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Circular Dichroism of Some Alkaloid Enaminoketones and γ-Pyridones

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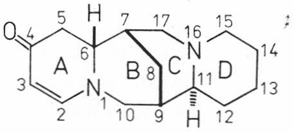
The CD spectra of multiflorine (*1*), seco(11,12)-12-dehydromultiflorine (*2*) and their 5-dehydroderivatives (*3, 4*) are reported. The effect of pH of the solution on the spectra of the enaminoketone and γ-pyridone chromophores is discussed.

Multiflorine (*1*) and seco(11,12)-12-dehydromultiflorine (*2*) were isolated from *Lupinus albus* seeds (cultivar BAC).[1] The stereochemistry of multiflorine (*1*) was studied and the negative n—π* Cotton effect, displayed in the ORD curve of *1*, was used to support the assignment of the absolute configuration of *1*.[2] The structure of *2*, originally formulated as *N*-methylalbine,[1] has recently been established on the basis of the NMR spectra.[3] Both alkaloids contain *Z-s-trans* enaminoketone chromophore, the spectral properties of which differ from those of simple enones, due to conjugation with the nitrogen *p*-orbital. Optically active compounds of this type are scarce, hence *1* and *2* provide unique opportunity to study the enaminoketone chromophore by circular dichroism, including solvent and protonation effects.



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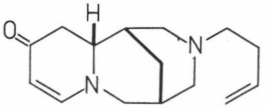

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In conjugated enones both n—π* and π—π* transitions can usually be observed by the UV and CD spectroscopy. In the UV spectra of enaminoketones *1* and *2* the weak n—π* band is completely obscured by the strong π—π* band red shifted due to conjugation with the nitrogen atom; hence only the π—π* band is observed in the UV spectra. As it is seen in Table I, both bands are observed in the CD spectra of *1* and *2*.

The n—π* band is uniformly negative and the π—π* band is positive regardless of the solvent used, both in the free bases and in their monoperchlorates. The opposite sign of n—π* and the π—π* Cotton effects are typically found in derivatives of 2-cyclohexenone.[4] The negative sign of the n—π* Cotton

TABLE I

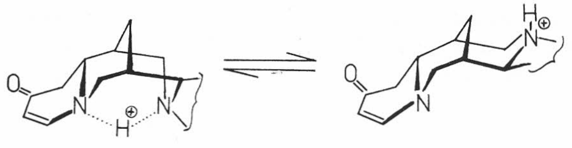
Chiroptical data for enaminoketones 1 *and* 2

Solvent	Free base (10^{-4} M)			Monoperchlorate (10^{-4} M)		
	Δε (nm)		ε (nm)	Δε (nm)		ε (nm)
	n—π*	π—π*	π—π*	π—π*	π—π*	π—π*
Multiflorine (*1*)						
Hexane	—1.0(346)	+4.5(296)	13300(302)		a	
Dioxane	—2.0(342)	+2.7(303)	12700(308)	—1.9(327)	+4.0(289)	12100(297)
Acetonitrile	—4.7(339)	+1.1(305)	14500(318)	—2.9(323)	+0.5(286)	12400(297)
Methanol	—4.5(337)	+1.1(298)	14300(326)	—4.6(327)	+2.5(294)	12600(316)
Water	—5.8(327)	+1.7(295)	15400(320)	—6.0(324)	+2.6(293)	14900(319)
Seco(11,12)-12-dehydromultiflorine (*2*)						
Hexane	—2.5(331)	+1.6(302)	12800(311)		a	
Dioxane	—9.8(332)	+1.9(303)	12900(317)	—2.2(327)	+1.1(283)	11500(294)
Acetonitrile	—6.6(338)	+0.5(299)	14400(324)	—2.7(323)	ca. 0	11400(296)
Methanol	—6.3(335)	+1.0(290)	15500(332)	—7.8(328)	+1.4(290)	9700(322)
Water	—7.6(323)	+2.5(292)	14400(317)	—6.6(322)	+1.9(291)	13300(317)

[a] Not soluble.

effect of *1* and *2* apparently conforms to Snatzke's sector rule for planar conjugated cyclohexenones (A).[5] It appears that the signs of the n—π* and π—π* Cotton effects of *1* and *2* are the same as the signs of the Cotton efefcts of structurally related steroidal (5α)-1-en-3-ones.[4] The position of the n—π* band of *1* is blue shifted in polar solvents (Figure 1), as judged from the CD spectra; in the case of *2* this shift is less evident because the position of the n—π* band in hexane is masked by its vibrational structure. On the other hand, the π—π* band is red shifted in polar solvents, as seen in the UV data (note larger red shift in the methanol solution, compared to the water solution). The π—π* Cotton effects are weak, except for nonpolar solvents, and their positions do not match the positions of the UV maxima due to the overlap with the strong CD n—π* band.

It is of interest to note that the intensity of the n—π* Cotton effect of *1* and *2* increases with solvent polarity while smaller changes are observed for the π—π* Cotton effect. Multiflorine *(1)* adopts halfchair-chair-boat-chair conformation *5b* of rings A—D both in the solid state[6] and in aprotic solvents,[7] whereas its monoperchlorate exists in a halfchair-chair-chair-chair conformation *5a*.[7,8] The latter conformation is ascribed to *2* and its monoperchlorate in solution, on the basis of the ^{13}C NMR measurements.[7] A comparable solvent



5a

5b

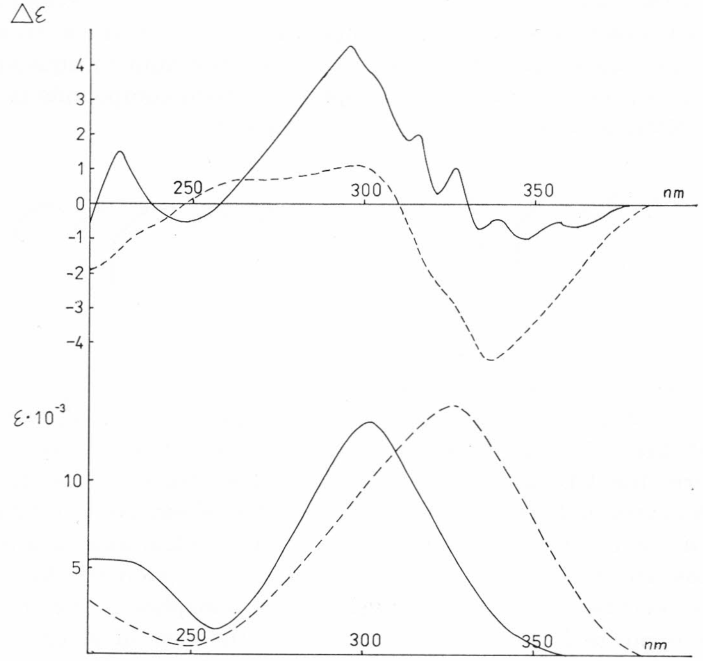
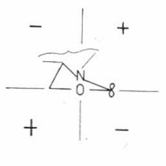
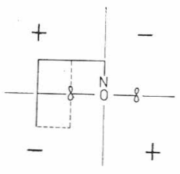


Figure 1. CD and UV spectra of multiflorine (*1*) in hexane (———) and methanol (— — —), c = 10^{-4} M.

effect on the intensities of the n—π* and π—π* CD bands of *1* and *2*, as well as their monoperchlorates, indicates conformational similarity of rings A and B in these molecules. Protonation strongly affects positions of the CD and UV bands, and to a lesser extent — their intensities. This is seen by comparing the data for *1* and *2* with the data for their monoperchlorates. The blue shift of the λ_{max} for the n—π* and π—π* bands upon protonation can be accounted for by the contribution made by the intramolecularly hydrogen bonded (N ... H ... N) alkaloid molecules having all-chair conformation (*5a*). In effect, this decreases electron density on N(1) and leads to an increase of the excitation energies for both transitions. The effect due to protonation is nearly completely washed-out in the water solution, probably due to a different protonation scheme. It should be noted that the IR spectra of *1* and *2*, as well as their monoperchlorates, retain the characteristic features of the enaminoketone chromophore (ν_{max} 1630 and 1580 cm^{-1}).

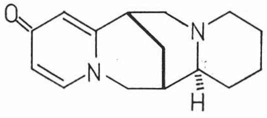


A



B

Two further alkaloids included in the series are 5-dehydromultiflorine *(3)* and 5-dehydro-seco(11,12)-multiflorine *(4)*. They are obtained from *1* and *2*, respectively, by catalytic dehydrogenation over platinum in aqueous solution.[9] The presence of the γ-pyridone chromophore in both compounds is ascertained by the IR, NMR and electronic absorption data.[1,3]



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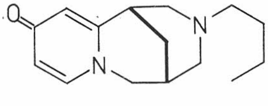


4

In particular, the UV absorption maximum of *3* and *4* is significantly blue-shifted, compared to *1* and *2*, and it appears at around 265 nm. The position of the UV maximum is relatively insensitive to solvent polarity. Furthermore, the CD and UV data for the free bases (Table II), and their monoperchlorates (not included) are very similar. From the CD data it appears that both n—π* bands (not observed in the UV spectra) and to a lesser extent π—π* bands are blue shifted on increasing solvent polarity. As expected for the highly symmetric planar γ-pyridone chromophore, the n—π* Cotton effects are opposite for *1*, *2* and *3*, *4*. Like in the case of structurally related steroidal 1,4-dien-3-ones,[10] the sign of the n—π* Cotton effect of *3* and *4* can be correlated with the stereostructure of these molecules through the use of the octant rule; positive Cotton effect results from the presence of ring B in the positive octant (B).

TABLE II

Chiroptical data for γ-pyridones 3 *and* 4

Solvent	Free base (10^{-4} M) Δε (nm) n—π*	Free base (10^{-4} M) Δε (nm) π—π*	ε (nm) π—π*	Solution acidified with 10-fold molar excess of $MeSO_3H$ Δε (nm)	Solution acidified with 10-fold molar excess of $MeSO_3H$ ε (nm)
5-Dehydromultiflorine (*3*)					
Hexane	+0.45(305)	—2.3(267)	10000(266)	a	
Dioxane	+1.0 (300)	—4.1(266)	14300(266)	+2.8(263)	10000(244)
Methanol	ca. 0	—2.6(261)	14400(264)	+2.7(263)	10400(245)
Water	+0.7 (275)	—1.5(254)	16600(254)	+3.0(261)	11000(244)
Seco(11,12-)-5-dehydrosecomultiflorine (*4*)					
Hexane	+0.75(306)	—2.5(267)	12400(266)	a	
Dioxane	+1.0 (304)	—3.3(267)	14700(266)	+2.0(262)	6300(244)
Methanol	+0.1 (300)	—2.0(259)	14100(265)	+1.8(262)	8800(245)
Water	+0.5 (278)	—2.2(254)	16700(264)	+3.6(261)	10100(243)[b]

[a] Not soluble. [b] With 100-fold molar excess of $MeSO_3H$.

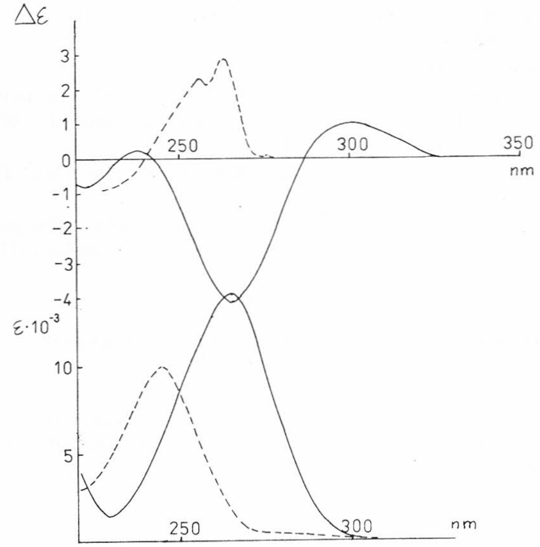
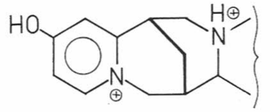


Figure 2. CD and UV spectra of 5-dehydromultiflorine (*3*) in dioxane (———), $c = 10^{-4}$ M, and in dioxane containing 10^{-3} M $MeSO_3H$ (— — —).

Although the structure of the γ-pyridone chromophore is retained in the monoprotonated *3* and *4* as mentioned earlier, the use of the excess of strong acid brings about substantial changes in the UV and CD spectra (Table II).* The UV maximum shifts to 243—245 nm and its position is not solvent sensitive. In the CD spectrum the positive Cotton effect is observed at 261—263 nm (Figure 2). The spectral changes upon protonation of *3* and *4* with excess acid can be best accounted for by the protonation of the carbonyl group, with subsequent formation of the resonance-stabilized pyridinium cation structure *6*.



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* The spectral changes due to protonation can be reversed by the addition of a base, providing that the acidified solution of *3* or *4* is not stored over a prolonged period of time.

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SAŽETAK

Cirkularni dikroizam nekih alkaloidnih enanminoketona i γ-piridona

W. Wysocka, D. Radocki i J. Gawroński

Izvještava se o CD spektrima multiflorina (*1*), seco(11,12)-dehidromultiflorina (*2*) i njihovih 5-dehidroderivata (*3, 4*). Raspravlja se o utjecaju pH otopine na kromofore u enaminoketonima i γ-piridonima.