



Circular Dichroism of Steroidal and Related Cisoid α,β -Unsaturated Ketones. Part II.

Jadwiga Frelek ^a, Wojciech J. Szczepek ^{*,b}, and Hans Peter Weiß ^c

^a Institute of Organic Chemistry, Polish Academy of Sciences, PL-01-224 Warszawa, Kasprzaka 44

^b Pharmaceutical Research Institute, PL-01-819 Warszawa, Rydygiera 8

^c Department of Chemistry, Ruhr-Universität Bochum D-44780 Bochum, Universitätstr. 150

Abstract - The circular dichroism (CD) of some steroidal and related cisoid conjugated enones in various solvents has been investigated. The relation between structure and observed Cotton effects (CE's) depending on the solvent or the temperature has been discussed in terms of previously published rules (Part I). It is also shown that CD spectra of these compounds are influenced by substituents located in the allylic axial or equatorial as well as α' -axial position.

Recently we have published¹ the CD data of over twenty cisoid enones of different types measured in acetonitrile. We have found that in all cases the sign of the $\pi\pi^*$ CE is governed by the helicity of the enone system, i.e. positive (negative) sign of the CE corresponds to the positive (negative) torsion angle. In some cases, however, we have observed a bisignate CD curve within $\pi\pi^*$ transition.

In general, the sign of the $\pi\pi^*$ transition CE should be opposite to the sign of the $\pi\pi^*$ CE,^{2,3} but we have shown that substitution in the vicinity of the chromophore contributes to this transition, which can lead to change of the sign. Similarly to the $\pi\pi^*$ transition some cisoid enones gave bisignate form CD curves in this spectral region. The nonfunctionalized enones 1-4 and the functionalized compounds 9-14 belong to the set of Δ^8 -octalin-1-one derivatives of P-configurational type and the enones 6-8 to the set of M-configurational type. Although the exo-methylene compound 5 is not a Δ^8 -octalin-1-one derivative, its assignment to the set of P-configurational type follows from structural feature as it is shown in Fig. 1.

The influence of the solvent polarity on the CD curves in the $\pi\pi^*$ region was studied in up to eight solvents of different acidity and basicity expressed by normalised E_T^N and B_{KT} values.^{5,6,7} This data is collected in Table 2 together with the CD values of the $\pi\pi^*$ transition. For the spectral range below 280 nm the data is shown in Table 3 and 4. The observed absorptions are divided in band I, which corresponds to the $\pi\pi^*$ transition, and band II. As we previously reported,¹ band II is always of opposite sign to the enone helicity. The sign of this band does not depend upon substitution or solvent used. Its intensity due to different solvents is unpredictable and can therefore not be discussed exactly.

Fig. 1: Unsubstituted enones

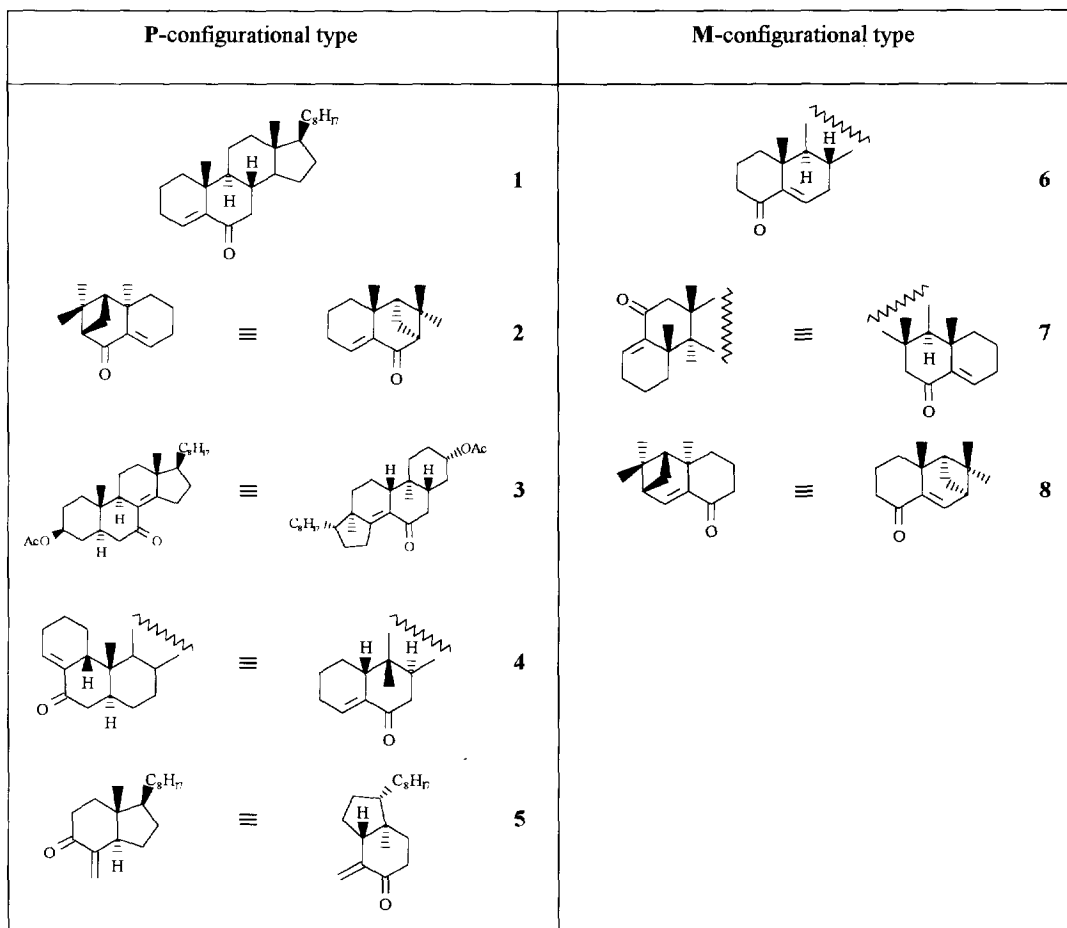
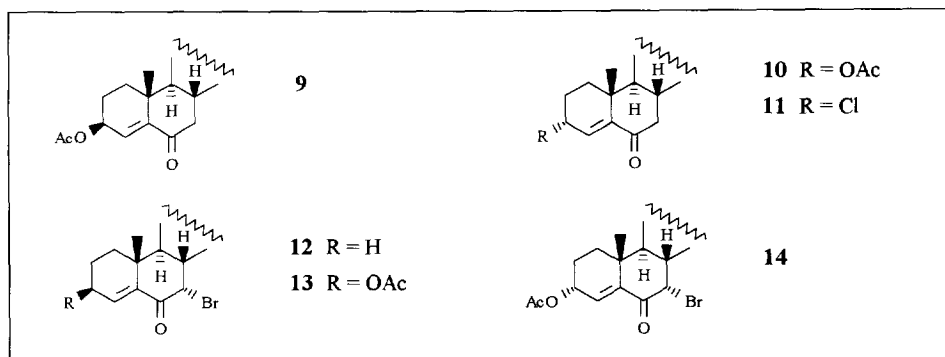


Fig. 2: Substituted enones (P-configurational type)



Calculated conformations of the enone systems

Compared to cyclic transoid enones, where the chromophore is located in one ring, in the case of cyclic cisoid enones we have two rings bearing the enone system (except in the case of *exo*-methylene compound **5**). Therefore, to determine the torsion angle of this cisoid enone unit we have to consider the possible conformations in both rings.

To get the most probable conformation of the investigated compounds we decided to do conformational analysis by molecular mechanics calculations with the MMX program.⁸ All geometries obtained were recalculated until constant value of steric energy was reached. In Table 1 we have collected the values of the enone torsional angles of the compounds **1-14** in the conformation of lowest energy. A second conformer of the next lowest energy also has the same sign of torsional angle, except for enones **3** and **5**, where a reversed torsion of the enone moiety was found. The obtained values of the enone torsional angles distinctly indicate that the chromophore in all cases is significantly skewed. For this reason substitution at the γ -allylic position in compounds **9-11**, **13** and **14** does not lead to substantial changes of the enone helicity compared to parent enone **1**. The calculated torsion angle (-43°) of compound **1**, although higher, agrees with that found from X-ray crystal data (ca. -32°).⁹

Table 1: Calculated torsional angles of the cisoid enones

Comp.	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Angle	-43°	-34°	-37°	-47°	-28°	$+40^\circ$	$+48^\circ$	$+49^\circ$	-43°	-45°	-43°	-49°	-52°	-54°

It is worth noting that P-configurational type is related to a negative and M-configurational type to a positive torsional angle for all conformers of lowest energy. Therefore the enones of M-type should give positive CE for the $n\pi^*$ transition according to the helicity rule for enones.³ Consequently, for P-configuration the sign of the transition should be negative.

Chiroptical Properties

$n\pi^*$ transition

As predicted from our calculations and according to the enone helicity rule^{1,3} the enones **1-5** should give negative CE's for this transition. The enones **1-3** follow this rule, as well in nonpolar as in polar solvents.

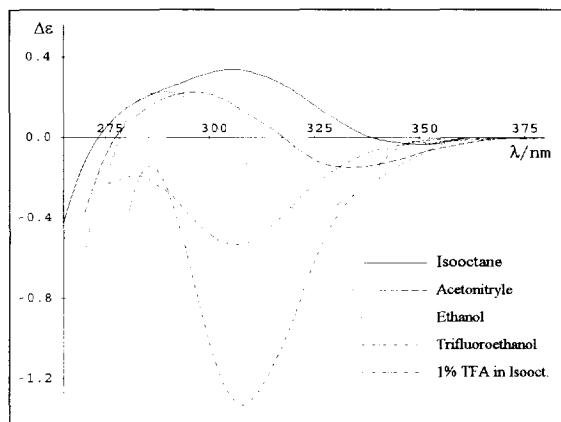


Fig.3: CD spectra of **4** in $n\pi^*$ region in different solvents.

However, the enones **4** and **5** show a bisignate curve shape in standard solvents as isooctane, acetonitrile and ethanol. Whereas for compound **5** the magnitude of positive and negative CE shows no distinct dependence upon the polarity of the solvent, in the case of enone **4** we can observe a significant influence of solvent polarity on the ratio of positive and negative part of the bisignate CD curve (Fig. 3). The increase of solvent polarity leads to an increase of the negative part (with decrease of the positive part) and finally in TFE and TFA/Oct only the negative CE is observed.

Table 2: CD data of the conjugated enones for the $n\pi^*$ transition { $\Delta\epsilon$ ($\lambda_{\text{max}}/\text{nm}$) }

Comp.	Solvent ^a		Isooctane	CCl ₄	Dioxane	CHCl ₃	CH ₃ CN	Ethanol	TFE ^b	TFA/Oct ^c
	E_{T}^{N}	B_{Rr}								
1	0.07	0.00	-2.09 (329)	-2.28 (328)	-2.40 (327)	-2.64 (322)	-2.43 (325)	-2.40 (322)	-5.24 (306)	-3.28 (306)
2			-0.32 (330)				-0.55 (321)	-0.63 (314)		
3			-1.08 (343)				-1.06 (336)	-1.15 (338)	-1.55 (325)	-1.57 (314)
4			-0.04 (350)				-0.15 (332)	-0.37 (324)	-0.84 (309)	-1.30 (308)
			+0.35 (306)				+0.23 (297)	+0.22 (289)		
5			-0.13 (359)				-0.10 (352)	-0.13 (342)		
			+0.08 (309)				+0.23 (301)	+0.10 (299)		
6			+1.10 (337)				+1.54 (329)	+1.72 (322)	+3.11 (308)	+3.18 (307)
7			+2.04 (330)		+2.10 (324)		+2.65 (324)	+2.42 (320)	+2.78 (303)	+3.88 (303)
8			+0.72 (328)				+0.73 (323)	+0.89 (318)		
9			-1.83 (329)	-2.08 (329)	-1.66 (328)	-2.58 (324)	-2.33 (326)	-2.02 (320)	-3.18 (310)	-2.99 (309)
10			-2.62 (330)	-3.16 (329)	-2.37 (330)	-2.90 (326)	-3.17 (328)	-3.42 (323)	-3.82 (313)	-3.51 (312)
11			-1.95 (334)				-2.65 (330)	-2.31 (327)	-3.35 (314)	-3.29 (312)
12				-0.04 (377)	-0.05 (374)	-0.17 (361)	-0.18 (365)	-0.05 (365)	-0.74 (336)	-0.09 (344)
			+1.41 (349)	+1.11 (325)	+0.97 (324)	+1.00 (316)	+0.82 (320)	+1.05 (317)	+0.72 (306) ^s	+1.18 (309) ^s
13			+1.61 (330)	+1.47 (325)	+2.25 (325)	-0.02 (380)	-0.03 (385)		-0.17 (353)	
						+1.39 (324)	+1.34 (326)	+1.29 (326)	+0.91 (309) ^s	+1.61 (312)
14			+1.31 (329)	+1.34 (327)	+1.23 (327)	-0.15 (369)	-0.17 (370)	-0.10 (371)	-0.60 (344)	-0.06 (359)
						+1.15 (322)	+0.79 (322)	+0.72 (319)	+0.58 (303) ^s	+1.14 (308)

^a The E_{T}^{N} and B_{Rr} values are taken from literature 5,6,7^b 2,2,2-Trifluoroethanol ^c 1% Trifluoroacetic acid in isooctane ^d not available ^s shoulder

Table 3: CD data of the unsubstituted conjugated enones in the 280-180 nm range { $\Delta\epsilon$ (λ_{\max} /nm) }

Comp.	Solvent	Band I		Band II
1	Oct	-0.46 (252)	+3.05 (228) ^s	+16.6 (193)
	Ace	-0.30 (261)	+2.23 (232) ^s	+10.5 (198)
	Eth	-0.23 (269)	+2.34 (236) ^s	+9.7 (200)
	TFE		+3.75 (249) ^s	+16.4 (208)
	TFA/Oct		+3.31 (245) ^s	+11.5 (208)
2	Oct		-4.15 (229)	a
	Ace		-4.01 (234)	a
	Eth		-2.87 (236)	+2.5 (195)
3	Oct		-5.87 (254)	+5.3 (207)
	Ace		-4.55 (257)	+4.9 (215)
	Eth		-5.14 (260)	+5.8 (214)
	TFE		-5.35 (267)	+7.0 (217)
	TFA/Oct		-5.02 (273)	+7.0 (221)
4	Oct	-2.70 (247)	+2.63 (218) ^s	+13.5 (195)
	Ace	-1.33 (255)	+ b	+4.8 (208)
	Eth	-1.30 (260)	+ b	+9.2 (209)
	TFE	-0.53 (271)	+ b	+6.3 (213)
	TFA/Oct	-1.49 (268)	+ b	+8.8 (215)
5	Oct		-3.34 (229)	a
	Ace		-3.25 (235)	+5.3 (204)
	Eth		-2.57 (237)	+5.0 (205)
6	Oct	+0.13 (262)	-8.09 (228)	-7.9 (219)
	Ace	+0.06 (269)	-8.51 (222) ^b	- c
	Eth		-8.49 (224) ^b	- c
	TFE		-11.35 (234)	-11.2 (221)
	TFA/Oct		-11.89 (232)	-11.5 (220)
7	Oct	+0.30 (254)	-3.49 (229)	-9.5 (195)
	Ace	+0.15 (265)	-4.33 (234)	-8.0 (197)
	Eth	+0.13 (272) ^s	-3.31 (236) ^s	a
	TFE		-2.73 (241) ^s	-6.5 (209)
	TFA/Oct		-5.04 (240) ^s	-9.3 (209)
8	Oct	+0.47 (264)	-2.37 (233)	
	Ace	+0.19 (272)	-2.23 (226) ^b	- c
	Eth	+0.11 (279) ^s	-2.36 (225) ^b	- c

Oct = Isooctane Ace = Acetonitrile Eth = Ethanol

TFE = 2,2,2-Trifluoroethanol TFA/Oct = 1% Trifluoroacetic acid in isooctane

a could not be measured b broad band c superimposed on Band I CE s shoulder

The calculated C=C-C=O torsional angles of enones **6-8** are positive, thus their $\pi\pi^*$ CE's should also be positive. In fact these compounds show a positive monosignate CD curve in all solvents studied.

The enone helicity of the functionalized derivatives of cholest-4-en-6-one **9-14** is negative and the same as for the parent enone **1**. However, the chiroptical behaviour of these compounds depends on the site of functionalization. Enones functionalized only at the γ -allylic position show strong negative $\pi\pi^*$ CE independently of the configuration of the substituent (β -OAc for **9**, α -OAc for **10** and α -Cl for **11**). The magnitudes of this CE are comparable with that of the parent enone **1**.

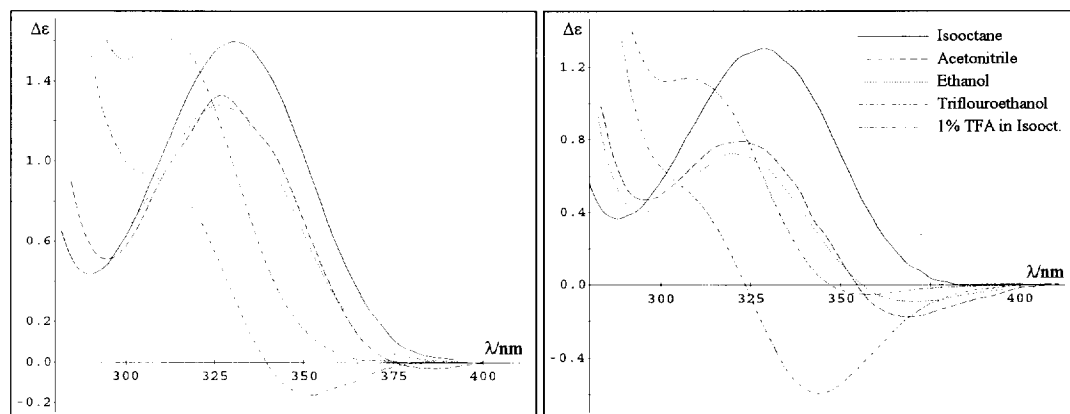


Fig. 4: CD spectra of **13** (left) and **14** (right) in $\pi\pi^*$ region in different solvents.

The remaining enones **12-14** bearing axial bromine substituent at α' -position exhibit moderate positive CE in nonpolar solvent (isooctane). The CD curve becomes bisignate on going to polar solvents. The intensity of the additional negative branch increases with increasing acidity of the solvent and reaches maximum in TFE solution. Unexpected low intensity of this branch (disappearance in the case of enone **13**) is observed in ethanol. Similar behaviour can be seen for TFA/Oct solutions.

$\pi\pi^*$ transition

According to the enone helicity rule the $\pi\pi^*$ band I CE should be of opposite sign to that of the enone torsional angle. In fact, among the unsubstituted enones the compounds **1**, **4** and **6-8** confirm this rule, although they display bisignate band I CE. The nonexpected additional negative branch for enones **1** and **4** and positive one for enones **6-8** appear at longer wavelength and is of weak intensity. The magnitude of this weak "preband" decreases strongly with increasing polarity of the solvent and for compounds **1**, **6** and **7** it totally disappears in very polar solvents as TFE.

Enone **4** displays an exceptionally strong negative "preband" of comparable intensity to the positive branch, which is obscured by strong band II CE. The magnitude of this "preband" is five times smaller in TFE than in isooctane, but increases on going to TFA/Oct as solvent.

Table 4: CD data of the substituted conjugated enones in the 280-180 nm range { $\Delta\epsilon$ (λ_{\max}/nm) }

Comp.	Solvent	Band I			Band II	
9	Oct		-4.83 (234)		+12.1 (195)	
	Ace		-4.80 (237)		+13.2 (197)	
	Eth		-3.78 (238)		+14.3 (197)	
	TFE		-3.73 (246)		+11.3 (202)	
	TFA/Oct		-2.84 (251)		+11.1 (204)	
10	Oct		+17.98 (224)		+21.5 (197)	
	Ace		+14.16 (225)		+14.8 (201)	
	Eth		+18.67 (223)		+20.6 (200)	
	TFE		+15.44 (221)		+14.7 (207) ^S	
	TFA/Oct		+14.58 (219)		+14.4 (208)	
11	Oct		+12.76 (226)		+12.0 (208)	
	Ace		+15.56 (225)		+15.1 (212)	
	Eth		+12.67 (222)		+12.1 (209)	
	TFE		+13.22 (222)		+12.4 (208)	
	TFA/Oct		+12.66 (216)		+12.1 (206)	
12	Oct	+7.55 (255)	-3.06 (224)		+8.4 (191)	
	Ace	+7.74 (260)	-0.87 (232)	+2.8 (211)	+4.7 (192)	
	Eth	+7.35 (263)	-0.58 (234)	+3.7 (211)	+4.6 (201)	
	TFE	+6.92 (270)		+6.2 (217)		
	TFA/Oct	+6.42 (271)	-0.16 (243)	+5.7 (218)	+4.2 (188)	
13	Oct	+5.24 (255)	-4.19 (229) ^S	-5.8 (218)	+7.0 (200)	
	Ace	+4.42 (260)	-2.27 (233)	-0.3 (217) ^S	+2.9 (202)	
	Eth	+4.52 (261)	-2.64 (233)	-1.2 (218) ^S	+3.8 (202)	
	TFE	+5.15 (266)	-1.44 (239)		+3.8 (218)	
	TFA/Oct	+4.38 (267)	-1.75 (239)		+2.7 (218)	
14	Oct	+12.97 (245)	+ b		+14.7 (200) ^S	
	Ace	+10.30 (251)	+ b		+8.7 (202)	
	Eth	+11.80 (249)	+ b		a	
	TFE	+12.54 (256)	+ b		+ c	
	TFA/Oct	+7.73 (257)	+ b		+ c	

The abbreviations are defined in Table 3.

The remaining unsubstituted enones **2**, **3** and **5** show a monosignate negative band I CE, although a positive one was expected according to the helicity rule.

The appearance of substituents in the vicinity of the chromophore dramatically changes the shape of the CD curve in the $\pi\pi^*$ region. Enone **9** bearing γ -equatorial substituent (OAc) displays monosignate negative CE of moderate intensity, whereas enones **10** and **11** - substituted axially (OAc, Cl) - show very strong monosignate positive CE. Introduction of axial bromine at the α' -position leads to more complicated spectra in this region accompanied by the appearance of a strong positive band at about 260 nm, which is obviously caused by this substituent.

Discussion

Nonfunctionalized enones

The enones **1** and **7** are almost enantiomorphous except that in the case of compound **7** we have a methyl group attached to the cyclohexanone ring at the β^1 -position instead of hydrogen. Therefore, as shown in Figure 5, the obtained CD curves are a quasi mirror image. The only remarkable difference is the intensity of band II CE, which is about two times stronger in the case of compound **1**.

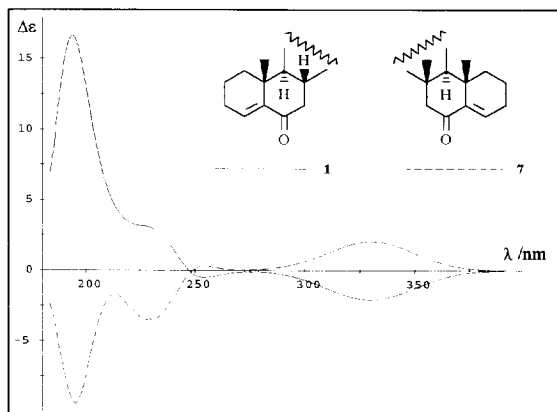


Fig. 5: CD spectra of **1** and **7** in isoctane

This can only depend on the different substitution in β^1 -position to the carbonyl group (hydrogene for comp. **1** and methyl group for comp. **7**), which also affects the torsional angle of the enone unit. For the more sterically hindered enone **7** we calculated $+48^\circ$ versus -43° for compound **1**. But it has no significant influence on the intensity and position neither of band I nor of $n\pi^*$ CE. The behaviour at low temperatures (Table 5) is also very similar, except the fact that for enone **1** an additional positive CE in the $n\pi^*$ region is observed, which leads to a bisignate curve shape.

The remaining enones strongly differ in their structural features and therefore can not be directly compared like above. However, comparison of the $n\pi^*$ CE's for the trans condensed compounds **1-3** and **5-8** shows that their magnitudes depend on the presence or absence of additional rings. Bicyclic enones (e. g. compounds **2**, **5** and **8**) display weaker CE's whereas the stronger ones are mostly characteristic for polycyclic enones (e. g. compounds **1** and **7**). This suggests that additional rings influence the intensity of the $n\pi^*$ CE. The rings which appear to make significant contributions are those directly fused to the cyclohexanone ring. Unexpectedly the signs of these contributions seem to follow the carbonyl octant rule. Therefore tetracyclic enone **1** and pentacyclic enone **7** show greater $n\pi^*$ CE's than tetracyclic enones **3** and **6**.

As it was mentioned before the lowest energy conformers of compounds **3** and **5** have negative torsional angle. For the next lowest energy conformers of both compounds the reversed helicity of the enone moiety was found. The calculated estimated population of these conformers, however, is low or very low and does not exceed 7.7 and 1.6%, respectively. Therefore the contribution of the conformer with the positive helicity to the CD should be negligible. In fact it is clearly seen for compound **3**. The bisignate curve shape of compound **5** within $n\pi^*$ transition may be only explained as a superposition of two vibrational progressions with CD's of different signs and may not be connected with equilibrium of the two conformers of opposite enone helicity.

The only investigated *cis* condensed enone **4** shows a bisignate and very weak $n\pi^*$ CE in common solvents although two lowest energy conformers of the same helicity were obtained by molecular mechanics calculations. The rings B and C of the cholestane skeleton lie as well in positive as in negative octant and the ring D exclusively in negative octant. Adapting the proposal done for *trans* condensed enones the sum of ring contributions may therefore be of no significant importance. At low temperatures a change of the ratio between negative and positive branch of the bisignate CD curve takes place. Although both values do increase, at -160° the negative CE is three times stronger than at $+20^\circ$ whereas the positive value is only 1.5 times stronger. According to our MMX calculations the conformers of lowest energy display a negative enone torsional angle and we would expect a monosignate negative $n\pi^*$ CE for both conformers. Therefore the unexpected behaviour of this compound as well for low temperatures as in different solvents can not be explained by the participation of another conformer. This implies that either solvation effects or rather the overlapping of vibrational progressions with CD's of different signs are responsible for the bisignate curve shape. A similar solvent dependence was reported by Gawronski¹⁰ for rigid (1*R*,4*S*)-bicyclo[2.2.1]heptan-2-one (+0.58 in *n*-heptane and +0.40 / -1.11 in 1,1,1,3,3,3-hexafluoro-2-propanol).

Table 5: Low temperature CD data of enones **1**, **4**, **7** and **14** in methylcyclohexane/isopentane (1:3) { $\Delta\epsilon$ (λ_{\max} /nm) }

Comp.	+20°C	-20°C	-60°C	-100°C	-140°C	-160°C
1	-2.2 (330)	-2.2 (330)	-2.3 (330)	-2.3 (330)	-2.2 (330)	-2.2 (330) ^a
			+0.08 (268)	+0.23 (269)	+0.42 (273)	+0.60 (273) ^a
	-0.63 (253)	-0.32 (252)	-0.16 (253)			
	+1.7 (228)	+2.0 (229)	+2.2 (231)	+2.6 (233)	+2.3 (233)	+2.2 (235) ^a
4	-0.07 (349)	-0.10 (347)	-0.12 (346)	-0.15 (343)		-0.21 (340)
	+0.38 (305)	+0.43 (305)	+0.49 (303)	+0.51 (302)		+0.55 (297)
7	+2.67 (326)		+2.93 (329)	+3.19 (325)	+3.25 (325)	+3.09 (324) ^b
	+0.87 (252)		+0.84 (257)	+0.52 (257)	+0.26 (259)	+0.07 (272) ^b
	-3.88 (228)		-4.36 (229)	-4.96 (229)	-5.27 (230)	-4.96 (231) ^b
14	-0.04 (386)	-0.05 (386)	-0.06 (383)	-0.05 (381)	-0.06 (380)	
	+1.30 (328)	+1.35 (328)	+1.32 (329)	+1.32 (329)	+1.26 (328)	

a) -175°C b) -170°C

C-3-Substituted cholest-4-en-6-ones

Introduction of 3β - or 3α - substituent only weakly changes the intensity and position of the $n\pi^*$ CE. The observed solvent dependence is very similar to that of unsubstituted enone **1**. However, they strongly influence band I CE. According to Beecham's rule¹¹ on the influence of γ -allylic oxygen substituent, band I CE of compound **9** is negative (negative AcO-C3-C4=C5 torsional angle). The intensity of this band becomes lower and λ_{\max} value is red shifted on going from non-polar to polar solvents. Band I CE's of compounds **10** and **11** (3α -OAc and 3α -Cl) are strongly positive because of strong positive contribution of the γ -allylic substituent.

This proves our previous proposal,¹ that not only oxygen containing substituents influence the sign of band I CE, furthermore α -chlorine has the same effect. As in the case of the equatorial 3β -chlorine substituent,¹ the contribution of axial chlorine (+13.3) is bigger than that for axial acetoxy- (+11.9) or hydroxy group (+5.8).¹ It is interesting, that this CE for compounds 10 and 11 is blue shifted in contrast to unsubstituted and 3β -OAc substituted cholest-4-en-6-one.

α' -Bromine substituted enones

As described above, the introduction of α' -bromine substituent has a dramatic influence on the chiroptical properties as well in the $n\pi^*$ as in the $\pi\pi^*$ region. To determine this influence exactly we subtracted the CD spectra of the correspondent enone without bromine substituent (1, 9 and 10) from the substituted one (12, 13 and 14), respectively. In all three cases the resulting curves are very similar. They indicate strong positive contributions to the $n\pi^*$ ($\delta\Delta\epsilon \approx +3$) and the $\pi\pi^*$ ($\delta\Delta\epsilon \approx +7$) transitions (Figure 6). This is in agreement with the positive helicity of the Br-C7-C6=O system (bromine lies in the positive octant regarding the carbonyl group). Furthermore a negative contribution to the band II CE can be observed.

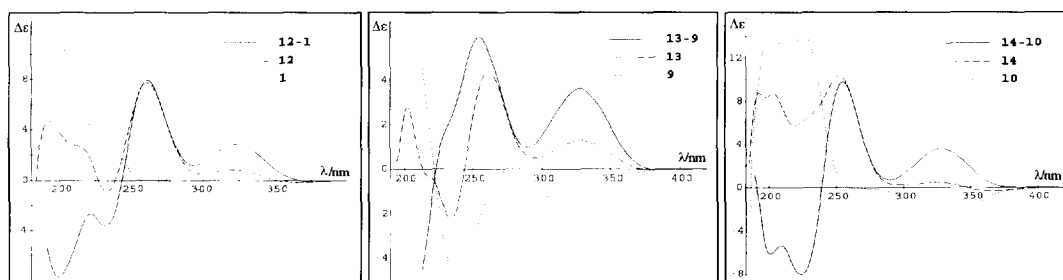


Fig. 6: Difference and original CD spectra of 1 and 12 (left), 9 and 13 (centre), 10 and 14 (right) in acetonitrile.

The low temperature investigations of bromo enones 13 (Table 6) and 14 (Table 5) show completely different behaviour of these compounds. For enone 14 no change in position or intensity of the CE's was observed, whereas for enone 13 dramatic changes for temperatures lower than -100°C in sign and intensity of the CE's took place. Since conformational changes leading to such a dramatic effect are highly improbable, this cannot be taken into account. Microcrystallisation was excluded, due to a slow temperature decrease down to -170°C and then a gentle rewarming of the solution, where repeated measurements led to the same results. Furthermore additional investigations with twice lower concentration ($c=2.18 \times 10^{-4}$ Mol/l, results listed in Table 6) have been made, but curve shapes and intensities remained almost the same. Solvation effects usually can occur but hence those effects are commonly much lower than the observed ones and the solvent used is unpolar, this should not be the determining factor for these drastic changes. A possible explanation may be the formation of some kind of aggregates, that does not lead to precipitation of the substance.

Table 6: Low temperature CD data of comp. **13** in methylcyclohexane/isopentane (1:3) { $\Delta\epsilon$ (λ_{\max}/nm) }

Temp.	$n\pi^*$		$\pi\pi^*$	
+20°C		+2.02 (328)		+7.78 (255)
-100°C		+2.15 (330)		+7.97 (256)
-110°C		+2.52 (330)		+9.34 (256)
-120°C		+2.34 (324)		+15.0 (256)
-130°C	-0.68 (362)	+0.90 (319)		+32.8 (257)
-140°C	-1.18 (357)	+0.44 (317)		+36.2 (257)
-150°C	-0.29 (366)	+1.69 (321)		+15.1 (257)
-155°C	-0.35 (365)	+1.61 (317)		+12.4 (256)
-160°C	-0.12 (371)	+1.86 (320)		+10.3 (251)
-165°C		+1.83 (323)	+1.27 (288) ^s	-8.37 (257)
-170°C		+2.12 (322)	+1.87 (290) ^s	-8.81 (256)

^s shoulder

Conclusions

(i) The sign of the CE associated with the $n\pi^*$ transition reflects the enone helicity as the dominant factor, as we have found for almost all investigated compounds, except those with bromine substitution in α' -position. It is worth noting that in the case of a bisignate CD curve the branch of the sign correlating with the enone helicity rule appears always at a longer wavelength and therefore it can be used to determine the helicity of the enone moiety. The magnitude of this branch depends on the solvent polarity and has its highest value if TFE is used as the solvent. There is also a contribution of rings adjoining the Δ^8 -octalin-1-one unit, whose sign follows ketone octant rule.

(ii) Neither geometry of the cyclohexene ring in the sense of its conformation nor chiral interaction of γ -allylic axial bond with the enone chromophore is the factor controlling the sign of band I CE of nonfunctionalized cisoid enones.

(iii) Substitution at the γ -allylic position slightly influence the intensity of $n\pi^*$ CE without the change of its sign. Axial and equatorial substituents - as well oxygen as chlorine - strongly affect the intensity and sign of band I CE by giving a contribution, whose sign depends on the helicity of the substituent-C3-C4=C5 system. In contrast to equatorially substituted and unsubstituted enones this band is blue shifted for axially substituted enones on going from nonpolar to polar solvents.

(iv) Introduction of α' -axial bromine substituent shows an overriding effect on $n\pi^*$, band I and band II CE's. The magnitude of the contribution to both $n\pi^*$ and band I CE's is strongly positive and the sign is in accord with Br-C7-C6=O helicity, whereas the contribution to band II CE is of opposite sign. This leads to inversion of the $n\pi^*$ CE and far more complicated spectra in the $\pi\pi^*$ region.

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Experimental

Melting points were determined on a Boetius micro-melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer PE 1310 spectrometer. ^1H NMR spectra were taken on a VARIAN Gemini spectrometer in CDCl_3 . Mass spectra (and high resolution) were measured on an AMD 604 Intectra spectrometer. UV measurements were made on a CARRY 1E apparatus in acetonitrile. The CD spectra were recorded in different solutions with a modified ISA-Jobin-Yvon Dichrograph Mark III (low temperature) and Mark VI or on AVIV 62 DS. Solutions with concentrations in the range 0.15-0.4 mg/ml were examined in cells with path length 0.05 to 2 cm.

The synthesis of the compounds 1-10, 13 and 14 has been described earlier.¹

3 α -Chlorocholest-4-en-6-one (11), m.p. 99-100°C (MeOH); UV (MeCN) [$\epsilon(\lambda_{\text{max}})$]: 160 (309), 8000 (236); ^1H NMR (200 MHz): 0.70 (3H, s, 18-H), 0.95 (3H, s, 19-H), 2.57 (1H, dd, $J=15.5, 3.8$ Hz, 7 β -H), 4.65 (1H, m, 3 β -H), 6.28 (1H, dd, $J=5.1, 0.8$ Hz, 4-H) was synthesised by dehydration of 3 β -tosyloxy-5-hydroxy-5 α -cholestan-6-one according to the published procedure¹² {lit.: m.p. 101°C¹³}.

7 α -Bromocholest-4-en-6-one (12). The synthesis was done in the same way as for compound 11 using 7 α -bromo-5-hydroxy-5 α -cholestan-6-one as the starting material. The product was obtained as a colourless oil (yield 82%). UV (MeCN) [$\epsilon(\lambda_{\text{max}})$]: 99 (338), 3000 (253); IR (film): 1691, 1628 and 757 cm^{-1} ; ^1H NMR (200 MHz): 0.72 (3H, s, 18-H), 0.97 (3H, s, 19-H), 4.34 (1H, d, $J=2.6$ Hz, 7 β -H), 6.44 (1H, t, $J=3.6$ Hz, 4-H); MS (m/z): 464/462 (M^+), 449/447, 384 (100%), 383, 369; HRMS for $\text{C}_{27}\text{H}_{43}\text{OBr}^{79}$ (M^+) found 462.2497, calcd. 462.2497.

References

1. Frelek, J.; Szczepiek, W.J.; Weiß, H.P. *Tetrahedron Asym.* **1993**, *4*, 411-424.
2. Kuball, H.-G.; Neubrech, S; Schönhofer, A. *Chem. Phys.* **1992**, *163*, 115-132.
3. Kirk, D.N. *Tetrahedron* **1986**, *42*, 777.
4. a) Gawronski, J. K. *Tetrahedron* **1982**, *38*, 3.
b) Gawronski, J. K. *The Chemistry of Enones*, ed. by S. Patai and Z. Rappaport, J. Wiley & Sons Ltd **1989**, 55.
5. Reichardt, C; Harbusch-Gömert, E. *Liebigs Annalen* **1983**, 721.
6. Krygowski, T.M.; Mielczarek, E; Wrona, P.K. *J.C.S. Perkin Trans. 2* **1980**, 1563.
7. Krygowski, T.M.; Radomski, J.P.; Rzeszowiak, A.; Wrona, P.K.; Reichardt, C. *Tetrahedron* **1981**, *37*, 119.
8. PC MODEL Vers. 3.2, Serena Software, Bloomington IN 47402-3076, USA.
9. Nassimbeni, L.R.; Russel, J.C.; Cragg G.M.L. *Acta Cryst.* **1977**, *B33*, 3755.
10. Gawronski, J. K.; Gawronska, K.; Koput, J. *Pol. J. Chem.* **1986**, *60*, 45.
11. Beecham, A.F. *Tetrahedron* **1971**, *27*, 5207.
12. Glotter, E.; Mandelovici, M. *J. Chem. Research (M)* **1991**, 2201.
13. Husain, M.; Khan, N.H. *Synth. Commun.* **1981**, *11*, 185.

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