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Microwave-Assisted Approach to the Hemiporphyrazine Synthesis

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Dedicated to the 80th anniversary of Academician of Russian Academy of Sciences O. I. Koifman

This work systematizes materials on the synthesis of hemiporphyrazines (Hps) using initialization by microwave irradiation. This approach makes it possible to significantly reduce the reaction time from 8-36 h to 20 min and avoid the use of a solvent for the synthesis. Thus, the interaction of m*-phenylenediamine, 1(H)- or 1-dodecyl-3,5-diamino-1,2,4-triazole with R-(+)- or S-(–)-camphoradicyanopyrazines produced optically active hemiporphyrazines.*

Keywords Hemiporphyrazine, microwave irradiation, synthesis, enthalpy of sublimation, optical activity.

Микроволновый подход к синтезу гемипорфиразинов

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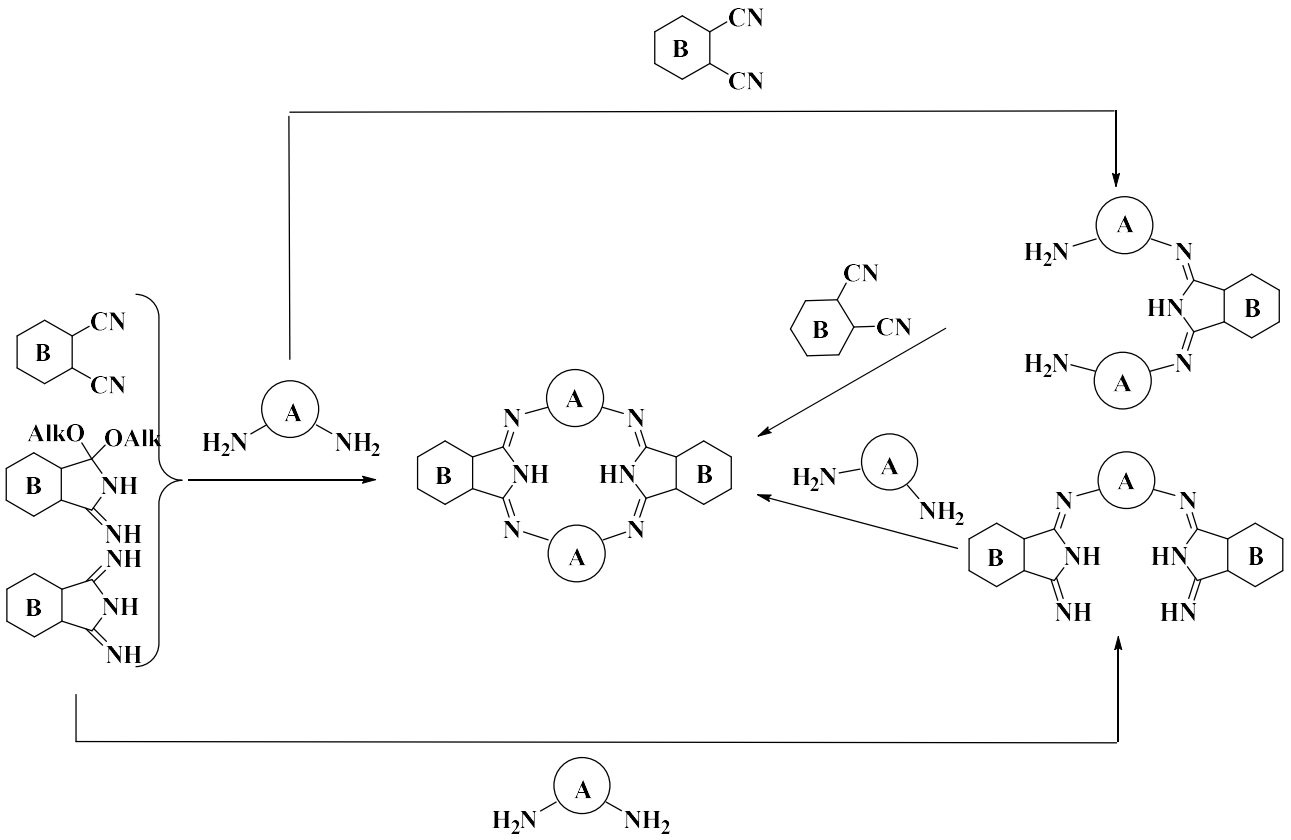
В работе систематизированы материалы о синтезе гемипорфиразинов (Hps) с применением микроволнового излучения. Использование этого подхода позволяет существенно сократить продолжительность синтеза с 8-36 ч до 20 мин, а также исключить применение растворителя. Так, взаимодействием м*-фенилендиамина, 1(H)- или 1-додецил-3,5-диамино-1,2,4-триазола с R-(+)- или S-(–)-камфорадицианопиразинами получены оптически активные гемипорфиразины.*

Ключевые слова: Гемипорфиразин, микроволновое излучение, синтез, энтальпия сублимации, оптическая активность.

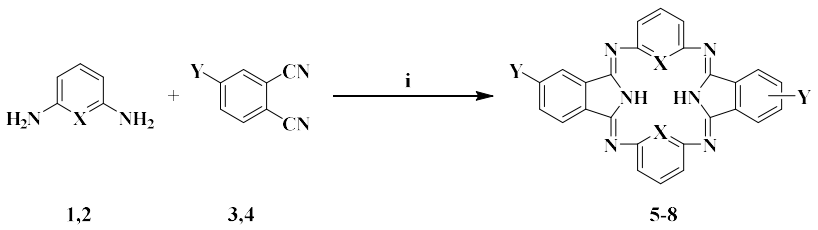
Introduction

Since their discovery,[1,2] hemiporphyrazines (Hps) – macroheterocycles of ABAB-type (where A – rest of aromatic diamines, B – pyrrole bearing subunits), have aroused sustained interest due to their diverse structural flexibilities, and wide range of practical useful properties,[3-7] for instance, luminescence,[8] optical activity,[9] optical limiting,[10] photo-chemical properties,[11] *etc*.

Main approach to the synthesis of Hps is a cross condensation of different substituted or unsubstituted phthalonitriles, as well as their derivatives, or of three-unit products ABA-type or BAB-type with various diamines,[1,12,13] which is realized by prolonged heating in organic solvents (Scheme 1).



Scheme 1. The routs for synthesis of hemiporphyrazines.



	X	Y	Yield,[20] %	Yield, %Lit
1	N	–	–	–
2	CH	–	–	–
3	–	H	–	–
4	–	^{t}Bu	–	–
5	N	H	29	38 [1]
6	CH	H	45	71 [21]
7	N	^{t}Bu	13	60 [22]
8	CH	^{t}Bu	56	62 [23]

Scheme 2. Synthesis of hemiporphyrazines **5-8** by solvent-free protocol, i: MWI (dynamic power ≤100 W), 150 °C, 20 min.

This process is associated with a long duration of synthesis (8–36 h), needs to use high-boiling organic solvents (ethylene glycol, methoxy- and ethoxyethanol, phenol, *etc*.) and a complicate process of separation and purification.

At the same time, microwave irradiation plays an important role in allowing synthesis to be carried out more quickly than with traditional methods and it can be considered a cost-effective and environmentally friendly solution.[14] Successful applications of microwave irradiation (MWI) in porphyrins and phthalocyanines chemistry both in organic solvents and in solid-phase have been reported in a number of works.[15-19] Before the development of our works, there was no information in the literature about the possibility of using microwave radiation in the synthesis of Hps. So, this mini-review summarizes the results of the Hps synthesis using MWI.

Unsubstituted and *tert*-Butylsubstituted Hemiporphyrazines

Microwave Synthesis

At the first stage, it was established,[20] that the treatment of 2,6-diaminopyridine **1** or 1,3-phenylene-diamine **2** and phthalonitrile **3** or 4-*tert*-butylphthalonitrile **4** by microwave irradiation at 150 °C for 20 min in open vessels leads to the corresponding hemiporphyrazines **5-8** (Scheme 2).

Hence two main advantages of microwave-assisted synthesis are demonstrated: the synthesis time has been significantly reduced from 8-10 hours to 20 minutes and no solvent was used during the synthesis process, which is more environmentally friendly.

The purification process was also simplified since it is realized without solvent eliminating from the reaction mass.

It was shown that the data of melting point, IR, UV-vis spectroscopies and elemental analysis for final products **5-8** were found to be similar to those described in the literature for corresponding Hps.[1,21-23] Also, the characterization of these compounds was completed with mass spectrometry data. Low yields of **5** and **7** are explained by formation of a large number of various condensation's products, which were detected by MALDI-TOF of the reaction mass.

Sublimation capability of organic substances in vacuum can be one of the effective methods of their purification and deposition on surfaces.

Sublimation Enthalpies and Gas-Phase Structures

Earlier it was established, that Hps[21] and NiHp[1] can be sublimated under vacuum. Recently the thermodynamic characteristics of these processes have been reported.[20] It was shown, that compounds **5**–**8** give stable streams of particles within 441–531 K temperature range with the dependences ln(I·T)=*f*(1000/T) close to straight lines (Figure 1).

The enthalpy of sublimation values ΔH_s for compounds **5-8** were calculated by linear regression using the Clausius-Clapeyron relation (Table 1).

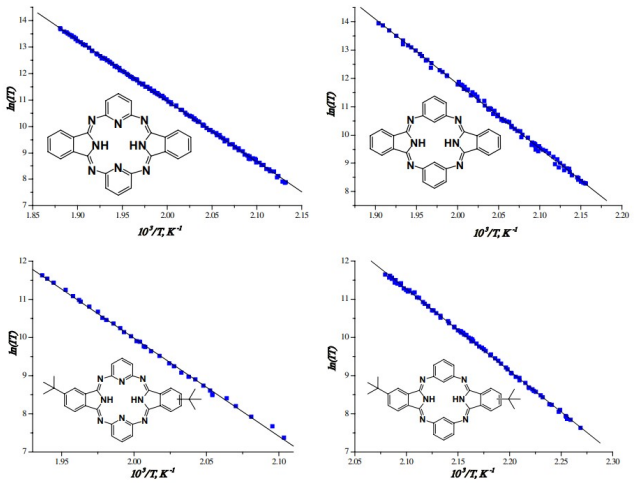


Figure 1. Dependences of the molecular ions intensities logarithms of Hps **5-8** on the temperature.

Table 1. Values of sublimation enthalpies for compounds **5-8.**

Compound	**5**	**6**	**7**	**8**
ΔH_s, kJ/mol	191 (1)*	189 (3)	214 (5)	178 (4)

*Parenthesized values are estimated errors calculated as 3σ

Ethoxy- and Camphor Substituted Hemiporphyrazines

Microwave Synthesis

In order to estimate applicability of microwave activation on the synthesis of both core and periphery modified Hps, a series of macroheterocyclic compounds bearing functionalized ethoxy groups **13-16** and camphorpyrazine motives **18a-c**, **21a-c** and **22a** were synthesized.[24-27]

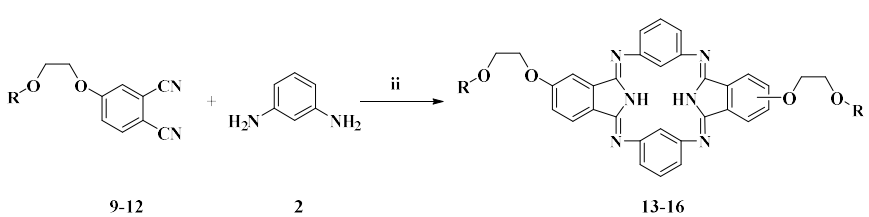
Synthesis of Hps bearing functionalized ethoxy groups **13-16** as mixtures of *cis*- and *trans*-isomers was carried out by interaction of the corresponding 4-substituted phthalonitriles[28] with 1,3-phenylenediamine using microwave assisted initialization at 130 °C, 20 min[24,25] (Scheme 3).

It is worthy to note that an attempt to synthesize methoxyethoxy- and ethoxyethoxy-substituted Hps under microwave initialization conditions described for unsubstituted macrocycle at a temperature of 150 °C leads to the destruction of the starting nitriles, so the synthesis temperature was reduced to 130 °C.

The presence of camphor subunits within macrocycles can induce their optical activity. Hence, racemic and chiral camphorcontaining Hps **18a-c** were synthesized by cross condensation of a racemic mixture **17a**, optical active R-(+)- **17b** or S-(–)-camphordicyanopyrazine **17c**[29] and 1,3-phenylenediamine **2** using microwave activation following solvent-free protocol (Scheme 4).[26] Triazolehemiporphyrazines **21a-c** and dodecyl-substituted triazolohemiporphyrazine **22a** were synthesized by condensation of a racemic mixture **17a** or optically pure R-(+)- **17b** and S-(–)-camphordicyanopyrazine **17c** with 1*H*-3,5-diamino-1,2,4-triazole **19** or 1-dodecyl-3,5-diamino-1,2,4-triazole **20** using microwave initialization at a temperature of 170 ° C for 20 min (Scheme 4).

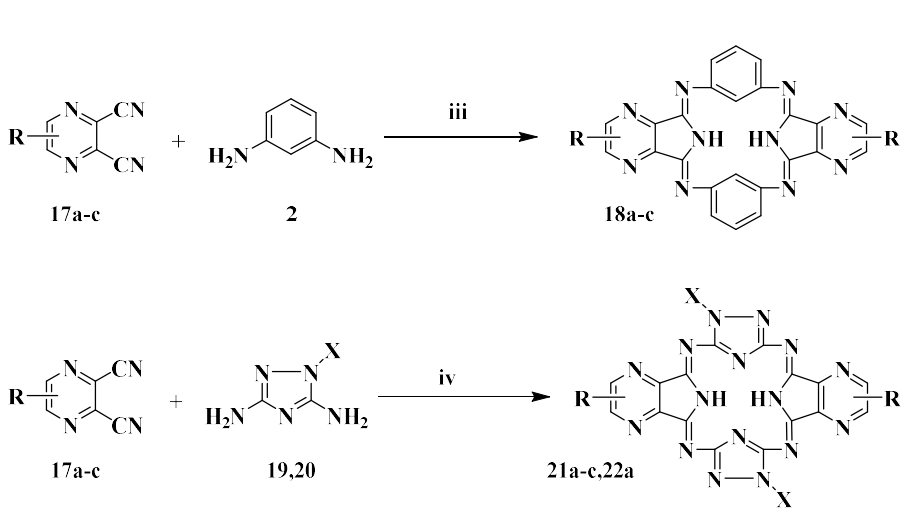
The signal at 10.59 ppm observed in the ^{1}H NMR spectrum of **18b** corresponds to the resonance of the protons of the pyrrole fragments that univocally indicates on nonaromatic character of macrocycle.

It is worthy to note that in the case, when **20** is used as a starting material, formation of a *cis*- and *trans*-isomers of **22** was expected, but this mixture could not be separated in this work.[30]



	R	Yield, %
9	CH_3	–
10	C_2H_5	–
11	C_2H_5OH	–
12	$C_2H_5OC_2H_5OH$	–
13	CH_3	5.5
14	C_2H_5	13.7
15	C_2H_5OH	2.2
16	$C_2H_5OC_2H_5OH$	1.65

Scheme 3. Synthesis of hemiporphyrazines **13-16** by solvent-free protocol, ii: MWI (dynamic power ≤100 W), 130 °C, 20 min.



	R	Yield, %
18a	Racemic mixture of R-(+) and S-(–)	21
18b	R-(+)	25
18c	S-(–)	21
21a	Racemic mixture of R-(+) and S-(–)	16
21b	R-(+)	20
21c	S-(–)	21
22a	Racemic mixture of R-(+) and S-(–)	17

Scheme 4. Synthesis of racemic and chiral camphor-containing hemiporphyrazines **18a-c**, **21a-c** and **22a** by solvent-free protocol. **iii**: MWI (dynamic power ≤100 W), 150 °C, 20 min. **iv**: MWI (dynamic power ≤100 W), 170 °C, 20 min. X = H (**19**, **21a-c**) or $C_{12}H_{25}$ (**20**, **22a**). For **22a** only *trans*-isomer is shown.

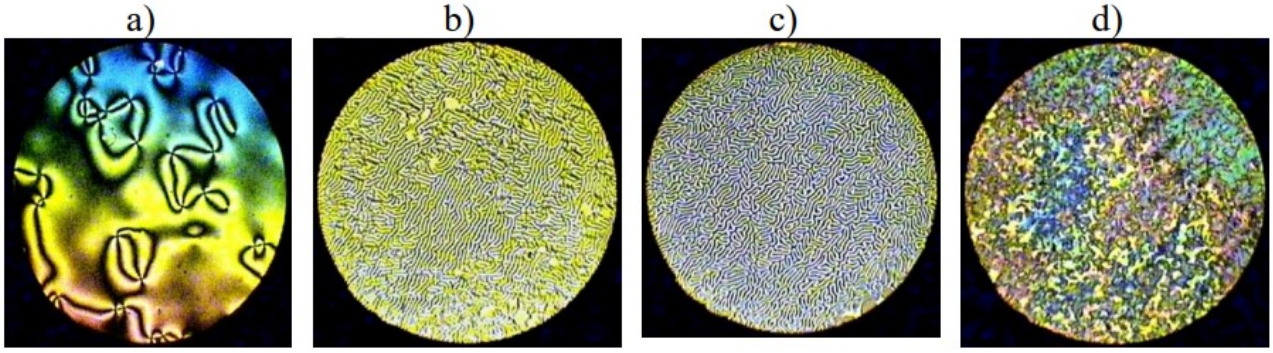


Figure 2. Textures of liquid crystal compositions: the texture of the schlieren nematic phase of the CB-6 liquid crystal mixture at 60 °C (a); the texture of the fingerprints of the CB-6 mixture with **18b** (0.92%) at 65 °C (b); the texture of the fingerprints of the CB-6 mixture with **18b** (1.8%) at 50 °C (c); the marble texture of the nematic phase of the CB-6 mixture with racemate **18a** (1.55%) at 50 °C (d).

Influence of Optical Active Camphor Substituted Hemiporphyrazines on Liquid Crystal Systems

A chiral nematic phase formation of the 4-(n)alkoxy-4-cyanobiphenyls (n=3–8) nematic mixtures (CB6) used as liquid crystal system under the influence of the chiral dopant Hp **18b** was observed by the method of polarizing microscopy (Figure 2).[26]

The formation of a "fingerprint" texture (Figure 2b,c) was detected, due to the induced chiral nematic phase formed in the system. The clearance temperatures and helix pitch were measured, and the helical twisting power β was found to be 2.19 μm^{-1}. At high concentrations of the chiral dopant drops in the temperature plots of the dielectric constants in the mesophase were detected.

Dielectric permittivity and its anisotropy and kinematic viscosity were determined for CB6 doped with racemic mixture **18a** and optical active **18b**. It was established that the negligible differences in optical properties of both systems is caused by the coincidence of the local orientational order in the nematic phase and in the quasi-nematic layers of the chiral nematic phase.

Conclusions

A method of hemiporphyrazines synthesis consisting in the interaction of phthalonitrile or substituted dinitriles with aromatic diamines under microwave radiation realized in the range of temperature within 130–170 °C for 20 min by solvent-free protocol is developed. This energy saving and environmentally friendly approach opens up prospects for further development of express-methods for obtaining macroheterocyclic compounds.

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