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A circular dichroism detection of stereostructural change due to amine protonation☆

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Abstract—Aromatic amine conformation can be controlled by protonation and this process can be followed by circular dichroism measurements.

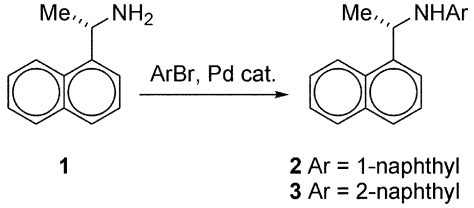
Control of molecular chirality by various external factors such as electrical means or light irradiation is the subject of current stereochemical studies, with applications foreseen in molecular devices and data storage systems.[1] Molecular and supramolecular ionic devices, responding to pH changes, have been previously studied.[2] Primary and secondary aliphatic amines invert rapidly;[3] their protonation, while retarding the inversion process, is not likely to result in a change of molecular stereostructure. For aromatic amines, on the other hand, protonation changes the configuration of the amine nitrogen atom from trigonal to tetragonal, with associated carbon skeleton conformational changes following. In solution, the change of molecular geometry cannot be easily followed by, for example, NMR spectral changes. However, the effect of protonation on molecular structure can be uniquely visualized by circular dichroism measurements on an appropriate optically active compound.

We have chosen a simple secondary aromatic amine **2**, with just one stereogenic center and two 1-naphthyl substituents. The presence of naphthyl substituents ensures high oscillator strength of the chromophores within the ^1B_b transition, which in turn may lead to intense exciton Cotton effects reflecting the conformation of the molecule.

Amine **2** was prepared from optically active (*S*)-(−)-1-(1-naphthyl)ethylamine (**1**) by Pd-catalyzed *N*-arylation[4] (Scheme 1). In a similar manner amine **3** was obtained for comparison purposes.[5]

Molecular modelling with MM3 force field (CONFLEX search)[6] followed by single point energy calculations (b3lyp/6-31g(d))[7] provided a number of conformers for each molecule **2** and **3**, among which the conformers with the extended structure were generally of the lowest steric energy. Namely, the lowest-energy conformer **2A** is characterized by a negative C1–N–C*–C1′ torsion angle (−143°), with the C–C* bond at the chiral center approximately in the plane of the vicinal 1-naphthyl group: the C(Me)–C*–C1′=C2′ torsion angle is 19°. The nitrogen atom is trigonal and the structure of **2A** is given in Scheme 2.[8]

The chirality of the two naphthalene rings system in **2A** is *positive*, considering the directions of the naphthalene long-axis polarized electric dipole transition moments, responsible for the strong allowed electronic transition at around 220 nm.[9] Protonation of **2A** by addition of two equivalents of methanesulfonic acid changes the conformation of the molecule. In the lowest-energy conformer the protonated nitrogen atom, now tetragonal, causes a *trans* arrangement of the



Scheme 1.

Keywords: circular dichroism; conformation; amine; protonation; DFT.

☆ Supplementary data associated with this article can be found at doi:10.1016/j.tetlet.2003.09.049

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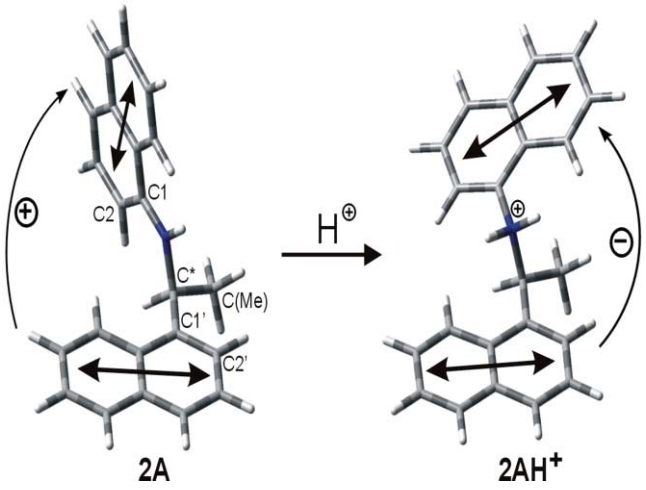

Scheme 2. Change of conformation of amine **2** on protonation.

C1–N⊕–C*–C1′ bond system (torsion angle −167°), while the plane of the naphthyl ring remains unchanged with regard to the position of substituents at the chiral center: the C(Me)–C*–C1′–C2′ angle is 20° (Scheme 2).[10] The most significant conformational difference between **2A** and **2AH+** is the rotation of the C2–C1–N–C* bond system from −3° in **2A** to +78° in **2AH+**. The chirality of the two naphthalene ring system in **2AH+** is *negative*, when defined as previously for **2A**. Accordingly, the CD spectra of **2** and its protonated form **2AH+** in acetonitrile are nearly mirror images, the first producing a strong positive exciton Cotton effect at around 215 nm (A = +190), the second a strong negative exciton Cotton effect (A = −210) at around 225 nm (Fig. 1). The observed CD change is reversible by sequential neutralization–acidification processes. Furthermore, these changes are not specific for the solvent and strong acid used: in methanol solution and with the use of excess hydrochloric acid or methanesulfonic acid the corresponding CD spectra differ (less than 10%) only in the amplitudes (A) of the exciton Cotton effects.

These exciton Cotton effects belong to the strong allowed transition of the ^1B_b type in the naphthalene chromophores, with λ_{max} 224 nm (ε 85100) for **2** and λ_{max} 217 nm (ε 98600) for protonated **2** in acetonitrile solution. This qualitative analysis is fully supported by calculations of the UV and CD transitions for the lowest-energy conformers of **2A** and **2AH+**. First, these structures were optimized by the DFT method at the b3lyp/3-21+g* level and subsequently the UV and CD spectra were computed with the use of hybrid functional mpw1pw91 and cc-pvdz basis.[7] The computed CD transitions shown in Figure 2 are in good agreement with the experiment and qualitative analysis. Thus, the chirality of the naphthyl groups system in **2** is efficiently controlled by the single act of protonation, changing from positive to negative. It should be noted that this conformational change cannot be determined from the ^{1}H NMR spectra.

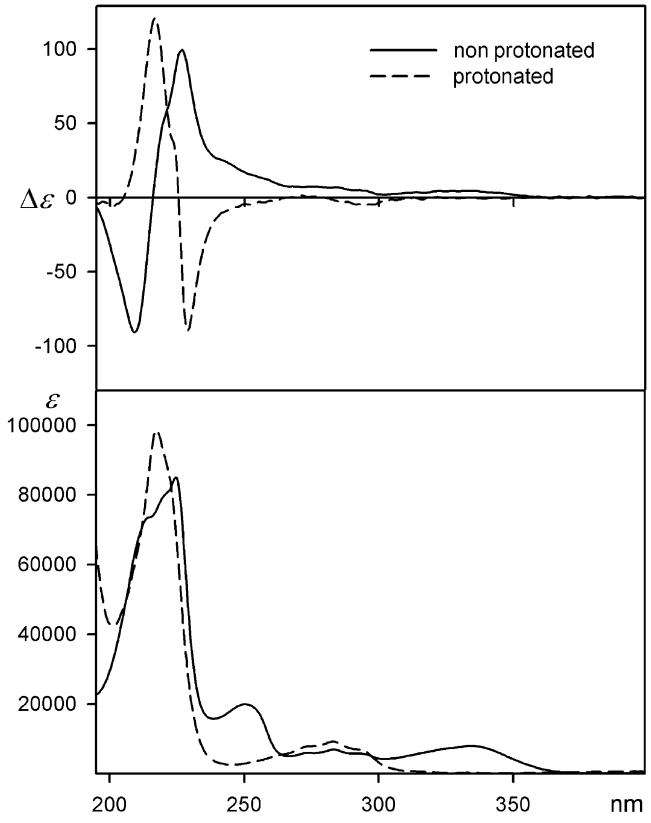

Figure 1. CD (upper panel) and UV (lower panel) spectra of **2** in acetonitrile.

In a similar chiral aromatic amine **3** protonation brings about a significant, although less dramatic change in the CD spectrum (Fig. 3). The strong positive exciton Cotton effect of the free amine (A = +220) is reduced nearly threefold (A = +77) on protonation. This can be readily rationalized in the following way. The structure of the protonated form **3H+** is quite similar to that of **2AH+**, however the 2-naphthylamine substituent in **3H+** can assume two different orientations of nearly the same steric energy, due to the rotation of the C2–N⊕ bond by 180°. The resulting rotatory power of the **3H+** conformer is on average positive but of much reduced strength.

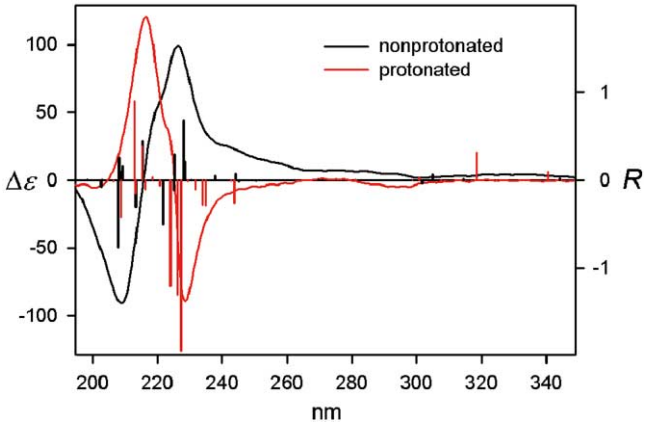

Figure 2. Experimental (solid lines) and calculated (using TD DFT method, vertical bars) CD spectra of **2**.

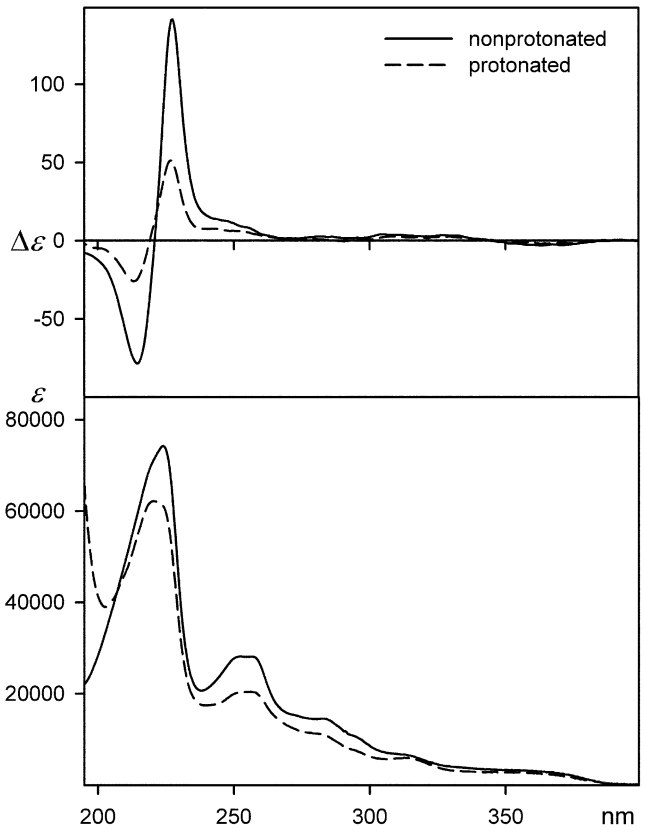

Figure 3. CD (upper panel) and UV (lower panel) spectra of **3** in acetonitrile.

In summary we have demonstrated that the shape and conformation of aromatic amines can be controlled by protonation of the nitrogen atom and this process can be readily followed by the CD spectra. Further applications of the control of aromatic (oligo)amine folding processes are under study in this laboratory.

Acknowledgements

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5. **General procedure**: 1- or 2-Bromonaphthalene (104 mg, 0.5 mmol), (*S*)-1-amino-1-naphthylethane (102 mg, 0.6 mmol), $Pd_2(dba)_3$ (9 mg, 0.01 mmol), *rac*-BINAP (12 mg, 0.02 mmol), NaO*t*Bu (67 mg, 0.7 mmol) and toluene (5 mL) were added to an oven-dried flask, which was capped with a septum, purged with argon and then heated with stirring to 110°C under argon for 20 h. The reaction mixture was then allowed to cool to room temperature, diluted with Et_2O (5 mL), and filtered through Celite. The filtrate was concentrated and the crude product was purified by column chromatography (20% CH_2Cl_2/hexane) on silica gel.
(*S*)-*N*-(1-Naphthyl)-1-(1-naphthyl)ethylamine 2: colorless crystals, yield 72% after crystallization (hexane); mp 143–144°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.80 (d, J=6.9 Hz, 3H), 4.86 (br, 1H), 5.48 (q, J=6.9 Hz, 1H), 6.25 (dd, J=7.5, 0.9 Hz, 1H), 7.06–7.17 (m, 2H), 7.36 (t, J=7.3 Hz, 1H), 7.46–7.61 (m, 4H), 7.67 (d, J=7.1 Hz, 1H), 7.73–7.81 (m, 2H), 7.90–8.00 (m, 2H), 8.23 (d, J=8.4 Hz, 1H); ^{1}H NMR ($CDCl_3$+TFA) δ 2.11 (d, J=6.8 Hz, 3H), 5.90 (q, J=6.8 Hz, 1H), 7.19–7.27 (m, 3H), 7.38–7.45 (m, 2H), 7.57–7.67 (m, 3H), 7.83–7.95 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 23.7, 49.6, 105.8, 117.2, 119.7, 122.0, 122.6, 123.2, 124.7, 125.4, 125.6, 125.9, 126.1, 126.6, 127.5, 128.8, 129.2, 130.7, 134.1, 134.3, 139.6, 141.8; HR EIMS found 297.1515 calcd for $C_{22}H_{19}N$ 297.1518.
(*S*)-*N*-(2-Naphthyl)-1-(1-naphthyl)ethylamine 3: solidified oil, yield 89% after chromatography, ^{1}H NMR ($CDCl_3$) δ 1.80 (d, J=6.9 Hz, 3H), 6.25 (q, J=6.9 Hz, 1H), 6.81 (dd, J=9.1, 2.2 Hz, 2H), 7.20–7.40 (m, 3H), 7.41–7.60 (m, 4H), 7.71–7.90 (m, 3H), 7.92 (d, J=7.1 Hz, 1H), 8.15 (d, J=7.1 Hz, 1H); ^{1}H NMR ($CDCl_3$+TFA) δ 2.11 (d, J=6.8 Hz, 3H), 6.10 (q, J=6.8 Hz, 1H), 7.10–8.10 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 29.7, 53.1, 118.7, 123.8, 124.2, 124.5, 124.6, 125.1, 125.6, 126.1, 126.6, 127.1, 127.5, 128.1, 128.5, 128.9, 129.7, 132.1, 133.8, 134.4, 138.3, 144.2; HR EIMS found 297.1516 calcd for $C_{22}H_{19}N$ 297.1518.
6. CAChe WS Pro 5.0, Fujitsu Ltd 2001.
7. Gaussian 98, Revision A10, Gaussian, Inc., Pittsburgh PA, 2001.
8. The conformer next to the minimum-energy **2A** has the torsion angles C1–N–C*–C1′=169.2 and C(Me)–C*–C1′–C2′=93.5 and its energy is 2.1 kJ mol^{-1} higher. The analogous energy difference between the two lowest-energy conformers of **3** is 2.3 kJ mol^{-1}.

9. Strictly speaking, in 1-naphthylamine derivatives the direction of the ^1B_b transition moment is not parallel to the naphthalene long molecular axis, but according to computations it is tilted toward the amine substituent. For qualitative analysis this difference is only of secondary importance. In protonated 1-naphthylamines the direction of the transition moment is approximately parallel to the naphthalene long molecular axis.
10. The two lowest-energy conformers of **2H$^+$** both have *negative* chirality of the naphthalene chromophoric system, hence only the conformer **2AH$^+$** is discussed.