RSC Advances

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

Journal Name

COMMUNICATION

New approach for post-functionalization of *meso*-formylporphyrins

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Kirill P. Birin[a,*], Yulia G. Gorbunova[a,b], Aslan Yu. Tsivadze[a,b]

A strategy for the post-functionalization of readily accessible *meso*-formylporphyrins affording *meso*-(2-imidazolyl)-porphyrins, containing substituents at the 4,5-positions of the imidazole fragment is developed. The reaction of 5-formyl-10,20-diarylporphyrins with phenanthrene- or phenanthroline-5,6-dione and ammonium acetate provides 5-(areneimidazol-2-yl)-10,20-diarylporphyrins with high yields. This methodology is used to prepare a set of representatives of this new type of substituted porphyrins. The distribution of the frontier orbitals of this class of compounds is evaluated by means of DFT calculations.

Post-modification of *meso*-arylporphyrins,[1-4] which are readily available on the gram scale, provides access to variety of functionalized compounds with multiple applications. Introduction of different substituents to porphyrin *meso*- and β-positions allows to modify the chemical, physicochemical and coordination properties of the resulting compounds, that determines their wide applications as molecular tectons for supramolecular chemistry, [5-9] in solar cells development[10], catalysis[11,12], molecular electronics[13], photovoltaics[14], molecular recognition[15-17], etc. Among various approaches for modification of porphyrin molecules, the application of Vilsmeier-Haak reaction occupies an outstanding position[18]. Formyl derivatives can be prepared efficiently from various metal porphyrins,[19] but examples of further employment of this functional group is limited because of its low reactivity. Interaction of formylporphyrins with phosphorus ylides,[20-22] the reduction of the carbonyl group,[23] formation of acetales,[24] interaction with Grignard reagents[22] and condensations with CH-acidic compounds[25,26] are described. In contrast, other reactions, typical for aromatic aldehydes, proceed with formylporphyrins notably different. For example, while oximes can be prepared from formylporphyrins by interaction with hydroxylamine, the related interaction with amines produces Schiff-bases with vanishing yields and the starting material is recovered.[27] The examples of chemical transformations of the formylporphyrins, in which the carbonyl group acts as a part of the constructed functional center of the molecule are virtually unknown. The application of formylporphyrins as carbonyl components in the heterocyclic condensations is limited to examples of interaction of β-formylporphyrin with acetylarenes under Kroehnke reaction conditions, providing substituted β-pyridylporphyrins in mixture with corresponding chalcones and substituted benzoporphyrins.[28]

The interaction of formylporphyrins with α-diketones providing 2,4,5-substituted imidazoles has not been described by now either for β- or for *meso*-formylporphyrins. Nevertheless this type of junction of the porphyrin and peripheral fragment is attractive for design of semi-rigid polytopic systems. The rigidity of the molecule along its axis with preservation of rotational lability of the fragments allows design of self-adapting molecular tectons for supramolecular chemistry. Moreover, the absence of the conjugation of the fragments, bridged by imidazole moiety, diminishes their mutual influence, allowing straightforward design of polytopic systems with desired properties. The balance between rigidity and conformational lability of the bridging fragment allows precise tuning of the electronic structure and self-association of the polytopic tectons under investigation. The introduction of heterocyclic fragment to the porphyrin allows to modify the coordination and physical-chemical properties of the obtained conjugate.

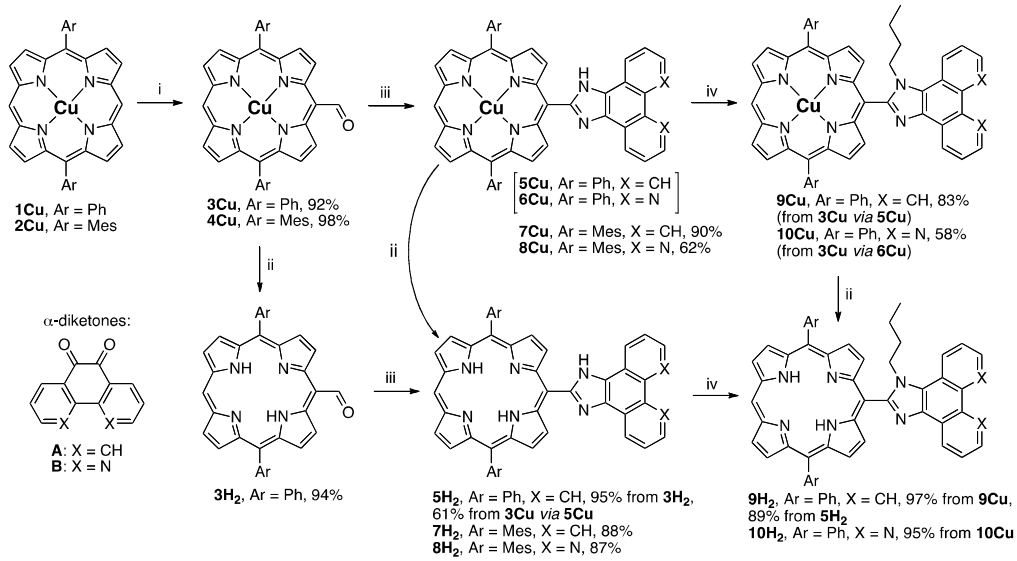
Meso-(2-imidazolyl)-porphyrins up to date were prepared from 2-formylimidazole or *meso*-(2-imidazolyl)-dipyrromethane[29-31] and consequently did not contain substituents at the 4,5-positions of the heterocycle. The only exception is the preparation of porphyrins, containing benzimidazol-2-yl substituents,[32] from corresponding 2-formyl-benzimidazole. Various *meso*-(2-imidazolyl)-porphyrins were found to be promising compounds for catalityc oxidation reactions,[30,33,34] self-assembly of supramolecular architectures,[35-39] two-photon absorption in organic media and in water,[35,37] non-linear optics,[38] intramolecular energy transfer[39] and modeling of photosynthetic "special pair".[31,40]

With this diversity of possible applications for functionalized *meso*-(2-imidazolyl)-porphyrins we focused on development of the general synthetic strategy towards *meso*-(2-imidazolyl)-porphyrins, containing substituents at the 4,5-positions of the imidazole

[a] A.N. Frumkin Institute of Physical Chemistry and Electrochemistry RAS, Leninsky prosp. 31, bldg. 4, Moscow, 119071, Russia. kirill.birin@gmail.com
[b] N.S. Kurnakov Institute of General and Inorganic Chemistry RAS, Leninsky prosp. 31, Moscow, 119991, Russia. yulia@igic.ras.ru
Electronic Supplementary Information (ESI) available: Synthetic procedures and all spectral data. See DOI: 10.1039/x0xx00000x

fragment. In present work we report efficient approach for condensation of *meso*-formylporphyrins and aromatic α-diketones with formation of imidazole heterocyclic bridge between the fragments.

Two diarylporphyrins, containing phenyl or mesityl groups at 5,15-positions and two aromatic α-diketones – phenathrene-5,6-dione and 1,10-phenanthroline-5,6-dione were selected for investigation. The application of two different diketones reveals their reactivity in the interaction under discussion, while two different types of *meso*-substituents of the porphyrin macrocycle allow to evaluate the influence of their bulkiness onto the reaction pathway. The studied sequence of chemical transformations is shown at **Scheme 1**. The formylation of copper(II) porphyrins **1Cu** and **2Cu** was performed similar to published procedure[20] with minor modification. The preparation of the Vilsmeier reagent in dichloroethane solution and decrease of Vilsmeier reagent/porphyrin ratio allowed to increase the yield of corresponding formylporphyrins **3Cu**-**4Cu** up to 98%. The demetalation of **3Cu** under acidic conditions[20] provided $\mathbf{3H_2}$ nearly quantitatively. The obtained *meso*-formylporphyrins $\mathbf{3H_2}$, **3Cu**, **4Cu** were further involved into interaction with α–diketones **A** and **B**.



Scheme 1. Reaction sequence and designation of the studied compounds (Mes = mesityl); i = DMF, $POCl_3$ in DCE, 60°C, 6h; ii = TFA, H_2SO_4 (7/1), r.t., 15 min; iii = α-diketone, NH_4OAc in $CHCl_3$, AcOH, reflux, 3 or 5 days; iv = BuBr, K_2CO_3 in DMF, 100°C, 24h.

While equimolar interaction of diketones **A** or **B** with typical aromatic aldehydes proceeds smoothly and provides high to quantitative yields,[41-44] in present case we encountered several peculiarities. Thus, the interaction of formylporphyrin **3Cu** with equimolar amount of diketone **A** and 10-fold excess of NH_4OAc upon reflux in $CHCl_3$/AcOH mixture did not provide complete conversion of the starting material, as revealed by TLC and MALDI-TOF MS. The stepwise addition of diketone **A** (3 equiv) and NH_4OAc (30 equiv) is unavoidable to achieve complete conversion of **3Cu** to condensation product upon reflux for 3 days. It is noteworthy, that simultaneous application of 3 equivalents of α-diketone **A** and 30-fold excess of NH_4OAc does not allow complete conversion of **3Cu**. We attribute this peculiarity to self-condensation of α-diketones under reaction conditions, which occurs faster than the condensation with *meso*-formylporphyrin. The treatment of **A** with 10-fold excess of NH_4OAc upon reflux in $CHCl_3$/AcOH mixture results in formation of inattributable aromatic compounds, while the starting α-diketone could hardly be detected in the mixture after 24 hours of reflux (Figures S1-S3). Eventually, formation of **5Cu** and **7Cu** requires 3-fold excess of **A**, while 6-fold excess of **B** is required for preparation of **6Cu** and **8Cu**. The interaction of $\mathbf{3H_2}$ with **A** under found conditions resulted in formation of corresponding free-base porphyrin $\mathbf{5H_2}$ with 95% yield, but the reaction rate was lower compared to copper complexes and reflux for 5 days required to achieve complete conversion.

Meso-imidazolylporphyrins, containing phenyl groups in 10,20-positions (**5Cu**, **6Cu**), are found to be virtually insoluble in organic media, even in $CHCl_3$, CH_2Cl_2 and their mixtures with MeOH, that makes their purification impossible. $\mathbf{5H_2}$ demonstrates slightly increased solubility, allowing its characterization by UV-Vis and NMR, but it is also inapplicable for chromatography. In contrast, mesityl-substituted analogues are sufficiently soluble in common organic solvents and can be easily purified by column chromatography. In order to solubilize $\mathbf{5H_2}$, **5Cu**, **6Cu** we have determined the conditions for their alkylation. These compounds were treated with 1-bromobutane in DMF, acetone and acetonitrile in the presence of K_2CO_3. It was found, that alkylation proceeds smoothly only in DMF at 60°C and its yield is estimated to be nearly quantitive since the overall yields of **9Cu** and **10Cu** for two stages is quite similar to the yields of **7Cu** and **8Cu**.

The prepared *meso*-(2-imidazolyl)-porphyrins **5Cu, 7Cu**-**10Cu** are found to be sufficiently stable to survive the treatment with mixture of trifluoroacetic and sulfuric acids (10/1) providing corresponding free-base porphyrins with high yields. A mild demetalation procedure with sulfuric acid in CH_2Cl_2 is described,[45] but its application did not allow conversion of metal complexes to free-

base porphyrins. Moreover, it should be mentioned, that porphyrins, containing N-alkylimidazole fragment are more stable upon acidic demetalation, than non-alkylated ones, that is revealed by higher yields of **9H$_2$** (97%) and **10H$_2$** (95%), compared to **7H$_2$** (88%) and **8H$_2$** (87%).

All the synthesized compounds were sufficiently characterized by UV-Vis and MALDI-TOF MS, while the structures of the free-base porphyrins were additionally proved by NMR (Figures S4 – S30). The UV-Vis spectroscopy reveals the sets of absorption bands, typical for 10,20-diarylporphyrins. Additional low-intensity absorptions are present in the 250-350 nm region and it can be attributed to areneimidazole transitions (Figures S23 – S30). The expected peaks are observed in the mass-spectra, demonstrating the well-defined isotopic pattern (Figures S13 – S21).

The analysis of NMR spectra in $CDCl_3$ revealed that behavior of areneimidazole NH-protons depends on the origin of the appended aromatic fragment (**Figure 1**). The interpretation of the spectra was based on the intensity and multiplicity of the signals as well as ^{1}H-^{1}H correlation pattern (Figures S6, S8, S12). In the case of imidazophenanthrene-appended porphyrins **7H$_2$** resolved sets of multiplets are observed, corresponding to phenanthrene protons and NH-proton. The observed set reveals the localization of NH-proton and dissymmetry of the phenanthrene fragment. In contrast, broadening of imidazophenanthroline fragment was revealed in the spectrum of **8H$_2$**. In this case the signal of NH-proton is not observed and we attribute this behaviour to inter- or intramolecular proton exchange between imidazole and phenanthroline nitrogen atoms. Moreover, a sharp signal of porphyrin inner NH-protons is observed in all cases, revealing that these protons do not participate this exchange. Moreover, in the case of **10H$_2$** in which imidazole nitrogen is alkylated, a resolved set of resonances of phenanthroline fragment is observed.

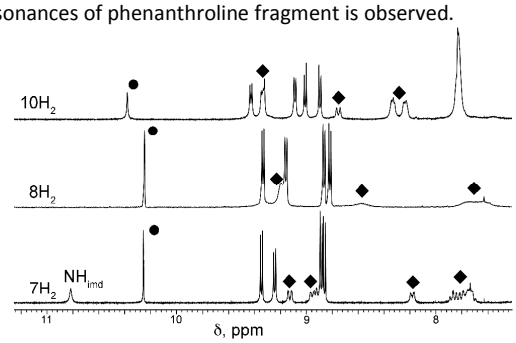
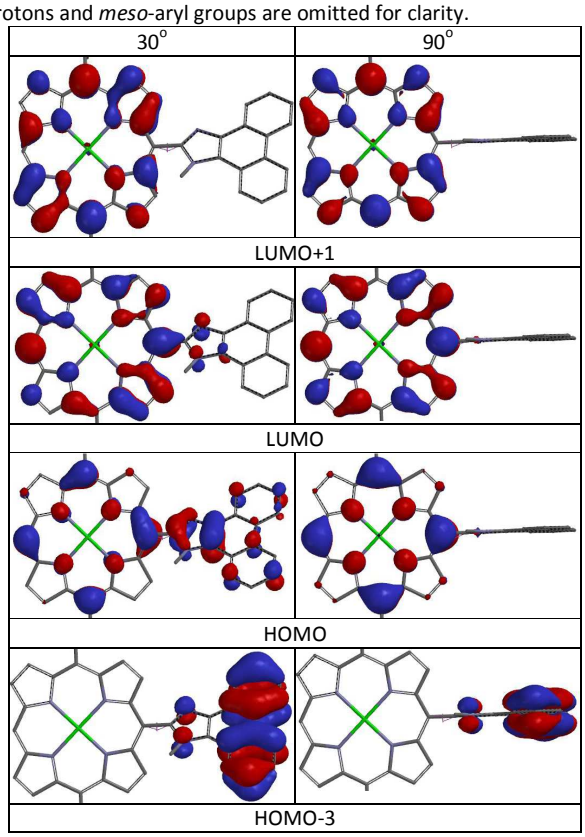


Figure 1. Aromatic regions of ^{1}H NMR spectra (300 MHz, $CDCl_3$) of **7H$_2$**, **8H$_2$** and **10H$_2$** (● = H_{meso}, ◆ = phenanthrene or phenanthroline protons).

A DFT analysis of the molecular orbitals of the synthesized compounds has been performed in order to reveal the mutual influence of the electronic structures of the aromatic fragments of the molecule. The calculation was carried out at B3LYP/6-31G(d) level of theory with model zinc 5,15-dimesitylporphyrin, bearing 10-imidazophenanthrene fragment, substituted with methyl group at nitrogen atom. In this case the orthogonal orientation of aromatic planes was found to be the most favorable. It was found that localization of frontier orbitals of the molecule depends on the respective orientation of porphyrin ring and areneimidazole unit. The first two unoccupied orbitals (LUMO and LUMO+1) are localized predominantly at porphyrin ring in tilted conformation and exclusively in orthogonal one. HOMO is distributed homogeneously between porphyrin macrocycle and aromatic moiety in tilted conformation, while in orthogonal one it is localized at porphyrin cycle exclusively. Moreover, an orbital HOMO-3 can be found, that is localized exclusively at polyaromatic fragment regardless the skew angle between aromatic planes.

Table 1. The localization of frontier orbitals in model imidazophenanthrene-appended porphyrin at varied skew angle. Protons and *meso*-aryl groups are omitted for clarity.



The observed behavior of the molecular orbitals reveals the possibility of the electron and charge transfer processes upon photoexcitation of the molecule with orthogonal orientation of aromatic planes. The energy gap for transitions HOMO-3 → LUMO and HOMO-3 → LUMO+1 correspond to 391 nm and 381 nm wavelengths, respectively. Since B3LYP functional tends to overestimate the energy of transitions up to 0.5 eV,[46] it can be presumed that the corresponding absorption bands are overlapped with Soret bands in the UV-Vis spectra of the synthesized compounds.

Conclusions

We have developed a new strategy for the post-functionalization of readily accessible *meso*-formylporphyrins. This approach allows introduction of 2-imidazolyl fragment, fused with functional polyaromatic moiety at 4,5-positions. This transformation

represents the first example of utilization of *meso*-formylporphyrins as carbonyl components in the heterocyclic condensation, despite the low reactivity of *meso*-formyl group. A set of compounds is synthesized with this approach and their further transformations are demonstrated. The preliminary DFT calculations have revealed the promising properties of the *meso*-areneimidazolyl-porphyrins for further investigation of charge and electron transfer properties.

The authors are grateful to the Council of the Russian President for support of young scientists (grant MK-272.2014.3).

Notes and references

1. J. A. S. Cavaleiro, A. C. Tome, and M. G. P. M. S. Neves, *Handbook of porphyrin science. 9. Meso-tetraarylporphyrin derivatives: new synthetic methodologies*, 2012.
2. C. M. A. Alonso, J. F. B. Barata, J. A. S. Cavaleiro, M. A. F. Faustino, D. Monti, S. Nardis, M. G. P. M. S. Neves, S. M. G. Pires, C. I. M. Santos, K. M. Smith, A. C. Tome, V. I. V. Serra, and J. Wojaczynski, *Synthesis and modifications of porphyrinoids*, Springer, 2014.
3. I. P. Beletskaya, V. S. Tyurin, A. Uglov, C. Stern, and R. Guilard, in *Handbook of porphyrin science*, eds. K. M. Kadish, K. M. Smith, and R. Guilard, 2012, vol. 23, pp. 82–281.
4. N. N. Sergeeva, M. O. Senge, and A. Ryan, in *Handbook of porphyrin science*, eds. K. M. Kadish, R. Guilard, and K. M. Smith, 2010, pp. 325–365.
5. V. Bulach and M. W. Hosseini, in *Handbook of porphyrin science*, eds. K. M. Kadish, K. M. Smith, and R. Guilard, 2012, pp. 299–390.
6. I. Beletskaya, V. S. Tyurin, A. Y. Tsivadze, R. Guilard, and C. Stern, *Chem. Rev.*, 2009, **109**, 1659–1713.
7. Y. Y. Enakieva, A. G. Bessmertnykh, Y. G. Gorbunova, C. Stern, Y. Rousselin, A. Y. Tsivadze, and R. Guilard, *Org. Lett*, 2009, **11**, 3842–3845.
8. E. V. Vinogradova, Y. Y. Enakieva, S. E. Nefedov, K. P. Birin, A. Y. Tsivadze, Y. G. Gorbunova, A. G. Bessmertnykh Lemeune, C. Stern, and R. Guilard, *Chem. Eur. J.*, 2012, **18**, 15092–15104.
9. A. A. Sinelshchikova, S. E. Nefedov, Y. Y. Enakieva, Y. G. Gorbunova, A. Y. Tsivadze, K. M. Kadish, P. Chen, A. Bessmertnykh-Lemeune, C. Stern, and R. Guilard, *Inorg. Chem.*, 2013, **52**, 999–1008.
10. L.-L. Li and E. W.-G. Diau, *Chem. Soc. Rev.*, 2012, **42**, 291–304.
11. R. De Paula, I. C. M. S. Santos, M. M. Q. Simões, M. G. P. M. S. Neves, and J. A. S. Cavaleiro, *J. Mol. Cat. A*, 2015, **404-405**, 156–166.
12. M. Goswami, V. Lyaskovskyy, S. R. Domingos, W. J. Buma, S. Woutersen, O. Troeppner, I. Ivanović-Burmazović, H. Lu, X. Cui, X. P. Zhang, E. J. Reijerse, S. DeBeer, M. M. van Schooneveld, F. F. Pfaff, K. Ray, and B. de Bruin, *J. Am. Chem. Soc.*, 2015, **137**, 5468–5479.
13. M. Jurow, A. E. Schuckman, J. D. Batteas, and C. M. Drain, *Coord. Chem. Rev.*, 2010, **254**, 2297–2310.
14. J. Chen, S. Ko, L. Liu, Y. Sheng, H. Han, and X. Li, *New J. Chem.*, 2015, **39**, 3736–3746.
15. S. Norrehed, P. Polavarapu, W. Yang, A. Gogoll, and H. Grennberg, *Tetrahedron*, 2013, **69**, 7131–7138.
16. K.-I. Hong, H. Yoon, and W.-D. Jang, *Chem. Commun.*, 2015, **51**, 7486–7488.
17. A. Brown and P. D. Beer, *Dalton Trans.*, 2012, **41**, 118–129.
18. G. V. Ponomarev, *Chem. Heterocycl. Compd.*, 1994, **30**, 1444–1465.
19. J. W. Buchler, C. Dreher, and G. Herget, *Eur. J. Org. Chem.*, 1988, **1988**, 43–54.
20. T. Morotti, M. Pizzotti, R. Ugo, S. Quici, M. Bruschi, P. Mussini, and S. Righetto, *Eur. J. Inorg. Chem.*, 2006, **2006**, 1743–1757.
21. O. B. Locos and D. P. Arnold, *Org. Biomol. Chem.*, 2006, **4**, 902.
22. K. Dahms, M. O. Senge, and M. B. Bakar, *Eur. J. Org. Chem.*, 2007, **2007**, 3833–3848.
23. N. V. Tkachenko, H. Lemmetyinen, J. Sonoda, K. Ohkubo, T. Sato, H. Imahori, and S. Fukuzumi, *J. Phys. Chem. A*, 2003, **107**, 8834–8844.
24. C. M. Carcel, J. K. Laha, R. S. Loewe, P. Thamyongkit, K.-H. Schweikart, V. Misra, D. F. Bocian, and J. S. Lindsey, *J. Org. Chem*, 2004, **69**, 6739–6750.
25. C. Muthiah, M. Taniguchi, H.-J. Kim, I. Schmidt, H. L. Kee, D. Holten, D. F. Bocian, and J. S. Lindsey, *Photochem. Photobiol.*, 2007, **83**, 1513–1528.
26. J. Warnan, L. Favereau, F. Meslin, M. Severac, E. Blart, Y. Pellegrin, D. Jacquemin, and F. Odobel, *Chem. Sus. Chem.*, 2012, **5**, 1568–1577.
27. G. V. Ponomarev, *Chem. Heterocycl. Compd.*, 1996, **32**, 1263–1280.
28. N. M. M. Moura, M. A. F. Faustino, M. G. P. M. S. Neves, A. M. S. Silva, A. C. Tome, and J. A. S. Cavaleiro, *Chem. Commun.*, 2012, **48**, 6142.
29. J. Bhaumik, Z. Yao, K. E. Borbas, M. Taniguchi, and J. S. Lindsey, *J. Org. Chem*, 2006, **71**, 8807–8817.
30. R. D. Paula, M. M. Q. Simões, M. G. P. M. S. Neves, and J. A. S. Cavaleiro, *Catal. Commun.*, 2008, **10**, 57–60.
31. H. Ozeki, A. Nomoto, K. Ogawa, Y. Kobuke, M. Murakami, K. Hosoda, M. Ohtani, S. Nakashima, H. Miyasaka, and T. Okada, *Chem. Eur. J.*, 2004, **10**, 6393–6401.
32. L. R. Milgrom, P. J. Dempsey, and G. Yahioglu, *Tetrahedron*, 1996, **52**, 9877–9890.
33. R. De Paula, M. M. Q. Simões, M. G. P. M. S. Neves, and J. A. S. Cavaleiro, *J. Mol. Cat. A*, 2011, **345**, 1–11.
34. Y. Miyazaki, A. Satake, and Y. Kobuke, *J. Mol. Cat. A*, 2008, **283**, 129–139.
35. K. Ogawa, H. Hasegawa, Y. Inaba, Y. Kobuke, H. Inouye, Y. Kanemitsu, E. Kohno, T. Hirano, S.-I. Ogura, and I. Okura, *J. Med. Chem.*, 2006, **49**, 2276–2283.
36. F. Hajjaj, Z. S. Yoon, M.-C. Yoon, J. Park, A. Satake, D. Kim, and Y. Kobuke, *J. Am. Chem. Soc.*, 2006, **128**, 4612–4623.
37. K. Ogawa, A. Ohashi, Y. Kobuke, K. Kamada, and K. Ohta, *J. Phys. Chem. B*, 2005, **109**, 22003–22012.
38. K. Ogawa, T. Zhang, K. Yoshihara, and Y. Kobuke, *J. Am. Chem. Soc.*, 2002, **124**, 22–23.
39. N. Nagata, Y. Kuramochi, and Y. Kobuke, *J. Am. Chem. Soc.*, 2009, **131**, 10–11.
40. M. Morisue, N. Haruta, D. Kalita, and Y. Kobuke, *Chem. Eur. J.*, 2006, **12**, 8123–8135.
41. M. Mao, J.-B. Wang, Z.-F. Xiao, S.-Y. Dai, and Q.-H. Song, *Dyes and Pigments*, 2012, **94**, 224–232.
42. N. N. Sergeeva, M. Donnier-Marechal, G. M. Vaz, A. M. Davies, and M. O. Senge, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 4385–4388.
43. Z. Wang, P. Lu, S. Chen, Z. Gao, F. Shen, W. Zhang, Y. Xu, H. S. Kwok, and Y. Ma, *J. Mater. Chem.*, 2011, **21**, 5451.

44. Y. Ooyama, H. Kumaoka, K. Uwada, and K. Yoshida, *Tetrahedron*, 2009, **65**, 8336–8343.
45. C. M. B. Carvalho, M. G. P. M. S. Neves, A. C. Tome, F. A. A. Paz, A. M. S. Silva, and J. A. S. Cavaleiro, *Org. Lett*, 2011, **13**, 130–133.
46. E. Baerends, G. Ricciardi, A. Rosa, and S. Van Gisbergen, *Coord. Chem. Rev.*, 2002, **230**, 5–27.