and degree of bromination of pyrrole rings in porphyrazine strongly depends on the brominating agent and solvent nature. The reaction of porphyrazine magnesium complex with molecular bromine and *N*-bromosuccinimide in pyridine gave magnesium complex of dibromotetraazaporphine. Increasing bromine substitution in porphyrazine enhances its acidic properties.

Tetraazaporphyrins (porphyrazines) are unique organic compounds. Tetraazaporphine (H_2TAP) is the parent compound for numerous porphyrazines.



H_2TAP

The molecule of tetraazaporphine possesses several reaction centers. These are the *meso*-nitrogen atoms, β-carbon atoms of the pyrrole rings, and intracyclic NH groups. Unlike porphine, the lone electron pairs of the *meso*-nitrogen atoms are capable of interacting with Lewis acids to form acid–base and charge-transfer complexes [1, 2]. The aromatic character of tetraazaporphine molecule and conjugation between the pyrrole ethylenic bonds and the main macrocyclic chromophore (C_8N_8) provide the possibility for electrophilic substitution of hydrogen [2]. Bromination of tetraazaporphine is the most studied and preparatively accessible reaction. We previously examined [3, 4] the bromination of tetraazaporphine with molecular bromine in glacial acetic acid and found that the process involves formation of 1:1 or 1:2 molecular adducts with bromine. Treatment of the complex $H_2TAPBr_4 \cdot 2Br_2$ with pyridine leads to formation of tetrabromotetraazaporphine [H_2TAPBr_4]. We also studied [5] the bromination of tetraazaporphine with *N*-bromosuccinimide in acetic acid and chloroform. The bromination of H_2TAR with *N*-bromosuccinimide is characterized by a lower selectivity, and a mixture of bromo derivatives is formed.

In the present work we examined the reaction of tetraazaporphine magnesium complex MgTAP with molecular bromine and *N*-bromosuccinimide in pyridine with the goal of increasing the selectivity and reducing the rate of the process. The magnesium complex was taken as starting compound to avoid acid–base interaction between pyridine and NH protons, which could complicate interpretation of the results. Labile complexes of magnesium with tetraazaporphine and their bromo derivatives are readily converted into the corresponding free ligands in glacial acetic acid.

The bromination of the pyrrole rings in MgTAP with bromine in pyridine proceeds at a lower rate than in acetic acid, and the reaction is not accompanied by formation of molecular complexes of porphyrazine with Br_2. Pyridine is a stronger base than tetraazaporphine; the formation of donor–acceptor complex of pyridine with bromine ($Br_2 \cdot Py$) is known [6] to reduce the electrophilicity of bromine. The progress of the reaction was monitored by thin-layer chromatography on Silufol plates, elemental analysis, and electronic absorption spectroscopy. In the presence of a 5- to 10-fold excess of bromine with respect to MgTAP, depending on the reaction time, the major product was magnesium complex of dibromotetraazaporphine. The maximal degree of bromination of the pyrrole rings in MgTAP was attained in 12 h at 20°C (porphyrazine–Br_2 molar ratio 1:10). Raising the excess of Br_2 to 20-fold and increasing the reaction time to 3 days led to reduced degree of bromination. Presumably, lability of bromine atoms in the β positions of the pyrrole rings of tetraazaporphine, as well as in diazines and triazines [7], originates from the strong electron-acceptor effect of nitrogen atoms in the macroring. After 5 days, oxidative decomposition processes clearly occurred.

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Electronic absorption spectra of tetraazaporphyrins in pyridine

Compound	λ_{max}, nm (log ε)			References
	I	II	Soret	
MgTAP	587 (5.07)	540 (4.04)	334 (4.80)	[8]
$MgTAPBr_2$	596 (4.22)	550 (3.52)	341 (4.23)	
$MgTAPBr_4$	612 (4.83)	560 (4.34)	360 (4.84)	[9]

The bromination of MgTAP with excess *N*-bromosuccinimide (NBS, 1:10) in pyridine at 20°C was slow. After 24 h, the shift of the first absorption band in the electron spectrum of the reaction mixture was as small as 2 nm. By increasing the amount of *N*-bromosuccinimide to 20 equiv and extending the reaction time to 2 days we succeeded in introducing up to two bromine atoms into the porphyrazine molecule. The electron spectrum of the product in pyridine was identical to that of the bromo derivative obtained from MgTAP and Br_2 in pyridine (see table).

The data in table show that introduction of two bromine atoms into the pyrrole rings of MgTAP induces red shift of the absorption spectrum due to enhanced polarization of the molecule (*–I* effect of bromine atoms). Comparison of the spectrum of the product with those of dibromotetraazaporphines [5] and substituted tetraphenylporphines [10] suggests that we obtained the *cis* isomer of $MgTAPBr_2$. The considerably lower molar absorption coefficient of $MgTAPBr_2$, as compared to the unsubstituted complex MgTAP and tetrabromo derivative $MgTAPBr_4$, also supports the structure of dibromoporphyrazine

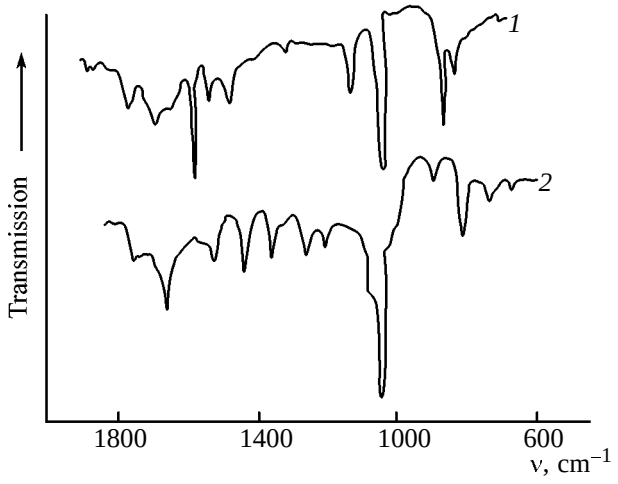

Fig. 1. IR spectra of magnesium complexes of (*1*) tetraazaporphine and (*2*) dibromotetraazaporphine.

with *cis* arrangement of the bromine atoms. The effect of bromine substitution is reflected in the IR spectrum of $MgTAPBr_2$: Some absorption bands change their position and increase in intensity, as compared with the unsubstituted complex (Fig. 1). We observed strengthening of C–H (840 cm^{-1}) and N–H bending vibrations (1004 cm^{-1}), whereas skeletal vibration bands at 1560 cm^{-1} (C⋯N) and 1632 cm^{-1} (C⋯C) remained almost unchanged.

Pyridine is capable of accelerating the bromination of tetraazaporphine and its magnesium complex in nonpolar and weakly polar organic solvents. We previously showed [5] that no bromination of tetraazaporphine with *N*-bromosuccinimide in chloroform occurs at room temperature. The reaction is initiated by irradiation or heating. In the presence of pyridine (4%) in $CHCl_3$ up to two bromine atoms can be introduced into the tetraazaporphine molecule with the aid of *N*-bromosuccinimide (4 days, 20°C). The rate of bromination of MgTAP with *N*-bromosuccinimide in 2-propanol strongly increases in the presence of pyridine. The shift of the first absorption band in the electronic spectrum of the reaction mixture obtained from MgTAP and *N*-bromosuccinimide (molar ratio 1:10) in 2-propanol is 13 nm (in 2 days at 20°C). With 2.5% of pyridine, the shift ($\Delta\lambda_I$) reaches 18 nm in 7 h at 20°C. After 2 days, $\Delta\lambda$ = 22 nm. Prolonged reaction (6 days and longer) results in oxidative decomposition of porphyrazine.

Porphyrazines are known to be weak NH acids [11, 12]. Whalley [13] was the first to reveal an interaction between tetraazaporphine and pyridine, which occured on photochemical initiation. Neither monobromotetraazaporphine nor unsubstituted porphyrazine react with pyridine at room temperature. In the electronic absorption spectrum of dibromotetraazaporphine in pyridine we observed a red shift of band III and a blue shift of band I (Fig. 2); the split value ($\Delta\lambda$) was 4.5 nm relative to the spectrum recorded in a neutral solvent (benzene). 2,12-Dibromotetraazaporphine in pyridine is characterized by a smaller $\Delta\lambda$ value (10 nm) than in benzene. The corresponding $\Delta\lambda$ value for the tribromo derivative in pyridine is 15 nm. In keeping with the data of [11], di- and tribromo derivatives of tetraazaporphine in pyridine are likely to form various monoamions differing by the degree of proton transfer from the acid to the base. As we showed in [3], on dissolution in pyridine tetrabromotetraazaporphine gives rise to an unstable dianion (Fig. 2) which decomposes in 2 days. The dianionic form of tetrabromotetraazaporphine in pyridine almost instantaneously coordinates metal ions (on mixing freshly prepared solutions of the porphyrazine and metal salt) [9]. However, in acetic acid electronic ef-

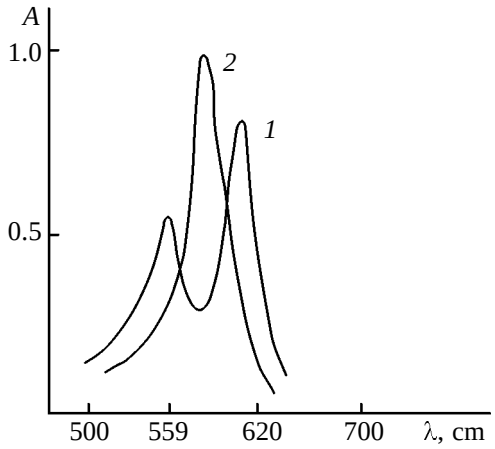

Fig. 2. Electronic absorption spectra of (*1*) dibromotetraazaporphine and (*2*) tetrabromotetraazaporphine in pyridine.

fects of bromine are not observed due to change in the solvation of the transition state [9].

Thus, the reactivity of tetraazaporphines strongly depends on the solvent nature. Pyridine with bromine forms a molecular adduct ($Py \cdot Br_2$), and the electrophilicity of bromine is reduced. The rate of bromination of tetraazaporphine in organic solvents increases in the presence of pyridine. Finally, bromo derivatives of tetraazaporphine are capable for acid–base interaction with pyridine. The strength of the acid–base interaction depends on the number of bromine atoms in the macroring.

EXPERIMENTAL

The electronic absorption spectra were recorded on a Specord-400 spectrophotometer. The IR spectra were measured in KBr on a UR-20 instrument. The magnesium complex of tetraazaporphine was synthesized by the procedure described in [14]. Bromine was purified according to [3].

Magnesium complex of dibromotetraazaporphine. Magnesium complex of tetraazaporphine (MgTAP), 0.05 g, was dissolved in 10 ml of pyridine, 0.08 ml of bromine in 5 ml of pyridine (molar ratio 1 : 10) was added with stirring, and the mixture was kept for 12 h at 20°C. The mixture was than poured into cold distilled water, and the precipitate was filtered off, washed with water until neutral reaction, and dried. The product was purified by column chromatography on silica gel using 4 : 1 benzene–acetone as eluent. Yield of $MgTAPBr_2$ 0.037 g (50%). R_f 0.37 (benzene–propanol, 10 : 0.2). Found, %: C 39.05; H 1.28; Br 32.07; Mg 4.83; N 22.33. $C_{16}H_6Br_2MgN_8$. Calculated, %: C 38.87; H 1.22; Br 32.32; Mg 4.92; N 22.66.

Free dibromoporphyrazine H_2TAPBr_2 was obtained by keeping $MgTAPBr_2$ in glacial acetic acid for 1 h at room temperature. Mono-, 2,12-dibromo-, and tribromo derivatives of tetraazaporphine were synthesized by the procedure reported in [5].

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