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CIRCULAR DICHROISM OF SOME CROWDED CYCLIC OLEFINS

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Abstract—Chiroptical data for sterically crowded olefins, i.e. cholest-5-enes and cholest-6-enes substituted in the 6- or the 4,4,6-positions suggest that the π-σ* transition may precede the olefinic π-π* transition. A comparison with short-wavelength Cotton effects in structurally related enones and dienes is also presented

The long standing problem of the optical activity of monoolefins has not been fully explored as far as the assignment of possible olefinic transitions and the relation of the observed Cotton effects to the olefin stereochemistry are concerned.

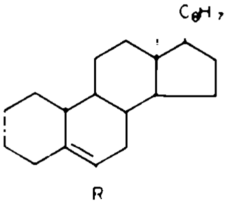
It is well known that the shape of the olefinic CD spectrum does not necessarily follow the shape of the UV absorption curve and that there is usually more than one Cotton effect within the region 220–185 nm. On the low frequency side of the electric dipole allowed π-π* transition Cotton effect (of which the maximum should coincide with the UV λ_{max}) there is observed an electric dipole forbidden, magnetic dipole allowed CD band, usually referred to as a π-3s Rydberg transition.[1] In the vicinity of the π-π* Cotton effect, but more to the blue side, there is observed another optically active transition, assigned as a $\pi\text{-}\sigma^*_{(CH)}$ or π-p, transition, which is not expected to contribute significantly to the isotropic absorption curve. At a higher frequency but still falling into a rather narrow energy span there may be observed a $\sigma_{(CH)}\text{-}\pi^*$ transition Cotton effect.[2]

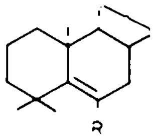
The sign of the π-π* transition Cotton effect has been correlated with olefin stereochemistry on the basis of an olefin octant rule[3] which assumes a planar ethylene chromophore. In the case of a ground state twisted olefinic bond another approach is possible, in which the olefin is treated as an inherently dissymmetric chromophore[4] of D_2 symmetry. In the allylic bond polarization model[5] a dominant role in the π-π* Cotton effect is assigned to the rotatory contribution of the polarizable allylic bonds. The dynamic coupling of the olefinic π-π* transition to the allylic bond transitions is thought, according to the recent calculations, to play a dominant role in determining olefin optical activity.[6]

Despite the continuing interest in properties of strained molecules[7] and the large number of available experimental CD data, both in cyclic[1a] and acyclic[2a] systems, only a limited number of strained olefins have been the subject of chiroptical studies. These include twisted ethylene derivative—*trans*-cyclooctene[9] and 2-bornanylidene-bornanes,[10] the latter being formally viewed as the derivatives of 2,3-di-t-butyl-2-butene. As no chiroptical data are available for crowded cyclohexene derivatives we were prompted to synthesize a series of endocyclic olefins including that with the degree of substitution equivalent to that in tri-t-butylethylene,[11] one of the most strained olefins known so far.

RESULTS AND DISCUSSION

We have chosen a series of olefins **1** and **2**, derivatives of Δ^5-cholestene (**1a**), with varying degree of substitution.





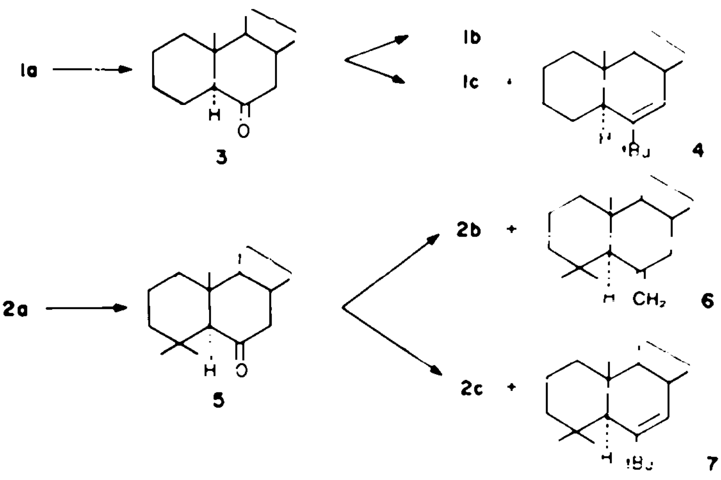
1a R = H **2a**
1b R = Me **2b**
1c R = tBu **2c**

The 6-substituted olefins were accessible in a sequence of reactions in which the olefins **1a** and **2a** were converted in a conventional manner into the corresponding 5α-cholestan-6-ones **3** and **5**, respectively.

Addition of MeLi or t-BuLi to the ketones **3** and **5** was quantitative in each case, except for the reaction of **5** with t-BuLi in which some ketone remained unreacted, evidently due to the severe strain in the reaction product and intermediate.

In both ketones the α-side of the molecule is less hindered and the formation of 6β-hydroxy derivatives should be favoured. Indeed, it has been reported that the addition of MeMgI to **3** yielded 6α-methylcholestan-6β-ol in *ca.* 70% yield,[12] while LAH reduction of **5** afforded exclusively 4,4-dimethylcholestan-6β-ol.[13] In our case PMR data indicated the presence of 6α-hydroxy products, when the steric approach to the CO group was hindered on both the α- and β-side. For example, the ratio of 6β- and 6α-alcohol as the products of t-BuLi addition to **3** was found to be 2:1.

Thionyl chloride-pyridine dehydration of the mixtures of epimeric carbinols from the alkyllithium addition afforded mixtures of olefins, recognized by PMR spectra and separated by means of preparative TLC on silver nitrate impregnated silicagel. In the exceptional case of dehydration of the product of MeLi addition to **3**, the 6β-OH group was suitably disposed for exclusive formation of the Δ^5-olefin **1b**. In the 4,4-dimethyl derivative **2b** the 6-Me group contributes substantially to the strain due to the nearly eclipsing interaction with 4α-Me group. This strain is partly released in the isomeric exocyclic



olefin **6**, the formation of which is indeed favoured. The Δ^5-olefin **2b** is converted into **6** by acid-catalyzed equilibration. Dehydration of the products of t-BuLi addition to **3** and **5** afforded the expected 6-t-butyl-Δ^5-olefins **1c** and **2c** along with their Δ^6-isomers **4** and **7**, respectively. The predominance of Δ^6-olefins is understandable, since the double bond is less hindered in them than in the Δ^5-isomers. The identity of each olefin was confirmed by means of PMR spectra (Table 1) as well as by MS.

The olefins studied here exhibit chiroptical properties that do not appear to fall into the framework of any of the existing rules. We note that the bisignate-type CD curves, characteristic of the π-bond twisted olefins[14] are clearly not observed in the case of the highly substituted Δ^5-olefins **1c**, **2a** and **2c**, for which the olefinic torsion should be more feasible. Secondly, in no case except the 6-methylene olefin **6**, could the lowest frequency Cotton effect be attributed to the olefinic UV π–π^* electric-dipole allowed transition (Table 2).

The π–π^* absorption maxima appear below 200 nm, at shorter wavelengths than the expected values for tri- and tetra-substituted endocyclic olefins[14] but generally in agreement with the values for corresponding Me-substituted ethylenes.[3] There is a noticeable red shift in the UV maximum position upon increasing substitution,

Table 1. PMR data for olefins and related compounds (δ)

Comp. No.	4,4-Me$_2$	10β-Me	13β-Me	Vinylic protons or alkyls
1a	—	1.00	0.68	5.29 (6-H)
1b	—	0.97	0.67	1.58 (6-Me)
1c	—	1.00	0.67	1.13 (6-tBu)
2a	1.08, 1.10	1.08	0.66	5.49 (6-H)
2b	1.20	1.04	0.67	1.75 (6-Me)
2c	1.29, 1.35	1.05	0.68	1.26 (6-tBu)
4	—	0.77	0.68	1.07 (6-tBu), 5.41 (7-H)
6	1.03	0.82	0.64	4.92 (6=CH$_2$)
7	1.05, 1.37	0.93	0.68	1.23 (6- tBu), 5.75 (7-H)
8	—	1.18	0.69	5.69 (6-H)
9	—	1.06	0.70	4.63, 4.85 (7=CH$_2$), 5.70 (6-H)
10	1.14, 1.19	1.23	0.70	5.89 (6-H)
11	1.12	1.12	0.71	4.70, 4.88 (7=CH$_2$), 5.89 (6-H)

Table 2. CD and UV data

Olefin	CD ($\Delta\epsilon$) π–3s	 π–σ^*	 π–π^*	UV (ϵ)
1a		+4.5 (202)	15.0! (188)	10000 sh (189)
1b	+6.65 (218)		−17.2 (190)	10000 sh (190)
1c	−1.4 sh (217)		−23.6 (194)	10600 (196.5) sh (*ca.* 220)
2a		−1.45 (209)	9.3! (188)	11500 sh (189)
2b	+1.25 (222)	−5.4 (204)	−7.0! (187)	9200 broad sh (196)
2c	−1.75 (223)		−18.1 (198.5)	11900 (198) sh (*ca.* 225)
4		+4.75 (208)	−17.0 (187)	10800 (191) sh (207)
6			+1.25 sh (204) +6.8 (191)	9700 (200.5)
7		+14.1 (207)	−14.2! (188)	10000 (191) sh (206)

although in some cases the UV maximum could be observed merely as the shoulder on the still rising absorption curve (olefins **1a**, **1b**, **2a** and **2b**). The intensity of the absorption does not vary significantly with substitution, whereas decrease of the $\pi-\pi^*$ transition energy and oscillator strength with an increase in the olefin π-bond twist is predicted by the semiempirical calculations.[4] The UV absorption curves of the t-Bu substituted olefins **1c**, **2c**, **4** and **7** show a shoulder on the lower energy side. This shoulder corresponds to the lower energy CD maximum (Table 2).

The $\pi-\pi^*$ Cotton effects in Δ^5-olefins are consistently negative, their magnitude increasing with the increasing bulk of the 6-alkyl substituent. The olefin octant rule[3] predicts a negative Cotton effect for **2a** and a positive one for **1a**. On the other hand, qualitative consideration of the conformation of Δ^5-olefins leads to the prediction of a positive olefinic torsional angle, as depicted in Fig. 1.

Fig. 1. Projection of the Δ^5-olefin torsion (exaggerated) as looked at along C6–C5 bond.

The sense of π-bond twist is thus the same as in *l-l-R-trans*-cyclooctene and a negative rotatory strength would be expected for the $\pi-\pi^*$ transition.[4] Small but positive olefinic torsional angles are displayed in the solid state by a number of unsubstituted steroidal Δ^5-olefins, as shown by X-ray analysis.[5]

The vinylic substituents (R = Me, t-Bu) increase π-bond torsional angle and this is followed by the increase of the $\pi-\pi^*$ Cotton effect. The allylic substitution (R′ = Me) will open the C(6)–C(5)–C(10)–C(9) torsional angle, thus reducing the olefinic C(10)–C(5)–C(6)–C(7) torsion. Again, this trend is seen in the reduced negative $\pi-\pi^*$ Cotton effects of 4,4-dimethylated olefins **2a**–**2c**. Additionally, the 4β-Me group partially offsets the negative rotatory power contribution of the 10β-Me group.

The olefins **1c**, **2b** and **2c** are roughly the cyclic equivalents of the highly strained ethylene derivatives, namely 2,3-di-t-butyl-*trans*-2-butene, 1,1-dimethyl-2,2-di-t-butylethylene and tri-t-butylethylene, for which π-bond torsional angles 21.9°, 29.4° and 16.4°, respectively, were calculated.[16] In substituted cyclohexenes the strain is lowered by the cyclic structure, in place of the C–H nonbonded interactions existing, for example, in *cis*-di-t-butylethylene. On the other hand, rigid cyclic structure disfavours other ways of molecular strain release, i.e. bond stretching and bond angle distortion. Hence, the π-bond torsion in substituted Δ^5-olefins cannot be neglected as the possible contribution to the $\pi-\pi^*$ Cotton effect.

The weak longer wavelength (217–223 nm) Cotton effects in tetrasubstituted olefins **1b**, **1c**, **2b** and **2c** are attributed to the π-3s Rydberg transition, as they fall in the expected energy span and correspond to at most weak shoulders in the isotropic absorption curves. Interestingly, these Cotton effects show a sign reversal in going from a 6-Me to a 6-t-Bu substituent. The longer wavelength transitions (202–209 nm) in trisubstituted olefins **1a**, **2a**, **4** and **7** are most probably of different origin, as judged by their higher CD intensity and low contribution to the eletronic absorption spectra. Consistently, they are referred to as $\pi-\sigma^*$ transitions and apparently they correlate with the stereochemistry of olefin within the prediction of olefin octant rule.[3] The contribution of the $\pi-\sigma^*$ transition to the 218 nm Cotton effect of **1b** may be responsible for its high intensity. The negative CD band at 204 nm in **2b** also falls into the $\pi-\sigma^*$ transition energy range.

Literature search of the CD data lends additional support for a little broader generalization of the CD behavior of cyclic olefins.

(a) Olefins substituted unsymmetrically in allylic positions generally display $\pi-\sigma^*$ Cotton effect at the longer wavelength side of the Cotton effect associated with the $\pi-\pi^*$ transition. The olefin should be tetra-, tri- or at least *cis*-disubstituted in order to bring the $\pi-\sigma^*$ transition below the $\pi-\pi^*$ energy region. Calculations predict that in strained polycyclic olefins $\pi-\sigma^*$. Rydberg transitions may precede the $\pi-\pi^*$ excitation.[17] Local symmetry of olefin allylic substitution may obscure the presence of the $\pi-\sigma^*$ CD band. This may explain the exceptional CD behavior of Δ^6-cholestene, for which only a single negative Cotton effect ($\Delta\epsilon$ −3.1 at 187 nm) was observed.[3] The related 6-substituted Δ^5-olefins **4** and **7** also show an intense negative CD band in the region of $\pi-\pi^*$ absorption (Table 2), probably resulting from the π-bond torsion. In highly twisted olefins the $\pi-\pi^*$ excitation energy is lowered more efficiently than that of the $\pi-\sigma^*$ transition, i.e. the sequence of the two transitions may be reversed.[4]

(b) The extreme complexity of the CD behavior of olefins complicates the use of any particular symmetry rule,[18] although some measure of success was noted in applying the olefin octant rule.[3] Incidentally, this might result from the persistent presence of the $\pi-\sigma^*$ transition in cyclic olefins, at long-wavelength side of the spectrum (previously referred to as λ_2 $\pi_x-\pi_x^*$ Cotton effect).

(c) In highly crowded cyclic olefins CD couplets and batochromic shifts are not necessarily observed, although this does not exclude the presence of olefin torsion. In fact, the CD band corresponding to the $\pi-\pi^*$ UV max retains the same sign in all olefins belonging to the same structural series, thus establishing the relation between $\pi-\pi^*$ Cotton effect and olefin geometry.

Interestingly, the same strongly negative Cotton effect, characteristic of twisted Δ^5-olefins, is found between 200 and 215 nm in the CD spectra of related cholest-5-en-7-ones **8** and **9** (Fig. 2). However, their 7-methylene derivatives **10** and **11** give more complex CD patterns: while the negative helicity diene **10** still retains a negative Cotton effect at the short-wavelength side of the strong conjugated diene Cotton effect, diene **11**, with a planar or slightly positive helicity chromophore, and a competitive chirality contribution of the C-4βMe and C-10βMe bonds,[20-22] displays a complex bisignate long wavelength Cotton effect, making assignment of the short-wavelength transitions less reliable.

EXPERIMENTAL

CD and UV spectra of the spectroscopic grade n-hexane solns (0.005–0.01 mol/l) were recorded on Jobin-Yvon Dichrographe III and a Cary 118C spectrophotometer, respectively, using 0.01 cm cells. PMR spectra were obtained on a Varian EM-360 spectrometer and refer to $CDCl_3$ solutions with TMS as reference. IR spectra were recorded on a Perkin–Elmer Model 580 instrument using KBr pellets and MS on a JEOL JMS D—100 spectrometer. Rotations were measured in CCl_4 solns.

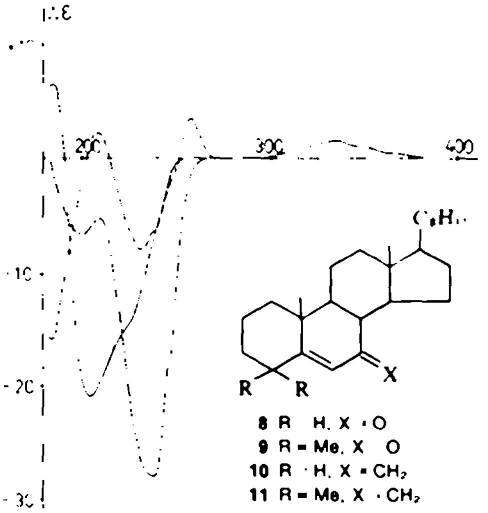


Fig. 2. CD curves (n-hexane): —— cholest-5-en-7-one (8), ······ 4,4-dimethylcholest-5-en-7-one (9), -·-·-· 7-methylenecholest-5-ene (10) and -·-·- 4,4-dimethyl-7-methylenecholest-5-ene (11).

Cholest-5-ene (**1a**), m.p. 91–91.5°, was prepared from cholesteryl bromide[20] by zinc reduction in AcOH. Nitration of **1a** or cholesteryl bromide, followed by Zn reduction in AcOH afforded **3**,[21] m.p. 98–100°.

4,4-*Dimethyl-5α-cholestan-6-one* (**5**). 3.986 g (10 mmoles) of **2a**, m.p. 73–75° (obtained from 4,4-dimethylcholest-5-en-3-one[22] by Wolff–Kishner reduction) was placed in a pressure flask equipped with septum cap, dissolved in anhyd. diethyl ether (40 ml) and treated with $BF_3 \cdot Et_2O$ (6.3 ml, 50 mmoles). The flask was purged with dry argone and at 0° 20 ml 2M LAH in diethyl ether was admitted. The content of the flask was stirred under B_2H_6 pressure for 2 hr, the excess of B_2H_6 was removed with argone and to the residue water (5 ml) was added. The resultant mixture was stirred for 24 hr with Brown reagent[23] (25 ml), extracted with ether and the oily mixture of products separated by means of column chromatography on silicagel. With petroleum ether there was recovered *ca.* 1 g (25%) of starting material, and with benzene-petroleum ether (1:1) there was eluted 1.20 g (29%) of crystalline **5**, m.p. 109–110° (from petroleum ether-EtOH; lit.[11] m.p. 108–109°), $\Delta\epsilon$(hexane): −0.347 (324 nm), −0.446 (313 nm), −0.333 (304.5 nm), +0.015 (265 nm), +5.9 (195 nm).

Reaction of ketones **3** *and* **5** *with alkyllithiums.* 1 mmole of **3** or **5** was stirred under argone with anhyd. diethyl ether (6 ml) and treated with 5-fold excess of either MeLi or t-BuLi in ethereal soln (in the latter case, ketone soln was added to the t-BuLi soln at −70° and after addition the soln was allowed to warm to room temp). Stirring was continued overnight, the excess of alkyllithium was destroyed with water and the residue extracted with ether. Addition products were obtained with essentially quantitative yield, with exception of the reaction of **5** with t-BuLi, where 30% of **5** was left unreacted.

Preparation of olefins **1b**, **1c**, **2b**, **2c**, **4**, **6** *and* **7**. The crude product of alkyllithium addition (after removal of diethyl ether from the dried soln) was dissolved in anhyd pyridine (2 ml) and treated at 0° with 10 drops of $SOCl_2$. After 3 hr at room temp. TLC indicated no starting material. The mixture was extracted with petroleum ether and the extract was filtered through silicagel to afford the olefinic products (the yield of this reaction step was almost quantitative).

Dehydration of the product of MeLi addition to **3** afforded crystalline **1b**, as the sole reaction product, m.p. 100–101° (from EtOAc-MeOH; lit.[12] m.p. 98–99°). In other cases oily mixtures of olefins were obtained and these were analyzed by PMR spectra (cf. the data collected in Table 1).

The mixture of olefins from the reaction of **5** with MeLi and $SOCl_2$ consisted of **2b** and **6**, in the ratio 7:3. Acid equilibration of the mixture ($HClO_4$ in CCl_4) increased the content of **6** to the ratio 3:7. Olefins from the reaction of **3** or **5** with t-BuLi and $SOCl_2$ were accordingly: **1c** + **4** (*ca.* 1:1) and **2c** + **7** (*ca.* 1:2). The above mixtures were separated with the aid of preparative TLC on Kieselgel G impregnated with 40% $AgNO_3$ (the plates were developed with n-pentane). In each case the Δ^4-olefin was the less polar component of the mixture. The products were crystallized from EtOAc–MeOH:

2b—M^+ 412, m.p. 89–91°, $[\alpha]_D^{21}$ +5.1° (c = 0.6)
6—M^+ 412, m.p. 94–96°, $[\alpha]_D^{21}$ +22.6° (c = 1.0), ν_{max} 1641 cm^{-1}
1c—M^+ 426, m.p. 71–74°, $[\alpha]_D^{21}$ −84.4° (c = 1.0)
4—M^+ 426, m.p. 70–73°, $[\alpha]_D^{21}$ −18.3° (c = 1.2)
2c—M^+ 454, m.p. 102–105°, $[\alpha]_D^{21}$ −45.9° (c = 0.6)
7—M^+ 454, not crystalline, $[\alpha]_D^{21}$ +5.9° (c = 1.7).

The Δ^5-7-ketones **8** (m.p. 128–131°, ϵ_{max} 14,640 at 230 nm) and **9** (m.p. 81–82°, ϵ_{max} 13,400 at 233 nm) were obtained from the corresponding olefins **1a** and **2a** in a photooxidation reaction[24] in cyclohexane soln. The eneones **8** and **9** were subsequently converted into the dienes **10** (not crystalline, ϵ_{max} 23,850 at 239.5 nm, $[\alpha]_D^{21}$ −205.8°, c = 1.2) and **11** (m.p. 76–77°, ϵ_{max} 19,600 at 242 nm, $[\alpha]_D^{21}$ −60.3°, c = 2.0), respectively, by means of Wittig reaction.

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