Synthesis of Hemipyrazinoporphyrazines Bearing Peripheral Pyrrolic Substituents

M. Salomé Rodríguez-Morgade,[a] G. Dan Pantos,[b] Esmeralda Caballero,[a] Jonathan L. Sessler,[b,@] and Tomás Torres[a,@]

[a]*Departamento de Química Orgánica, Universidad Autónoma de Madrid, Cantoblanco,28049 Madrid, Spain*
[b]*Department of Chemistry and Biochemistry and Institute for Cellular and Molecular Biology 1 University Station - A5300, University of Texas at Austin, Austin, Texas 78712-0165, USA*
[@]*Corresponding authors E-mail: sessler@mail.utexas.edu, tomas.torres@uam.es*

Described in this report is the synthesis and optical spectroscopic characterization of two new dipyrrolylquinoxaline analogues. These new systems consist of novel hemipyrazinophyrazines that are functionalized on their respective peripheries with four pyrrole rings. The electronic features of these compounds are typical of those expected for hemiporphyrazines, although slight bathochromic shifts are observed for the absorption bands in the violet-blue region of the electromagnetic spectrum.

Introduction

Hemiporphyrazines (Figure 1) are members of the generalized class of porphyrin analogues known as azaporphyrins.[1-5] They can be considered as ABAB phthalocyanine analogues in which two isoindole subunits have been replaced by heterocycles other than pyrroles. As a consequence, hemiporphyrazines generally display D_{2h} symmetry, that is, they bear two opposite faced isoindole moieties. This feature has made them interesting building-blocks for the construction of linear arrays, such as ribbon- or ladder-type polymers. Hemiporphyrazines also offer the advantage of being easy to prepare. For instance, the first example of this nonaromatic, cross-conjugated compounds, the 28 π-electron macrocycle **1** (Figure 1) reported by Elvidge and Linstead[6] was obtained through condensation of 1,3-diiminoisoindoline with 2,6-diaminopyridine. This synthetic procedure, like the name originally proposed, has now been extended to the whole hemiporphyrazine class. In fact, the general procedure currently used to obtain any of a number of hemiporphyrazines is to condense a suitable 1,3-diimino-isoindoline derivative with the corresponding (hetero)-aromatic ring endowed with two primary amines. Here, the position of the two amino functions should be such that it permits the crossover [2+2] cyclotetramerization of the two components. Further, metallation with appropriate metal salts can be used to access the corresponding metallohemiporphyrazines.

The Madrid group has been involved in the modification of the tetraazaporphyrin structure in order to obtain other macrocycles structurally related to phthalocyanines and porphyrazines but exhibiting non conventional physicochemical features.[2,3,8] One of the modifications that we have carried out involves the incorporation of the 1,2,4-triazole or 1,3,4-thiadiazole heterocycles into the tetrazaporphyrin structure. Thus, we have described the synthesis, characterization and properties of *triazoleazaporphyrins* (**2**, Figure 1),[9,10] intrinsically unsymmetrical compounds that constitute aromatic azaporphyrin analogues in which one isoindole moiety has been formally replaced by a 1,2,4-triazole subunit. The introduction of this heterocycle into the phthalocyanine framework leads to a lower degree of electronic delocalization, which results in an hypsochromic shift of its *Q*-band in relation to the corresponding phthalocyanine absorption.[5,11] This property, coupled with the lack of symmetry center, has made these derivatives good targets for the development of materials with non-linear optical applications.[12,13,14] In addition, their amphiphilic structure, characterized by a polar 1,2,4-triazole head and an aromatic macrocycle, is especially appropriate for Langmuir-Blodgett film formation.[9]

The replacement of two isoindole subunits in a Pc by two 1,2,4-triazoles affords the so-called

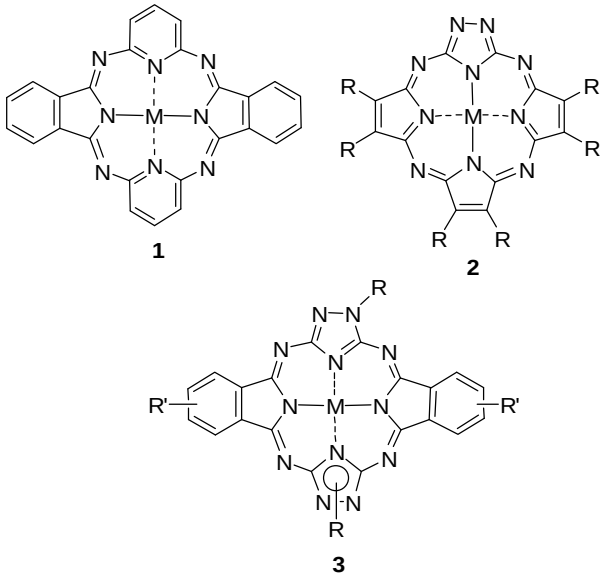


Figure 1. Chemical structures of hemiporphyrazine (**1**), triazoleazaporphyrin (**2**) and triazolehemiporphyrazine (**3**).

triazolehemiporphyrazines (**3**, Figure 1),[3] macrocycles that possess a 20 π-electron cross-conjugated system and therefore, nonaromatic character. We have functionalized these hemiporphyrazines to produce materials with special optical and liquid crystalline properties.[3,15] Furthermore, we have taken advantage of the hemiporphyrazine ABAB symmetry to prepare heterobinuclear and heterotrinuclear phthalocyanine-hemiporphyrazine hybrids with extended conjugation.[16] We have also extended the π system of the hemiporphyrazines by preparing the first examples of expanded triazolehemiporphyrazine[17] and thiadiazolehemiporphyrazine.[18] These expanded heteroannulenes display unusual coordination features, including an ability to bind two or three metal ions, respectively, within their central cavity.

Recently, the group in Austin has developed a variety of pyrrole-based anion receptors, including some based on calixpyrroles, sapphyrins, and dipyrrolylquinoxalines.[19,20] Several of the latter systems allow for the direct, so-called naked eye detection of several biologically relevant anions. Others have served to underscore the fact that small changes in the structure can produce receptors with very different anion binding properties. Thus, we had a two-fold motivation to combine the chemistry of pyrrolic macrocycles with that of the hemiporphyrazines: First, it would allow the effect of structure on pyrrole-based anion recognition to be further probed. Second, the reddish color of hemiporphyrazines could enable the use of these compounds as colorimetric anion sensors. With this medium-term purpose in mind, we decided to incorporate the dipyrrolylquinoxaline motif into the hemiporphyrazine structure. Thus, in this paper we wish to report briefly on a new class of dipyrrolylquinoxaline analogues consisting in triazolehemiporphyrazines further functionalized with peripheral pyrrole rings.

Experimental

UV-vis spectra were recorded with a Hewlett-Packard 8453 spectrophotometer. IR spectra were recorded with Bruker Vector 22 spectrophotometer. MALDI-TOF MS spectra were recorded with a Bruker Reflex III spectrometer. NMR spectra were recorded with a Bruker AC-300 instrument. Column chromatographies were carried out on silica gel Merck-60 (230-400 mesh, 60 Å) and TLC was performed on aluminium sheets precoated with silica gel 60 F_{254} (E. Merck). Chemicals were purchased from Aldrich Chemical Co. and used as received without further purification.

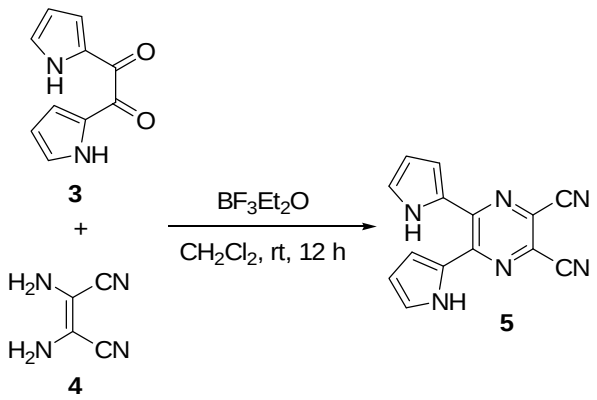
General procedure for the synthesis of hemipyrazinoporphyrazines ***8a,b:*** A mixture of pyrazinocarbonitrile **5** (1 mmol) and the corresponding diaminotriazole derivative **7a,b** (1 mmol) was dissolved in ethyleneglycol and the solution was heated at 100º C for 4 h. After this time a precipitate was observed. The temperature was raised to 160º C and the mixture was heated for other 20 h at this temperature. The suspension was cooled to r.t., the solid was filtered and washed with ethanol. The obtained solid was suspended in ethanol and triturated at reflux, filtered, washed with ethanol and dried at 10^{-1} mm Hg.

7,17(18)-Dihydrodi(5',6'-bis(1''H-pyrrol-2''-yl)pyrazino)[b,g]-5,7,8,10,15,17,18,20-octaazaporphyrin **8a:** (58%). *m/z* (MALDI-TOF) 685 (100) $[(M+H)^+]$. ν_{max} (KBr)/cm^{-1} 3283, 2966, 1722, 1641, 1547, 1425, 1398, 1358, 1263, 1182, 1047, 804. λ_{max} (DMF) 387, 432 nm.

7,17(18)-Didodecyl-7,17(18)-dihydrodi(5',6'-bis(1''H-pyrrol-2''-yl)pyrazino)[b,g]-5,7,8,10,15,17,18,20-octaazaporphyrin **8b:** (52%). *m/z* (MALDI-TOF, dithranol) 1021 (100) $[(M+H)^+]$. ν_{max} (KBr)/cm^{-1}, 3290, 2925, 2856, 1718, 1651, 1539, 1435, 1398, 1356, 1258, 1190. λ_{max} (DMF) 390, 435 nm.

Results and Discussions

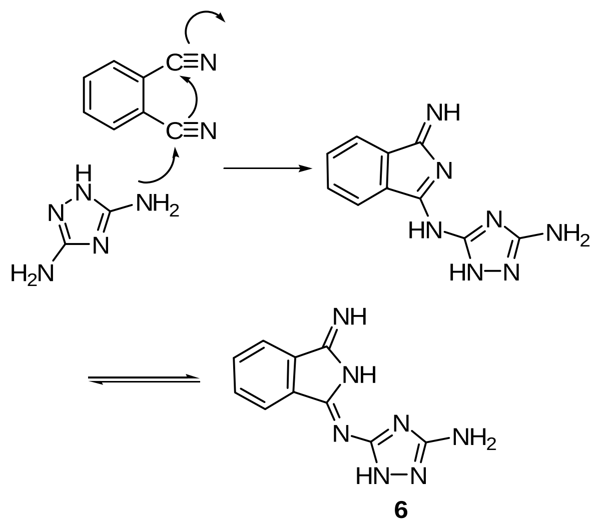
Appropriate dinitrile precursors were prepared using synthetic procedures previously reported by the Austin group.[19] Specifically, condensation of 1,2-bis-(1*H*-pyrrol-2-yl)ethane-1,2-dione (**3**) with diaminomaleonitrile (DAMN, **4**) was found to afford the corresponding 5,6-bis(1*H*-pyrrol-2-yl)pyrazine-2,3-dicarbonitrile **5** in 55% yield (Scheme 1).



Scheme 1. The synthesis of the pyrazinedicarbonitrile **5**.

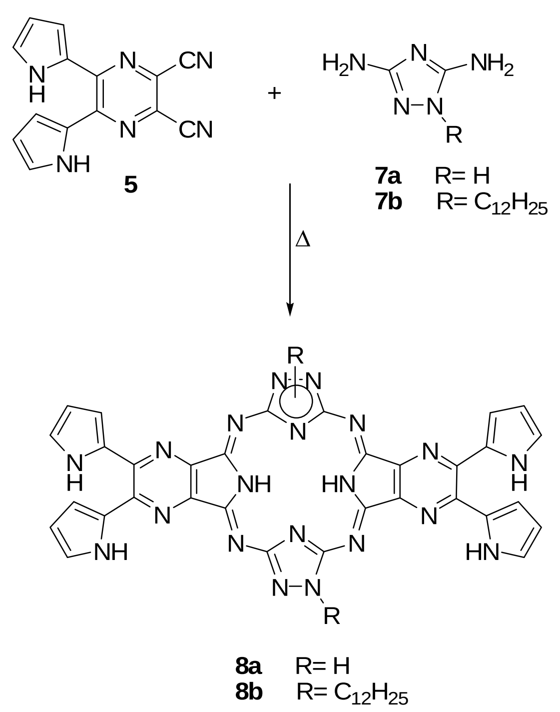
As mentioned above, the synthesis of hemiporphyrazines usually involves the condensation reaction of a diamine with a diiminoisoindoline derivative which in turn, is obtained by reaction of the corresponding phthalonitrile with ammonia in an alcoholic solvent and catalyzed by a sodium alkoxide. However, in some cases it is also possible to obtain a hemiporphyrazine directly from an appropriately chosen dinitrile precursor. In the latter case, harsher conditions are necessary to complete the cyclotetramerization reaction. This is thought to reflect the fact that diiminoisoindolines are reaction intermediates under these conditions. In fact, the condensation of a diamine with a phthalonitrile should begin with the nucleophilic attack of one of the amino moieties on one of the nitrile groups. Subsequently, a pyrrole ring is produced from the dicyano compound, to yield a two-unit intermediate of type **6**, which already contains the iminoisoindoline moiety (see Scheme 2). The further dimerization of this two-unit intermediate affords the hemiporphyrazine macrocycle.

Triazolehemiporphyrazines have also been obtained both from diiminoisoindoline, or directly from the condensation reaction of phthalonitrile precursors and 2,5-diamino-1,2,4-triazole derivatives.[21] In the latter case, treatment of the starting materials at high temperature (198º C at reflux in ethyleneglycol) proved to be the most convenient method in terms of reaction time and efficiency. The thermal instability of the dicyano derivative **5** precludes prolonged heating at high temperatures. Therefore, hemiporphyrazine **8a** was prepared *via* a cyclotetramerization reaction involving the pyrazinocarbonitrile **5** and guanazole (**7a**), which could be carried out at a temperature of 160 °C (Scheme 3). Under these conditions, an yield of 58% was obtained.



Scheme 2. The mechanism of the formation of a triazolehemiporphyrazine starting from a phthalonitrile precursor.

Macrocycle **8a** proved to be extremely insoluble in organic solvents. However, it was appreciated that functionalization of 1,2,4-triazole derivatives at the 1 position with dodecyl chains leads to enhanced solubility in organic solvents.[21] Accordingly, we have prepared the triazolehemiporphyrazine **8b**; it was produced following the same methodology but using 3,5-diamino-1-dodecyl-1,2,4-triazole (**7b**)[21] as the triazole precursor. Unfortunately, the solubility of this compound was not greatly improved relative to its non substituted congener.



Scheme 3. Synthesis of hemipyrazinoporphyrazines **8a,b**

All new compounds were characterized using standard spectroscopic techniques. Compounds **8a,b** displayed a single peak at m/z = 685 and 1021, respectively corresponding to $[M+H]^+$ in the MS (MALDI-TOF). In addition, the UV-vis spectra of both hemipyrazinoporphyrazines **8a** and **8b** were found to be almost identical.

In Figure 2 the electronic spectra of a typical Ni^{II} triazolehemiporphyrazine, compound **8b**, and the associated pyrazinecarbonitrile precursor are shown.

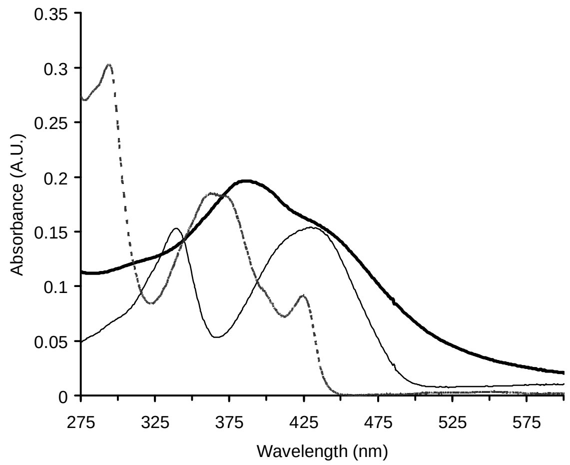


Figure 2. UV-vis spectra of hemipyrazinoporphyrazine **8b** (thick solid line), a typical triazolehemiporphyrazine (**3**, R = $C_{12}H_{25}$, R' = OC_8H_{17}, M = Ni, dotted line), and 5,6-bis(1*H*-pyrrol-2-yl)-pyrazine-2,3-dicarbonitrile (**5**) (thin solid line) in DMF.

The electronic properties of macrocycle **8b** are typical for a triazolehemiporphyrazine, in that two bands are seen at 390 and 435 nm, respectively. As expected, neither the fused pyrazino rings nor the peripheral pyrrole moieties produces any substantial alteration in the optical properties of the triazolehemiporphyrazine, apart from a slight bathochromic shift in the absorption bands of ca. 20 nm. While not yet fully established, this shift is likely due to the incorporation of the four pyrazino nitrogens within the hemiporphyrazine structure.

Conclusion

In summary, two new dipyrrolylquinoxaline analogues are described. They consist of novel hemipyrazinoporphyrazines that are functionalized on their respective peripheries with four pyrrole rings. The electronic properties of these compounds are typical of those expected for hemiporphyrazines, in that UV-vis absorption bands in the violet-blue region of the electromagnetic spectrum are displayed. However, slight bathochromic shifts are seen. Unfortunately, the poor solubility of these macrocycles in typical organic solvents precluded their testing as anion sensors. Further studies in order to obtain soluble compounds are currently underway and will be published in due course.

Acknowledgements. The work in Madrid was supported by the Spanish MEC (CTQ-2005-08933-BQU), the Comunidad de Madrid (S-0505/PPQ/000225), and the ESF-MEC (project SOHYD). M. S. R.-M. thanks the Spanish MEC for a R & C contract. The work in Austin was supported by the National Science Foundation (CHE 0515670 to J.L.S.).

References

1. Campbell J.B. *U.S. Patent* 2765308, **1956**; *Chem. Abstr.* **1956**, *51*, 8143f.
2. Fernández-Lázaro F., Torres T., Haushel B., Hanack M. *Chem. Rev*. **1998**, *98*, 563-575.
3. Rodríguez-Morgade M.S., de la Torre G., Torres T. Design and Synthesis of Low-Symmetry Phthalocyanines and Related Systems, in *The Porphyrin Handbook*, Vol. 15, Ch. 99 (Kadish K.M., Smith K.M., Guilard R., Eds) San Diego, Academic Press, **2003**, 125-159.
4. Rodriguez-Morgade M.S., Stuzhin P.A. *J. Porphyrins Phthalocyanines* **2004**, *8*, 1129-1165.
5. Rio Y., Rodríguez-Morgade M.S., Torres T. *Org. Biomol. Chem.* **2008**, *6*, 1877-1894.
6. Elvidge J.A., Linstead R.P. *J. Chem. Soc.* **1952**, 5008-5012.
7. de la Torre G., Nicolau M., Torres T. Phthalocyanines: Synthesis, Supramolecular Organization, and Physical Properties, in *Supramolecular Photosensitive and Electroactive Materials* (Ed. Nalwa H.R.) New York, Academic Press, **2001**, 1-111.
8. Claessens C.G., González-Rodríguez D., Torres T. *Chem. Rev*. **2002**, *102*, 835-853.
9. Nicolau M., Cabezón B., Torres T. *Coord. Chem. Rev.* **1999**, *190-192*, 231-243.
10. Islyaikin M.K., Rodríguez-Morgade M.S., Torres T. *Eur. J. Org. Chem.* **2002**, 2460-2464.
11. Cabezon B., Rodríguez-Morgade S., Torres T. *J. Org. Chem.* **1995**, *60*, 1872 -1874.
12. de la Torre G., Vázquez P., Agulló-López F., Torres T. *J. Mat. Chem.* **1998**, *8*, 1671-1683.
13. de la Torre G., Vazquez P., Agullo-Lopez F., Torres T. *Chem. Rev*. **2004**, *104*, 3723-3750.
14. Rojo G., Agulló-López F., Cabezón B., Torres T., Brasselet S., Ledoux I., Zyss J. *J. Phys. Chem. B* **2000**, *104*, 4295-4299.
15. Diaz-Garcia M.A., Ledoux I., Fernandez-Lazaro F., Sastre A., Torres T., Agullo-Lopez F., Zyss J. *J. Phys. Chem.* **1994**, *98*, 4495–4497.
16. de la Torre G., Martínez-Díaz M.V., Ashton P.R., Torres T. *J. Org. Chem.* **1998**, *63*, 8888-8893.
17. Rodríguez-Morgade M.S., Cabezón B., Esperanza S., Torres T. *Chem. Eur. J.* **2001**, *7*, 2407-2413.
18. Islyaikin M.K., Danilova E.A., Yagodarova L.D., Rodríguez-Morgade M.S., Torres T. *Org. Lett.* **2001**, *3*, 2153-2156.
19. Sessler J.L., Pantos G.D., Katayev E., Lynch V.M. *Org. Lett.* **2003**, *5*, 4141-4144.
20. Ghosh T., Maiya B.G., Wong M.W. *J. Phys. Chem. A* **2004**, *108*, 11249-11259.
21. Fernández-Lázaro F., de Mendoza J., Mó O., Rodríguez-Morgade S., Torres T., Yáñez M., Elguero J. *J. Chem. Soc. Perkin Trans. 2* **1989**, 797-803.

Received 12.06.2008
Accepted 13.06.2008