Detection of Chirality by Colour

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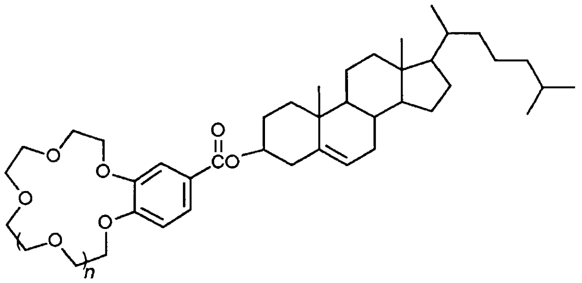
On addition of optically-active ammonium ions the helical pitch of cholesteric liquid crystals containing steroidal crown ethers changes in an enantioselective manner: in certain cases the difference in the colour change can be visually detected.

Crown ethers with chiral substitutents or chiral frameworks are capable of discrimination of racemic ammonium ions through crown $\cdots$ H_3N^+–R^* interactions.[1,2] This discovery provided a strong cross-link between enzyme chemistry and host–guest chemistry because chiral recognition is the first step in enzymic reactions. In the past, the chiral recognition ability was estimated by indirect methods such as determination of association constants, membrane transport rates, reaction rates, *etc.*[1,2] More recently, Kaneda *et al.*[3] introduced an ingenious method to estimate directly the chiral recognition ability: they combined the concept of chromogenic crown ethers[4–7] with that of chiral crown ethers and designed novel chiral azophenolic acerands. Thus, enantioselective complexation with optically-active amines could be readily detected by the colour change.

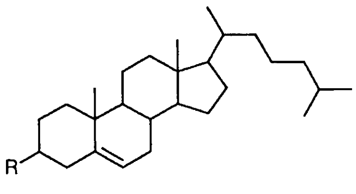
We recently synthesized new steroidal crown compounds **1a** and **b**.[8–10] When alkali metal cations were added to a mixture of cholesterol nonanoate **2** and cholesterol chloride **3** (a room temperature liquid crystal) containing **1a** or **b**, the helical pitch of the mixed cholesteric liquid crystals was changed.[9] This indicates that the metal binding to **1a** or **b** in the liquid crystals can be detected by the colour change. This finding led us to test if the system can discriminate optically-active ammonium ions through a diastereoisomeric interaction because the steroidal skeleton is optically-active. If it can, one can directly detect the chirality of ammonium ions by the colour change.

Preparation of **1** has been described previously.[8,9] Compound **2** (1.2×10^{-5} mol), **3** (0.8×10^{-5} mol), **1b** (or 4-methoxycarbonylmonobenzo-18-crown-6 **4**, used as a reference compound; 0.9×10^{-5} mol) and chiral amine hydrochloride ($R^*NH_3^+Cl^-$) were dissolved in chloroform (1.0 ml). An aliquot (usually 200 μl) of this solution was spread on a glass plate and mixed with minute glass beads with a uniform diameter (10 ± 0.2 μm). The solution was dried and then sandwiched with another glass plate. The thickness of the sample thus prepared is regulated by the glass beads. The wavelength of maximum reflection ($\lambda_R = nP$, where n is the mean index of reflection and P is the helical pitch of the cholesteric mesophase) was measured spectrophotometrically at 27 °C.[11]

Fig. 1 shows plots of λ_R *vs.* [PA (phenylalanine methyl ester hydrochloride)]/[**1b**]. It is seen from Fig. 1 that with increasing PA concentration, the λ_R for D-PA increases whereas that for L-PA decreases. The difference at [PA]/[**1b**] = 0.08 amounts to 64 nm. This colour change could be visually detected. In contrast, the λ_R for **4** was scarcely affected by the addition of PA (Fig. 2). Similarly, the addition of optically-active *N,N,N*-trimethyl-1-phenylethylammonium iodide, which does not interact with the crown ring, did not change the λ_R to a significant extent (Table 1). These results indicate that the interaction between the additive and the crown ring and the covalent linkage between the cholesterol moiety and the crown ring are essential to the λ_R change. This provides an important clue to explain why the λ_R for the **1b–2–3** ternary system changes upon addition of PA. Since PA is scarcely soluble in the **2–3** mixed medium, it should be solubilized through complexation with the crown ether moiety. If the NH_3^+-binding crown site is orientated in the structure-form-



1a: *n* = 1
1b: *n* = 2
4 : *n* = 2, Me replaces steroid substituent



2: R = $Me[CH_2]_7CO_2$
3: R = Cl

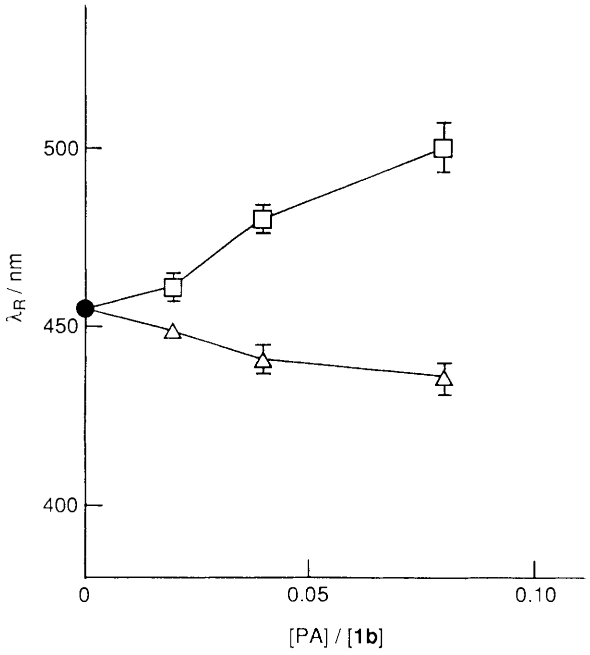


Fig. 1 Plots of λ_R *vs.* [PA(phenylalanine methyl ester hydrochloride)]/[**1b**]. The λ_R values are the average of four repeated runs. □, D-isomer; △, L-isomer; the error range is shown by bars.

Table 1 Shift (nm) of λ_R induced by added amine hydrochlorides ($R^*NH_3^+Cl^-$)[a]

	1b–2–3[b]		**4–2–3**[c]	
$R^*NH_3^+Cl^-$	D-Isomer	L-Isomer	D-Isomer	L-Isomer
1-Phenylethylamine hydrochloride	+81 ± 3	+25 ± 3	−2 ± 1	+2 ± 4
Phenylglycine methyl ester hydrochloride	+39 ± 7	−26 ± 3	+6 ± 1	−2 ± 1
Alanine methyl ester hydrochloride	−11 ± 1	−16 ± 4	—	—
Phenylalanine methyl ester hydrochloride	+45 ± 7	−19 ± 4	−8 ± 2	−2 ± 5
Valine methyl ester hydrochloride	+35 ± 2	−1 ± 1	—	—
Tryptophan methyl ester hydrochloride	+31 ± 1	−6 ± 7	—	—
N,N,N-Trimethyl-1-phenylethylammonium iodide	−1 ± 4	−5 ± 5	—	—

[a] **1b** (or **4**) : **2** : **3** = 9 : 12 : 8, [$R^*NH_3^+Cl^-$]/[**1b**(or **4**)] = 0.08. The λ_R values are the average of four repeated runs. [b] The λ_R in the absence of $R^*NH_3^+Cl^-$ is 455 nm. [c] The λ_R in the absence of $R^*NH_3^+Cl^-$ is 670 nm.

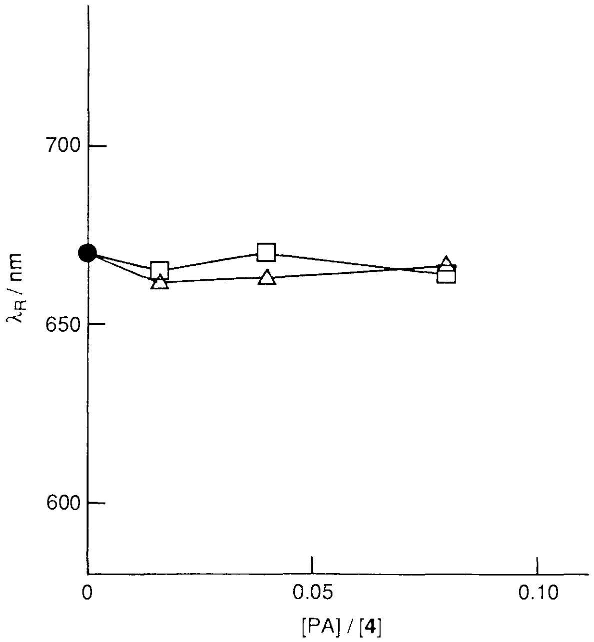


Fig. 2 Plots of λ_R *vs.* [PA(phenylalanine methyl ester hydrochloride]/[**4**]; □, D-isomer; △, L-isomer

ing cholesteric mesophase (as in **1b–2–3**), the complexation event is transduced to the cholesteric site and changes the helical pitch. However, if the NH_3^+-binding crown site is not specifically fixed in the cholesteric mesophase (as in **4–2–3**) or if the additive is not specifically bound to the crown site (as in *N,N,N*-trimethyl-1-phenylethylammonium iodide), the complexation event is not reflected by the cholesteric pitch.

We tested several chiral amine hydrochlorides in the **1b–2–3** system (Table 1). Examination of Table 1 reveals that (i) the large λ_R difference between D- and L-isomers is observed for ammonium ions having bulky substituents (such as phenyl and indolyl), (ii) although the λ_R moves in the same direction in a few cases, the λ_R values for D-isomers always appear at the longer wavelengths, and (iii) in every case, the perceptible λ_R shift is not induced in the **4–2–3** system.

The foregoing results indicate that chiral amine hydrochlorides bound to the crown ring in **1b** change the helical pitch in an enantioselective manner. Thus, this system is regarded as a novel detection of chirality by the colour change. These findings consistently suggest that the present system serves as a new chiral sensory system.

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