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Isomerism of Bis(7-azaindolyl)methane

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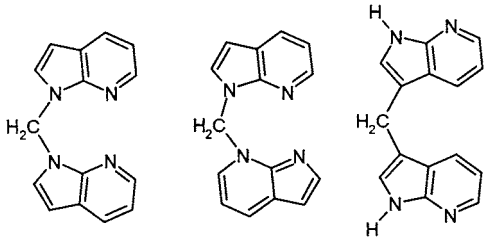
ABSTRACT



1 **2** **4**

Three isomers of bis(7-azaindolyl)methane have been synthesized and fully characterized. Isomers 1 and 2 contain 7-azaindolyl groups that are bound to the CH_2 group through nitrogen atoms. However, 1 contains two "normal" 7-azaindolyl groups, whereas 2 contains both a normal 7-azaindolyl group and a tautomer form of 7-azaindolyl. The third isomer 4 contains two 7-azaindolyl groups that are bound to the CH_2 group through the carbon atom at the position-3. These three isomers show distinct absorption and emission spectra, attributable to the different forms of 7-azaindolyl groups in the isomers, as indicated by the results of ab initio calculations.

7-Azaindole and derivatives have attracted much attention recently because of their many uses. For example, the 7-azaindole moiety has been used as a chromophore of the optical probe for both protein structures and protein dynamics[1] and as an aza analogue of an indole whose skeleton is often found in naturally occurring alkaloids. 7-Azaindole and its derivatives show interesting biological activities.[2] 7-Azaindole is also a useful building block for organic syntheses.[3] Some of the 7-azaindolyl derivatives developed by our group have been used successfully as blue emitters in organic light-emitting devices (OLEDs).[3b−e] Complexes of 7-azaindolyl-containing ligands also showed good luminescence properties[3c,4] and intriguing reactivities.[5] One interesting and much investigated phenomenon of 7-azaindole is its tautomerism and proton transfer in solution. Isomers of methylated 7-azaindole compounds that mimic untautomerized ("normal") and tautomerized 7-azaindole have been used successfully as probes and model compounds for the study of tautomerism and proton-transfer process of 7-azaindole, due to their distinct absorption and emission spectra.[6] In contrast to the extensively studied isomers of methylated 7-azaindole compounds, information on isomers of 7-azaindole derivatives involving alkylation by a methylene group is scarce. During our recent efforts to synthesize bis(7-azaindol-1-yl)-

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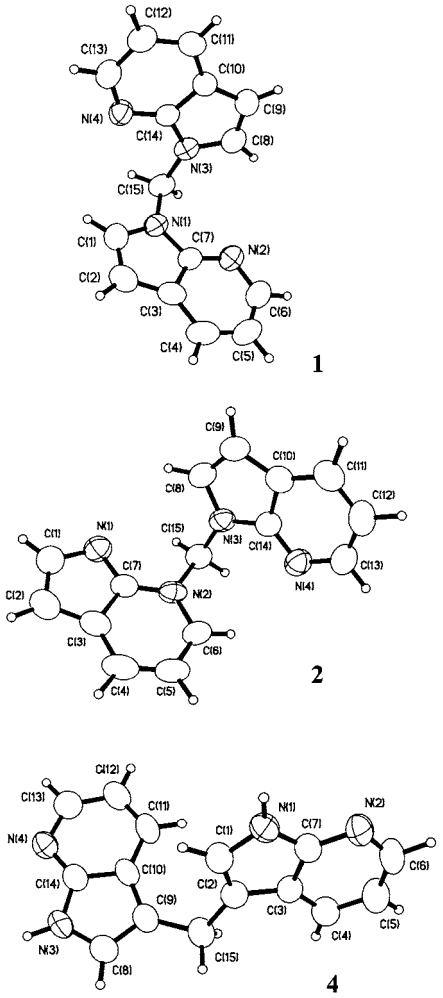


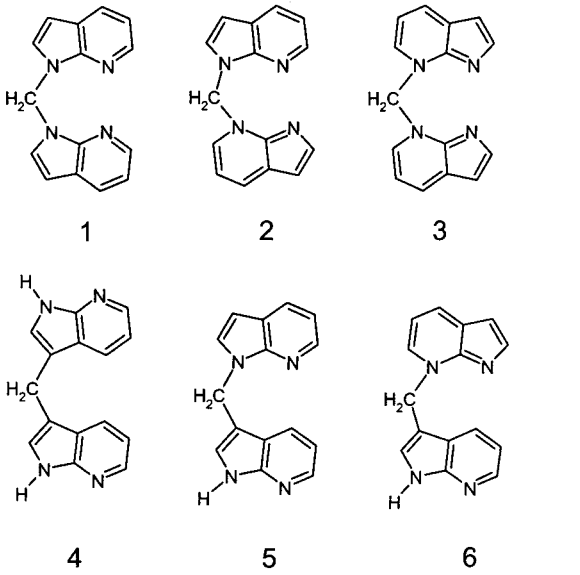
Figure 1. Molecular structures of **1**, **2**, and **4** with 50% thermal ellipsoids and labeling schemes.

methane, **1**, a potentially useful luminescent chelate ligand for metal ions, we have observed the formation of unexpected isomers, in addition to compound **1**, that are unusual and unprecedented in 7-azaindole chemistry. In view of the importance of isomerism in 7-azaindole chemistry and the scarcity of methylene-substituted 7-azaindole derivatives, we carried out a detailed study on these isomers, and the results are reported herein.

The synthesis of compound **1** was carried out by the reaction of CH_2Br_2 with 7-azaindole in the presence of KOH and the phase-transfer catalyst, NBu_4Br, in refluxing toluene and water. When the reaction was carried out in the presence of a large excess of KOH, compounds **1** and **2** were obtained as the major products (~90% yield, ~3:2 ratio), while only a trace amount of compound **4** was obtained, as determined by ^{1}H NMR. When a diluted solution of 1.5 equiv (relative to the amount of 7-azaindole) of KOH was used, compound **4** was isolated in ~25% yield as a crystalline solid by filtration from the reaction mixture because of its poor solubility in toluene. All three isomers are air-stable in the solid state and in solution. There is no interconversion between the three isomers, as evident from ^{1}H NMR spectroscopic study in the temperature range of 25−80 °C. The structures of compounds **1**, **2**, and **4** were confirmed by single-crystal X-ray diffraction analyses.[7]

As shown in Figure 1, compound **1** has two 7-azaindolyl groups bound to the CH_2 group via the 1-N atoms; hence both 7-azaindolyl groups in **1** have the normal structure. Compound **2**, on the other hand, has a 1-N-bound 7-azaindolyl (7-azaindol-1-yl) group and a 7-N-bound 7-azaindoly (7-azaindol-7-yl) group, i.e., it contains both the normal form and the tautomer form of 7-azaindolyl. The N-alkylation of nitrogen-heterocycles (such as pyrazoles, pyrroles, imidazoles, and indoles) by means of a phase-transfer technique is a well-established and very convenient method for preparing the corresponding N-alkyl derivatives.[8] 7-Azaindole is known to have multiple active sites toward electrophilic substitution.[3a] The three possible isomers from the reaction of CH_2Br_2 with 7-azaindole due to the alkylation of the nitrogen sites are shown as compounds **1**−**3** in Scheme 1. Since the 7-azaindol-1-yl anion intermediate is more stable

Scheme 1



than the 7-azaindol-7-yl anion, one would expect isomer **1** to be the major product. In our synthesis, however, both isomers **1** and **2** were obtained from one-pot reaction in good yields (total yield ≈ 90%) with isomer **1** being slightly more favored. Isomer **3** was not observed. The results from ab initio calculations[9] on compounds **1**−**3** indicate that among the three isomers, **1** is the most stable and **3** the least stable.

(7) All data were collected on a Siemens Smart CCD 1000 X-ray diffractometer operated at 50 kV and 30 mA at 293(2) K. Structural solutions and refinements were performed on a PC using the Bruker AXS SHELXTL software package (version 5.10).

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The total energy of **1** is about 20 mHartree (0.54 eV) lower than that of **2**, and the total energy of **2** is about 20 mHartree lower than that of **3**. The experimental results seem to be in agreement with the ab initio calculation results. The absence of compound **3** from the reaction could be attributed to its relatively poor thermodynamic stability.

Compound **4** is the most unusual isomer from the reaction where the alkylation occurs on the carbon atom at position-3, as shown by the crystal structure in Figure 1. Previous theoretical study indicated that the carbon atom at position-3 has a relatively high electron density,[10] compared to other carbon atoms in 7-azaindole; hence, electrophilic substitution at the C-3 atom is theoretically possible. However, most previously reported substitution reactions at position-3 were achieved either under acidic conditions or in the presence of Lewis acid.[3a] A few rare examples of alkylation at the 3-position of 7-azaindole under basic conditions have been reported recently.[11] On the basis of the observed reactivity of the C-3 atom and the nitrogen atoms, two additional isomers **5** and **6** are theoretically possible, but we did not find any evidence for their presence.

X-ray diffraction analysis established unequivocally that in compound **4**, the acidic protons are on the 1-N atoms in both 7-azaindolyl groups. The presence of these acidic protons and the availability of lone pairs from the 7-N atoms make it possible for the formation of an extended hydrogen bonded network in the crystal lattice of **4**. Indeed, as shown in Figure 2, intermolecular hydrogen bonds are formed

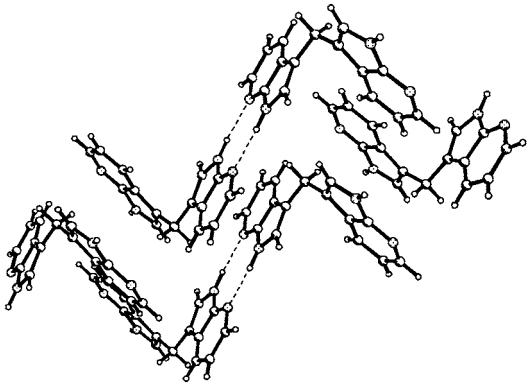

Figure 2. Diagram showing intermolecular hydrogen bonds of **4**.

between the 7-N atoms and protons on the 1-N atoms of adjacent molecules, resulting in the formation of wavelike chains. The distance between the two hydrogen bonded nitrogen pair is 2.929(3) Å, and the N−H···N angle is 167.1(17)°. Compounds **1** and **2** are soluble in common organic solvents. In contrast, compound **4** is only soluble in polar solvents such as THF and methanol. The melting point of **1**, **2**, and **4** are 141, 145, and 260 °C, respectively. The poor solubility and high melting point of compound **4** are likely caused by the intermolecular hydrogen bonds.

The UV−vis absorption spectra of **1** and **4** in solutions are similar. The UV−vis spectrum of compound **2**, in contrast, is very different. In addition to the extra shoulder peak at 308 nm, it has a weak broad absorption band with λ_{max} = 380 nm, which is tailing to the purple-blue region. Consequently, **2** has a distinct light yellow color, while **1** and **4** are colorless. Compounds **1**, **2**, and **4** are luminescent at room temperature in solutions. The absorption and emission spectra of **1**, **2**, and **4** in THF solutions are shown in Figure 3. The emission maxima of **1**, **2**, and **4** are 353,

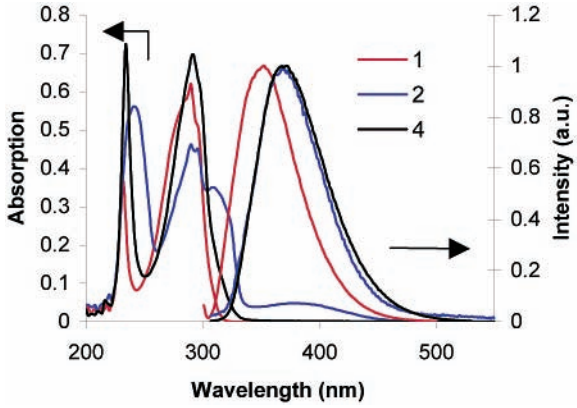

Figure 3. Absorption and emission spectra of **1**, **2**, and **4** recorded in THF (0.040 mM) at ambient temperature.

370, and 372 nm, respectively, when excited at λ_{max} = 298 nm. The results of ab initio molecular orbital calculations show that the HOMO−LUMO band gap of **1** is much bigger than that of **2** (∼35 mHartree), which is consistent with the trend of the emission spectra. The HOMO and LUMO orbitals of **1** involve π orbtials from both 7-azaindoly-1-yl groups. In contrast, as shown in Figure 4, the HOMO and LUMO orbitals of **2** consist of π orbtials from the 7-azaindol-7-yl group only. Therefore, the emission of **1** can be attributed to a $\pi^* \rightarrow \pi$ transition centered on the normal 7-azaindolyl, whereas the emission of **2** can be attributed to a $\pi^* \rightarrow \pi$ transition centered on the "tautomer" 7-azaindolyl. This observation is consistent with the results of previous

(9) Ab initio calculations for compounds **1**−**3** were performed on the restricted Hartree−Fock (RHF) level using a standard split-valence polarized (6-31G*) basis set, employing the Gaussian 98 suite of programs. Geometric parameters for **1** and **2** were obtained from crystal data, while the geometric parameters for **3** were obtained from a computer-optimized model. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.6; Gaussian, Inc.: Pittsburgh, PA, 1998.

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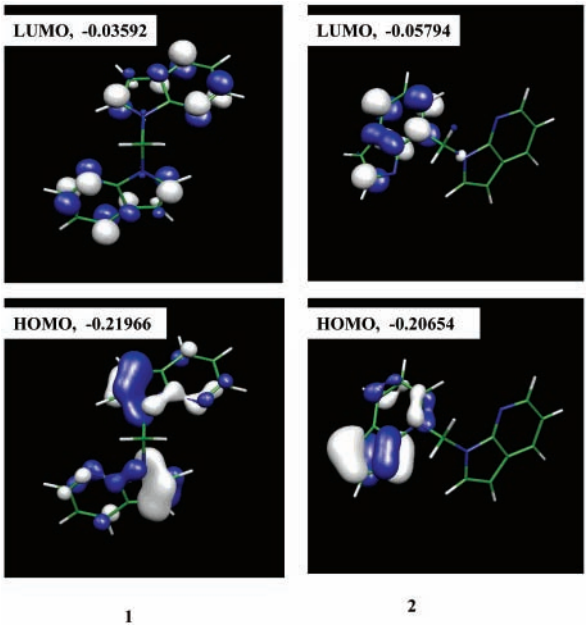

Figure 4. Diagrams showing the HOMO and LUMO levels of **1** and **2**.

studies on isomers of 7-N and 1-N methylated 7-azaindoles.[6] If compound **4** retains the same normal 7-azaindolyl structure in solution as it does in the solid state, its emission spectrum should resemble that of **1** instead of **2**. The fact that **4** has an emission spectrum similar to of **2** leads us to suggest that in solution, at least one of the 7-azaindolyl groups in the molecule of **4** exists in the tautomer form similar to that in **2**, due to proton transferring between 1-N and 7-N atoms. Our preliminary study shows that compounds **1**, **2**, and **4** can bind to metal centers readily to form a variety of interesting luminescent complexes. The details will be published in due course.

In summary, we have shown that three isomers from the alkylation of 7-azaindole by a methylene group can be obtained readily from the reaction of CH_2Br_2 with 7-azaindole. These three isomers have distinct structural features and electronic properties and are promising candidates both as model compounds for the study of isomerism and tautomerism of 7-azaindole and derivatives and as ligands for new luminescent metal complexes.

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Supporting Information Available: Experimental procedures, characterization data, and tables of detailed crystallographic data for all compounds reported in this paper. This material is available free of charge via the Internet at http://pubs.acs.org.

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