Elucidation of the formation of cation–π complexes and their conformational behavior in solution by CD spectroscopy

Shinji Yamada,* Chisako Morita and Jun Yamamoto

Department of Chemistry, Faculty of Science, Ochanomizu University, Bunkyo-ku, Tokyo 112-8610, Japan

Abstract—Circular dichroic exciton Cotton effects were observed for some pyridinium salts and a quinolinium salt having a benzyl or a naphthylmethyl group, which revealed the existence of an intramolecular cation–π interaction. The sign of the Cotton effects deduced the relative position of the two chromophores.
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The circular dichroic exciton Cotton effect is significantly important in determination of the absolute configuration of a variety of compounds.[1,2] In addition, this effect reflects the conformations of the chiral molecules in solution when the steric and electronic effects favorably restrict the conformational flexibility.[1,2]

In the course of our studies on the conformation control of pyridinium compounds,[3,4] we have found that **2b** having a pyridinium ring and a benzyl group is geometrically restrained[4] by an intramolecular cation–π interaction.[5] The X-ray analysis clarified that the pyridinium and phenyl rings lie parallel to each other and the two rings are arranged face-to-face (Fig. 1).[4] The ^{1}H NMR studies suggested the conformation in solution to be similar to the X-ray structure.[4]

To clarify its conformational details in solution and to obtain further evidence for the existence of an intramolecular cation–π interaction, we focused on CD spectroscopy due to its remarkable ability for conformational analysis in solution. We report here that CD exciton Cotton effects provide evidence for the existence of a cation–π interaction and reveal the conformation of the cation–π complex.

a : R = Ph
b : R = CH$_2$Ph
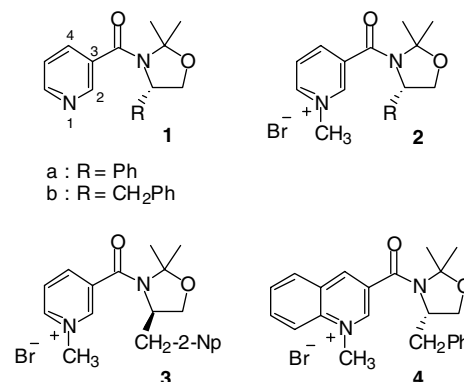
Nicotinic amides **1a** and **1b** and pyridinium salts **2a**, **2b**[4] and **3**,[6] and quinolinium salt **4**[7] were employed for the conformational studies. The UV and CD spectra[8] of **1a** and **1b** in CH$_3$CN are shown in Figure 2. The UV spectra of both **1a** and **1b** exhibit two bands around 270 and 220 nm, which can be assigned to the π–π* transition (B band) of the pyridine moiety[9] and the π–π* transitions (K band) of the phenyl and pyridine rings, respectively.[9] In the CD spectra, positive Cotton effects appear at the π–π* (B band) region of the pyridine moiety (Fig. 2a and b). This positive sign would be associated with the directionality of the twisting of the C3–CO bond toward the pyridine ring.[10] Another strong positive Cotton effect is present at the 223 nm region of **1a** with respect to the π–π* absorption of the phenyl group attached to the chiral center (Fig. 2a), whereas no such band is present in **1b** (Fig. 2b).

* Corresponding author. Tel.: +81 (0)3 5978 5349; fax: +81 (0)3 5978 5715; e-mail: yamada@cc.ocha.ac.jp
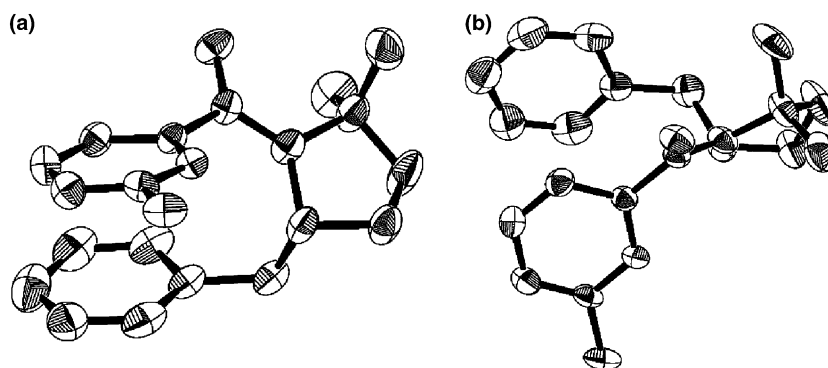
(a)   **(b)**

Figure 1. Reported ORTEP drawings of **2b**. (a) Side view; (b) top view.
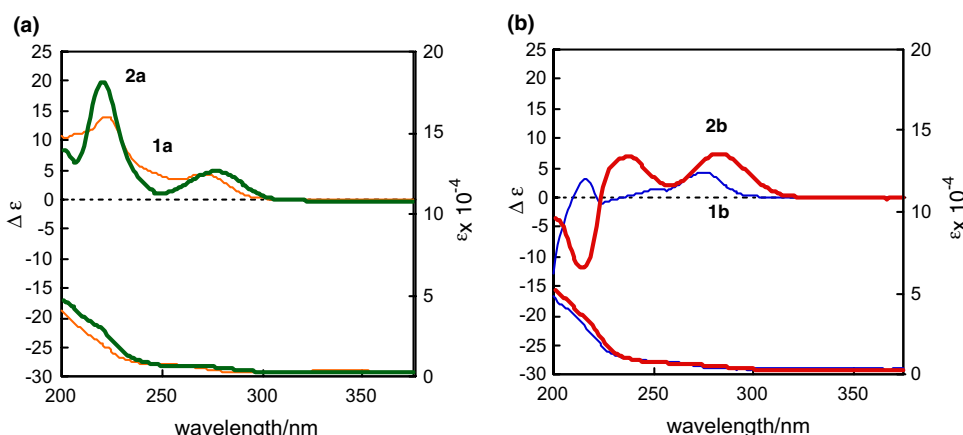

Figure 2. CD and UV spectra of (a) **1a** and **2a** and those of (b) **1b** and **2b** in CH₃CN.

The UV spectra for **2a** and **2b** are very close to those of **1a** and **1b** as shown in Figure 2. The absorption bands of them can be analogously assigned to the case of **1**. The CD spectrum of **2a** shows two positive Cotton effects, which closely resembles that of **1a**. In contrast, the spectrum of **2b** is significantly different from that of **1b**, suggesting the larger contribution of a cation–π interaction into the conformation of **2b**. A remarkable feature is the significant difference in the CD curves between **2a** and **2b** in spite of a small structural difference between them. The CD spectrum of **2b** exhibits exciton couplet at the 200–260 nm region with the first strong positive exciton Cotton effect at around 236 nm and the second strong negative exciton Cotton effect at around 214 nm. The crossover point of 224 nm is very close to the absorption bands of π–π* of the phenyl and pyridinium rings, indicating that this couplet would be a result of the exciton coupling between the two chromophores. These observations strongly suggested that the conformational flexibility of **2b** is significantly diminished by an intramolecular cation–π interaction. The benzyl group is a much better substituent than a phenyl group to take an effective orientation for the formation of a cation–π complex, which would cause significant differences in the CD spectra between **2a** and **2b**.

The plus sign of the observed CD couplet in **2b** implies that the two chromophores take a disposition as shown in Figure 3. This is in agreement with the previously re-

ported X-ray geometry of **2b** with respect to the relative position of the two moieties (Fig. 1b).[4] The positive Cotton effect around 282 nm suggests that the chirality about the C3–CO axis will be *M* according to the literature,[10] which is also consistent with that of the X-ray structures (Fig. 1).[4] These observations lead to a conclusion that the conformation of **2b** in solution is very similar to that in the crystal.

It should be noted that the Δε values receive temperature effects but scarcely receive solvent effects. When the measurements were carried out in the range of 5–60 °C in CH₃CN, the Δε values decreased with raising of the temperature.[11] This phenomenon is a general feature of flexible molecules because the higher temperature enhances the molecular motion and results in the decreasing of the Δε values.[12] Although it has been known that polar solvents weaken a cation–π inter-
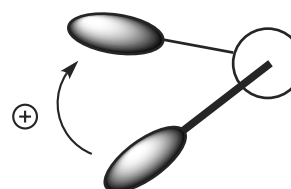

Figure 3. Schematic relative position of the two chromophores down the N–C bond with chirality.
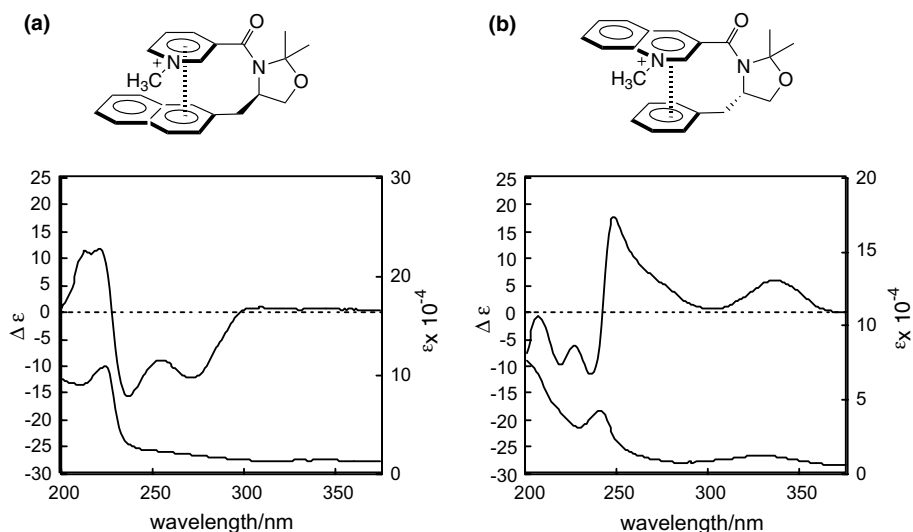
Figure 4. CD and UV spectra of (a) **3** and those of (b) **4** in CH₃CN.

action,[13] little effect was observed in the present system,[14] suggesting a larger interaction energy in this intramolecular complex.

The CD measurements of **3** and **4** were also carried out to clarify their conformations and the existence of a cation–π interaction in solution. Since they have a naphthylmethyl or quinolinium moiety possessing a long-axis polarized electric dipole transition moment, it is easy to evaluate the exciton Cotton effects. Both CD spectra[6,7] exhibit splitting Cotton effects as expected (Fig. 4a and b). The crossover points of **3** and **4** are 228 and 241 nm, respectively, which are closely associated with the π–π* absorption of the naphthylmethyl group (226 nm for **3**) and the quinolinium ring (241 nm for **4**). The CD curve for **3** is nearly a mirror image to that of **2b** due to the opposite absolute configuration of the chiral auxiliary. The CD spectrum of quinolinium **4** does not resemble the corresponding pyridinium derivative **2b** because of the different absorption behavior of the quinolinium moiety from that of the pyridinium ring. However, an exciton couplet with a positive sign around 220–260 nm and a positive Cotton effect associated with the B band of the quinolinium around 336 nm reflect similar conformational behavior to **2b** (Fig. 4b). These observations apparently provide evidence for the existence of a cation–π interaction in **3** and **4** in solution.

In summary, the observation of an exciton couplet between a pyridinium (quinolinium) and a benzyl (naphthylmethyl) group clarified the existence of an intramolecular cation–π interaction in the pyridinium and quinolinium salts **2b**, **3**, and **4**. Moreover, the sign of the chirality reveals the relative position of the two chromophores. To the best of our knowledge, these are the first examples for the elucidation of cation–π interactions by CD spectroscopy. These findings should be useful in the studies of cation–π interactions in various systems. Further studies on the related conformation switching system are now in progress.

References and notes

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6. Spectral data of **3**: white crystal, mp: 137.5–139 °C; IR (KBr) 3461, 3402, 3051, 2935, 2935, 1646, 1630, 1409, 1364, 1217 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.04 (s, 1H), 8.49 (d, *J* = 5.4 Hz, 1H), 7.83 (dd, *J* = 6.0, 3.6 Hz, 1H), 7.70 (dd, *J* = 6.0, 3.6 Hz, 1H), 7.54–7.50 (m, 4H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.12 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.10 (dd, *J* = 8.1, 5.4 Hz, 1H), 5.25–5.21 (m, 1H), 4.63 (dd, *J* = 9.2, 4.9 Hz, 1H), 4.36 (s, 3H), 4.07 (d, *J* = 9.2 Hz, 1H), 3.11 (dd, *J* = 12.9, 3.4 Hz, 1H), 3.06 (dd, *J* = 12.9, 10.0 Hz, 1H), 2.02 (s, 3H), 1.71 (s, 3H); UV (CH₃CN) λ_max (ε) 228 (9.04 × 10⁴) nm; CD (CH₃CN, 0.019 mM) λ_ext (Δε) 272 (−12.3), 237 (−15.7), 222 (+11.7), 213 (+11.3) nm; [α]_D^27 = −116.4 (c 0.868, CH₃CN).
7. Spectral data of **4**: white crystal, mp: 219–220 °C; IR (KBr) 3444, 2983, 2938, 1640, 1409 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.44 (s, 1H), 8.41 (s, 1H), 8.23–8.14 (m, 3H), 7.98–7.94 (m, 1H), 6.92–6.81 (m,

5H), 5.22–5.18 (m, 1H), 4.94 (dd, J = 9.3, 4.4 Hz, 1H), 4.92 (s, 3H), 4.00 (d, J = 9.3 Hz, 1H), 2.94 (dd, J = 13.7, 10.7 Hz), 2.88 (dd, J = 13.7, 4.4 Hz), 2.02 (s, 3H), 1.80 (s, 3H); UV (CH$_3$CN) λ_{max} (ε) 241 (4.21×10^4) nm; CD (CH$_3$CN, 0.034 mM) λ_{ext} ($\Delta\varepsilon$) 336 (+5.9), 248 (+17.6), 235 (−11.7), 219 (−9.9) nm; $[\alpha]_D^{27}$ = +137.7 (c 1.05, CH$_3$CN).

8. CD spectral data in CH$_3$CN solution (0.06 mM) for **1a**, **1b** and **2a**, **2b** at rt: **1a**: λ_{ext} ($\Delta\varepsilon$) 271 (+4.2), 222 (+13.9); **1b**: λ_{ext} ($\Delta\varepsilon$) 275 (+4.2), 224 (−1.1), 215 (+3.0) nm; **2a**: λ_{ext} ($\Delta\varepsilon$) 276 (+4.9), 220 (+20.0) nm; **2b**: λ_{ext} ($\Delta\varepsilon$) 282 (+7.5), 236 (+7.1), 214 (−11.8) nm.

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11. CD measurements of **2b** were carried out in CH$_3$CN (6.0×10^{-5} M); 5 °C: λ_{ext} ($\Delta\varepsilon$) 281 (+7.9), 236 (+7.1), 213 (−13.9) nm; 25 °C: λ_{ext} ($\Delta\varepsilon$) 282 (+7.5), 236 (+7.1), 214 (−11.8) nm; 60 °C: λ_{ext} ($\Delta\varepsilon$) 283 (+6.7), 236 (+5.7), 214 (−11.0) nm.

12. For an example, see: Roschester, J.; Sandström, J. *Tetrahedron* **1989**, *45*, 5091–5100.

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14. CD (CH$_3$CN) λ_{ext} ($\Delta\varepsilon$) 282 (+7.5), 236 (+7.1), 214 (−11.8) nm; CD (EtOH) λ_{ext} ($\Delta\varepsilon$) 283 (+6.6), 235 (+6.2), 214 (−12.1) nm; CD (H$_2$O) λ_{ext} ($\Delta\varepsilon$) 280 (+6.4), 234 (+8.7), 214 (−15.4) nm.