Synthesis and Separation of *meso*-Tetraarylporphyrins with C_i Symmetry

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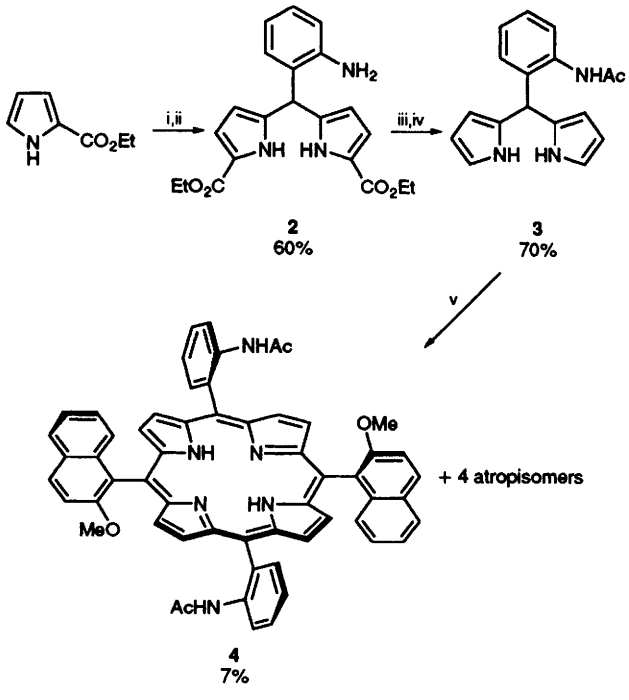
5,15-Di(*o*-acetylaminophenyl)-10,20-di-1-(2-methoxynaphthyl)porphyrin was prepared by way of o-acetylaminophenyl-2,2′-dipyrrylmethane; the expected 5 atropisomers (αα′ββ′, αα′βα′, αβ′αβ′, αα′αβ′, αα′αα′) have been separated and characterised on the basis of their spectroscopic properties and thermal isomerisation behaviour.

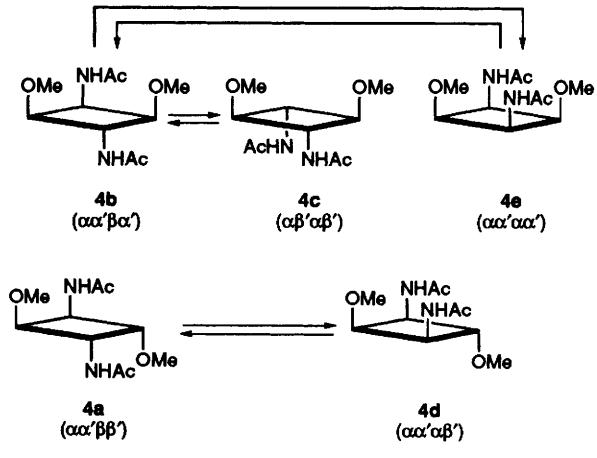
Tetraarylporphyrins with two different aryl groups attached alternately at the 5, 10, 15 and 20 positions have been prepared through the statistical pyrrole condensation with two different aryl aldehydes followed by chromatographic separation of the resulting six component mixture.[1] The sequential condensation of pyrroles with the first aldehyde and then the resulting dipyrrylmethanes with the second aldehyde has recently been shown to provide a more elegant pathway to these C_2 symmetric porphyrins, particularly to 5,15-diarylporphyrins.[2] However, this synthetic methodology has never been applied to tetraarylporphyrins, while some C_2-symmetric porphyrins have recently been synthesised by modified MacDonald [2 + 2] condensations.[3] If two differently *ortho*-substituted aryl groups were used in this procedure, 5 atropisomers (αα′ββ′, αα′βα′, αβ′αβ′, αα′αβ′, αα′αα′) arising from the restriction of rotation of the *meso*-aryl groups should occur for the resulting porphyrin. Although atropisomerism in tetraarylporphyrins has been well known,[4–8] there has been no such report for a tetraarylporphyrin with mixed *meso*-aryl groups. The C_i symmetric atropisomer (αα′ββ′) is of special interest because two sides of the porphyrin plane have opposite chirality and thus diastereotopic interaction is expected toward optically active substrates depending on which side interacts with the substrates. This molecular recognition is relevant to the design of new biomimetic catalysts.[9] Here we disclose the preparation and separation of this C_i-symmetric porphyrin along with the other 4 atropisomers.



Scheme 1 *Reagents and conditions*: i, *o*-nitrobenzaldehyde, $TiCl_4$, CH_2Cl_2, 0 °C, 22 h; ii, H_2, 10% Pd-C, THF, room temp., 10 h; iii, NaOH, $(CH_2OH)_2$, reflux, 2 h; iv, Ac_2O, Et_3N, 0 °C, 2 h; v, 2-methoxynaphthaldehyde, $EtCO_2OH$, $Zn(OAc)_2$, reflux, 5 h

$TiCl_4$-catalysed condensation of 2-ethoxycarbonylpyrrole with *o*-nitrobenzaldehyde at 0 °C in CH_2Cl_2 afforded *o*-nitrophenyl-5,5′-diethoxycarbonyl-2,2′-dipyrrylmethane **1** along with a small amount of an isomeric 2,3′-dipyrrylmethane. *o*-Aminophenyl-5,5′-diethoxycarbonyl-2,2′-dipyrrylmethane **2** which was obtained by the reduction of **1** with H_2/Pd-C was decarboxylated in boiling alkaline ethylene glycol and then *N*-acetylated with acetic anhydride. This *o*-acetylaminophenyl-2,2′-dipyrrylmethane **3** was condensed with 2-methoxy-1-naphthaldehyde in refluxing propionic acid in the presence of $Zn(OAc)_2$ to give 5,15-di(*o*-acetylaminophenyl)-10,20-di-1-(2-methoxynaphthyl)porphyrin **4** as a mixture of 5 atropisomers in 7% total yield after demetallation and purification through silica gel chromatography. When this cyclisation was carried out in CH_2Cl_2 under the catalysis of BF_3–Et_2O, decomposition of **3** into the aldehyde and pyrrole followed by their random recombination with 2-methoxy-1-naphthaldehyde took place.

The chromatographic separation of the porphyrin **4** on silica gel using solvents with a gradient from benzene to CH_2Cl_2 and finally to CH_2Cl_2–acetone (10:1) afforded 5 fractions **4a–e** in the order of elution.† The ^1H NMR spectra showed that the second fraction **4b** and the fourth fraction **4d** are *Cs*-symmetric. A pair of acetylamino signals with 1:1 ratio were observed at δ 6.81 and 6.80 (NH) and at δ 1.25 and 1.24 (MeCO) for **4b**. Two methoxy signals with a 1:1 ratio were observed at δ 3.66 and 3.64 and the 7- and 8-naphthyl protons appeared as two pairs of signals (triplets at δ 7.04 and 6.99; and doublets at δ 6.88 and 6.77) for **4d**. Therefore, **4b** and **4d** are unambiguously associated with the αα′βα′‡ and the αα′αβ′ isomer, respectively. Although the ^1H NMR data do not give decisive evidence to assign the remaining fractions, **4a**, **c**, **e**, because of the inherently identical spectral pattern of these three isomers, they were characterized on the basis of their thermal interconversion behaviour. It is known that an αααα isomer of tetra(*o*-pivaloylaminophenyl)porphyrin **5** undergoes isomerisation to other atropisomers under reflux in xylene for 45 min[4] while that of tetra-1-(2-hydroxynaphthyl)porphyrin **6** is totally



Scheme 2

unaffected under reflux in toluene for 2 h.[5]§ Therefore, it is reasonable to assume that a *o*-acetylaminophenyl group rotates and a 2-methoxynaphthyl group does not during refluxing in a xylene solution. HPLC analysis (SiO_2/$CHCl_3$) of a *m*-xylene solution of **4b** ($\alpha\alpha'\beta\alpha'$) or **4d** ($\alpha\alpha'\alpha\beta'$) after reflux for 1 h showed that **4b** was isomerised to both **4c** and **4e** whereas **4d** was isomerised only to **4a**. The interconversion between the two groups, (**4b**, **4c**, **4e**) and (**4a**, **4d**), has never been observed under the above reaction conditions. This means that the latter two isomers have an *anti* 2-methoxynaphthyl arrangement whereas the former three isomers have an *syn* arrangement as is anticipated. The observed isomer ratio after equilibration based on HPLC peak areas was 3.4 : 1.0 for the mixture of (**4b** + **4c**)¶ and **4e** and 1.0 : 1.0 for the mixture of **4a** and **4d**. The ratios are in good accordance with the theoretical ratios (1 : 1 for the latter two isomers, 2 : 1 : 1 for the former three isomers), assuming that the rate of rotation of an *o*-acetylaminophenyl group is independent of the arrangement of the other three *meso*-aryl substituents in an atropisomer. Thus, the fraction **4a** is assigned to the C_i-symmetric isomer ($\alpha\alpha'\beta\beta'$),‖ while both **4c** and **4e** are C_2-symmetric isomers ($\alpha\beta'\alpha\beta'$ and $\alpha\alpha'\alpha\alpha'$). The fraction **4e** with the most elution volume on silica gel HPLC is considered to have all the polar substituents directed to one side of the porphyrin plane ($\alpha\alpha'\alpha\alpha'$), taking into account a general tendency that the larger the difference in the polarity between both sides of the porphyrin plane, the more polar is that atropisomer. This tendency is reported in a number of tetra(*o*-substituted aryl)porphyrins including **5** and **6**.[4–8] Thus, the remaining fraction **4c** must possess an $\alpha\beta'\alpha\beta'$ arrangement. It is reasonable that the C_i-symmetric porphyrin has the least elution volume in silica gel chromatography since it is the only isomer in which both sides of the porphyrin plane has the same spatial arrangement of the substituent groups except for chirality. The desired C_i-symmetric porphyrin **4a** was obtained through the equilibration (in boiling mesitylene overnight)-separation (silica gel column chromatography) sequence three times in 31% total yield based on the whole mixture of the porphyrin atropisomers.

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Footnotes

† The five fractions showed the R_f values (0.17, 0.15, 0.10, 0.04, and 0.015) on Merck Kiesel Gel 60PF_{254} with CH_2Cl_2 elution.

‡ A dash notation in $\alpha\alpha'\beta\alpha'$ is for the arrangement of 2-methoxynaphthyl groups.

§ We have confirmed that an $\alpha\alpha\alpha\alpha$ isomer of tetra-1-(2-methoxynaphthyl)porphyrin is stable in a refluxing xylene solution.

¶ As two peaks due to **4b** and **4c** were not resolved satisfactorily, the peak area was counted as a whole.

‖ **4a**: ^{1}H NMR (δ, $CDCl_3$) 8.67, 8.60 (dx2, 4Hx2, β-pyrrole), 8.62 (d, 2H, phenyl-3-H), 7.97 (d, 2H, phenyl-6-H), 7.76 (t, 2H, phenyl-4-H), 7.44 (t, 2H, phenyl-5-H), 8.36 (d, 2H, naphthyl-3-H), 8.09 (d, 2H, naphthyl-5-H), 7.75 (d, 2H, naphthyl-4-H), 7.36 (t, 2H, naphthyl-6-H), 7.02 (t, 2H, naphthyl-7-H), 6.83 (d, 2H, naphthyl-8-H), 6.78 (s, 2H, NHAc), 1.26 (s, 6H, COMe), 3.66 (s, 6H, OMe), −2.40 (bs, 2H, pyrrole-NH). FABMS (*m*/*z*) 889 $(M + 1)^+$. UV–VIS [λ_{max} (log ε) in CH_2Cl_2] 421 (5.44), 514 (4.22), 546 (3.24), 589 (3.69), 652 (3.82) nm. IR ν/cm^{-1} (KBr) 1700 (NHCO).

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