π-Cation and π-Dipole-Stabilizing Interactions in a Simple Model System with Cofacial Aromatic Rings

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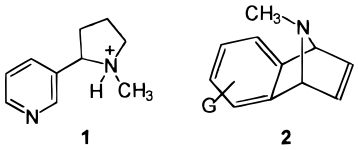
Four 1,8-disubstituted naphthalenes having a 1-naphthyl ring cofacial to a second ring were prepared by a Suzuki-type coupling of a bromide with a borane, a boronic acid, or a boronic ester in the presence of Pd(0). The second ring is either a positively charged N-methylated 3-pyridyl (**4A**) or a 3-(trimethylammonio)phenyl group (**7A**) or a neutral 3-tolyl (**5**) or 3-(dimethylamino)phenyl (**7**) ring. At ambient temperatures, all exhibit atropisomerism. The syn isomer predominates over the anti form, suggesting that π-charge and π-dipole electrostatic through-space interactions preferentially stabilize the more sterically hindered syn isomer. The largest preference for the syn isomer, a factor of 3.1, was found for the trimethylammonio substrate **7A** in $CDCl_3$. Semiempirical computations (AM1 and PM3) predict that the syn isomer is lower in energy than the anti form of the positively charged compounds, but the preference for the neutral compounds is small enough to be ambiguous.

Noncovalent attractive interactions are important for molecular recognition.[1,2] These include ion as well as dipole attractions to the π-electrons of aromatic rings.[3−7] The interaction between the π-electrons of an aromatic ring and a positive charge such as that in a trimethylammonio group constitutes one such electrostatic attraction, only recently recognized.[4] In biological systems, for example, such an attraction exists between the neurotransmitters acetylcholine and protonated nicotine (**1**) at their natural receptor sites, heavily constituted with aromatic rings.[8] Similar interactions are important for protein structure.[7,9] A large number of model systems have been constructed to show that such an attractive interaction also exists in purely chemical systems.[4,10−12]

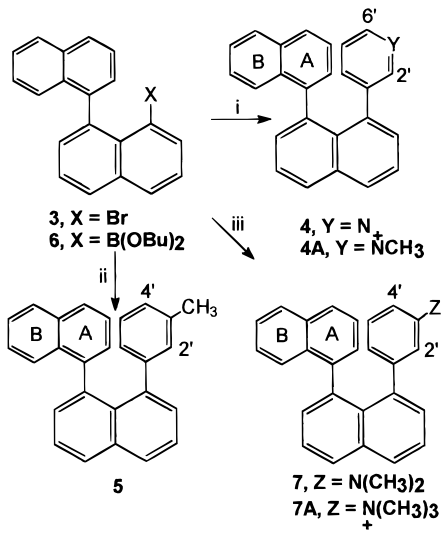


1 **2**

An interesting example of an aromatic ring interacting with a dipole to generate a weak noncovalent bond is found in the preferred syn conformation of azanorbornadiene **2**. Here, the methyl group is positioned over and not away from the benzene ring.[13]

We have constructed a simple model system containing two cofacial aromatic rings held in place by a 1,8-disubstituted naphthalene frame in order to search for π-charge- and π-dipole-stabilizing interactions (Scheme 1). One cofacial ring, a 1-naphthyl group, was chosen to have a large π-facial surface area for interaction as well as dissymmetry to allow for the formation of equilibrating stereoisomers. The second monosubstituted ring was

Scheme 1[a]



[a] Key: (i) diethyl(3-pyridyl)borane, then MeI; (ii) 3-toluneboronic acid; (iii) *N*,*N*-dimethyl-3-bromoaniline, then MeI.

(1) Whitesides, G. M.; Simanek, E. E.; Mathias, J. P.; Seto, C. T.; Chin, D. N.; Mammen, M.; Gordon, D. M. *Acc. Chem. Res.* **1995**, *28*, 37.
(2) Hunter, C. A. *Chem. Soc. Rev.* **1994**, *23*, 101.
(3) Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303.
(4) Dougherty, D. A. *Science* **1996**, *271*, 163.
(5) Naray-Szabo, G.; Ferenczy, G. G. *Chem. Rev.* **1995**, *95*, 829.
(6) Schneider, H.-J.; Schiestel, T.; Zimmerman, P. *J. Am. Chem. Soc.* **1992**, *114*, 7698.
(7) Burley, S. K.; Petsko, G. A. *Adv. Protein Chem.* **1988**, *39*, 125.
(8) Harel, M.; Quinn, D. M.; Nair, H. K.; Silman, I.; Sussman, J. L. *J. Am. Chem. Soc.* **1997**, *118*, 2340.
(9) Rebek, J., Jr. *Chem. Soc. Rev.* **1996**, *25*, 255.
(10) Arnecke, R.; Böhmer, V.; Cacciapaglia, R.; Dalla Cort, A.; Mandolini, L. *Tetrahedron* **1997**, *53*, 4901.
(11) Aoki, K.; Murayama, K.; Nishiyama, H. *J. Chem. Soc., Chem. Commun.* **1995**, 2221.
(12) Caldwell, J. W.; Kollman, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 4177.
(13) Bushweller, C. H.; Brown, J. H.; DiMeglio, C. M.; Gribble, G. W.; Eaton, J. T.; LeHoullier, C. S.; Olson, E. R. *J. Org. Chem.* **1995**, *60*, 268.

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selected to be monocyclic with a substituent located at position 3 to interact with the 1-naphthyl ring. These include a pyridinium ring (**4A**) to model a delocalized positive charge and a (trimethylammonio)phenyl (**7A**) group to provide a more localized positive charge. The two other dipolar models made use of a substituted benzene ring with a methyl (**5**) or a dimethylamino (**7**) group, the latter giving rise to a larger dipole. All the substrates make use of a methyl substituent as a reporter group in their proton NMR spectra, thereby making easy the determination of syn/anti isomer ratios reflecting restricted rotation.

Our results show for the first time that it is possible to have the more sterically hindered syn atropisomer predominate over the more commonly favored anti stereoisomer in such cofacial compounds, consistent with the presence of the suggested stabilizing interactions. The B-ring of the naphthalene and the substituent on the other cofacial ring are syn to each other.

Results

Syntheses. All the important compounds were synthesized by $Pd(PPh_3)_4$-catalyzed cross-coupling reactions of a bromide and a borane or boronic acid or ester in aqueous alkali (Suzuki coupling[14]). It was important to use 1,2-dimethoxyethane[15] (DME) in place of the more common THF in order to promote solubility. Application of a tetrabutylammonium phase-transfer catalyst also was beneficial.[16−18] An 8-substituted 1,1′-binaphthyl[19] was prepared first, and then the variable second ring was added in a coupling reaction to give a racemic mixture.

8-Bromo-1,1′-binaphthyl[19] (**3**) and diethyl(3-pyridyl)borane gave 1-(1′-naphthyl)-8-(3′-pyridyl)naphthalene (**4**) (72%). The starting bromide was prepared from 1,8-dibromonaphthalene[20] and 1-naphthaleneboronic acid[21] in a Pd-catalyzed coupling reaction.[19] Quaternization with methyl iodide gave the desired product **4A** (80%).

The preparation of 1-(3′-tolyl)-8-(1′-naphthyl)naphthalene (**5**) again made use of bromide **3**,[19] which then was coupled with 3-tolueneboronic acid[22] (87%).

1-(1′-Naphthyl)-8-[3′-(*N*,*N*-dimethylamino)phenyl]naphthalene (**7**) required the use of 1,1′-binaphthyl boronate ester[19] **6** and *N*,*N*-dimethyl-3-bromoaniline[23] (81%). Heating **7** with MeI gave the *N*,*N*,*N*-trimethylammonio derivative **7A** (89%).

Proton NMR Spectra. All the positively charged and neutral methylated materials existed as mixtures of syn and anti atropisomers present in unequal amounts in a number of solvents at room temperature. Two signals were present for the methyl protons in each substrate. While the aromatic portions of the spectra are complex due to extensive signal overlap, the pair of methyl signals associated with each substance has a chemical shift separation of at least 0.3 ppm that allows the ready determination of syn−anti ratios at ambient temperatures, Table 1.

Table 1. Chemical Shifts for Stereoisomeric Methyl Protons and Associated Syn/Anti Isomer Quotients at 20 °C

compd	solvent	anti, ppm	syn, ppm	[syn]/[anti]
4A	DMSO-d_6	3.97	3.62	1.2
	DMSO-d_6[a]	4.01	3.61	1.1
	CD_3OD	4.03	3.72	1.4
	$CDCl_3$	4.30	3.95	2.2
5	DMSO-d_6	1.99	1.37	1.5
	$CDCl_3$	2.04	1.44	1.4
7	$CDCl_3$	2.78	2.30	1.5
7A	DMSO-d_6	3.44	3.05	1.1
	CD_3COCD_3	3.80	3.42	1.5
	$CDCl_3$	3.80	3.41	3.1

[a] At 100 °C.

Structural assignments of the stereoisomers are based on the common observation that a proton when positioned over an aromatic ring is shielded.[24−26] A methyl group in position 3 of the monocyclic ring of our compounds will largely experience the shielding effect of the A-ring of the cofacial naphthalene when it is anti, but it will be shielded by both the A and B rings when located syn as verified by the results of computational studies considered below. Therefore, the signal of the methyl group in the syn isomer will be at higher field than that in the anti structure, and it will be found at considerably higher field than in a simple model compound where such shielding is not present.

Confirmation of the proposed relationships between stereochemical assignments and chemical shifts in systems such as ours is found among individually isolated stereoisomers, including those for cofacial rings found in the more extensively studied cyclophanes,[25] some characterized by X-ray crystallography. Often only one of the isomers is examined, occasionally syn as with **2**,[13] more generally anti.[19,27] But when steric hindrance is large, both isomers may be separated and characterized.[28]

The chemical shifts of the methyl protons in syn- and anti-[2.2]metacyclophanes are highly supportive of our analysis. When the methyl groups at the 4 and 12 ("internal") positions are situated over and inside the phenylene ring, their signal is found at 0.56 ppm, but when they are directed outside and away from the neighboring ring in the other isomer the signal is located at 4.75 ppm.[25] These two isomeric forms correspond, respectively, to our syn and anti isomers where a methyl group is directed toward the B-ring or away from it.

Comparison of the *N*-methyl shifts for the iodide salt of cation **4A**, Table 1, with that of *N*-methylpyridinium ion reference compound (bromide and iodide, 4.3 ppm, DMSO-d_6[29]) shows that the position of the signal for the anti isomer is moved upfield by 0.3 ppm and the signal for the syn isomer is shifted to higher field by 0.7 ppm. This is consistent with the chemical shift of the *N*-methyl group in quaternized pyridinophanes.[30] Similarly, the

(14) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
(15) Alcock, N. W.; Brown, J. M.; Hulmes, D. I. *Tetrahedron: Asymmetry* **1993**, *4*, 743.
(16) Jeffery, T. *Tetrahedron Lett.* **1994**, *35*, 3051.
(17) Crisp, G. T.; Gebauer, M. G. *Tetrahedron* **1996**, *52*, 12465.
(18) Reetz, M. T.; Breinbauer, R.; Wanninger, K. *Tetrahedron Lett.* **1996**, *37*, 4499.
(19) Zoltewicz, J. A.; Maier, N. M.; Lavieri, S.; Ghiviriga, I.; Abboud, K. A.; Fabian, W. M. F. *Tetrahedron* **1997**, *53*, 5379.
(20) Kuroda, M.; Nakayama, J.; Hoshino, M.; Furusho, N.; Kawata, T.; Ohba, S. *Tetrahedron* **1993**, *49*, 3735.
(21) Yarbroff, D.; Branch, G. E. K.; Bettman, B. *J. Am. Chem. Soc.* 1934, *56*, 1850.
(22) Thompson, W. J.; Gaudino, J. *J. Org. Chem.* **1984**, *49*, 5237.
(23) Gilman, H.; Banner, I. *J. Am. Chem. Soc.* **1940**, *62*, 344.
(24) Balaban, A. T.; Dinculescu, A.; Koutrakis, N.; Chiraleu, F. *Tetrahedron Lett.* **1979**, *20*, 437.
(25) Boekelheide, V. *Top. Curr. Chem.* **1983**, *113*, 87.
(26) Lai, Y.-H.; Yong, Y.-L. *J. Org. Chem.* **1997**, *62*, 4500.
(27) Katoh, T.; Ogawa, K.; Inagaki, Y.; Okazaki, R. *Tetrahedron* **1997**, *53*, 3557.
(28) Ibuki, E.; Ozasa, S.; Fujioka, Y.; Hiroshi, M. *Chem. Pharm. Bull.* **1981**, *29*, 2103.
(29) Reynolds, W. F.; Priller, U. R. *Can. J. Chem.* **1968**, *46*, 2787.

signals at 1.44 ppm for 3-tolyl compound **5**-syn are located upfield from those of toluene (2.09 ppm) by 0.65 ppm and even upfield of the shifts for the methyl groups in 1,8-di(3-tolyl)- (2.14 and 1.99 ppm)[31] and 1,8-di(4-tolyl)naphthalene (2.17 ppm).[32]

The *N*,*N*-dimethyl signals in **7** are upfield of those for *N*,*N*-dimethyl-3-bromoaniline[23] (2.89, $CDCl_3$) by 0.6 ppm for the syn structure, consistent with shielding. The stereolabile dimethyl unit provides just a single signal for each isomer present in unequal amounts. The *N*,*N*,*N*-trimethylammonio pair of singlets in **7A** shows a signal for the syn isomer upfield by 0.55 ppm of those found for the methyl protons in *N*,*N*,*N*-trimethylanilinium ion (3.61 ppm, DMSO-d_6).

Chemical shifts for annular protons when not present as overlapped multiplets also support the stereochemical assignments. Thus, with cation **4A** in $CDCl_3$ (500 MHz), there are two such pairs of signals, one proton pair for each cofacial ring. Especially interesting and confirmatory is the order of intensities within a pair. The doublets (J = 6.0 Hz) at 8.74 and 8.62 ppm are due to H-6′ of the pyridinium ring as verified by an NOE experiment in which the *N*-methyl group was irradiated selectively. The second pair of signals consists of two doublet of doublets (J = 6.0, 6.5 Hz) at 7.12 and 6.88 ppm; they are associated with H-3′ of the A-ring of the cofacial naphthalene. At lower field, the smaller signal appears before the larger, but at higher field the intensity order is reversed. Here, H-6′ is on the same ring as the *N*-methyl group and points in a similar direction and so the shift pattern anti and then syn is the same for both types of protons; both experience the enhanced shielding effects of the A- and B-naphthalene rings when syn but not when anti. But for the proton at H-3′ on the naphthalene A-ring, greater shielding occurs in the anti than in the syn isomer due to greater overlap with the pyridine ring in the anti form. This same pattern of anti at higher field than syn is observed in ternaphthalenes,[19] azaternaphthalenes,[19] and 1,8-di(3,3-dipyridyl)naphthalenes[33] and for equivalent positions in [2.2]paracyclonaphthalenes.[34] The isomer preference of syn over anti as given by the pyridine and naphthalene ring protons is a factor of 2.2 and 2.1, respectively, while the value from the methyl protons is 2.2.

For aniline **7**, broadened singlets due H-2′ appear at 6.02 and 5.68 ppm with the former being less intense than the latter. This is the same pattern observed for H-6′ of the pyridine ring in **4A** and has the same explanation for the shift order. The syn to anti isomer preference (1.5) established by the ring protons is the same as that (1.5) provided by the methyl groups.

Ratio of Diastereomers. The syn/anti population quotients for the four compounds are listed in Table 1 for several solvents, mostly DMSO-d_6 and $CDCl_3$, and for **4A** values are given at two temperatures. The syn form is favored for all four compounds under all conditions, the syn to anti preference factors ranging in value from 1.1 to 3.1 at ambient temperatures. As expected for an equilibrium between isomers with a ratio close to 1 in value, the influence of temperature on the value for **4A** is insignificant.

Table 2. Gas-Phase Enthalpies of Formation (kcal/mol) of Anti and Syn Atropisomers in One or More Conformations As Computed by AM1 and PM3

compd	anti-1[a]	anti-2[a]	syn-1[a]	syn-2[a]	anti-1[b]	anti-2[b]	syn[b]
4	133.31	**133.22**	133.73	same	125.32	same	125.61
4A,I[c]	**279.56**	280.02	278.76	same	271.16	same	270.11
5	116.75	**116.55**	**116.65**	116.72	109.43	same	109.42
7	133.73	**133.44**	133.64	**133.49**	115.52	**115.22**	115.01
7A,I[c]	289.75	**289.16**	287.63	same	269.45	**268.89**	267.24

[a] AM1. [b] PM3. The lower energy anti or syn conformation is printed in bold type. [c] Iodide.

The two cations were investigated the most extensively. The syn/anti abundance quotient for **4A** increased modestly as the amount of syn isomer increased when the solvent polarity was changed on going from DMSO-d_6 (1.2) to CD_3OD (1.4) to $CDCl_3$ (2.2). For **7A**, this factor increased somewhat more when DMSO-d_6 (1.1) was changed to acetone-d_6 (1.5) and to $CDCl_3$ (3.1). This latter quotient is the largest observed in our study. In this least polar solvent the large trimethylammonio substituent of **7A** preferentially occupies the more sterically hindered conformation by a wide margin.

For neutral compound **5** with its weakly electron-donating methyl group and resultant small dipole moment, the nature of the solvent had essentially no influence on the syn/anti values, 1.5 for DMSO-d_6 and 1.4 for $CDCl_3$. A similar value was observed for in **7** in $CDCl_3$ with its larger and more strongly electron-donating dimethylamino group; the syn isomer was favored by a factor of 1.4.

The unquaternized pyridyl precursor **4** to monocation **4A** was not examined extensively. In DMSO-d_6, its spectrum at 19 °C was sharp and complex due to signal overlap. Judging from the integer intensity ratio of the multiplets, an anti−syn pair was present in approximately a 1:1 ratio. Heating this sample to 70 °C kept the 1,8-naphthalene signals sharp, but the *ten* pyridyl protons broadened considerably as the rate of ring rotation increased, thereby verifying that two isomers indeed were present.

Semiempirical Computations, Isomer Preferences, and Conformations. On the basis of the computed enthalpies of formation, Table 2, the AM1 method correctly predicted that the syn diastereomer is lower in energy than the anti isomer in the case of cations **4A** and **7A** while the PM3 data provided the same conclusion for these two as well as for neutral **7**. For **4A**, the syn isomer is favored by 0.80 (AM1) and 1.0 (PM3) kcal/mol, giving a syn/anti ratio of 4 and 5:1, respectively, and for **7A** the syn diastereomer is preferred by 1.5 (AM1) and 0.81 (PM3) kcal/mol or by factors of 13 and 4.0, respectively. The PM3 computation indicated that in the case of **7** the syn form is lower by 0.21 kcal/mol, giving a preference of a factor of 1.4. However, the computations indicated that the anti isomer is favored for neutral **5** and **7** but the preference is small, about 0.1 kcal/mol, and therefore not meaningful. The computed preferences for the syn compound based on enthalpies are larger than those observed. In the case of unsubstituted **4**, the anti isomer is favored by 0.51 (AM1) or 0.29 (PM3) kcal/mol, factors of 2.4 and 1.6, respectively. Experimentally, there is no real preference for a

(30) Kang, H. C.; Boekelheide, V. *J. Am. Chem. Soc.* **1984**, *106*, 2672.
(31) Vögtle, F.; Wingen, R. *Tetrahedron Lett.* **1978**, 1459.
(32) Clough, R. L.; Mison, P.; Roberts, J. D. *J. Org. Chem.* **1976**, *41*, 2252.
(33) Zoltewicz, J. A.; Maier, N. M.; Fabian, W. M. F. *Tetrahedron* **1996**, *52*, 8703.
(34) Wasserman, H. H.; Keehn, P. M. *J. Am. Chem. Soc.* **1969**, *91*, 2374.

sample in DMSO-d_6, a solvent that tends to level the populations.

Although the 3-*tert*-butyl analog of trimethylammonio **7a** was not prepared, both AM1 (0.35 kcal/mol) and PM3 (0.42 kcal/mol) computations indicate that the anti isomer of the neutral compound is lower in energy than the syn, giving an anti to syn population quotient of 1.8 and 2.0, respectively. Therefore, since the sizes of the *tert*-butyl and trimethylammonio groups are about the same, the degree of steric crowding between these groups and the cofacial ring is similar. The change in the predominant isomer from syn to anti on removing the positive charge is consistent with the idea that a π-charge electrostatic-stabilizing interaction is a major factor causing a change in the ground-state orientation of the cofacial rings.

There are two anti and two syn limiting ground-state conformations with small differences in enthalpies depending on the orientation of the 1-naphthyl B-ring and the group at position 3 of the other cofacial ring, taking the 1,8-disubstituted naphthalene frame as a reference for the geometry, Table 2. In the anti isomer, both of these fragments can be located "inside" over the disubstituted naphthalene ring or both may be "outside". In the syn orientation, one of these fragments is rotated "outside" and the other is "inside". Interconversion between the two limiting conformations is rapid because only simple rotations about the σ-bonds are required. A similar suggestion regarding conformations and their ease of interconversion was made for the position of the methyl groups in the di(2-tolyl) cofacial analog.[35] The AM1 method generally provided an energy difference for both forms of the syn and anti diastereomers while the PM3 treatment was much less sensitive to conformational changes, in no case differentiating between the two possible syn forms. For **4A**, **5**, **7**, and **7A**, the preferred conformation (AM1) for the syn isomer usually has the B-naphthyl ring "outside" and the substituent "inside" over the naphthalene frame.

Discussion

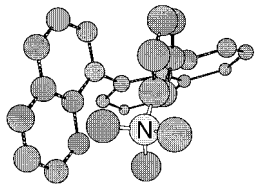
With the many cofacial 1,8-diarylnaphthalenes reported to date, the anti diastereomer is favored. This holds for simple uncharged diaryl and dihetaryl compounds where the anti to syn ratio often is about 3:1.[19,27,33,35−38] For systems with two positively charged cofacial pyridine rings, again the anti isomer is more abundant,[19] but the ratio is, as expected, modestly dependent on solvent polarity.[39]

The presence of two cofacial naphthalene rings[19,28] or a pair of cofacial naphthalene and isoquinoline rings[19] or a pair of cofacial polycyclic pyrenyl aromatic rings[38] does not cause the syn isomer to predominate. The necessary feature for the preferential population of a syn stereoisomer in our examples is the presence of one cofacial polycyclic aromatic ring, here a 1-substituted naphthalene, and a monocyclic ring with a group at position 3.

Structural Deformations and Conformational Preferences. Crystal structures[19,27,38,40−42] as well as the results of computations[19,33,37,39,43,44] reveal that the cofacial rings generally are not perpendicular to the main naphthalene ring plane but instead are twisted away. Carbon atoms at the 1,8 positions in the naphthalene frame lie above and below the main plane defined by the remainder of the ring, and the σ-bonds to these atoms adopt an arrangement allowing the faces of the cofacial rings to move laterally apart and to be offset. The rings are not parallel; they are skewed outward from their bonding sites in a V-shaped pattern in order to minimize repulsions between the rings. Semiempirical computations show all these deformations, but the computed deformations tend to be larger than those observed in the crystal.[19]

The distances between the cofacial A- and B-naphthyl rings and the substituent at position 3 are dependent on the identity of the isomer and the extent of the "in" and "out" rotations of the rings about their σ-bonds. The group at position 3 is closer on average to the B-naphthyl ring in the syn than in the anti isomer.

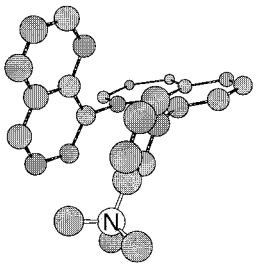
In the syn conformation (AM1) shown in structure **7A-*syn*** (hydrogen atoms omitted for clarity), the B-ring is "outside" and the trimethylammonio group is "inside"; the computed energy for this conformation is the same as that for the other limiting conformation where the positions of the two rings are interchanged. The positively charged nitrogen atom is almost equidistant from all the carbon atoms of the B-ring, varying from 4.26 to 4.48 Å. Distances from this same atom to the carbons of the A-ring are slightly larger, increasing from 4.86 Å at C-1′ to 5.51 Å at C-3′. The nitrogen atom therefore interacts with both rings, more with the B-ring. In the same conformation for **4A**-syn (AM1), the separation between the centroids of the pyridinium and the naphthalene rings is only about 3.88 Å, and this is similar to the van der Waals contact distance of 3.4 Å for a benzene ring.[45]



7A-*syn*

In the lower energy **7A-*anti*-2** conformation (AM1, Table 2) illustrated by the structure, the B-ring and the trimethylammonio substituent are located "inside". In this conformation, the distances from the nitrogen atom to the carbon atoms of the A-ring increase from 3.89 Å at C-3′ to 5.17 Å at C-8a′ (AM1). Distances to the B-ring are much larger. The conformation of **4A-*anti*-1** (AM1, Table 2) with the lower energy has both the B-ring and

(35) Clough, R. L.; Roberts, J. D. *J. Am. Chem. Soc.* **1976**, *98*, 1018.
(36) Cozzi, F.; Cinquini, M.; Annunziata, R.; Dwyer, T.; Siegel, J. *J. Am. Chem. Soc.* **1992**, *114*, 5729.
(37) Zoltewicz, J. A.; Maier, N. M.; Fabian, W. M. F. *J. Org. Chem.* **1997**, *62*, 3215.
(38) Wahl, P.; Krieger, C.; Schweitzer, D.; Staab, H. A. *Chem. Ber.* **1984**, *117*, 260.
(39) Zoltewicz, J. A.; Maier, N. M.; Fabian, W. M. F. *J. Org. Chem.* **1996**, *61*, 7018.
(40) Jones, P. G.; Grahn, W.; Bahl, A.; Chrapkowski, A. *Z. Kristallogr.* **1995**, *210*, 229.
(41) Tsuki, R.; Komatsu, K.; Takeuchi, K.; Shiro, M.; Cohen, S.; Rabinovitz, M. *J. Phys. Org. Chem.* **1993**, *6*, 435.
(42) House, H. O.; Koepsell, D. G.; Campbell, W. J. *J. Org. Chem.* **1972**, *37*, 1003.
(43) Cosmo, R.; Sternhell, S. *Aust. J. Chem.* **1987**, *40*, 1107.
(44) Zoltewicz, J. A.; Maier, N. M.; Fabian, W. M. F. *J. Org. Chem.* **1997**, *62*, 2763.
(45) Bickelhaupt, F. *Pure Appl. Chem.* **1990**, *62*, 373.



7A-*anti*-2

the *N*-methyl group located "inside" over the frame. The distance between the ring centroids is 3.75 Å. In an *ab initio* study the favorable distance between a benzene ring and an interacting tetramethylammonium ion was 4.2 Å.[12,46]

Ground-state electrostatic potential surfaces distributed into positive and negative regions that are computed with *ab initio* and AM1 methods for a variety of uncharged aromatic rings provide a simple yet good model to indicate the presence of π-charge interactions.[47] Attractive interactions require the face and not the edge of an aromatic ring to participate. For naphthalene, the highest negative potential is at the center of each ring and not the center of the molecule. For aniline, the highest positive potential is at the nitrogen site.[47] These conclusions are consistent with our observations concerning the presence of the preferred syn isomer for **4A**, **7**, and **7A**. Our least understandable result is for **5**, the least polar compound, where the positive and negative electrostatic potentials of the 3-tolyl ring are only slightly perturbed relative to those of benzene.

Solvent Dependent Isomer Ratios. The two faces of the cofacial rings are not symmetrically solvated. On one side is the neighboring ring and on the other face is solvent. No solvent molecules can be situated between the rings due to a lack of space. As solvent became more polar and better able to interact in a stabilizing manner with the charge on the exposed faces in **4A** and **7A**, the less sterically hindered anti isomer increased in abundance, Table 1.

Conclusions. Compounds **4A**, **5**, **7**, and **7A** show a preference for the syn over the anti atropisomer, suggesting the presence of π-charge- and π-dipole-stabilizing interactions that are stronger in the syn than in the anti orientation. The ionic or dipolar site interacts in a stabilizing fashion with both the A- and B-naphthyl rings when oriented syn, but the group in the anti isomer largely interacts with just the A-ring.

Experimental Section

General Methods. Because compounds consist of mixtures of anti and syn diastereomers in varying amounts, areas of multiplets generally are not in integral ratios and so areas are not reported. Spectra usually were obtained at 19−20 °C on a 300 MHz instrument.

1-(1′-Naphthyl)-8-(3′-pyridyl)naphthalene (4). To a degassed solution of 100 mg (0.30 mmol) of 8-bromo-1,1′-binaphthyl[19] (**3**) and 17 mg (0.013 mmol, 5 mol %) of $Pd(PPh_3)_4$ in 2 mL of DME was added 48 mg (0.33 mmol) of diethyl(3-pyridyl)borane followed by 50 mg (0.33 mmol) of Na_2CO_3 in 1 mL of water. After the mixture under nitrogen was magnetically stirred in a sealed container at 100 °C for 2 h, it was diluted with 50 mL of CH_2Cl_2 and 100 mL of water. The organic phase was separated, and the water layer was extracted with CH_2Cl_2 (10 mL). The combined organic layer was adsorbed onto 1 g of silica and chromatographed on silica using hexanes/EtOAc (1/2). After removal of the solvent, 72 mg (0.22 mmol, 72%) of a colorless oil was obtained. On stirring with hexanes, the material formed a white solid: mp 132−134 °C; ^{1}H NMR (DMSO-d_6) δ 8.18 (m), 7.96 (d, J = 1 Hz), 7.8−7.2 (m), 7.07 (m), 6.89 (d, J = 8.4 Hz), 6.6 (m), 6.2 (m). Anal. Calcd for $C_{25}H_{17}N$: C, 90.60; H, 5.17; N, 4.23. Found: C, 90.18: H, 5.32; N, 4.19.

1-(1′-Naphthyl)-8-(1′-methyl-3′-pyridinium-3′-yl)naphthalene Iodide (4A). To 20 mg (0.060 mmol) of **4** dissolved in 0.5 mL of MeOH was added 50 μL of MeI. After the mixture was allowed to stand for 24 h at rt, the solvent was removed and the residue was recrystallized from EtOH/ether to give 23 mg (0.51 mmol, 86%) of slightly yellowish needles: mp 225−227 °C; ^{1}H NMR 500 MHz ($CDCl_3$ at 25 °C) δ 8.74 (d, J = 6 Hz), 8.62 (d, J = 6.0 Hz), 8.15 (dd, J = 1.5, 8.5 Hz), 7.86 (s), 7.81 (d, J = 8.0 Hz), 7.77 (m), 7.70 (m), 7.6 (m), 7.45 (m), 7.28 (m), 7.12 (dd, J = 6, 7 Hz), 7.02 (d, J = 8.5 Hz), 6.88 (t, J = 6.5 Hz), 4.29 (Me), 3.94 (Me). Anal. Calcd for $C_{26}H_{20}IN$: C, 65.97; H, 4.26; N, 2.97. Found: C, 65.79; H, 4.31; N, 2.88.

1-(1′-Naphthyl)-8-(3′-methylphenyl)naphthalene (5). A mixture of 600 mg (1.80 mmol) of 8-bromo-1,1′-binaphthyl[19] (**3**), 266 mg (1.96 mmol) of (3-methylphenyl)boronic acid,[22] and 140 mg (0.12 mmol, 6.7 mol %) of $Pd(PPh_3)_4$ in 8 mL of DME was degassed by bubbling nitrogen. After the addition of 300 mg (2.83 mmol) of Na_2CO_3 in 4 mL of H_2O, the mixture was heated at reflux for 1 h under nitrogen with stirring. The mixture was diluted with 30 mL of CH_2Cl_2, the layers were separated, the organic phase was dried (Na_2SO_4), and the solvent was removed. The residue was dissolved in 40 mL of CH_2Cl_2, 3 g silica was added, and the solvent was removed. The adsorbed material then was applied to a silica gel column equilibrated with hexanes, followed by elution with hexanes to give 540 mg (1.57 mmol, 87%) of an off-white solid. Recrystallization from hexanes gave a white solid: mp 142−143 °C; ^{1}H NMR (DMSO-d_6) δ 8.11 (m), 7.76 (m), 7.45 (m), 7.1 (m), 6.94 (m), 6.68 (m), 6.43 (m), 6.14 (m), 1.99 (Me), 1.37 (Me). Anal. Calcd for $C_{27}H_{20}$: C, 94.15; H, 5.85. Found: C, 94.10. H, 5.89.

1-(1′-Naphthyl)-8-[3′-(*N*,*N*-dimethylamino)phenyl]naphthalene (7). *N*,*N*-Dimethyl-3-bromoaniline was prepared by methylating 3-bromoaniline using aqueous dimethyl sulfate.[23] The product was substantially contaminated with the monomethyl product and removed by chromatography on alumina with hexanes followed by Kugelrohr distillation.

The binaphthyl boronate ester[19] (**6**) (1.32g, 3.2 mmol) in 7 mL of DME, 468 mg (2.34 mmol) of *N*,*N*-dimethyl-3-bromoaniline, and 100 mg (0.87 mmol) of $PdP(PPh_3)_4$ (dark brown solution) was degassed by bubbling nitrogen. After an aqueous solution of 562 mg (10 mmol) of KOH and 60 mg (0.19 mmol) of tetra-*n*-butylammonium bromide was added, the mixture was heated at reflux under nitrogen with stirring for 3 h (the mixture turned black after 10 min) and then was diluted with CH_2Cl_2−H_2O (50 mL/50mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL). After the combined layers were dried and concentrated under reduced pressure, the residue was dissolved in 30 mL of CH_2Cl_2, and 3 g silica was added. The solvent again was removed to give adsorbed material that was applied to a silica column equilibrated with hexanes. Elution with EtOAc in hexanes (0−7%) gave 710 mg (1.90 mmol, 81% over two steps starting with **3**) of a colorless oil that crystallized on standing at rt. Recrystallization from hexane gave a white solid: mp 114−116 °C; ^{1}H NMR ($CDCl_3$) δ 8.0 (m), 7.54−7.1 (m), 6.70 (t, J = 7.5 Hz), 6.27 (d, J = 7.5 Hz), 6.02 (s), 6.1 (m), 5.75 (d, J = 7.5 Hz), 5.68 (s), 2.78 (Me), 2.30 (Me). Anal. Calcd for $C_{28}H_{23}N$: C, 90.04, H, 6.21, N, 3.75. Found: C, 89.75; H, 6.35; N, 3.73.

1-(1′-Naphthyl)-8-[3′-(trimethylammonio)phenyl]naphthalene Iodide Monohydrate (7A). To 100 mg (0.27 mmol) of 1-(1′-naphthyl)-8-[3′-(*N*,*N*-dimethylamino)phenyl]naphtha-

(46) Kim, K. S.; Lee, J. Y.; Lee, S. J.; Ha, T.-K.; Kim, D. H. *J. Am. Chem. Soc.* **1994**, *116*, 7399.
(47) Mecozzi, S.; West, A. P., Jr.; Dougherty, D. A. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, 10566.

lene (**7**) in 2 mL of chloroform was added 0.1 mL (1.7 mmol) of iodomethane. After being allowed to stand for 24 h at rt, the product was precipitated by the addition of 10 mL of ether, filtered, and washed with ether. Drying in vacuo gave 127 mg (0.238 mmol, 89%) of a yellowish solid: mp 171−173 °C; ^{1}H NMR ($CDCl_3$) δ 8.09 (m), 7.7−7.1 (m), 6.92 (s, b), 6.62 (m), 3.80 (Me), 3.42 (Me). Anal. Calcd for $C_{29}H_{27}IN\cdot H_2O$: C, 65.17; H, 5.47; N, 2.62. Found: C, 65.46; H, 5.16; N, 2.68.

Semiempirical Computations. Details appear in other papers.[33,37]

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