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Syntheses of shuttlecock- and bowl-equipped phenylazopyridines and photomodulation of their coordination ability to Zn-porphyrin

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ABSTRACT

Shuttlecock- and bowl-equipped 4-(phenylazo)pyridine derivatives, which bear substituents that allow the pyridine moiety to protrude in the trans form but hinder it in the cis form, have been designed and synthesized. These molecules show cis/trans photoisomerization despite the presence of bulky substituents. ^{1}H NMR titration with Zn-porphyrin showed that the trans isomers coordinate to Zn-porphyrin much stronger than the cis isomers.

Azobenzene and its derivatives are expected to be applied to molecular switches and devices, making use of differences in the properties such as structures, absorption spectra, and dipole moments between the two isomers, trans and cis forms.[1] Phenylazopyridine derivatives, which bear a pyridyl ring in place of a phenyl ring of azobenzenes, are utilized in a field of coordination chemistry because of their coordination ability to a metal ion. We previously reported a supramolecular photoswitches wherein the fluorescence from Zn-porphyrin can be controlled by photoirradiation making use of the difference in axial coordination ability between the trans and the cis isomers of 3-(phenylazo)pyridine derivatives,[2] which incorporate a bulky group in such a way that the association with Zn-porphyrin is hindered in the cis configuration. However, the cis isomer did not dissociate from Zn-porphyrin completely. In this work, to solve this problem, we designed and synthesized shuttlecock- and bowl-equipped 4-(phenylazo)pyridine derivatives, TbetNNPy **5** and BmtNNPy **10**, which bear a tetra(*tert*-butylethynyl)-1,1′:3′,1″-terphenyl group and a 4-*tert*-butyl-2,6-bis[(2,2″,6,6″-tetramethyl-*m*-terphenyl-2′-yl)methyl]phenyl group[3], respectively. For these phenylazopyridine ligands, it was expected that the cis isomers mostly lose the coordination ability to Zn-porphyrin but the trans isomer is able to coordinate to it because the pyridine-*N* of the cis isomer is covered by the shuttlecock- and bowl-shaped framework but that of the trans isomer is not, as shown schematically in Figure 1. We then investigated the difference in coordination ability between the trans and the cis isomers of these compounds.

TbetNNPy **5** was synthesized as shown in Scheme 1. 1,3-Dibromo-2-nitrosobenzene **2** was obtained by the oxidation of 2,6-dibromoaniline **1** by *m*-chloroperbenzoic acid (*m*CPBA)[4] in 50% yield. Azo compound **3** was prepared by a coupling reaction between **2** and 4-aminopyridine with NaOH[5] in 10% yield. Terphenyl azopyridine **4** was synthesized by Suzuki–Miyaura cross-coupling reaction between **3** and 3,5-dichlorophenylboronic acid[6] in 66% yield. Finally, TbetNNPy **5** was synthesized by Sonogashira cross-coupling reaction[7] between **4** and *t*-butylacetylene in 72% yield. This linear route was employed because a more convergent route, in which the incorporation of the 3,5-bis(*tert*-butylethynyl)phenyl group to **1** was followed by a coupling of the resulting amino compound and 4-aminopyridine[5], was unsuccessful because the latter coupling of the amino compounds did not proceed.

BmtNNPy **10** was synthesized as shown in Scheme 2. Compound **6** was prepared according to a reported procedure.[8–12] Nitrosopyridine 1-oxide **7** was prepared from 4-nitropyridine 1-oxide by reduction to the hydroxylamino compound followed by oxidation with H_2SO_4/$KMnO_4$.[13] The coupling reaction of **6** and **7** under basic conditions with K_2CO_3 in DMF produced azoxy compound **8** in 57% yield (route 1). Only the pyridine-*O* in **8** was reduced to produce azoxy compound **9** when PCl_3[14] was used. The subsequent

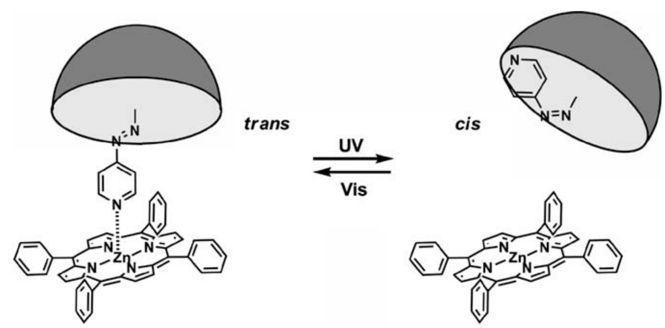

Figure 1. Supramolecular photoswitch using 4-(phenylazo)pyridines bearing a shuttlecock- and a bowl-shaped framework.

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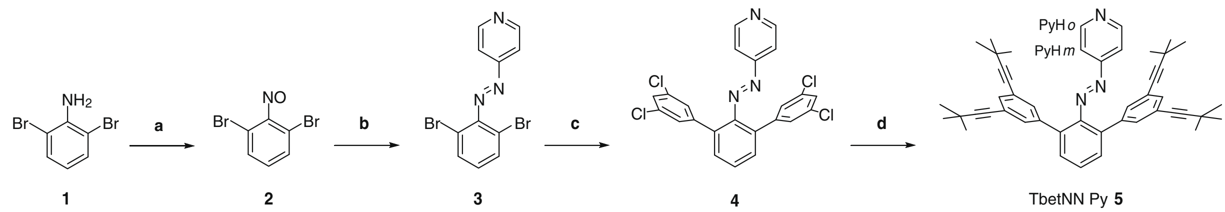
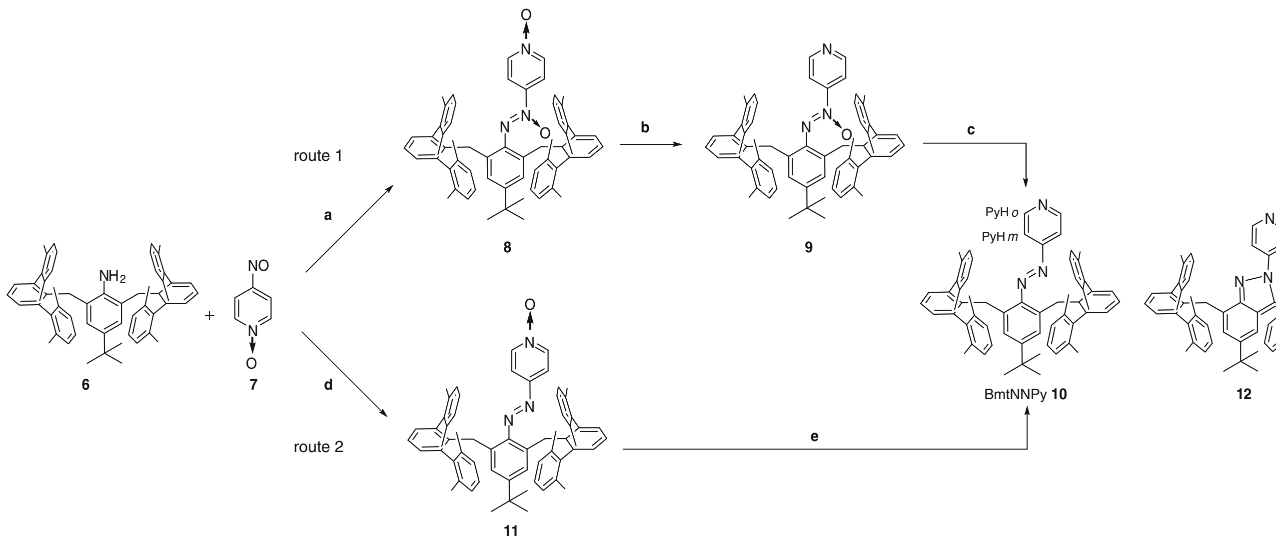


Scheme 1. Preparation of TbetNNPy (**5**). Reagents and conditions: (a) *m*CPBA, CH_2Cl_2, 20 °C, 4 h, 50%; (b) 4-aminopyridine, 50% NaOH aq, benzene, reflux, 10%; (c) *m*-dichlorophenylboronic acid, $Pd(PPh_3)_4$, K_2CO_3, DME, reflux, 66%; and (d) (i) $PdCl_2(CH_3CN)_2$, 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl, $CsCO_3$, anhydrous CH_3CN, and (ii) *tert*-butylacetylene, 72%.



Scheme 2. Preparation of BmtNNPy (**10**). Reagents and conditions: (a) K_2CO_3, DMF, 50 °C, overnight, 57%; (b) PCl_3, $CHCl_3$, reflux, 2 h, 100%; (c) (i) Zn, AcOH, THF, rt, 6 h, (ii) Zn, rt, 16 h, 11%; (d) AcOH, $CHCl_3$, 50 °C→rt→70 °C, overnight, 93%; (e) $TiCl_4$, In, dry THF, rt, 5 min, 31%.

reduction of **9** with Zn/AcOH afforded **10** in 11% yield.[15] The coupling of **6** and **7** under acidic conditions (route 2) in the presence of AcOH in $CHCl_3$[16] produced azo pyridine oxide **11** in 93% yield without formation of azoxy compound **8**. The reduction of pyridine-*O* in **11** with $TiCl_4$/In[17] produced BmtNNPy **10** in 31% yield. In these final steps from **9** or **11** to **10**, compound **12** formed in 6–16% yield via cyclization between the azo-*N* adjacent to the pyridyl group and the benzyl carbon, along with a trace amount of **6**. Route 2 has been found to be better than route 1 because steps are shorter and the yield of **10** is higher.

Large $\pi\pi^*$ absorption bands for *trans*-TbetNNPy and *trans*-BmtNNPy appear at about 330 nm, as a shoulder to the absorption of the terphenyl group, and 348 nm, respectively, while small and broad $n\pi^*$ bands appear at 450 or 469 nm, respectively, which are shown in Supplementary data (Figs. S1 and S2). These absorption bands are characteristic to azobenzene derivatives. Upon UV light ($\pi\pi^*$) irradiation to a solution of *trans*-TbetNNPy or *trans*-BmtNNPy (e.g., in toluene at 25 °C), the trans isomer was converted to the cis isomer. The cis isomer was converted back to the trans isomer by irradiating visible light ($n\pi^*$). Thus, TbetNNPy and BmtNNPy behaved as photochromic compounds regardless of the bulky substituents.

To investigate the difference in coordination ability to Zn-porphyrin between the trans and the cis isomers, we carried out ^1H NMR titration of the azo ligands with Zn-porphyrin in C_6D_6. We monitored chemical shift changes for pyridine protons of TbetNNPy and BmtNNPy, in addition to 4-(phenylazo)pyridine (4-PhNNPy) as a model, upon incremental addition of Zn-porphyrin to mixed solutions of the trans and the cis isomers. For 4-PhNNPy, the signals of pyridine protons of the cis isomer were shifted upfield almost as

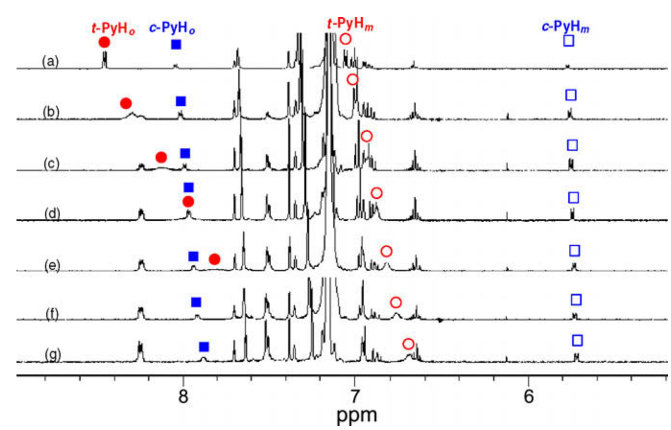


Figure 2. ^1H NMR upfield shifts in C_6D_6 for *trans*- and *cis*-TbetNNPy **5** (2.5 mM) upon addition of Zn-tetraphenylporphyrin ((a) 0, (b) 0.1, (c) 0.2, (d) 0.3, (e), 0.4, (f) 0.5, and (g) 0.6 mM).

much as those of the trans isomer (Fig. S3). In contrast, in the case of TbetNNPy, the chemical shifts for the trans isomer were shifted upfield significantly, while those for the cis isomer were shifted only a little (Fig. 2). For BmtNNPy, although the resonance for the *ortho* protons cannot be compared because they disappear on addition of the porphyrin, the chemical shift change for the *meta* protons of the trans isomer was much lager than that of the cis isomer (Fig. 3). Plots of these chemical shifts of pyridine protons vs. the concentration of Zn-porphyrin clearly indicate the difference in coordination ability between the two isomers (Fig. S4). The association

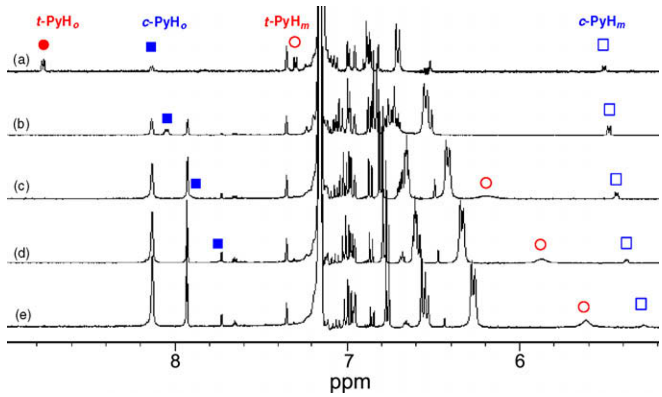


Figure 3. ^{1}H NMR upfield shifts in C_6D_6 for *trans*- and *cis*-BmtNNPy **10** (2.5 mM) upon addition of Zn-5,15-bis(3′,5′-di-*tert*-butylphenyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin19 ((a) 0, (b) 0.6, (c) 1.2, (d) 1.8, and (e) 2.4 mM).

constants of the trans and cis isomers of 4-PhNNPy with Zn-tetraphenylporphyrin (ZnTPP) were estimated as 1300 and 920 M^{-1}, respectively, while those of the trans and cis isomers of TbetNNPy were 860 and 120 M^{-1}.[18] For BmtNNPy, the association constants of the trans and cis isomers with Zn-5,15-bis(3′,5′-di-*tert*-butylphenyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin[19,20] were estimated as 2000 and 100 M^{-1}, respectively. These results clearly indicate that the affinities of the trans and cis isomers of 4-PhNNPy toward Zn-porphyrins are similar, while those of BmtNNPy and TbetNNPy depend heavily on whether they are in the trans or in the cis configuration.

In conclusion, we have synthesized shuttlecock-equipped (TbetNNPy) and bowl-shaped (BmtNNPy) phenylazopyridine derivatives, which bear substituents that allow the pyridine moiety to protrude in the trans form but hinder it in the cis form. These molecules show cis/trans photoisomerization by irradiation. The cis isomers only weakly interact with Zn-porphyrins, while the trans isomers coordinate to Zn-porphyrins significantly. Work is in progress toward the application of these compounds to photoresponsive switches.

Acknowledgment

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Supplementary data

The synthesis of new compounds: **3**, **4**, **5**, **8**, **9**, **10**, **11** and **12**, the absorption changes due to the photoisomerization for **5** and **10**, and plots of chemical shifts for pyridine protons versus the concentration of Zn-porphyrin are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.02.126.

References and notes

1. (a) *Molecular Switches*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, 2001; (b) Muraoka, T.; Kinbara, K.; Kobayashi, Y.; Aida, T. *J. Am. Chem. Soc.* **2003**, *125*, 5612; (c) Yagai, S.; Karatsu, T.; Kitamura, A. *Chem. Eur. J.* **2005**, *11*, 4054.
2. (a) Otsuki, J.; Narutaki, K.; Bakke, J. M. *Chem. Lett.* **2004**, *33*, 356; (b) Otsuki, J.; Narutaki, K. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1537.
3. Goto, K.; Okazaki, R. *Liebigs Ann. Recl.* **1997**, 2393.
4. Smirnov, O. Y.; Churakov, A. M.; Tyurin, A. Y.; Streleko, Y. A.; Ioffe, S. L.; Tartakovsky, V. A. *Russ. Chem. Bull. Int. Ed.* **2002**, *51*, 1849.
5. Brown, E. V.; Granneman, G. R. *J. Am. Chem. Soc.* **1975**, *97*, 621.
6. Cravotto, G.; Beggiato, M.; Penoni, A.; Palmisano, G.; Tallari, S.; Leveque, J.; Bonrath, W. *Tetrahedron Lett.* **2005**, *46*, 2267.
7. Gelman, D.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 5993.
8. Lüning, U.; Wangnick, C.; Peters, K.; Schnering, H. G. V. *Chem. Ber.* **1991**, *124*, 397.
9. Field, J. E.; Hill, T. J.; Venkataraman, D. *J. Org. Chem.* **2003**, *68*, 6071.
10. Tashiro, M.; Yamato, T. *J. Org. Chem.* **1985**, *50*, 2939.
11. Goto, K.; Holler, M.; Okazaki, R. *Tetrahedron Lett.* **1996**, *37*, 3141.
12. Tan, B.; Goto, K.; Kobayashi, J.; Okazaki, R. *Chem. Lett.* **1998**, *10*, 981.
13. Gowenlock, B. G.; Cameron, M.; Boyd, A. S. F. *J. Chem. Res. (S)* **1995**, 358.
14. Jones, R. A.; Roney, B. D.; Sasse, W. H. F.; Wade, K. O. *J. Chem. Soc. (B)* **1967**, 106.
15. Demmark, S. E.; Fan, Y. *J. Am. Chem. Soc.* **2002**, *124*, 4233.
16. Peters, M. V.; Stoll, R. S.; Goddard, R.; Buth, G.; Hecht, S. *J. Org. Chem.* **2006**, *71*, 7840.
17. Yoo, B. W.; Choi, K. H.; Choi, K. I.; Kim, J. H. *Synth. Commun.* **2003**, *33*, 4185.
18. The association constants were estimated by a least-squares method using the equilibria of the association of the trans and the cis ligands with ZnTPP:

$$K_t = P_t/(P_0 - P_t - P_c)(t_0 - P_t)$$
$$K_c = P_c/(P_0 - P_t - P_c)(c_0 - P_c)$$

Here P_t and P_c are the concentrations of the trans-azo ligand·Zn-porphyrin and the cis-azo ligand·Zn-porphyrin, respectively, P_0 is the total concentration of Zn-porphyrin, t_0 and c_0 are the total concentration of the trans- and cis-azo ligands, respectively. The value of K_t was obtained with experiments with pure trans isomers. The value of K_c was obtained from titration of mixtures of trans and cis isomers, assuming the limiting values of chemical shift changes of pyridyl protons in the ligand in the cis isomer, $\Delta\delta c^{\infty}$, are the same as those in the trans isomer $\Delta\delta t^{\infty}$.

19. Osuka, A.; Liu, B.; Maruyama, K. *J. Org. Chem.* **1993**, *58*, 3582.
20. Zn-5,15-bis(3′,5′-di-*tert*-butylphenyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin was used for its better solubility in C_6D_6 and its less overlap of ^{1}H NMR spectrum with that of BmtNNPy, as compared to ZnTPP.