Synthesis of Benzihemiporphyrazine Bearing tert-Butylquinoxaline[2,3-c]pyrrole Fragments

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Dedicated to Academician Aslan Yusupovich Tsivadze on the occasion of his 75-th birthday

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A new representative macroheterocyclic compound of the ABAB-type was synthesized by crossover-condensation of \textit{m}-phenylenediamine and 6-tert-butylquinoxaline-2,3-dicarbonitrile by refluxing in fresh distillated BuOH. The crude product was washed by hot hexane and purified by column chromatography on silica gel using an eluent mixture comprised of methylene chloride:methanol:hexane. Solvents were then evaporated and orange powder was dried at reduced pressure. The obtained substance was characterized by UV-Vis, IR, \textsuperscript{1}H NMR spectroscopy and mass-spectrometry data. The signal located at 655.5 Da which corresponds to \([\text{M+H}]^+\) ions was detected in MALDI-TOF (without matrix). Using of \(\alpha\)-cyano-4-hydroxycinnamic acid (CHCA) as matrix induces the appearance of a reduced form of the macrocycle which is detected by a signal at 656 Da \([\text{M+2H}]^+\). The structures of two regioisomers with different positions of tert-butyl groups in pyrroloquinoxaline fragments were optimized at DFT/B3LYP/6-31G(d,p) level. It was predicted that both isomers have nonplanar saddle-shape structures and that the cis-isomer was found to be of 0.75 kcal/mol more stable than alternative regioisomer. The positive values of NICS calculated at the centers of molecules confirm the nonaromatic character of their macrorings.

Keywords: Synthesis, macroheterocyclic compound, benzihemiporphyrazine, \textit{m}-phenylenediamine, 6-tert-butylquinoxaline-2,3-dicarbonitrile.

Синтез бензигемипорфиразина с фрагментами \textit{t}рет–бутилхиноксалин[2,3–с]пиррола

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Взаимодействием \textit{m}-фенилендиамина и 6-трет-бутилхиноксалин-2,3-дикарбонитрила в кипящем бутаноле было получено макрогетероциклическое соединение ABAB-типа. Очистку проводили промыванием горячим гексаном и далее колоночной хроматографией на силикагеле с использованием элюирующей смеси: хлористый метилен:метанол:гексан. После отгонки растворителей оранжевый порошок сушили в вакууме. Полученное соединение охарактеризовано данными электронной, ИК, \textsuperscript{1}Н ЯМР спектроскопии и масс-спектрометрии. В масс-спектре MALDI-TOF (без использования матрицы) обнаружен сигнал 655.5 Да, соответствующий молекулярному иону \([\text{M+H}]^+\). Использование \(\alpha\)-циано-4-гидроксикоричной кислоты (СНСА) в качестве матрицы индуцирует появление восстановленной формы макроцикля с сигналом 656 Да \([\text{M+2H}]^+\). Структуры
Introduction

Pyrazino-annelated phthalocyanines (Pcs) have attracted much attention.[1,2] Indeed, they demonstrate properties which are inherent to Pcs and, moreover, the presence of auxiliary nitrogen atoms which results in supplementary coordination abilities and a basic character of macroheterocyclic core.[3] Therefore these compounds reveal a number of practically interesting properties.[4,5]

A substitution of two opposite faced isoindole moieties in Pc molecule with aromatic diamines led to ABAB-type macrocycles known as hemiporphyrines (Hps).[6,7] Various aspects of their synthesis, structure particularities, coordination characteristics, and practical applications have been reviewed.[8-11] New optical limiting[12] and photophysical properties[13-15] of Hps have also been reported. Therefore multiloop conjugation systems, which can be highlighted in Hps molecules, stimulate considerable theoretical interest.[16-18] Moreover, the presence of quinoxaline fragments in Mcs structure could enlarge the conjugation chain and expand their coordination abilities. However, Mcs of the ABAB-type with quinoxaline rings have not been studied due to the lack of preparative methods of their synthesis.

It's worthy to note that Mcs are typically very poorly soluble in organic solvents. The introduction of bulky substituents (t-Butyl groups, for instance) onto the periphery of macrocycle increases the solubility in common organic solvents, facilitates their purification, and opens larger areas for their application.[19,20] Hence the subject of this work is synthesis and characterization of dibenzihemiporphyrine of the ABAB-type with 1,3-phenylene (A) and pyrroloquinoxaline rings (B) bearing tert-butyl groups.

Experimental

6-tet-butylquinoxaline-2,3-dicarbonitrile has been prepared following the method described in the literature.[21] Butanol was distilled before use. Column chromatography was carried out on silica gel Merck-60. Thin-layer chromatography (TLC) was performed on aluminum sheets precoated with aluminum oxide 60 F254 (Merck). MALDI-TOF spectra were obtained with a Shimadzu Biotech Axima Confidence in positive ion mode without matrix and using a-cyano-4-hydroxycinnamic acid (CHCA) as matrix. Nitrogen elemental analysis was carried out with a FlashEA 1112 CHN-O Analyzer. 1H NMR spectra were recorded on an Avance-300 instrument in DMSO-D6. UV-Vis (CHCl3) spectra were recorded on a Shimadzu Biotech Axima Confidence with a Shimadzu UV-1601PC spectrometer.

Scheme 1.
Results and Discussion

Following the protocol applied previously in the synthesis of the tert-butylpyrrolepyrazine macroheterocycle,[20] compound 3 was obtained by crossover condensation of equimolecular amounts of 6-tert-butylquinoxaline-2,3-dicarbonitrile 1 and m-phenylenediamine 2 in boiling butanol (Scheme 1).

The reaction was monitored by TLC. After 24 hours stirring at reflux, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel using the eluent mixture: CH2Cl2:MeOH:C6H14 (10:1:3). Based on the proposed synthetic scheme, the resulting orange substance is expected to be a mixture of regioisomers which differed by the tert-butyl groups positions on the pyrroloquinoxaline fragments. This mixture could not be separated under the experimental conditions.

The product was characterized by mass-spectrometry, UV-Vis, IR and 1H NMR spectroscopies and elemental analysis data. Quantum chemistry calculations of the two regioisomers, which differ in the position of tert-butyl groups, were carried out at DFT level using B3LYP hybrid functional with 6-31G(d,p) basis set.

The signal located at 655.5 Da which corresponds to [M+H]+ ion was detected in MALDI-TOF (Figure 1). A good conformity between the calculated isotopic distributions and those derived from experimental data proves this assignment. The signal located at 672.5 Da corresponds to [M+H2O]+ ion.

The use of α-cyano-4-hydroxycinnamic acid as matrix induces the appearance of a reduced form of the macrocycle which can be detected by a signal at 656 Da [M+2H]+ in MALDI-TOF spectrum.

The main bands in the IR spectra are induced by C–H bonds vibrations belonging to the tert-butyl group (2854, 2922, 2954 cm⁻¹). The bands at 1604 and 1454 cm⁻¹ can be correlated to deformations of C=C and C=N bonds, correspondingly.

Along with signals of 1.44 ppm, which result from the resonance of the protons of the tert-butyl groups, there are two groups of signals observed in the 1H NMR spectrum of macrocycle measured in deuterated dimethyl sulfoxide in the region of 6.39–7.72 ppm and 8.19–8.39 ppm. These result from the resonance of the protons of the 1,3-phenylene fragments and those of benzene nucleus of quinoxaline fragments, respectively.

To reveal the difference between regioisomers (3a – cis, 3b – trans), the quantum chemistry calculations at the DFT level using B3LYP hybrid functional with 6-31G(d,p) basis have been carried out. It was found that both 3a and 3b exhibit nonplanar saddle-shape structures, and 3a was found to be of 0.75 kcal/mol more stable than alternative regioisomer (Figure 3). The benzene and pyrroloquinoxaline fragments deviate from the median plane of molecule in opposite directions. In particular, the angles between the planes formed by the exocyclic nitrogen atoms and pyrroloquinoxaline fragments are calculated to be equal to –26.2° and –26.7°, whereas the angles between the planes of benzene fragments are equal to 49.0° and 49.8° for 3a and 3b isomers, correspondingly. It’s worthy to note the position of tert-butyl groups doesn’t much affect the bond lengths and angles in macrocycle.

To analyse aromatic character of 3a and 3b, the NICS values were calculated. NICS values pertaining to global
Synthesis of Benzihemiporphyrazine

Figure 3. View of optimized configurations 3a and 3b and calculated energies.

Table 1. Calculated magnitudes of NICS (ppm) for isomers 3a and 3b.

|     | i   | ii  | iii | iv  | v   | vi  | vii | viii | ix  |
|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|
| 3a  | 1.16| –8.82| –6.36| 1.89| –8.48| –8.50| 1.89| –6.36| –8.82|
| 3b  | 1.15| –8.86| –6.33| 1.89| –8.50| –8.51| 1.94| –6.24| –9.41|

The positive values of NICS calculated at the center i of 3a and 3b confirm nonaromatic character of macroring. But 1,3-phenylene moieties save their aromaticity (points v and vi) what can be most probably explained by the fact that lost of their local aromaticities is not compensated by energy advantage when global aromaticity is established. Five-membered rings demonstrate nonaromatic character due to strong perturbations induced by double bonds located in 1,3-positions.

Analysis of orbital structure of 3a and 3b shows that HOMO and LUMO are orbitals of π-character and that the electron transition between them is of π-π*-character. Computed energies of frontier orbitals and excitation energy are shown in the Table 2.

Table 2. Calculated magnitudes of HOMO/LUMO (eV) and excitation energy ΔE (eV) of isomers 3a and 3b.

|     | Energy of MO*, eV |            |            |            | 3a  | 3b  | ΔE  |
|-----|-------------------|------------|------------|------------|-----|-----|------|
| LUMO+1 | –2.29            | –2.30      |            |            |     |     |      |
| LUMO   | –2.32             | –2.35      |            |            |     |     |      |
| HOMO   | –5.65             | –5.66      |            |            |     |     |      |
| HOMO-1 | –5.85             | –5.85      |            |            |     |     |      |
| ΔE, eV| 3.33              | 3.31       |            |            |     |     |      |

*HOMO is corresponds to \( \psi_{1,2} \), LUMO – \( \psi_{1,3} \)

The structures of the HOMO and LUMO of 3a and 3b are shown in Figure 4.

In order to estimate whether there is the difference in light absorption ability of the regioisomers or not, absorption spectra of 3a and 3b were calculated by TDDFT method using the configurations optimized at the B3LYP/6-31G(d,p) level. The analysis of TDDFT calculations of the first singlet-singlet electron transfers showed that isomers are spectrally indistinguishable. Calculated maxima of their absorption located at 436 nm are nearby to that found in experimental UV-Vis spectrum of 3 (Table 3).

Table 3. Calculated and experimental wavelengths (nm), oscillator strengths (f) for 3a.

| Experimental spectrum (CHCl3) of 3 | Calculated data (TDDFT) of 3a |
|-----------------------------------|-------------------------------|
| \( \lambda, \text{nm} \) | \( A \) | \( \lambda, \text{nm} \) | \( f \) |
| 416 | 0.05 | 436 | 0.15 |

Conclusions

A new example of a benzihemiporphyrazine with tert-butyl-pyrroloquinoxaline fragments was synthesized. The product was characterized by mass-spectrometry, UV-Vis, IR and 1H NMR spectroscopies, and elemental analysis data. To reveal the difference between regioisomers, quantum chemistry calculations at the DFT level using B3LYP hybrid functional with 6-31G(d,p) basis set have been carried out. It was found that both cis- and trans-isomers exhibit nonplanar
saddle-shape structures and cis-isomer was found to be of 0.75 kcal/mol more stable than alternative regioisomer. To analyse aromatic character of isomers, the NICS values were calculated. It was shown that positive values of NICS found in the centre of molecules confirm the nonaromatic character of the macrocycle.

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Figure 4. Views of HOMO and LUMO of 3a and 3b.