

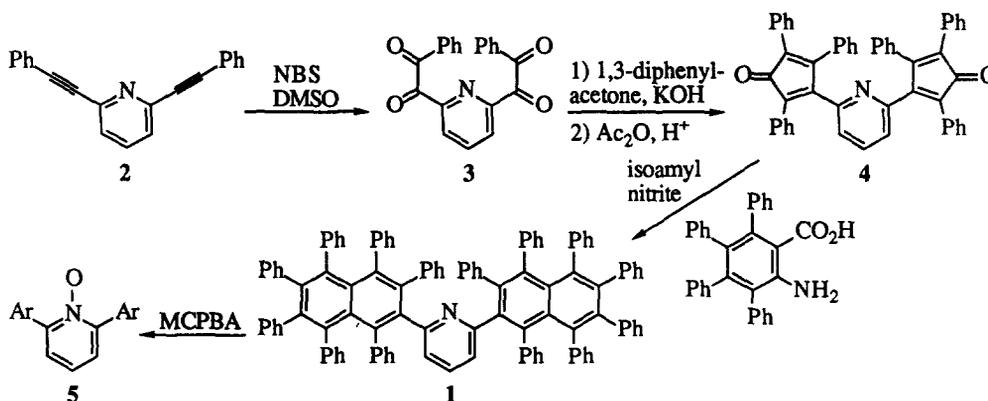
Albatrossidine: A Large, Easily Synthesized Molecular Cleft

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Abstract: 2,6-Bis(heptaphenyl-2-naphthyl)pyridine (**1**) was prepared in three steps from 2,6-bis(phenylethynyl)pyridine, and its X-ray structure was determined. The pyridine nitrogen lies at the base of a broad, chiral molecular cleft created by the perphenylnaphthyl "wings" of **1**.
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We recently described the synthesis of octaphenylnaphthalene by the addition of tetraphenylbenzyne, generated from 3,4,5,6-tetraphenylanthranilic acid, to tetraphenylcyclopentadienone.¹ Octaphenylnaphthalene is a roughly rectangular slab with a 12 Å × 14 Å surface, and its ease of synthesis suggested that large organic structures containing clefts or cavities defined by appropriately placed perphenylnaphthyl groups should be easily accessible. We report here the preparation and characterization of the first such compound, 2,6-bis(heptaphenyl-2-naphthyl)pyridine (**1**), in which a pyridine nitrogen is buried deep between two perphenylnaphthyl "wings", to which we give the trivial name albatrossidine.



The synthesis of **1** is very short. Oxidation of 2,6-bis(phenylethynyl)pyridine² with NBS/DMSO³ gives the tetraketone **3** in 49% yield.⁴ Condensation of **3** with two equivalents of 1,3-diphenylacetone then yields the

perphenylnaphthyl “wings” are roughly perpendicular to the central pyridine, and the naphthalenes are oriented *trans* to one another. Although **1** appears to have many rotational degrees of freedom, its conformation is highly constrained by severe steric interactions. First, the C-1 phenyl of each naphthalene strongly interacts with the C-3 phenyl of the opposite naphthalene, with an *ortho*-hydrogen of each C-1 phenyl pressing into the face of the opposing C-3 phenyl. Thus the edges of the C(1')- and C(1'')-phenyls (see Figure 1), press into the faces of the C(3'')- and C(3')-phenyls, so that the C(10')- and C(10'')-hydrogens are only 2.72 Å and 2.92 Å, respectively, from the centers of the opposing phenyl groups. It is probably these two protons which give rise to the most upfield resonances in the ¹H NMR spectrum of **1**. Second, the naphthyl groups themselves cannot be planar because of the steric bulk of the eight aryl substituents on each. Octaphenylnaphthalene exhibits an undulating, approximately *C_i*-symmetric conformation,¹ but each of the naphthyl groups in **1** is twisted; both have an end-to-end twist¹³ of 20°. In fact, AM1 calculations indicate that such twisted conformations should be slightly favored in octaarylnaphthalenes,¹ and the collision of the C-1 and C-3 phenyls may provide a further bias in favor of the twisted conformation. Finally, the interaction of the four C-1 and C-3 phenyl groups also tends to lock the wings of **1** in place. Molecular mechanics calculations (SYBYL) show only two low energy conformations, the *trans* geometry found in the X-ray structure and a similar *cis* conformation less than one kcal/mol higher in energy. However, if both conformations are present to a significant extent in solution, then they must be able to interconvert by rotation about the pyridine-naphthalene bonds (since only one isomer of **1** is observed), and this exchange process may be responsible for the broadening observed in the NMR spectra of **1**.

This last hypothesis was confirmed in an unexpected way. The pyridine nitrogen of **1**, deep within the cleft (see Figure 2), appears to be sterically encumbered, but it is in fact accessible to common reagents. Most significantly, compound **1** was smoothly oxygenated with MCPBA to give *two separable isomers* of the corresponding N-oxide **5**, which presumably arise from the *cis* and *trans* conformations of the parent **1**. The ¹H NMR spectra of the oxides are distinct and sharp,^{14,15} unlike that of **1**. Thus the introduction of the oxygen substituent is sufficient to halt the rotation about the pyridine-naphthalene bonds on both the NMR and laboratory time scales. The assignment of the two oxides is uncertain at this time, but the *trans*-oxide should have *C₂* symmetry and a large chiral cleft, and, because of the high barrier to rotation, it should be resolvable.

The syntheses of a variety of albatross molecules are now underway, as are studies of their use as molecular hosts.

Acknowledgment. This work was supported by NSF Grant CHE-9408295 (to R.A.P.) and NIH Grant GM44038 (to C.E.S.). We thank Prof. F. M. Hughson for use of the X-ray diffractometer.

References and Notes

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4. For **3**: mp 127-130 °C; ¹H NMR (CDCl₃, 270 MHz) δ 7.16 (m, 4H), 7.38 (m, 6H), 8.05 and 8.20 (A₂B system, 3H); ¹³C NMR (CDCl₃) δ 126.6, 128.6, 128.8, 132.6, 134.4, 139.4, 151.0, 193.9, 195.5 (9 of 9 expected resonances); MS, *m/z* 343 (M⁺, 15), 105 (100), 72 (40).

5. For **4**: mp 115-117 °C; ¹H NMR (CDCl₃, 270 MHz) δ 6.83-7.38 (m); MS, *m/z* 691 (M⁺, 100), 662 (M-HCO, 54).
6. For **1**: mp 350-352 °C; ¹H NMR (CDCl₃, 500 MHz) δ 5.04 (br s, 1H), 5.68 (br s, 1H), 5.81 (br s, 2H), 5.93 (br s, 1H), 6.12 (br s, 1H), 6.25 (br s, 1H), 6.34 (br s, 1H), 6.40-6.94 (br m, 65H); ¹³C NMR (CDCl₃) δ 123.4, 124.8, 125.2, 125.4, 126.4*, 126.7*, 127.6, 127.8, 128.4, 128.6, 129.1, 129.4, 130.2, 130.9, 131.4*, 131.8*, 132.6*, 132.9, 133.5*, 134.2*, 138.8, 139.0, 140.4*, 141.3, 141.4, 142.3*, 142.7, 142.9 (28 of 41 expected resonances, but starred resonances are broad and/or multiple); FAB MS, *m/z* 1396 (M+H, 100), 1319 (M - C₆H₅, 14).
7. A crystal of **1** measuring 0.02 mm x 0.31 mm x 0.58 mm, and mounted in a sealed glass capillary containing a small amount of the mother liquor to inhibit loss of solvent, was used for X-ray measurements. Crystal data: C₁₀₉H₇₃N·CHCl₃; monoclinic, space group *P*2₁/*c*; *a* = 21.88 (7) Å, *b* = 34.57 (7) Å, *c* = 13.72 (2) Å, β = 98.04 (11)°, *V* = 10274 (41) Å³, *Z* = 4, *D*_{calcd} = 0.980 g/cm³. Intensity data were collected out to 2θ = 90° by using Cu Kα radiation (λ = 1.54178 Å) at 298 K on a Rigaku R-AXIS IIC image plate system equipped with a rotating anode and double-focusing mirrors. 293 frames of data were collected with 2° of oscillation per frame. The 29537 observed reflections were indexed, integrated, and corrected for Lorentz and polarization effects (using the program DENZO⁸), and then the reflections were scaled and merged (SCALEPACK⁸). The final data set contained 7502 unique reflections (*R*_{int} = 0.096). The structure was solved by molecular replacement (PATSEE⁹), and refined by full-matrix least-squares on *F*² (SHELXL-93¹⁰) to *R*(*F*) = 0.174 with all heavy atoms anisotropic and inclusion of hydrogen atoms with a riding model [*U*(H) = 1.2*U*(C)]. A difference-Fourier synthesis at this stage revealed no peak larger than 1.7 eÅ⁻³ in the two symmetry related channels running parallel to the *c*-axis, but the clustering of peaks was suggestive of two badly disordered CHCl₃ sites. However, all attempts to fit the electron density within the channels with discrete solvent molecules were without success, so the SQUEEZE/BYPASS¹¹ procedure implemented in PLATON-94¹² was used to account for the solvent electron density. A total electron count of 205.9 e in a total volume of 3181.7 Å³ was found for the two channels, consistent with approximately four CHCl₃ (58 e) per cell. (Attempts to determine independently the identity and amount of solvent present by NMR analysis were without success due to rapid solvent loss by the crystals during handling in the absence of the mother liquor.) The SQUEEZE-processed data was used for all subsequent cycles of refinement, which converged to *R*(*F*) = 0.098, *wR*(*F*²) = 0.274, and *S* = 1.15 for 6183 reflections with *F* > 4σ(*F*), and *R*(*F*) = 0.107, *wR*(*F*²) = 0.286, and *S* = 1.08 for 7502 unique reflections and 992 variables.
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14. For **5** isomer A (major): *R*_f 0.31 (9:1 hexanes-EtOAc); ¹H NMR (CDCl₃, 500 MHz) δ 5.80 (t, *J* = 8 Hz, 1H), 5.90 (br s, 2H), 6.05 (br s, 2H), 6.09 (d, *J* = 8 Hz, 2H), 6.42 (m, 8H), 6.50-6.75 (m, 54H), 6.78 (t, *J* = 7 Hz, 2H), 6.85 (t, *J* = 7 Hz, 2H); FAB MS, *m/z* 1412 (M+H, 100), 1307 (56).
15. For **5** isomer B (minor): *R*_f 0.15 (9:1 hexanes-EtOAc); ¹H NMR (CDCl₃, 500 MHz) δ 5.72 (t, *J* = 8 Hz, 1H), 5.93 (d, *J* = 8 Hz, 2H), 6.05 (m, 6H), 6.23 (t, *J* = 8 Hz, 2H), 6.30 (d, *J* = 8 Hz, 2H), 6.33 (t, *J* = 7 Hz, 2H), 6.40 (m, 4H), 6.52-6.82 (m, 46H), 6.94 (m, 6H), 7.12 (d, *J* = 7 Hz, 2H); FAB MS, *m/z* 1412 (M+H, 100), 1307 (46).

(Received in USA 5 September 1996; revised 5 November 1996; accepted 8 November 1996)