DOI: 10.1002/ejoc.201000670

Facile Synthesis of Substituted Mono-, Di-, Tri- and Tetra-2-aryl-2,3-dihydro-1*H*-perimidines

Marta Martínez Belmonte,[a] Eduardo C. Escudero-Adán,[a] Jordi Benet-Buchholz,[a] Robert M. Haak,[a] and Arjan W. Kleij*[a,b]

Keywords: Nitrogen heterocycles / Perimidines / Zinc catalysis

The efficient synthesis of a variety of substituted 2-aryl-2,3-dihydro-1*H*-perimidines using Zn-catalysis is reported. A series of 2,3-dihydroperimidines with various functional groups have been isolated in high yield by simple filtration from the reaction mixture. The new compounds have been fully characterized by spectroscopic and spectrometric analyses and in some cases also by X-ray diffraction. The synthetic approach was subsequently also tested for di-, tri-, and tetra-(salicyl)aldehyde reagents and afforded the corresponding multi-perimidines in good yields. In the present studies also an unexpected bis(2,3-dihydro-1*H*-perimidine) decomposition product has been identified. The current approach underlines the simplicity of creating a series of perimidines which may be post-altered by using the functional group diversity introduced through the aldehyde reagents.

Introduction

Perimidines[1] are tricyclic heterocycles consisting of a dihydropyrimidine ring *ortho*- and peri-fused to a naphthalene fragment. These structures have been shown to be interesting candidates for biological activity studies and find widespread application in industry, agriculture and medicine.[2] A generally applied synthetic route towards perimidines comprises the reaction of 1,8-diaminonaphthalene with a carbonyl compound such as carboxylic acids, anhydrides, acid halides, ketones or aldehyde reagents.[3] In the latter case 2,3-dihydro-1*H*-perimidines are produced which can be easily converted to perimidines by dehydrogenation. The preparation of (2,3-dihydro-1*H*-)perimidines has been subject of many investigations using Lewis acid promoted reactions[4] or other methods.[5] Although aryl-functionalized 2,3-dihydro-1*H*-perimidines have been known for quite some time, their corresponding derivatives constructed from salicylaldehyde reagents remain remarkably unexplored. Properly functionalized salicylaldehydes would allow post-functionalization of the perimidine structure and/or combination with other scaffolds by coupling procedures to give rise to new (multi-)perimidines with potentially interesting properties relevant for pharmaceutical applications. On the other hand, recent literature has witnessed the communication of various multi-perimidinal systems that find use as ligand scaffolds for catalytically active complexes,[6] as convenient "stoppers" of supramolecular systems such as [2]- and [4]rotaxanes,[7] and as fragments of *N*-salicylideneaniline structures.[8]

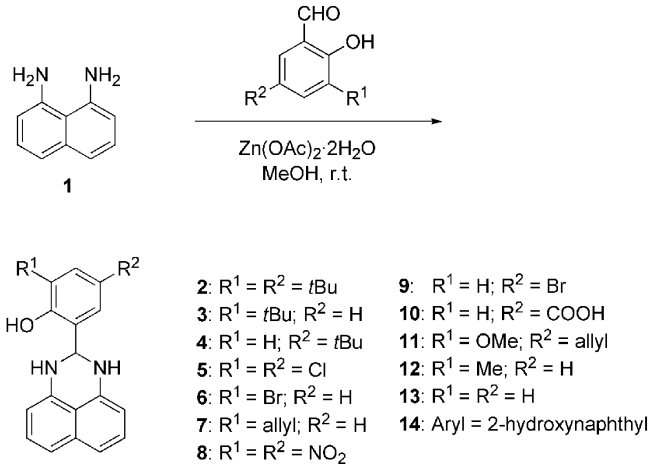
We here report a versatile Zn-mediated approach towards a small library of functionalized 2-aryl-2,3-dihydro-1*H*-perimidines with ample scope that is among the mildest and most efficient methods reported to date. Additionally, we report on various multi-2,3-dihydro-1*H*-perimidinal systems that can also easily be obtained from di-, tri- and tetra-aldehyde precursors.

Results and Discussion

Our interest in using 1,8-diaminonaphthalene as a scaffold originates from the studies we have undertaken to explore various salen structures as versatile building blocks for new materials[9] and supramolecular structures.[10] We are particularly attracted to diamino-aryl scaffolds that are able to induce a planar geometry around the ligated metal ion, and have reported on the unusual properties of Zn-centred salphen complexes [salphen = *N*,*N*′-salicylidene-1,2-diaminophenyl].[11] We envisioned that 1,8-diaminonaphthalene would be a useful starting point for the creation of other types of geometrically planar ligands that, upon ligation of Zn ions, should be able to amplify the arsenal of intriguing structures potent as a molecular building block. Molecular modelling studies[12] revealed that indeed a rather planar geometry may be obtained and therefore we set out to prepare the corresponding salen complex derived from 1,8-diaminonaphthalene using conditions that have previously been proven to be successful for salphen deriva-

[a] Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans 16, 43007 Tarragona, Spain
Fax: +34-977920224
E-mail: akleij@iciq.es
[b] Catalan Institute for Research and Advanced Studies (ICREA), Passeig Lluís Companys 23, 08010 Barcelona, Spain
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201000670.

tives.[13] Combination of 2 equiv. of 3,5-di-*tert*-butylsalicylaldehyde with 1,8-diaminonaphthalene **1** and an excess of $Zn(OAc)_2{\cdot}2H_2O$ in MeOH (see Exp. Sect. and Scheme 1) gave a fast precipitation of a white solid. This solid was first analyzed by ^1H NMR spectroscopy ([D_6]acetone solution) and showed a single, pure compound with a resonance pattern that could not be associated with a Zn(salen) complex. Typical peaks at δ = 6.20 and 5.75 ppm (2:1 integral ratio) were observed that indicated the formation of a distinct species. Closer inspection of the NMR spectrum and mass spectroscopic data confirmed the isolation of 2-(2-hydroxy-3,5-di-*tert*-butylphenyl)-2,3-dihydro-1*H*-perimidine (**2**, Scheme 1) in 48% yield. The selective formation and isolation of **2** was further supported by X-ray diffraction (XRD) analysis (Figure 1).



Scheme 1. Synthesis of 2,3-dihydro-1*H*-perimidines **2**–**14** via a Zn-mediated procedure.

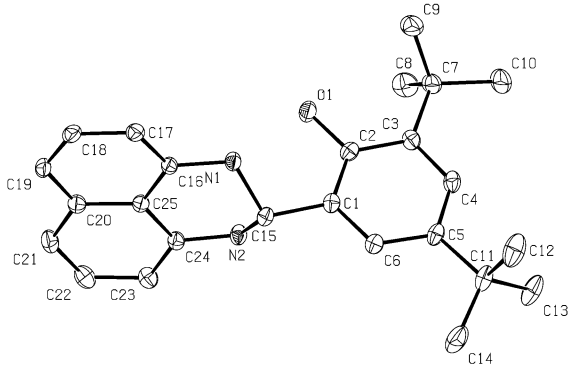


Figure 1. Molecular structure for **2** determined by XRD with the adopted numbering scheme; co-crystallized solvent molecules and H-atoms are omitted for clarity.[14]

From the reaction described above a second fraction of product was also isolated but proved to be impure and contained, besides **2**, another compound (**2b**) with an NMR pattern having characteristic peaks a 13.94 and 9.08 ppm (Supporting Information). These chemical shifts pointed to the formation of an imine species and fortunately this component selectively crystallized from the NMR solvent mixture ([D_6]acetone/[D_6]DMSO). The result of these XRD studies is shown in Figure 2. The 1,5-substitution of the two salicylidene groups in **2b** probably originates from an impurity (i.e., 1,5-diaminonaphthalene) in the starting material 1,8-diaminonaphthalene.[15]

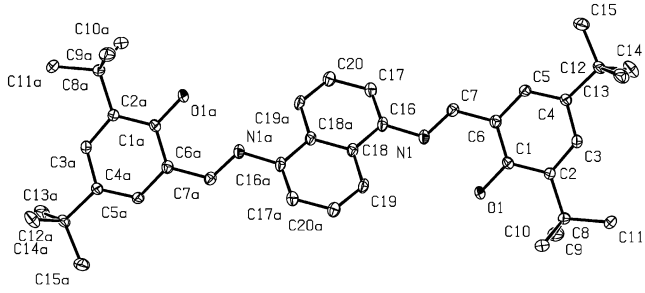
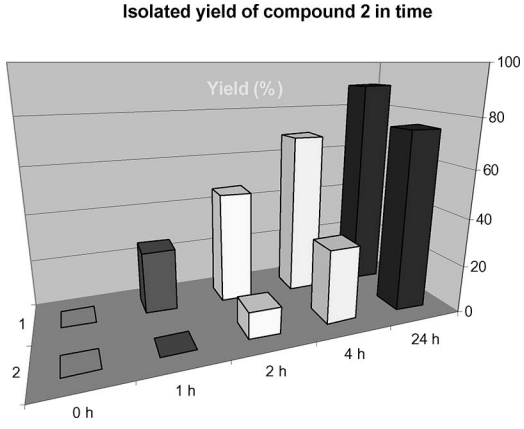


Figure 2. Molecular structure for **2b** (minor product) determined by XRD with the adopted numbering scheme; co-crystallized solvent molecules and H-atoms are omitted for clarity.[14]

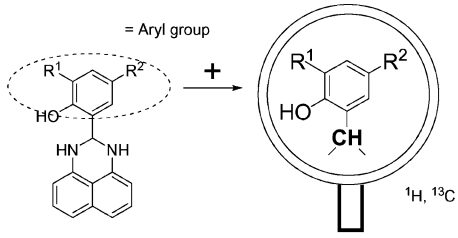
The synthesis of **2** was then probed with and without the presence of a catalytic amount of $Zn(OAc)_2{\cdot}2H_2O$ (8–10 mol-%) and with a slight excess of salicylaldehyde reagent. The isolated yield in the presence of Zn catalyst proved to be significantly higher at different stages of the reaction (Scheme 2, scale: 4 mmol of 1,8-diaminonaphthalene using 1.2 mol equiv. of salicylaldehyde). The simple isolation of compound **2** prompted us to investigate the scope of this reaction in more detail. We therefore screened a number of salicylaldehyde reagents for the preparation of a series of substituted 2-aryl-2,3-dihydro-1*H*-perimidines (Scheme 1, **2**–**14**) with the use of $Zn(OAc)_2{\cdot}2H_2O$ as catalyst. In particular, salicylaldehydes with functional groups that allow for post-modification were utilized and the results of this screening are summarized in Table 1.

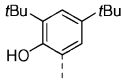
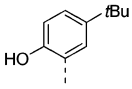
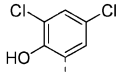
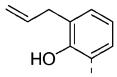
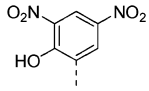
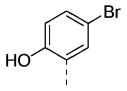
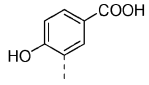
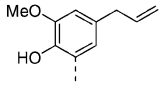
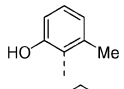
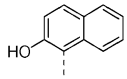


Scheme 2. Time-dependent isolated yield in the presence (lane 1) and absence (lane 2) of $Zn(OAc)_2{\cdot}2H_2O$.

Both apolar, aliphatic as well as distinct polar groups can be readily introduced in the perimidine structure (Table 1).[16] With the exception of **11**, all isolated yields are beyond 70%. It should be noted that for the majority of the cases simple filtration of the reaction mixture afforded the pure product in high yield. In some cases the isolation of the product was carried out by concentration and/or cooling of the reaction mixture. The products **6** and **9** (the

Table 1. Synthesis of various substituted 2-aryl-2,3-dihydro-1*H*-perimidines **2**–**14** and ^{1}H and ^{13}C{^{1}H} NMR spectroscopic data for the aryl-*CH* fragment.



	Aryl group	Yield[a] [%]	δ_{1H}(CH)[b] [ppm]	δ_{13C}(CH)[b] [ppm]
2		82	5.75	71.01
3		77	5.48	70.62
4		78	5.59	68.09
5		85	5.67	61.98[c]
6		99	5.58[d]	64.02[c]
7		76	5.49	67.39[e]
8		83	6.04	60.57[c]
9		92	5.63[c]	60.09[c]
10		85	5.66[c]	60.28[c]
11		66	5.78	60.91[c]
12		79	5.48	67.52[d]
13		72	5.65[c]	60.89[c]
14		76	6.46	62.53[e]

[a] Isolated yield. [b] NMR spectroscopic data recorded in [D$_6$]-acetone unless stated otherwise. [c] Recorded in [D$_6$]DMSO. [d] Recorded in 90:10 v/v [D$_6$]acetone/[D$_6$]DMSO. [e] Recorded in 70:30 v/v [D$_6$]acetone/[D$_6$]DMSO.

brominated derivatives) behaved completely different. While compound **6** was isolated in nearly quantitative yield after one single filtration, the isolation of its isomeric **9** proved to be complicated when an excess of salicylaldehyde reagent was used. Therefore, the synthesis of **9** was finally carried out with equimolar amounts of 1,8-diaminonaphthalene and 5-bromosalicylaldehdye and the product was isolated through precipitation of the product by addition of water to the reaction mixture.

Although the reactions of Table 1 were not followed in time, there are strong indications that the products are formed much faster than the experimental conditions indicate. For instance, the syntheses of **5** (30 min reaction time, 85% yield) and **6** (5 min reaction time, 99% yield) suggest that 2,3-dihydro-1*H*-perimidine formation might indeed be a fast process and the use of stoichiometric amounts of salicylaldehyde (see **9**) should be sufficient to reach full conversion of the starting materials. All compounds showed ^{1}H and ^{13}C{^{1}H} consistent with their structures: the data of the characteristic aryl-CH fragment is listed in Table 1. The structure for **12** was also determined by XRD (Figure 3).

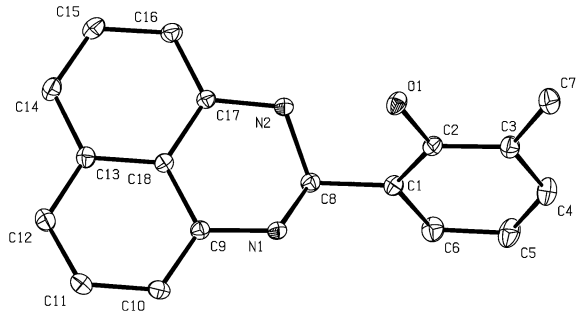
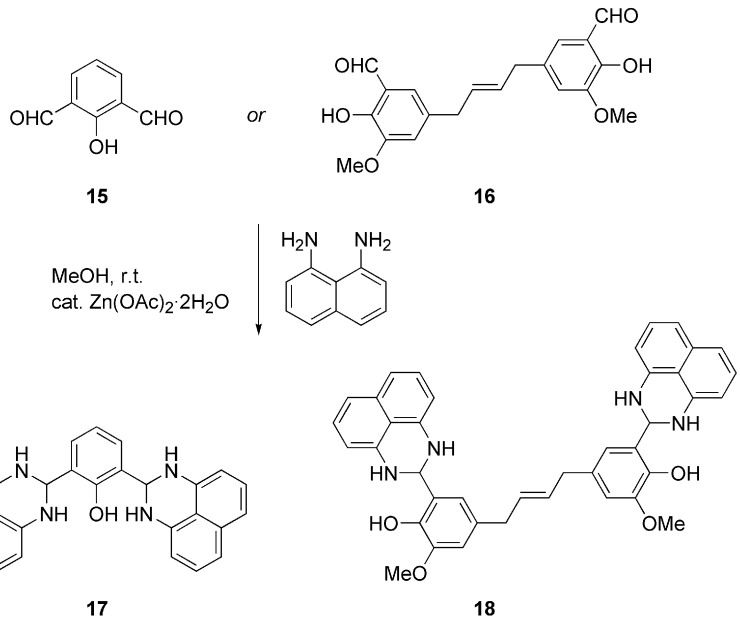


Figure 3. Molecular structure for **12** determined by XRD with the adopted numbering scheme; co-crystallized solvent molecules and H-atoms are omitted for clarity. Note that only one of the independent molecules in the unit cell is shown.[14]

As the 2,3-dihydro-1*H*-perimidine compounds **2**–**14** (Table 1, Scheme 1) are easily obtained, we then focused on more challenging substrates such as 2-hydroxyisophthaldehyde **15** and previously reported di-salicylaldehyde **16** (Scheme 3).[17] Using the same synthetic methodology, the bis(2,3-dihydro-1*H*-perimidine) compounds **17** and **18** were isolated in 94% and 85% yield, respectively. The identity of **17** and **18** could be simply deduced from the NMR spectroscopic data through the diagnostic integral ratio (1:4:2 for **17** and 2:4:2 for **18**) between the OH, the NH and aryl-CH groups, and the ESI(–)-MS data. The proposed structure for **17** was also supported by XRD (Figure 4).[18]

The synthesis of **20** from known trialdehyde **17**[19] proved to be more cumbersome (Scheme 4). Our initial intent failed due to precipitation of partially substituted **17** as identified by both NMR and MS analysis. We then used a more dilute reaction mixture and short heating time to reflux temperature in order to prevent precipitation of both the tri-aldehyde reagent as well as incompletely substituted **17** at an early stage of the process. Much to our surprise we discovered the formation of bis(2,3-dihydro-1*H*-perimidine) **21** as the major isolated product under these conditions. Compound **21** has two 2,3-dihydro-1*H*-perimidine fragments but surprisingly comprises a protonated central aryl unit instead of the expected, unreacted aryl-CHO group.



Scheme 3. Synthesis of bis(2,3-dihydro-1*H*-perimidines) **17** and **18** using dialdehydes **15** and **16**.

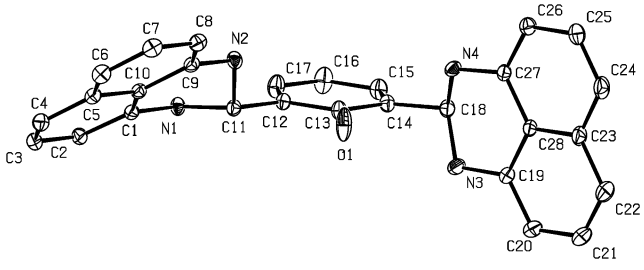
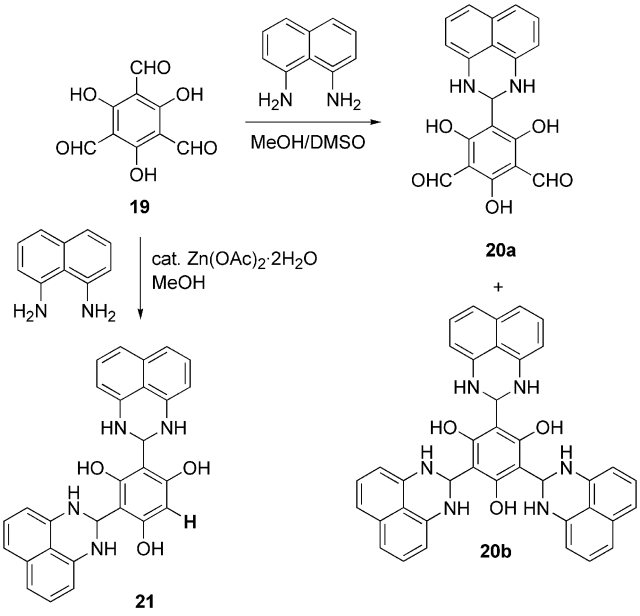


Figure 4. Molecular structure for **17** determined by XRD with the adopted numbering scheme; co-crystallized solvent molecules and H-atoms are omitted for clarity.[14]

The isolation of **21** was fully supported by NMR and mass spectrometric analyses.[20] For instance, the $^{13}C\{^1H\}$ NMR spectrum recorded for **21** did not show the characteristic aldehyde carbon around 190 ppm and displayed one carbon peak less than would be expected for the bis(2,3-dihydro-1*H*-perimidine) product having the aldehyde function still intact. An alternative synthesis of **20** was then probed by using DMSO as co-solvent (see Exp. Sect.). Under these latter conditions a homogeneous mixture results at the beginning of the reaction, after which rapidly a solid starts to precipitate. The identity of this precipitate was established with NMR and MS and the product turned out to be the mono-2,3-dihydro-1*H*-perimidine **20a** (61% isolated yield, Scheme 3). From the mother liquor a second fraction was isolated and this was analyzed as the tris(2,3-dihydro-1*H*-perimidine) **20b** (14% isolated yield, Scheme 3). These findings emphasize the low solubility of the intermediate structures in the conversion **19**→**20b**. Crystals of **20b** could be obtained from DMSO/Et_2O, and the structure (Figure 5) comprises the three perimidine units in a non-planar arrangement around the aromatic core.[21] To the best of our knowledge, solid-state structures of tri-perimidines have not been reported to date.



Scheme 4. Use of trialdehyde **19** for the synthesis of **20a**, **20b** and **21**.

We then also investigated the possibility to create multi-perimidine structures supported by calixarenes by treatment of known tetraformylcalix[4]arene **22**[22] with an excess of 1,8-diaminonaphthalene in THF (Scheme 5). This procedure afforded calix[4]-perimidine **23** in 55% isolated yield. The structure of **23** was fully supported by NMR analysis showing only one pattern for the calixarene scaffold and perimidine fragments, with a correct integral ratio. The proposed structure of **23** was further supported by MALDI-TOF mass spectrometry.

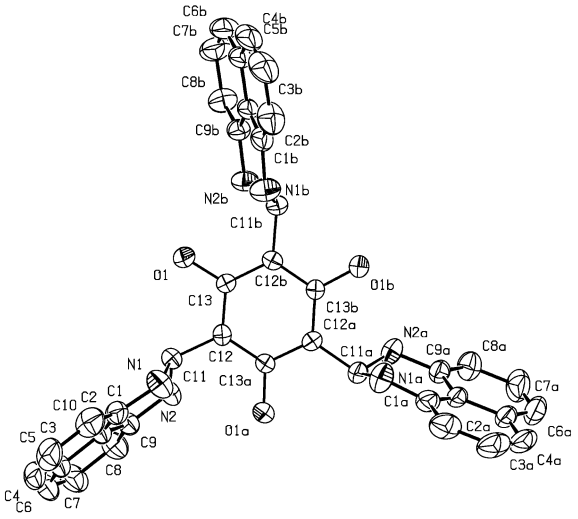
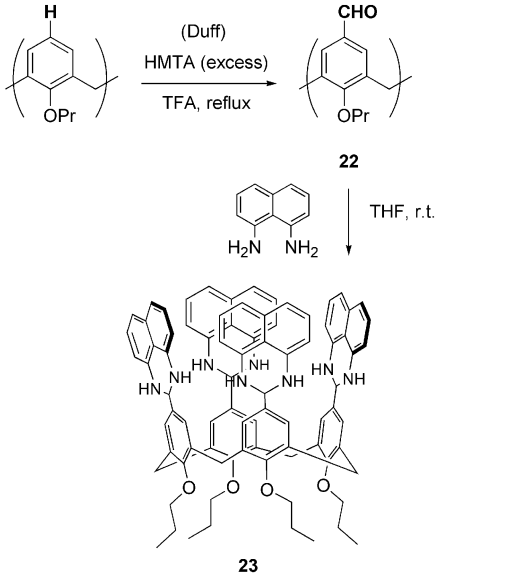


Figure 5. Molecular structure for **20b** determined by XRD with the adopted numbering scheme; co-crystallized solvent molecules, H-atoms and disorders are omitted for clarity.



Scheme 5. Use of calixarene **22** in the synthesis of tetrakis-perimidine **23**.

The calixarene structure **23** comprises a set of eight NH fragments that might be of use as hydrogen bond partners. Recently, deep cavity calix[4]arenes appended on the upper rime with four 1*H*-phenanthro[9,10-*d*]imidazol-2-yl groups were reported by de Mendoza and co-workers,[23] and they showed that the cavity of these systems can be stabilized by hydrogen bonding to suitable H-acceptors. Since these calixarene structures are potentially useful in molecular recognition processes and catalysis, compound **23** may form a good starting point for achieving these objectives.

Conclusions

Here we present a general synthetic method for 2-aryl-substituted 2,3-dihydro-1*H*-perimidines employing $Zn(OAc)_2{\cdot}2H_2O$ as catalyst. The procedure involves the use of salicylaldehydes equipped with various functionalities that may be useful in further synthesis. The developed protocol has also been proven to be successful for the synthesis of various bis(2,3-dihydro-1*H*-perimidines) such as **17** and **18**. In the case of tri-aldehyde **19** as reagent we have encountered an unusual product, viz. bis(2,3-dihydro-1*H*-perimidine) **21** that is believed to result from a cleavage of one aryl–C(perimidine) bond within **20b**. An alternative synthetic approach afforded both the mono- as well as tris-(2,3-dihydro-1*H*-perimidine) compounds **20a** and **20b**, and the isolation of the mono-, di- and tris(2,3-hydro-1*H*-perimidines) derived from **19** shows the synthetic versatility of this interesting scaffold. The preparation of tetrakis-perimidine **23** having a calix[4]arene support shows that multi-perimidines are easily accessed. This latter compound has an array of NH donors potentially useful to create a molecular receptor. Studies towards the use of this (**23**) and other multi-perimidinal compounds as hydrogen-bond donors in recognition events are in progress.

Experimental Section

General Information: All manipulations were done in air without any necessary precautions. All reagents [1,8-diaminonaphthalene, all salicylaldehydes, 2-hydroxyisophthalaldehyde, $Zn(OAc)_2{\cdot}2H_2O$ and solvents] were commercially purchased and used as received. The NMR spectra were recorded on a Bruker 400 MHz spectrometer, the mass spectral measurements and X-ray analyses were performed by the Research Support Unit from ICIQ, and the elemental analyses were obtained from the University of Santiago de Compostela (Spain), Unidad de Análisis Elemental.

2-(3,5-Di-*tert*-butyl-2-hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (2): To a solution of 1,8-diaminonaphthalene (0.59 g, 3.73 mmol) in MeOH (20 mL) was added a solution of 3,5-di-*tert*-butylsalicylaldehyde (1.08 g, 4.61 mmol) dissolved in MeOH (10 mL). Then solid $Zn(OAc)_2{\cdot}2H_2O$ (71.6 mg, 0.326 mmol, 8.7 mol-%) was added and the mixture stirred at room temperature for 18 h. In due course, a precipitate was noted which was collected by filtration after 18 h and dried. Off-white solid, yield 1.15 g (3.07 mmol, 82%). Crystals were obtained from hot CH_3CN and also from MeOH. Only in the latter case the crystals proved to be suitable for X-ray diffraction. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 9.09 (s, 1 H, OH), 7.36 (d, ^4J = 2.4 Hz, 1 H, ArH), 7.22–7.29 (m, 4 H, ArH), 7.18 (d, ^4J = 2.4 Hz, 1 H, ArH), 6.78 (d, ^3J = 7.0, ^4J = 1.2 Hz, 2 H, ArH), 6.20 (br. s, 2 H, NH), 5.75 (s, 1 H, Ar-CH), 1.42 [s, 9 H, C(CH$_3$)$_3$], 1.30 [s, 9 H, C(CH$_3$)$_3$] ppm. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]acetone): δ = 155.03, 143.56, 141.48, 137.00, 135.90, 127.72, 125.58, 125.28, 124.02, 118.70, 114.99, 107.57, 71.01, 35.78, 34.84, 32.05, 30.17 ppm. ESI(+)-MS (MeOH): *m*/*z* = 771.4 (2M + Na)$^+$ (calcd. 771.5), 397.2 [M + Na]$^+$ (calcd. 397.2), 375.2 [M + H]$^+$ (calcd. 375.2). $C_{25}H_{30}N_2O{\cdot}CH_3CN$ (415.57): calcd. C 78.03, H 8.00, N 10.11; found C 77.91, H 8.20, N 9.61.

Synthesis of 2 without Zn Catalyst: To a solution of 1,8-diaminonaphthalene (0.51 g, 3.22 mmol) in MeOH (20 mL) was added a solution of 3,5-di-*tert*-butylsalicylaldehyde (0.90 g, 3.84 mmol) dissolved in MeOH (10 mL). The mixture was stirred at room temperature for 18 h. In due course, a precipitate was noted which was collected by filtration after 18 h and dried; yield 0.78 g (2.08 mmol, 65%). Spectroscopic features are as reported above.

2-(3-*tert*-Butyl-2-hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (3): To a solution of 1,8-diaminonaphthalene (0.61 g, 3.86 mmol) in MeOH (20 mL) was added a solution of 3-*tert*-butylsalicylaldehyde (0.77 g, 4.32 mmol) dissolved in MeOH (10 mL). Then solid $Zn(OAc)_2{\cdot}2H_2O$ (72.7 mg, 0.331 mmol, 8.6 mol-%) was added and the mixture stirred at room temperature. The off-white solid that precipitated in due course was collected by filtration after 18 h and dried (fraction 1: 352.8 mg). A second fraction of product was obtained by concentration of the mother liquor to 15 mL (fraction 2: 588.3 mg); total yield 941.1 mg (2.96 mmol, 77%). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 9.32 (s, 1 H, OH), 7.22–7.30 (m, 5 H, ArH), 7.13 (d, ^3J = 7.4, ^4J = 1.5 Hz, 1 H, ArH), 6.79 (t, ^3J = 7.7 Hz, 1 H, ArH), 6.77 (d, ^3J = 7.0, ^4J = 1.2 Hz, 2 H, ArH), 6.21 (br. s, 2 H, NH), 5.48 (s, 1 H, Ar-CH), 1.41 [s, 9 H, C(CH$_3$)$_3$] ppm. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]acetone): δ = 157.50, 143.37, 137.76, 135.86, 128.91, 128.39, 127.72, 124.77, 119.42, 118.80, 114.98, 107.68, 70.62, 35.52, 30.06 ppm. ESI(–)-MS (MeOH): *m*/*z* = 317.2 (M – H)$^-$ (calcd. 317.2). $C_{21}H_{22}N_2O$ (318.41): calcd. C 79.21, H 6.96, N 8.80; found C 79.03, H 6.96, N 8.77.

2-(5-*tert*-Butyl-2-hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (4): To a solution of 1,8-diaminonaphthalene (0.47 g, 2.97 mmol) in MeOH (20 mL) was added a solution of 5-*tert*-butylsalicylaldehyde (0.62 g, 3.48 mmol) dissolved in MeOH (10 mL). Then solid $Zn(OAc)_2{\cdot}2H_2O$ (55.5 mg, 0.253 mmol, 8.5 mol-%) was added and the mixture stirred at room temperature. The off-white solid that precipitated in due course was collected by filtration after 18 h and dried (fraction 1: 527.3 mg). A second fraction of product was obtained by cooling the concentrated mother liquor (15 mL) to –25 °C (fraction 2: 207.9 mg); total yield 735.2 mg (2.31 mmol, 78%). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 8.54 (s, 1 H, OH), 7.44 (d, ^4J = 2.5 Hz, 1 H, ArH), 7.29 (d, ^3J = 8.5, ^4J = 2.6 Hz, 1 H, ArH), 7.22–7.26 (m, 2 H, ArH), 7.17 (d, ^3J = 8.3, ^4J = 0.9 Hz, 2 H, ArH), 6.79 (d, ^3J = 8.5 Hz, 1 H, ArH), 6.71 (d, ^3J = 7.3, ^4J = 1.0 Hz, 2 H, ArH), 6.05 (br. s, 2 H, NH), 5.59 (s, 1 H, Ar-CH), 1.28 [s, 9 H, C(CH$_3$)$_3$] ppm. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]-acetone): δ = 155.50, 143.80, 142.59, 135.92, 127.71, 127.69, 127.04, 124.95, 118.20, 116.86, 114.78, 107.04, 68.09, 34.66, 31.95 ppm. ESI(–)-MS (MeOH): *m*/*z* = 317.2 (M – H)$^-$ (calcd. 317.2). $C_{21}H_{22}N_2O$ (318.41): calcd. C 79.21, H 6.96, N 8.80; found C 78.94, H 6.96, N 8.78.

2-(3,5-Dichloro-2-hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (5): To a solution of 1,8-diaminonaphthalene (0.49 g, 3.10 mmol) in MeOH (35 mL) was added a solution of 3,5-dichlorosalicylaldehyde (0.75 g, 3.93 mmol) dissolved in MeOH (15 mL). Then solid $Zn(OAc)_2{\cdot}2H_2O$ (57.3 mg, 0.261 mmol, 8.4 mol-%) was added and the mixture stirred at room temperature. Instantaneously an off-white precipitate was formed which was collected after 30 min by filtration (fraction 1: 584.9 mg). A second fraction of the product was obtained by concentration of the mother liquor to 15 mL (fraction 2: 286.4 mg); total yield 871.3 mg (2.63 mmol, 85%). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 9.64 (br. s, 1 H, OH), 7.45 (d, ^4J = 2.4 Hz, 1 H, ArH), 7.40 (d, ^4J = 2.4 Hz, 1 H, ArH), 7.24–7.31 (m, 4 H, ArH), 6.75 (d, ^3J = 7.0, ^4J = 0.9 Hz, 2 H, ArH), 6.27 (br. s, 2 H, NH), 5.67 (s, 1 H, Ar-CH) ppm. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]DMSO): δ = 150.62, 142.25, 134.30, 130.89, 128.71, 127.40, 126.93, 123.11, 121.86, 116.25, 112.62, 105.33, 61.98 ppm. ESI(–)-MS (MeOH): *m*/*z* = 329.0 (M – H)$^-$ (calcd. 329.0). $C_{17}H_{12}Cl_2N_2O$ (331.20): calcd. C 61.65, H 3.65, N 8.46; found C 61.52, H 3.62, N 8.19.

2-(3-Bromo-2-hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (6): To a solution of 1,8-diaminonaphthalene (0.25 g, 1.58 mmol) in MeOH (15 mL) was added a solution of 3-bromo-salicylaldehyde (0.35 g, 1.74 mmol) dissolved in MeOH (5 mL). Then solid $Zn(OAc)_2{\cdot}2H_2O$ (33.5 mg, 0.153 mmol, 9.7 mol-%) was added and the mixture stirred at room temperature for 5 min. The precipitate that had formed was collected by filtration and dried. Off-white solid, yield 535.0 mg (1.57 mmol, 99%). ^{1}H NMR (400 MHz, [D$_6$]acetone + 10% [D$_6$]DMSO): δ = 7.54 (d, ^3J = 8.0, ^4J = 1.6 Hz, 1 H, ArH), 7.43 (d, ^3J = 7.6, ^4J = 1.5 Hz, 1 H, ArH), 7.22 (t, ^3J = 7.8 Hz, 2 H, ArH), 7.14 (d, ^3J = 8.3, ^4J = 0.9 Hz, 2 H, ArH), 6.85 (t, ^3J = 7.7 Hz, 1 H, ArH), 6.67 (d, ^3J = 7.3, ^4J = 0.9 Hz, 2 H, ArH), 5.58 (s, 1 H, Ar-CH) ppm. Both the NH as well as the OH protons are not observed. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]DMSO): δ = 152.70, 142.47, 134.31, 132.88, 128.68, 128.47, 126.90, 120.85, 116.46, 112.91, 110.79, 105.62, 64.02 ppm. ESI(–)-MS (MeOH): *m*/*z* = 339.0 (M – H)$^-$ (calcd. 339.0). $C_{17}H_{13}BrN_2O$ (341.20): calcd. C 59.84, H 3.84, N 8.21; found C 59.82, H 3.84, N 8.05.

2-(3-Allyl-2-hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (7): To a solution of 1,8-diaminonaphthalene (0.24 g, 1.52 mmol) in MeOH (15 mL) was added a solution of 3-allylsalicylaldehyde (0.34 g, 2.10 mmol) dissolved in MeOH (5 mL). Then solid $Zn(OAc)_2{\cdot}2H_2O$ (30.0 mg, 0.137 mmol, 9.0 mol-%) was added and the mixture stirred at room temperature for 18 h. Then the reaction mixture was concentrated to 10 mL upon which a white precipitate was formed. Filtration afforded 205.5 mg of product (fraction 1). Cooling of the mother liquor to –25 °C afforded a second fraction of microcrystalline product (142.5 mg). Total yield 348.0 mg (1.15 mmol, 76%). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 8.97 (s, 1 H, OH), 7.22–7.29 (m, 4 H, ArH), 7.15–7.17 (m, 2 H, ArH), 6.81 (t, ^3J = 7.5 Hz, 1 H, ArH), 6.75 (d, ^3J = 7.0, ^4J = 1.1 Hz, 2 H, ArH), 6.16 (br. s, 2 H, NH), 5.97–6.07 (m, 1 H, -CH$_2$-C(*H*)=CH$_2$), 5.49 (s, 1 H, Ar-CH), 5.09 [d, $^2J_{AB}$ = 17.1, ^4J = 1.9 Hz, 1 H, one of -CH$_2$-C(H)=C*H*$_2$], 5.01 [d, $^2J_{AB}$ = 10.0 Hz, 1 H, one of -CH$_2$-C(H)=C*H*$_2$], 3.39 [d, ^3J = 6.7 Hz, 2 H, -C*H*$_2$-C(H)=CH$_2$] ppm. ^{13}C{^{1}H} NMR (10 MHz, 70% [D$_6$]acetone + 30% [D$_6$]DMSO): δ = 155.13, 143.40, 137.58, 135.16, 130.71, 128.31, 127.97, 127.25, 125.50, 119.50, 117.35, 115.68, 114.08, 106.58, 67.39, 34.28 ppm. ESI(–)-MS (MeOH): *m*/*z* = 301.1 (M – H)$^-$ (calcd. 301.1). $C_{20}H_{18}N_2O$ (302.37): calcd. C 79.44, H 6.00, N 9.26; found C 79.13, H 5.89, N 9.07.

2-(2-Hydroxy-3,5-dinitrophenyl)-2,3-dihydro-1*H*-perimidine (8): To a solution of 1,8-diaminonaphthalene (0.24 g, 1.52 mmol) in MeOH (20 mL) was added a solution of 3,5-di-nitro-salicylaldehyde (0.34 g, 1.60 mmol) dissolved in MeOH (10 mL). Then solid $Zn(OAc)_2{\cdot}2H_2O$ (28.8 mg, 0.131 mmol, 8.6 mol-%) was added and the mixture stirred at room temperature. Instantaneously an orange-brown precipitate was formed which was collected after 18 h by filtration and dried; yield 441.8 mg (1.25 mmol, 83%). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 8.87 (d, ^4J = 2.8 Hz, 1 H, ArH), 8.67 (d, ^4J = 2.5 Hz, 1 H, ArH), 7.26 (t, ^3J = 7.8 Hz, 2 H, ArH), 7.19 (d, ^3J = 8.2 Hz, 2 H, ArH), 6.71 (d, ^3J = 7.2 Hz, 2 H, ArH), 6.04 (s, 1 H, Ar-CH), 2.93 (br., 2 H, NH) ppm. The OH was not observed. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]DMSO): δ = 157.85, 141.24, 136.86, 136.16, 134.23, 133.34, 127.56, 126.97, 121.72, 116.66, 112.52, 105.79, 60.57 ppm. ESI(–)-MS (MeOH): *m*/*z* = 351.1 (M – H)$^-$ (calcd. 351.1). $C_{17}H_{12}N_4O_5{\cdot}1/3H_2O$ (358.31): calcd. C 56.99, H 3.56, N 15.64; found C 57.10, H 3.33, N 15.44.

2-(5-Bromo-2-hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (9): To a solution of 1,8-diaminonaphthalene (0.41 g, 2.59 mmol) in MeOH (20 mL) was added a solution of 5-bromo-salicylaldehyde (0.53 g, 2.64 mmol) dissolved in MeOH (10 mL). Then solid $Zn(OAc)_2{\cdot}2H_2O$ (51.3 mg, 0.234 mmol, 9.0 mol-%) was added and the mixture stirred at room temperature. After 18 h, the mixture was concentrated to dryness and the residue triturated with MeOH (10 mL)

and filtered to yield 330.7 mg of a beige solid. To the mother liquor was added distilled water (10 mL) which caused the precipitation of a beige solid, which was collected by filtration and dried in vacuo (486.6 mg); total yield 817.3 mg (2.40 mmol, 92%). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.13 (br., 1 H, OH), 7.53 (d, ^4J = 2.5 Hz, 1 H, ArH), 7.33 (d, ^3J = 8.6, ^4J = 2.5 Hz, 1 H, ArH), 7.16 (t, ^3J = 7.8 Hz, 2 H, ArH), 7.00 (d, ^3J = 8.0 Hz, 2 H, ArH), 6.86 (d, ^3J = 8.6 Hz, 1 H, ArH), 6.60 (br., 2 H, NH), 6.52 (d, ^3J = 7.3 Hz, 2 H, ArH), 5.63 (s, 1 H, Ar-CH) ppm. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]DMSO): δ = 154.82, 142.87, 134.38, 131.59, 130.86, 129.88, 126.89, 117.71, 115.56, 112.36, 110.06, 104.65, 60.09 ppm. ESI(–)-MS (MeOH): *m*/*z* = 339.0 (M – H)$^-$ (calcd. 339.0), 681.1 (2M – H)$^-$ (calcd. 681.0). $C_{17}H_{13}BrN_2O\cdot1/3H_2O$ (347.21): calcd. C 58.81, H 3.97, N 8.07; found C 58.80, H 3.65, N 7.78.

2-(5-Carboxy-2-hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (10): To a solution of 1,8-diaminonaphthalene (0.21 g, 1.33 mmol) in MeOH (15 mL) was added a solution of 2-formyl-3-hydroxybenzoic acid (0.27 g, 1.60 mmol) dissolved in MeOH (5 mL). Then solid Zn(OAc)$_2\cdot$2H$_2$O (24.5 mg, 0.112 mmol, 8.4 mol-%) was added and the mixture stirred at room temperature. After 18 h the reaction mixture was concentrated to 10 mL and filtered to afford a beige solid; yield 349.3 mg (1.13 mmol, 85%). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 12.46 (br., 1 H, COOH), 10.60 (br., 1 H, OH), 8.14 (d, ^4J = 2.1 Hz, 1 H, ArH), 7.79 (d, ^3J = 8.5, ^4J = 2.2 Hz, 1 H, ArH), 7.15 (t, ^3J = 7.8 Hz, 2 H, ArH), 6.99 (d, ^3J = 7.7 Hz, 2 H, ArH), 6.95 (d, ^3J = 8.5 Hz, 1 H, ArH), 6.58 (br. s, 2 H, NH), 6.52 (d, ^3J = 7.1 Hz, 2 H, ArH), 5.66 (s, 1 H, Ar-CH) ppm. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]DMSO): δ = 167.76, 159.49, 143.23, 134.47, 131.05, 130.77, 127.10, 126.92, 121.91, 115.54, 115.33, 112.44, 104.65, 60.28 ppm. ESI(–)-MS (MeOH): *m*/*z* = 305.1 (M – H)$^-$ (calcd. 305.1). $C_{18}H_{14}N_2O_3\cdot3/4H_2O$ (319.83): calcd. C 67.60, H 4.88, N 8.76; found C 68.01, H 4.38, N 8.67.

2-(5-Allyl-2-hydroxy-3-methoxyphenyl)-2,3-dihydro-1*H*-perimidine (11): To a solution of 1,8-diaminonaphthalene (0.13 g, 0.822 mmol) in MeOH (5 mL) was added a solution of 3-methoxy-5-allylsalicylaldehyde (0.16 g, 0.832 mmol) dissolved in MeOH (5 mL). Then solid Zn(OAc)$_2\cdot$2H$_2$O (14.7 mg, 0.0670 mmol, 8.1 mol-%) was added and the mixture stirred at room temperature. After 18 h the reaction mixture was concentrated to 5 mL and cooled to –25 °C. The beige solid that precipitated was collected by filtration and dried; yield 181.1 mg (0.545 mmol, 66%). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.96 (br. s, 1 H, OH), 7.21 (t, ^3J = 7.8 Hz, 2 H, ArH), 7.11 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.00 (d, ^4J = 1.6 Hz, 1 H, ArH), 6.83 (d, ^4J = 1.8 Hz, 1 H, ArH), 6.65 (d, ^3J = 7.4 Hz, 2 H, ArH), 5.90–6.00 [m, 1 H, -CH$_2$-C(*H*)=CH$_2$], 5.86 (br. s, 2 H, NH), 5.78 (s, 1 H, Ar-CH), 5.09 [d, $^2J_{AB}$ = 17.0, ^4J = 1.6 Hz, 1 H, one of -CH$_2$-C(H)=C*H*$_2$], 5.00 [d, $^2J_{AB}$ = 10.2, ^4J = 1.0 Hz, 1 H, one of -CH$_2$-C(H)=C*H*$_2$], 3.86 (s, 3 H, OMe), 3.31 [d, ^3J = 6.7 Hz, 2 H, -C*H*$_2$-C(H)=CH$_2$] ppm. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]-DMSO): δ = 147.46, 143.44, 142.92, 137.91, 134.40, 129.96, 126.86, 126.75, 119.93, 115.55, 115.36, 112.49, 111.91, 104.53, 60.91, 55.99, 39.38 ppm. ESI(–)-MS (MeOH): *m*/*z* = 331.2 (M – H)$^-$ (calcd. 331.1). $C_{21}H_{20}N_2O_2\cdot1/3H_2O$ (338.41): calcd. C 74.53, H 6.16, N 8.28; found C 74.71, H 5.86, N 8.08.

2-(2-Hydroxy-3-methylphenyl)-2,3-dihydro-1*H*-perimidine (12): To a solution of 1,8-diaminonaphthalene (0.45 g, 2.84 mmol) in MeOH (30 mL) was added a solution of 3-methylsalicylaldehyde (0.43 g, 3.16 mmol) dissolved in MeOH (10 mL). Then solid Zn(OAc)$_2\cdot$2H$_2$O (60.1 mg, 0.274 mmol, 9.6 mol-%) was added and the mixture stirred at room temperature. After 18 h the reaction mixture was filtered to furnish 525.9 mg of a microcrystalline solid. Concentration of the mother liquor to 10 mL afforded a second fraction (96.9 mg) of product; total yield 622.8 mg (2.25 mmol, 79%). Crystals suitable for X-ray diffraction were obtained from MeOH. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 8.86 (s, 1 H, OH), 7.21–7.28 (m, 4 H, ArH), 7.14 (t, ^3J = 7.4 Hz, 2 H, ArH), 6.76 (t, ^3J = 7.5 Hz, 1 H, ArH), 6.74 (d, ^3J = 7.1, ^4J = 1.2 Hz, 2 H, ArH), 6.11 (br., 2 H, NH), 5.48 (s, 1 H, Ar-CH), 2.20 (s, 3 H, Me) ppm. ^{13}C{^{1}H} NMR (10 MHz, [D$_6$]acetone + 10% [D$_6$]DMSO): δ = 155.31, 143.02, 134.90, 131.19, 127.42, 126.84, 125.33, 124.56, 118.85, 117.11, 113.84, 106.26, 67.52, 15.49 ppm. ESI(–)-MS (MeOH): *m*/*z* = 275.1 (M – H)$^-$ (calcd. 275.1). $C_{18}H_{16}N_2O$ (276.33): calcd. C 78.24, H 5.84, N 10.14; found C 77.63, H 5.78, N 10.02.

2-(2-Hydroxyphenyl)-2,3-dihydro-1*H*-perimidine (13): To a solution of 1,8-diaminonaphthalene (0.66 g, 4.17 mmol) in MeOH (30 mL) was added a solution of salicylaldehyde (0.62 g, 5.08 mmol) dissolved in MeOH (15 mL). Then solid Zn(OAc)$_2\cdot$2H$_2$O (80.6 mg, 0.367 mmol, 8.8 mol-%) was added and the mixture stirred at room temperature. After 18 h the reaction mixture was concentrated to 15 mL and filtered to yield 488.1 mg of product. A second fraction (299.8 mg) was obtained from the mother liquor at room temp. in due course; total yield 787.9 mg (3.00 mmol, 72%). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.67 (s, 1 H, OH), 7.46 (d, ^3J = 7.6, ^4J = 1.6 Hz, 1 H, ArH), 7.17 (t, ^3J = 7.7, ^4J = 1.6 Hz, 1 H, ArH), 7.14 (t, ^3J = 7.8 Hz, 2 H, ArH), 6.98 (d, ^3J = 7.6 Hz, 2 H, ArH), 6.88 (d, ^3J = 8.1, ^4J = 0.7 Hz, 1 H, ArH), 6.83 (t, ^3J = 7.4 Hz, 1 H, ArH), 6.54 (br., 2 H, NH), 6.52 (d, ^3J = 7.4, ^4J = 0.5 Hz, 2 H, ArH), 5.65 (s, 1 H, Ar-CH) ppm. ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]-DMSO): δ = 155.45, 143.27, 134.41, 129.11, 128.41, 127.09, 126.83, 118.90, 115.44, 115.38, 112.50, 104.59, 60.89 ppm. ESI(+)-MS (MeOH): *m*/*z* = 263.1 [M + H]$^+$ (calcd. 263.1), 285.1 [M + Na]$^+$ (calcd. 285.1). $C_{17}H_{14}N_2O\cdot1/3H_2O$ (268.32): calcd. C 76.10, H 5.51, N 10.44; found C 76.44, H 5.20, N 10.22.

2-(2-Hydroxynaphthyl)-2,3-dihydro-1*H*-perimidine (14): To a solution of 1,8-diaminonaphthalene (0.43 g, 2.72 mmol) in MeOH (30 mL) was added a solution of 2-hydroxy-1-naphthaldehyde (0.49 g, 2.85 mmol) dissolved in warm MeOH (10 mL). Then solid Zn(OAc)$_2\cdot$2H$_2$O (49.5 mg, 0.226 mmol, 8.3 mol-%) was added and the mixture stirred at room temperature. After 18 h the reaction mixture was filtered to yield a first fraction (531.4 mg). Concentrated of the mother liquor to 10 mL and cooling to –25 °C afforded a second fraction (116.8 mg); total yield 648.2 mg (2.08 mmol, 76%). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 9.88 (s, 1 H, OH), 8.26 (d, ^3J = 8.3 Hz, 1 H, ArH), 7.86 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.47 (t, ^3J = 7.7, ^4J = 1.1 Hz, 1 H, ArH), 7.27–7.36 (m, 6 H, ArH), 7.16 (d, ^3J = 8.9 Hz, 1 H, ArH), 6.80 (d, ^3J = 6.8, ^4J = 1.2 Hz, 2 H, ArH), 6.46 (s, 1 H, Ar-CH), 6.24 (br., 2 H, NH) ppm. ^{13}C{^{1}H} NMR (10 MHz, [D$_6$]acetone + 20% [D$_6$]DMSO): δ = 156.16, 144.56, 135.64, 133.94, 131.22, 129.46, 128.89, 127.34, 126.58, 123.30, 119.49, 117.17, 117.10, 115.81, 114.24, 106.35, 62.53 ppm. ESI(–)-MS (MeOH): *m*/*z* = 311.1 (M – H)$^-$ (calcd. 311.1). $C_{21}H_{16}N_2O$ (312.36): calcd. C 80.75, H 5.16, N 8.97; found C 80.30, H 5.17, N 9.09.

1,3-Bis[2,3-dihydro-1*H*-perimidin-2-yl]phenol (17): To a solution of 1,8-diaminonaphthalene (269.3 mg, 1.70 mmol) in MeOH (15 mL) was added a solution of 2-hydroxyisophthalaldehyde (121.5 mg, 0.809 mmol) dissolved in MeOH (5 mL). Then solid Zn(OAc)$_2\cdot$2H$_2$O (18.4 mg, 0.0838 mmol, 10.4 mol-%) was added and the mixture stirred at room temperature. After 18 h the reaction mixture was filtered to yield a beige solid (327.2 mg, 0.76 mmol, 94%). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.62 (s, 1 H, OH), 7.41 (d, ^3J = 7.6 Hz, 2 H, ArH), 7.19 (t, ^3J = 7.8 Hz, 4 H, ArH), 7.05 (d, ^3J = 7.8 Hz, 4 H, ArH), 6.88 (t, ^3J = 7.6 Hz, 1 H, ArH), 6.71 (br., 4 H, NH), 6.60 (d, ^3J = 7.3 Hz, 4 H, ArH), 5.65 (s, 2 H, Ar-CH)

ppm. $^{13}C\{^1H\}$ NMR (10 MHz, [D$_6$]acetone + 20% [D$_6$]DMSO): δ = 156.02, 143.41, 135.55, 129.61, 127.97, 127.55, 119.53, 117.30, 114.10, 106.46, 65.01 ppm. ESI(–)-MS (MeOH): *m/z* = 429.2 (M – H)$^-$ (calcd. 429.2), 859.4 (2M – H)$^-$ (calcd. 859.4). $C_{28}H_{22}N_4O\cdot 2/3H_2O$ (442.51): calcd. C 76.00, H 5.31, N 12.66; found C 75.81, H 5.30, N 12.45.

Bis(2,3-dihydro-1*H*-perimidine) Compound 18: To a solution of 1,8-diaminonaphthalene (59.7 mg, 0.377 mmol) in MeOH (10 mL) was added a solution of dialdehyde **16**[14] (56.3 mg, 0.158 mmol) dissolved in THF (20 mL). Then solid $Zn(OAc)_2\cdot 2H_2O$ (8.9 mg, 0.0405 mmol, 8.9 mol-%) was added and the mixture stirred at room temperature for 1 h. The reaction mixture was concentrated to dryness and triturated with MeOH (10 mL) to afford, after filtration, a beige solid (85.0 mg, 0.133 mmol, 85%). ^1H NMR (400 MHz, [D$_6$]acetone + 30% [D$_6$]DMSO): δ = 8.74 (br. s, 2 H, OH), 7.17 (t, ^3J = 7.8 Hz, 4 H, ArH), 7.04 (d, ^3J = 8.2 Hz, 4 H, ArH), 7.02 (s, 2 H, ArH), 6.82 (s, 2 H, ArH), 6.60 (d, ^3J = 7.3 Hz, 4 H, ArH), 6.25 (br., 4 H, NH), 5.74 (s, 2 H, Ar-CH), 5.65 (m, 2 H, -CH=CH-), 3.77 (br. s, 6 H, OMe), 3.29 (m, 4 H, Ar-CH$_2$) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, [D$_6$]DMSO): δ = 147.42, 143.51, 142.82, 134.40, 130.72, 130.21, 126.80, 126.76, 119.75, 115.35, 112.51, 111.80, 104.52, 60.86, 55.88, 38.12 ppm. ESI(–)-MS (MeOH): *m/z* = 635.3 (M – H)$^-$ (calcd. 635.3). $C_{40}H_{36}N_4O_4\cdot H_2O$ (654.75): calcd. C 73.38, H 5.85, N 8.56; found C 73.08, H 5.53, N 8.32.

2,3-Dihydro-1*H*-perimidine Derivative 20a and Tris(2,3-dihydro-1*H*-perimidine) Compound 20b: To a solution of 1,8-diaminonaphthalene (223.5 mg, 1.41 mmol) in MeOH (30 mL) was added a hot solution of trialdehyde **19**[15] (90.4 mg, 0.430 mmol) in DMSO (5 mL). Shortly hereafter a suspension was obtained which was filtered to yield **20a** (92.1 mg, 0.262 mmol, 61% based on **19**). The mother liquor was further stirred at room temp. and in due course a second precipitate was obtained. This was collected by filtration and analyzed as **20b** (38.5 mg, 0.0610 mmol, 14% based on **19**).

Data for 20a: ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 9.88 (s, 2 H, CHO), 7.57 (s, 1 H, OH), 7.14 (t, ^3J = 7.8 Hz, 2 H, ArH), 7.07 (d, ^3J = 8.2 Hz, 2 H, ArH), 6.46 (d, ^3J = 7.2 Hz, 2 H, ArH), 5.61 (br. s, 1 H, Ar-CH) ppm. The other two OH and NH protons were not observed. $^{13}C\{^1H\}$ NMR (100 MHz, [D$_6$]DMSO): δ = 190.75, 170.85, 147.32, 138.34, 135.04, 128.45, 122.49, 119.66, 107.73, 104.81, 92.44, 40.42 ppm. ESI(–)-MS (MeOH): *m/z* = 349.1 (M – H)$^-$ (calcd. 349.1). HRMS (ESI-, MeOH): calcd. for $C_{19}H_{13}N_2O_5$: 349.0824; found 349.0822.

Data for 20b: ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 10.15 (s, 3 H, OH), 7.25 (t, ^3J = 7.8 Hz, 6 H, ArH), 7.18 (d, ^3J = 7.6 Hz, 6 H, ArH), 6.76 (d, ^3J = 6.9 Hz, 6 H, ArH), 6.66 (s, 6 H, NH), 5.86 (s, 3 H, Ar-CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, [D$_6$]DMSO): δ = 157.63, 142.53, 134.22, 126.81, 117.36, 113.35, 106.99, 103.15, 60.52 ppm. ESI(–)-MS (MeOH): *m/z* = 629.3 (M – H)$^-$ (calcd. 629.3). HRMS (ESI-, MeOH): calcd. for $C_{39}H_{29}N_6O_3$: 629.2301; found 629.2297. $C_{39}H_{30}N_6O_3\cdot H_2O$ (648.71): calcd. C 72.21, H 4.97, N 12.95; found C 72.28, H 4.77, N 12.83.

Bis(2,3-dihydro-1*H*-perimidine) Compound 21: To a solution of 1,8-diaminonaphthalene (211.6 mg, 1.34 mmol) in MeOH (20 mL) was added a suspension of trialdehyde **19**[14] (88.8 mg, 0.423 mmol) in MeOH (20 mL). Then solid $Zn(OAc)_2\cdot 2H_2O$ (28.0 mg, 0.128 mmol) was added and the mixture shortly brought to reflux. After cooling to room temp., the mixture was stirred for 18 h and filtered to yield a beige solid (64.2 mg, 0.139 mmol, 33% based on **19**). Subsequent fractions contained mixtures of products. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 9.84 (s, 1 H, OH), 9.57 (s, 2 H, OH), 7.22 (t, ^3J = 7.8 Hz, 4 H, ArH), 7.13 (d, ^3J = 7.7 Hz, 4 H, ArH), 6.70 (d, ^3J = 7.0 Hz, 4 H, ArH), 6.65 (s, 4 H, NH), 5.98 (s, 1 H, Ar-H), 5.76 (s, 2 H, Ar-CH) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, [D$_6$]DMSO): δ = 158.28, 157.50, 142.94, 134.26, 126.72, 116.98, 113.37, 106.54, 102.86, 94.95, 60.46 ppm. ESI(–)-MS (MeOH): *m/z* = 461.2 (M – H)$^-$ (calcd. 461.2). HRMS (ESI-, MeOH): calcd. for $C_{28}H_{21}N_4O_3$: 461.1614; found 461.1626.

Tetrakis(2,3-dihydro-1*H*-perimidine) Compound 23: To a solution of tetraformylcalix[4]arene **22**[22] (95.7 mg, 0.136 mmol) and 1,8-diaminonaphthalene (180.6 mg, 1.14 mmol) was added solid $Zn(OAc)_2\cdot 2H_2O$ (20.0 mg, 0.0911 mmol). The reaction mixture was stirred for 18 h after which ^1H NMR ($CDCl_3$) confirmed a full conversion. Concentration in vacuo and trituration with MeOH followed by filtration afforded an off-white solid (95.3 mg, 0.0753 mmol, 55%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.13 (s, 8 H, ArH), 7.08 (d, ^3J = 6.3 Hz, 8 H, ArH), 6.98 (t, ^3J = 6.2 Hz, 8 H, ArH), 6.17 (d, ^3J = 5.8 Hz, 8 H, ArH), 5.22 (s, 4 H, Ar-CH), 4.59 (d, ^2J = 10.5 Hz, 4 H, CH_AH$_X$), 4.24 (br. s, 8 H, NH$_2$), 3.98 (t, ^3J = 6.0 Hz, 8 H, OCH_2CH$_2$CH$_3$), 3.34 (d, ^2J = 10.5 Hz, 4 H, CH$_A H_X$), 2.07 (m, 8 H, OCH$_2$CH_2CH$_3$), 1.10 (t, ^3J = 6.0 Hz, 12 H, OCH$_2$CH$_2$CH_3) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 157.41, 141.98, 135.57, 134.91, 134.37, 127.77, 126.79, 177.99, 113.59, 106.21, 77.45, 68.02, 31.20, 23.51, 10.54 ppm. MALBIS(+)-MS (dctb): *m/z* = 1264.7 (M)$^+$ (calcd. 1264.6). HRMS (MALDI+, dctb): calcd. for [M]$^+$ ($C_{84}H_{80}N_8O_4$): 1264.6297; found 1264.6297.

CCDC-765488 (for **2**), -765489 (for **2b**), -765882 (for **12**), -765883 (for **17**) and -776256 (for **20b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see also the footnote on the first page of this article): Selected copies of NMR and MS spectra.

Acknowledgments

We thank the Institute of Chemical Research of Catalonia (ICIQ), the Catalan Institute for Research and Advanced Studies (ICREA) and the Ministereo de Ciencia e Innovación (MICINN) (project CTQ-2008–02050/BQU), and Consolider Ingenio 2010 (project CSD2006-0003) for support. Dr. Noemí Cabello and Alba González Arandilla are thanked for the MS measurements.

[1] a) K. Undheim, C. Benneche, in: *Comprehensive Heterocyclic Chemistry II* (Eds.: A. R. Katritzky, C. W. Rees, E. F. Scriven), Pergamon, Oxford, **1996**; b) A. F. Pozharskii, V. V. Dalnikovskaya, *Russ. Chem. Rev.* **1981**, *50*, 816–835.

[2] a) J. M. Herbert, P. D. Woodgate, W. A. Denny, *J. Med. Chem.* **1987**, *30*, 2081–2086; b) X. Bu, L. W. Deady, G. J. Finlay, B. C. Baguley, W. A. Denny, *J. Med. Chem.* **2001**, *44*, 2004–2014; c) D. R. Luthin, A. K. Rabinovich, D. R. Bhumralkar, K. L. Youngblood, R. A. Bychowski, D. S. Dhanoa, J. M. May, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 765–770.

[3] For some examples see: a) V. Paragamian, M. B. Baker, B. M. Puma, J. Reale Jr., *J. Heterocycl. Chem.* **1968**, *5*, 591–597; b) A. Shaabani, A. Maleki, *Chem. Pharm. Bull.* **2008**, *56*, 79–81; c) J. B. Hendrickson, M. S. Hussoin, *J. Org. Chem.* **1987**, *52*, 4137–4139; d) J. J. Vanden Eynde, F. Delfosse, A. Mayence, Y. V. Haverbeke, *Tetrahedron* **1995**, *51*, 5813–5818; e) V. A. Ozeryanskii, E. A. Filatova, V. I. Sorokin, A. F. Pozharskii, *Russ. Chem. Bull.* **2001**, *50*, 846–853.

[4] a) A. Maquestiau, L. Berte, A. Mayence, L. Vanden Eynd, *Synth. Commun.* **1991**, *21*, 2171–2180; b) A. Mobinikhaledi, P. J. Steel, *Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry* **2009**, *39*, 133–135; c) S.-L. Zhang, J.-M. Zhang, *Chin. J. Chem.* **2008**, *26*, 185–189; d) J. Zhang, S. Zhang, *Synth. Commun.* **2007**, *37*, 2615–2614.

[5] a) L. W. Deady, T. Rodemann, *J. Heterocycl. Chem.* **1998**, *35*, 1417–1419; b) N. Morita, J. I. Dickstein, S. I. Miller, *J. Chem. Soc. Perkin Trans. 1* **1979**, *1*, 2103–2106; c) I. Yavari, F. Jahanimoghaddam, F. Adib, H. R. Bijanzadeh, *Tetrahedron* **2002**, *58*, 6901–6906; d) I. A. S. Smellie, A. Fromm, R. M. Paton, *Tetrahedron Lett.* **2009**, *50*, 4104–4106; e) A. Mobinikhaledi, N. Foroughifar, N. Basaki, *Turk. J. Chem.* **2009**, *33*, 555–560; f) M. Tajbakhsh, M. M. Heravi, B. Mohajerani, A. Ahmadi, *J. Mol. Catal. A* **2006**, *247*, 213–215.

[6] I. G. Jung, S. U. Son, K. H. Park, K.-C. Chung, J. W. Lee, Y. K. Chung, *Organometallics* **2003**, *22*, 4715–4720.

[7] S.-Y. Hsueh, K.-W. Cheng, C.-C. Lai, S.-H. Chiu, *Angew. Chem. Int. Ed.* **2008**, *47*, 4436–4439.

[8] M. Sauer, C. Yeung, J. H. Chong, B. O. Patrick, M. J. MacLachlan, *J. Org. Chem.* **2006**, *71*, 775–788.

[9] a) S. J. Wezenberg, A. W. Kleij, *Angew. Chem. Int. Ed.* **2008**, *47*, 2354–2364; b) A. W. Kleij, *Chem. Eur. J.* **2008**, *14*, 10520–10529.

[10] a) A. W. Kleij, *Dalton Trans.* **2009**, 4635–4639; b) S. J. Wezenberg, E. C. Escudero-Adán, J. Benet-Buchholz, A. W. Kleij, *Inorg. Chem.* **2008**, *47*, 2925–2927; c) S. J. Wezenberg, E. C. Escudero-Adán, J. Benet-Buchholz, A. W. Kleij, *Chem. Eur. J.* **2009**, *15*, 5695–5700.

[11] a) E. Escudero-Adán, J. Benet-Buchholz, A. W. Kleij, *Chem. Eur. J.* **2009**, *15*, 4233–4237; b) M. M. Belmonte, E. C. Escudero-Adán, J. Benet-Buchholz, A. W. Kleij, *Eur. J. Inorg. Chem.* **2009**, 5307–5318.

[12] Software used: CAChe 7.5 WS (MM2 level).

[13] a) A. W. Kleij, *Eur. J. Inorg. Chem.* **2009**, 193–205; b) A. W. Kleij, D. M. Tooke, M. Lutz, A. L. Spek, J. N. H. Reek, *Eur. J. Inorg. Chem.* **2005**, 4626–4634; c) A. W. Kleij, D. M. Tooke, M. Kuil, M. Lutz, A. L. Spek, J. N. H. Reek, *Chem. Eur. J.* **2005**, *11*, 4743–4750.

[14] Crystallographic data for **2**: $C_{25}H_{30}N_2O$, M = 374.51, monoclinic, $P2_1/c$, a = 18.854(2) Å, b = 11.8258(12) Å, c = 9.5335(10) Å, β = 96.995(3)°, V = 2109.8(4) Å^3, Z = 4, ρ(calcd.)= 1.179 g/cm^3, F(000) = 808, μ = 0.072 mm^{-1}, crystal size 0.02 × 0.03 × 0.40 mm, T = 100(2) K, θmin–max = 2.8–29.8°, total/unique data = 27695/5907, R(int) = 0.096, data/restraints/parameters = 5907/0/268, GOF = 1.029, R_1/wR_2 = 0.0581/0.1362 [$I > 2\sigma(I)$], R_1/wR_2 = 0.1036/0.1576 (all data), min./max. residual density = –0.268/0.373 e/Å^3. Crystallographic data for **2b**: $C_{45.80}H_{62}N_2O_4S_{0.20}$, M = 710.99, triclinic, $P\bar{1}$ (no. 2), a = 6.3817(10) Å, b = 10.5794(17) Å, c = 16.884(4) Å, α = 103.763(15)°, β = 96.927(16)°, γ = 107.213(11)°, V = 1034.9(4) Å^3, Z = 1, ρ(calcd.) = 1.141 g/cm^3, F(000) = 386, μ = 0.081 mm^{-1}, crystal size 0.01 × 0.05 × 0.30 mm, T = 100(2) K, θmin–max = 1.3–28.7°, total/unique data = 17513/5212, R(int) = 0.065, data/restraints/parameters = 5212/22/252, GOF = 1.051, R_1/wR_2 = 0.0594/0.1669 [$I > 2\sigma(I)$], R_1/wR_2 = 0.1130/0.2105 (all data), min./max. residual density = –0.362/0.748 e/Å^3. Crystallographic Data for **12**: $C_{18}H_{16}N_2O$, M = 276.33, orthorhombic, $Pca2_1$ (no. 29), a = 12.4883(12) Å, b = 12.0727(11) Å, c = 9.1089(9) Å, V = 1373.3(2) Å^3, Z = 4, ρ(calcd.) = 1.337 g/cm^3, F(000) = 584, μ = 0.084 mm^{-1}, crystal size 0.01 × 0.20 × 0.30 mm, T = 100(2) K, θmin–max = 3.2–36.5°, total/unique data = 15140/5091, R(int) = 0.033, data/restraints/parameters = 5091/1/198, GOF = 1.038, R_1/wR_2 = 0.0489/0.1188 [$I > 2\sigma(I)$], R_1/wR_2 = 0.0633/0.1282 (all data), min./max. residual density = –0.234/0.622 e/Å^3. Crystallographic data for **17**: $4(C_{28}H_{22}N_4O)\cdot0.5(C_2H_6O_2)\cdot3(CH_3O)\cdot4.08(H)$, M = 1850.23, monoclinic, $P2_1/c$ (no. 14), a = 14.5809(4) Å, b = 7.4563(2) Å, c = 21.2371(7) Å, β = 104.455(1)°, V = 2235.80(11) Å^3, Z = 1, ρ(calcd.) = 1.374 g/cm^3, F(000) = 976, μ = 0.088 mm^{-1}, crystal size 0.20 × 0.40 × 0.40 mm, T = 100(2) K, θmin–max = 3.1–36.4°, total/unique data = 48152/10917, R(int) = 0.031, data/restraints/parameters = 10917/15/327, GOF = 1.064, R_1/wR_2 = 0.0565/0.1698 [$I > 2\sigma(I)$], R_1/wR_2 = 0.0710/0.1840 (all data), min./max. residual density = –1.115/0.687 e/Å^3.

[15] We used the 1,8-diaminonaphthalene from Aldrich (99% purity).

[16] Note that compounds **13** and **14** have been reported previously. Nonetheless the synthesis and analysis data for these compounds have been included for completeness. See for more details: a) O. Maloshitskaya, J. Sinkkonen, V. Ovcharenko, K. N. Zelenin, K. Pihlaja, *Tetrahedron* **2004**, *60*, 6913–6921; b) M. Zendehdel, A. Mobinikhaledi, A. Asgari, *J. Inclusion Phenom. Macrocyclic Chem.* **2008**, *60*, 353–357; see also ref.[4b]

[17] R. M. Haak, M. M. Belmonte, E. C. Escudero-Adán, J. Benet-Buchholz, A. W. Kleij, *Dalton Trans.* **2010**, *39*, 593–602.

[18] The structure for **17** closely resembles the one reported by Chung et al., which does not comprise the phenol function; see ref.[6]

[19] J. H. Chong, M. Sauer, B. O. Patrick, M. J. MacLachlan, *Org. Lett.* **2003**, *5*, 3823–3826.

[20] This result proved to be reproducible and was checked in a separate synthesis. NMR and MS data were identical in this latter preparation.

[21] The structure of **20b** was determined by XRD but the crystal data proved to be poor (R1 = 0.137) and the structure could not be solved satisfactorily. Despite this quality, the proposed connectivity pattern could be unequivocally established. The crystallographic data has been deposited at the CCDC with reference number CCDC-776256.

[22] See: A. Dondoni, A. Marra, M.-C. Scherrmann, A. Casnati, F. Sansone, R. Ungaro, *Chem. Eur. J.* **1997**, *3*, 1774–1782.

[23] E. Botana, K. Nalttinen, P. Prados, K. Rissanen, J. de Mendoza, *Org. Lett.* **2004**, *6*, 1091–1094.

Received: May 10, 2010
Published Online: July 15, 2010
After publication in Early View, the name of an additional co-author has been included.

