



Dynamic stereochemistry of 1,8-bis(2,2'-disubstituted-4,4'-dipyridyl)naphthalenes and their *N,N'*-dioxide derivatives

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Abstract—The dynamic stereochemistry of axially chiral 2,2'-disubstituted 1,8-bis(4,4'-dipyridyl)naphthalenes and their *N,N'*-dioxide derivatives has been investigated using variable-temperature NMR spectroscopy. Computational studies and NMR data show that these constrained atropisomers exist as almost equimolar mixtures of *syn*- and *anti*-isomers and undergo rapid interconversion at ambient temperature. Introduction of electron-donating substituents into the pyridyl moieties facilitates isomerization, which proceeds via a T-shaped transition state. The decrease in conformational stability was attributed to destabilization of the ground state as a result of enhanced Coulombic repulsion between the cofacial hetaryl rings. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

1,8-Disubstituted naphthalenes display striking properties because of their unusual geometry and related atropisomerism. A variety of *peri* substituted naphthalene derivatives exhibiting alkyl,¹ aryl,² and hetaryl groups³ has been synthesized to study the nature of steric and electronic interactions between π -stacked arenes. In the ground state of 1,8-diarylnaphthalenes, both aryl rings are cofacial and almost perpendicular to the nonplanar naphthalene group. The naphthalene moiety is twisted and the two aryl groups are splayed out to minimize steric interactions and through-space Coulombic repulsion between the *peri* substituents. Rotation about the aryl-naphthalene bond of 2,2'-disubstituted 1,8-diarylnaphthalenes causes interconversion of diastereoisomers via a T-shaped transition state exhibiting the edge of the rotating aromatic ring directed towards the face of the neighboring ring. Conformational stability of 1,8-disubstituted naphthalenes increases with steric restriction in the T-shaped transition state. Introduction of substituents into the *peri* aryl rings has been reported to significantly increase the energy barrier to isomerization.⁴ Despite their interesting stereochemical and electronic properties, only a few applications of 1,8-diarylnaphthalenes

have been investigated. Bahl et al. designed new blue-transparent frequency-doubling devices using nonlinear optically active 1,8-dihetarylnaphthalenes.⁵ Watkinson et al. developed a 1,8-diarylnaphthalene-derived bis-(manganese) complex exhibiting water splitting activity upon irradiation of visible light.⁶

We report herein an investigation of electronic effects on the conformational stability of new 2,2'-disubstituted 1,8-bis(4,4'-dipyridyl)naphthalene derivatives and their *N,N'*-dioxides, **1–4** (Fig. 1).⁷

The 1,8-bis(2,2'-disubstituted-4,4'-dipyridyl)naphthalene framework displays shielding groups, such as phenyl rings, in close proximity to a metal binding heteroatom.

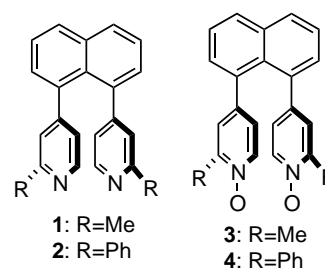


Figure 1. Structure of 2,2'-disubstituted 1,8-bis(4,4'-dipyridyl)naphthalene derivatives and their *N,N'*-dioxides.

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Thus, bidentate atropisomers **1–4** combine chelating properties with unique structural features. Based on the conformational flexibility inherent to these compounds, atropisomeric *N,N'*-dioxides **3** and **4** might be useful as molecular probes for chiral recognition studies as well as molecular switches. Bidentate *N,N'*-dioxides are known to form strong Lewis acid–base complexes with a variety of metal ions.⁸ Pyridine *N*-oxides have been reported to exhibit catalytic activity in various organic reactions, such as oxidation of alkyl amines to *N*-oxides and ozonolysis of olefins.⁹ Recently, chiral pyridine *N*-oxides and 2,2'-biquinoline *N,N'*-dioxides have been introduced to asymmetric catalysis.¹⁰ The development of suitably substituted, and therefore conformationally stable, derivatives of *anti* 1,8-dihetarylnaphthalene *N,N'*-dioxide **3** and **4** would afford a new class of chiral ligands for enantioselective catalysis.

2. Results and discussion

Rotation of either pyridyl ring about the axially chiral pyridyl–naphthalene bond of 2,2'-disubstituted 1,8-bis(4,4'-dipyridyl)naphthalenes **1** and **2** and their *N,N'*-dioxides **3** and **4** causes *syn/anti*-isomerization. Variable temperature NMR spectroscopy¹¹ allowed us to determine the rotational energy barrier for atropisomers **1–4** by the coalescence method (Table 1).¹² The NMR temperature was varied between –50 and 45°C

Table 1. Energy barrier to *syn/anti*-isomerization of **1–4**

Entry	T_c (°C)	ΔG^\ddagger (kJ/mol)
1	40.3	67 ^a
2	40.3	73 ^b
3	12.1	64 ^a
	27.5	65 ^b
4	27.5	69 ^b

T_c = coalescence temperature.

^a Based on coalescence of methyl signals.

^b Based on coalescence of pyridyl signals.

and measured following a procedure reported by Merbach et al.¹³ The proton NMR signals of the naphthalene moiety undergo only minor changes with varying temperature. By contrast, lineshapes of pyridyl as well as methyl and phenyl signals change significantly and show coalescence at ambient temperature (Fig. 2). At low temperature, the methyl signals of the *syn* and *anti* isomers of **1** and **3**, respectively, are well resolved in the proton NMR spectrum.

The rotational energy barrier of **1** was determined as 67 kJ/mol at 40.3°C. At the same temperature, **2** exhibits a higher energy barrier to isomerization, i.e. 73 kJ/mol. The corresponding *N,N'*-dioxides **3** and **4** exhibit slightly lower rotational energy barriers, i.e. 65 and 69 kJ/mol, respectively, at 27.5°C.

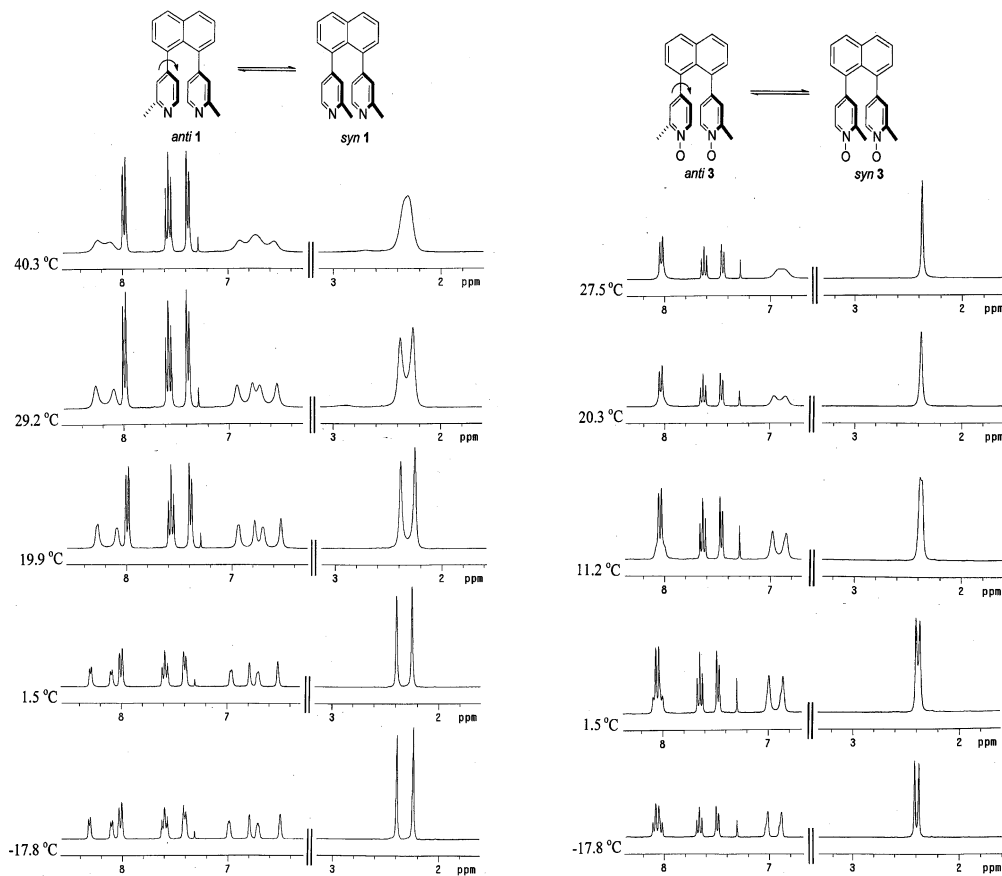


Figure 2. Variable-temperature NMR spectroscopy of 1,8-bis(2,2'-dimethyl-4,4'-dipyridyl)naphthalene, **1**, and its *N,N'*-dioxide derivative **3**.

We assume that the unsubstituted side of the rotating pyridyl ring points towards the neighboring pyridyl ring in the T-shaped transition state. Therefore, steric effects from substituents at position 2 of the pyridyl moieties on the rotational energy barrier of atropisomers **1–4** should be negligible. The increase in the energy barrier observed when replacing a methyl by a phenyl group is probably a result of electronic effects. It is likely that the aromatic π -systems as well as lone electron pairs on the heteroatoms of the two cofacial pyridyl rings exhibit repulsive through-space Coulombic interactions. Stacked aryl rings have been reported to undergo strong repulsive Coulombic interactions that overcompensate charge-transfer and van der Waals interactions.¹⁴ According to our PM3 calculations, 1,8-dipyridylnaphthalenes and their N,N' -dioxides adopt a conformation with both aromatic moieties being splayed away from each other to minimize intramolecular Coulombic repulsion and dipole–dipole interactions (Fig. 3).

At room temperature, the proton NMR spectra of atropisomers **1–4** were consistent with almost equimolar mixtures of C_2 -symmetric *anti* and meso *syn* isomers. These results are in good agreement with PM3 calculations that suggest only small energetic preferences of 1–3 kJ/mol for the *anti* isomer of **1–4**. One might expect that steric repulsion between the phenyl groups in position 2 of the pyridyl rings of compounds **2** and **4** would favor the *anti* isomer over the sterically crowded *syn* isomer. Such repulsive steric interactions could be partially compensated for by attractive π – π interactions between the phenyl moieties. Similar effects on the *syn/anti*-populations of 1,8-diarylnaphthalenes have been reported by Lavieri et al.¹⁵ However, PM3 computations of the *syn* isomer of **2** reveal that the two phenyl rings are splayed away (Fig. 3). The distance between their mass centers was determined as 5.5 Å, indicating that both phenyl moieties are too far apart to undergo significant π – π interactions.¹⁶

For geometric reasons, repulsive Coulomb interactions can only occur in the parallel-stacked ground state but not in the T-shaped transition state. Introduction of phenyl groups into 1,8-dipyridylnaphthalenes should reduce the electron density in the cofacial pyridyl moieties and decrease destabilizing Coulombic interactions in the ground state. Electronic effects on the stability of the face-to-edge transition state, such as enhancement of CH/ π -interactions, should be negligible.¹⁷ As a result, incorporation of a phenyl group into the 1,8-dipyridylnaphthalene framework increases the rotational energy barrier. Atropisomer **1** affords a lower rotational energy barrier than its phenyl derivative **2**, since introduction of a methyl group into the 1,8-dipyridylnaphthalene moiety increases repulsive Coulomb interactions. Consequently, destabilization of the ground state results in decreased conformational stability of **1**. It is well known that conversion of a pyridine ring to its N -oxide increases the π -electron density in the aromatic moiety. Oxidation of the atropisomers **1** and **2** to their N,N' -dioxide derivatives **3** and **4** should result in enhanced Coulombic repulsion and reduced stability of the cofacial ground state. Accordingly, the energy barrier to *syn/anti*-isomerization obtained for 1,8-dipyridylnaphthalene N,N' -dioxides **3** and **4** is lower than the energy barrier observed for the corresponding dipyrityls **1** and **2**, respectively.

In summary, the rotational energy barrier of 2,2'-disubstituted 1,8-bis(4,4'-dipyridyl)naphthalenes and their N,N' -dioxides has been studied by variable-temperature NMR spectroscopy. 1,8-Bis(4,4'-dipyridyl)naphthalenes exhibit a higher energy barrier to *syn/anti*-isomerization than their N,N' -dioxide derivatives. Introduction of a phenyl group into the pyridyl or pyridine N -oxide moiety increases the rotational energy barrier, whereas introduction of a methyl group decreases the conformational stability. It was concluded that an increase of π -electron density in the pyridyl moieties enhances destabilizing Coulomb interaction in the cofacial ground state and thus facilitates *syn/anti*-isomerization.

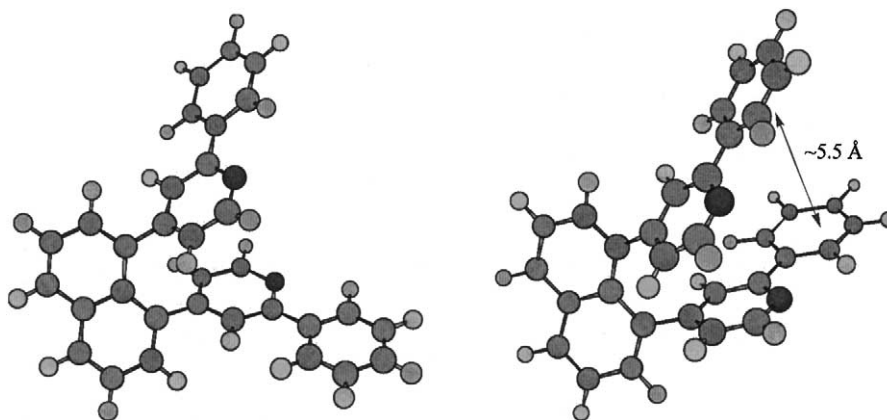


Figure 3. Ground state conformation of *anti* (left) and *syn* (right) 1,8-bis(2,2'-diphenyl-4,4'-dipyridyl)naphthalene, **2**, calculated by PM3.

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- Equation 1: $\Delta G^\ddagger = -\ln(k_c h / 2k_B T_c) RT_c$, equation 2: $k_c = \pi \Delta\nu / \sqrt{2}$, T_c = coalescence temperature, k_c = rate constant at T_c , h = Planck's constant, k_B = Boltzmann's constant, R = Gas constant, $\Delta\nu$ = chemical shift difference at low temperature. Factor 2 in equation 1 accounts for the two possible isomerization pathways, i.e. rotation of either pyridyl ring. It is assumed that both rotations have the same energy barrier.
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