

## CD spectra of pharmaceuticals substances - Steroids (3)

### 1. Estradiol

Estradiol is the most effective estrogen and is primarily found in the ovary and placenta. The secretion of estradiol from mammalian ovaries increases during the follicular maturation phase, reaches a maximum just before ovulation (40 to 200 pg/1 ml blood plasma) and decreases rapidly after ovulation to 10 to 30 pg/1 ml blood plasma.<sup>2)</sup> Estradiol is not described in the Japanese Pharmacopoeia.

Figure 1 shows the CD/UV spectra of estradiol. According to the assignments for chiral substituted benzenes,<sup>3)</sup> the <sup>1</sup>L<sub>b</sub>-band in UV and negative CD can be assigned to absorption in the wavelength range from 300 to 250 nm, the <sup>1</sup>L<sub>a</sub>-band in UV and positive CD to that of 300 to 250 nm and the <sup>1</sup>B<sub>a,b</sub>-band in UV and positive CD to that of around 200nm. A spectroscopic moment, namely a transition moment induced by the substitution to benzene ring, is simply evaluated using a 6-substituted tetralin as a model compound of estradiol, as shown in the figure below. This figure well demonstrates that the Cotton effect for the <sup>1</sup>L<sub>a</sub>-band of estradiol possessing a B-ring with right (P)-helicity is negative.

### 2. Estriol

Estriol is used as a follicular hormone agonist for estrogen insufficiency in women after menopause, and also as a drug for osteoporosis.<sup>5)</sup>

Figure 2 shows the CD/UV spectra of estriol. Both are quite similar to those of estradiol, as shown in Figure 1.

### 3. Estradiol benzoate

Estradiol benzoate has higher durability of action than estradiol and therefore it is extensively used for the various problems accompanying the disorder of follicular hormones. Figure 3 shows the CD/UV spectra of estradiol benzoate. They are different from those of estradiol or estriol. The difference is due to the effect of the benzoate group bound to the phenol group. Particularly, the <sup>1</sup>L<sub>b</sub>-band in the UV spectrum of estradiol benzoate shows a shift to a shorter wavelength in comparison with estradiol and estriol, and the sign of the CD for the former reverses to positive, while it is negative for the latter.

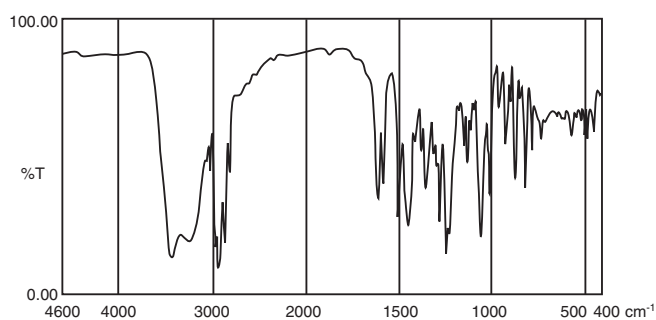
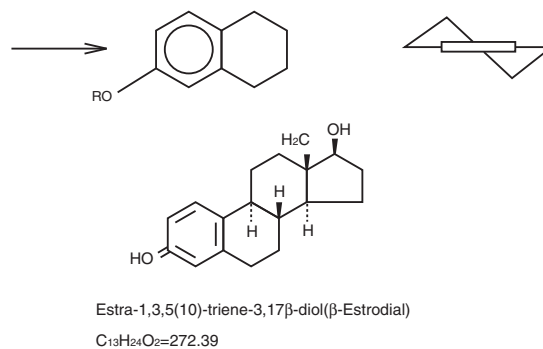
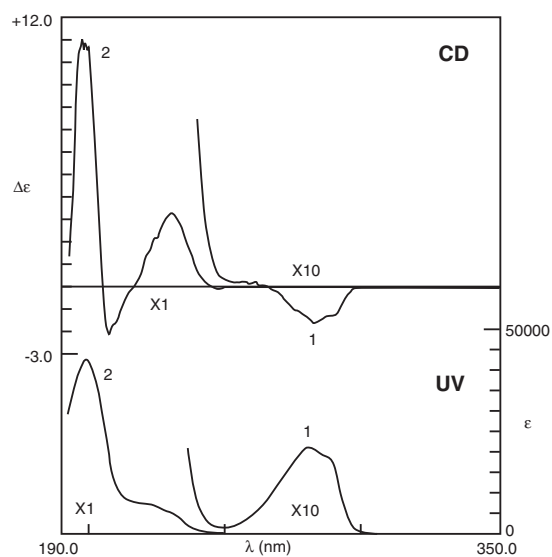
### 4. Sodium prasterone sulfate

Sodium prasterone sulfate, a water-soluble androgen secreted by adrenal glands, changes to a precursor of estrogen at pregnancy. It is applied for cervical ripening insufficiency at the end stage of pregnancy.<sup>5)</sup> Figure 4 shows the CD/UV spectra of sodium prasterone sulfate. In both of the spectra, the absorptions are assigned to the R-band of the carbonyl group at the 17th site. The cyclopentanone ring in the 14 $\alpha$ -17-ketosteroid has an envelope-type conformation, as shown in the right figure and its octant projection chart explains the positive Cotton effect.<sup>6)</sup>

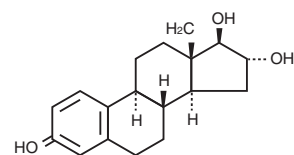
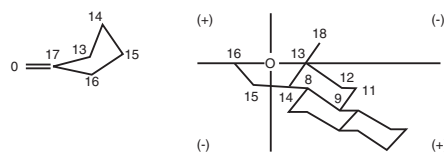
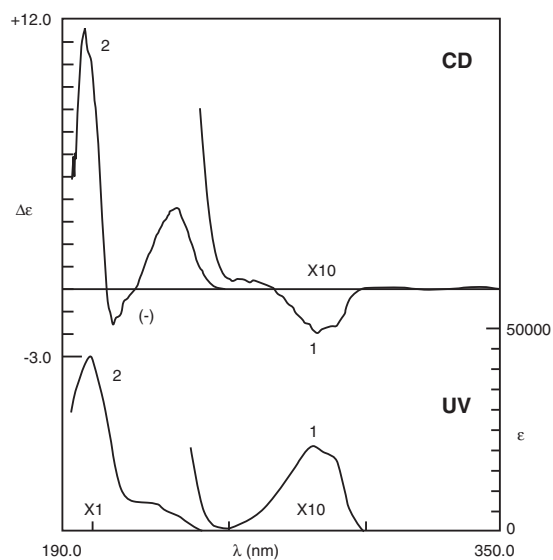
#### References and Comments

- 1) Dioxane, usually used as a solvent in this series, has a minimum observable shorter wavelength around 200nm, whereas ethanol, used in this report, has a minimum around 190nm.
- 2) The Dictionary of Biochemistry, Tokyo Kagaku Dojin, 1st Edition, 1984.
- 4) Snatzke, G., Kajtar, M., Werner-Zamojska, F., Tetrahedron, 1972, vol. 28, pp.281-288 Related reference: Sagiv, J., Tetrahedron, vol. 33, pp.2315-2320, 1977.
- 5) The Manual of Japanese Pharmacopoeia, 12th Edition, Hirokawa Shoten, 1991.
- 6) Kuriyama, K., Experimental Chemistry Series, Sequel vol. 5, Japan Chemical Society Ed., Maruzen, 1996. Optical Rotatory Dispersion, pp 1241-1341.

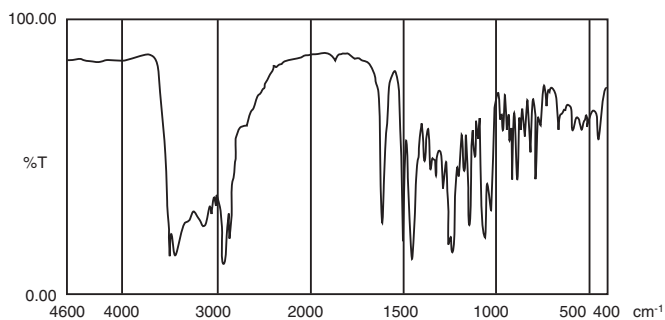
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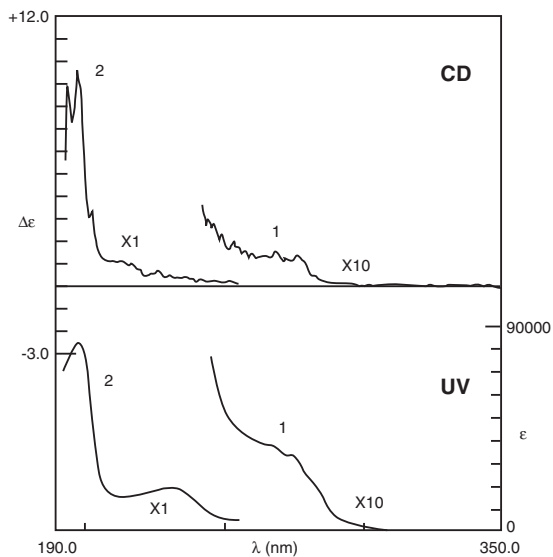
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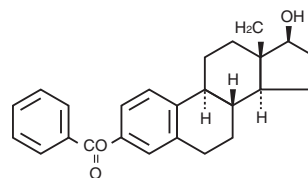
Estra-1,3,5(10)-triene-3,16 $\alpha$ ,17 $\beta$ -triol(Estriol)  
C<sub>18</sub>H<sub>24</sub>O<sub>3</sub>=288.39



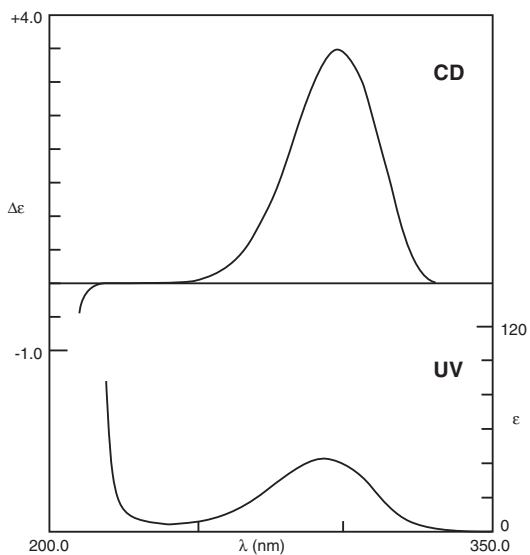
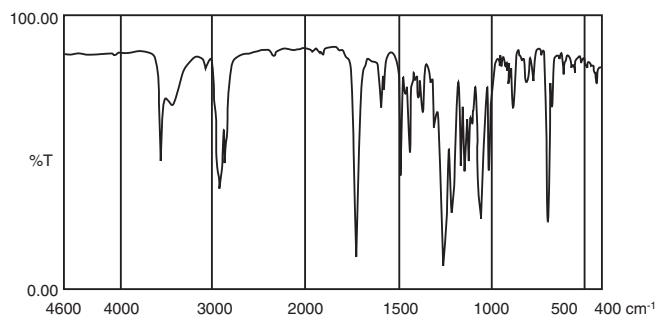
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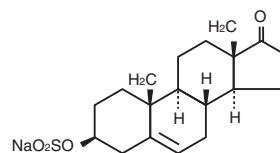
Sample : SIGHA E8515  
 CD/UV : Ethanol Solution  
 1: 5.0 mg/50 ml (0.27 mM), 10 mm Cell  
 2: 5.0 mg/25 ml (0.53 mM) and 5.0 mg/100 ml (0.13mM), 1 mm Cell



1,3,5(10)-Estratriene-3,17 β-diol 3-benzoate(β-Estradiol 3-benzoate)  
 $C_{25}H_{28}O_3=376.50$



Sample: SIGHA D5297  
 CD/UV : Ethanol Solution  
 5.0 mg/10 ml (1.2 mM), 10 mm Cell



Dehydroisoandrosterone 3-sulfate Sodium Salt(Prasterone Sulfate Sodium Salt)  
 $C_{19}H_{27}O_5SNa \cdot 2H_2O=426.51$

