Tetrahedron Vol. 35, pp. 1649 to 1652
Pergamon Press Ltd., 1979. Printed in Great Britain

CIRCULAR DICHROISM OF OLEFINS—IV†

A SEMIQUANTITATIVE PREDICTION OF THE INTENSITY OF THE COTTON EFFECT OF ALLYL ALCOHOLS AND ETHERS

JEAN-MARIE BERNASSAU*, MARCEL FETIZON and ISSAM HANNA‡
Ecole Polytechnique, Laboratoire de Synthese Organique, 91128 Palaiseau Cedex, France

(*Received in UK* 11 *November* 1976; *Accepted for publication* 9 *December* 1976)

Abstract—A semi quantitative prediction of the intensity of the Cotton effect of a few allyl alcohols and ethers in the steroid and diterpene series has been derived. It relies on a calculation of the weight of the various conformations and on the allylic bond polarization model.

1. INTRODUCTION

No thorough theoretical understanding of the electronic spectrum of mono-olefins has been reputed, although a great deal of work has been devoted to the subject.[1] As a consequence, prediction of the sign of the Cotton effect associated with the allowed electronic transitions of chiral olefins relies on empirical rules only.[2] Among these, the reversed octant rule of Scott and Wrixon (S.W. rule)[3] seems to be fairly reliable, as far as the low frequency transitions (λ_2 band) is concerned. However there are still some discrepancies.[4] More recently it has been shown that allylic bonds play a very important role in the CD of a variety of olefinic compounds. As suggested by Andersen[5] in the so-called allylic bond polarization (ABP) model, the Cotton effect due to the λ_2 transition should be dominated by the contribution of the polarizable allylic bonds (Fig. 1). In order to test the validity of this model some allylic ethers in diterpenes series (1, 2, 3) as well as allylic alcohols in the steroid series (4, 5) have been studied (Fig. 2). While it was necessary to investigate the stability of the various conformations of these flexible molecules, this could be achieved by using the "force-field" model. Eventually it led to a rough estimate of the $\Delta\epsilon_{max}$ for the Cotton effect associated with the λ_2 transition.

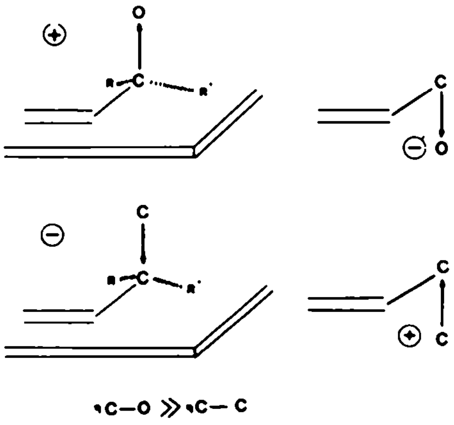


Fig. 1.

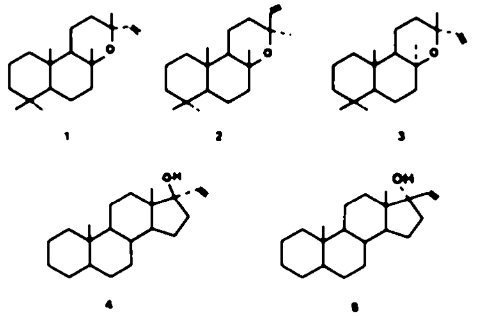


Fig. 2.

2. RESULTS AND DISCUSSION

Manoyl oxide 1, 13-epimanoyloxide 2 and 8-epimanoyloxide 3 are naturally occurring compounds. Preparation of 17α-vinyl androstane 17-ol 4 is straightforward. Synthesis of its epimer 5 has been carried out according to the following Scheme: (Fig. 3) formylolefination of androstane 17-one gives the E-unsaturated aldehyde 6[7] which was treated with H_2O_2 under weakly basic conditions.[8] The resulting α,β-epoxyaldehyde 7 was then submitted to a Wolff-Kishner reduction[9] leading to the expected 17α-alcohol.

The energy of a conformer of compounds 1 to 5 was then calculated as a function of the dihedral angle ϕ counted anticlockwise in the oriented coordinate system indicated on Fig. 4. For each of these five substances,

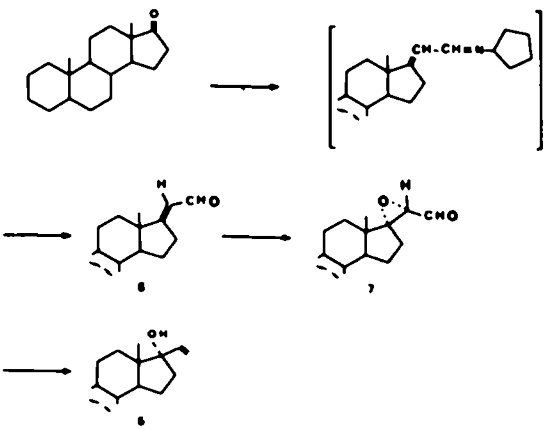


Fig. 3.

---

†Part III see Ref. 4d.

‡Present address: Faculté des Sciences, Université Libanaise, Hadet-Beyroute, Liban.

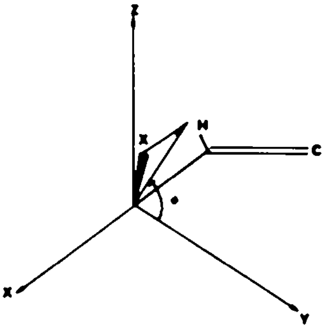


Fig. 4.

several (two in general) conformations of nearly equal energy have been found (Fig. 5). The relative weight of these conformations was calculated by using Boltzmann's law.

On the basis of the ABP model[1a] *the sign of the Cotton effect could correctly be predicted, as well as the order of magnitude of its intensity.*

The contribution of an X group bonded to the allylic carbon depends on the angle ϕ and the nature of X. If X is oxygen, the contribution to the Cotton effect is positive when X lies *above* the xCy plane. The opposite sign is found for alkyl groups (Fig. 4). In both cases, this contribution $\eta(X, \phi)$ vanishes when $\phi = 0$ or π and is maximum for $\phi = \pi/2$ or $3\pi/2$.

Since it is a periodic function of ϕ, an approximation of $\eta(X, \phi)$ might be of the form:†

$$\eta(X, \phi) = \eta_x \sin \phi$$

with $\eta_{OH} > 0$, $\eta_{alkyl} < 0$ and $|\eta_{OH}| \gg |\eta_{alkyl}|$.

If, on the other hand, the contribution of two groups bonded to the same allylic carbon can be considered as additive, then in a given conformation‡

$$\Delta\epsilon_i = \eta_O \sin \phi_i + \eta_{alkyl}[\sin(\phi_i + 2\pi/3) + \sin(\phi_i + 4\pi/3)]$$

or

$$\Delta\epsilon_i = (\eta_O - \eta_{alkyl}) \sin \phi_i.$$

Finally, if p_i is the weight of the corresponding conformation, the calculated $\Delta\epsilon_{max}$ value for the Cotton

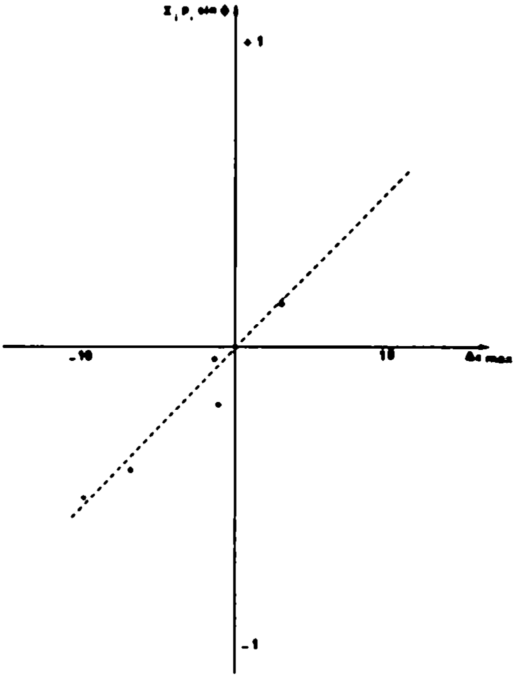


Fig. 6.

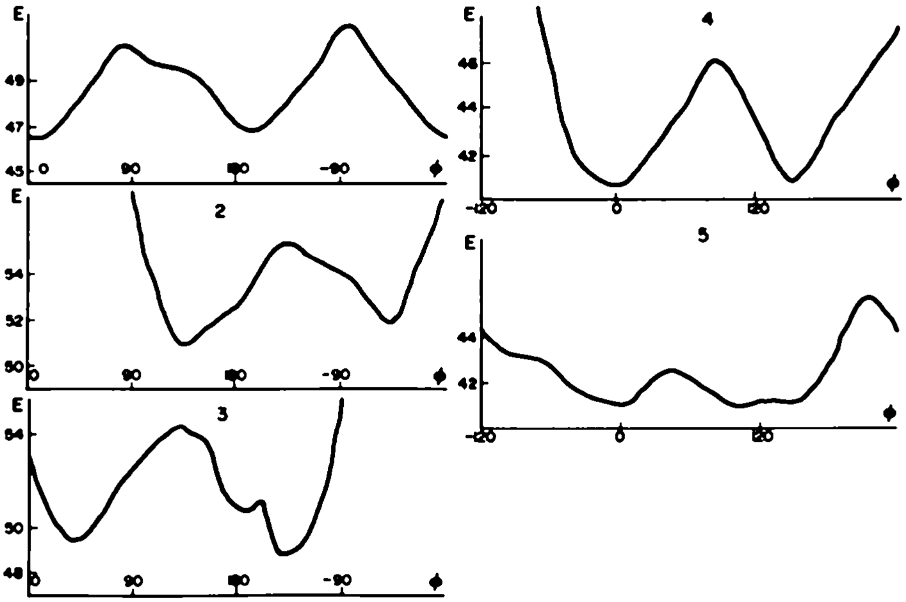


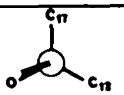
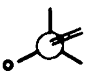
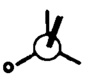
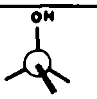
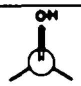
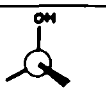
Fig. 5.

---

†This type of approximation is currently used for the rotation barrier of simple compounds (e.g. ethane).

‡ϕ_i is the dihedral angle between the nodal plane of the double bond and the plane containing the X group with the largest atomic number.

Table 1.

			λ_{max}	$\Delta\epsilon$
1	 $\phi = 10°$ E = 46.5 kcal	 $\phi = -170°$ E = 46.0 kcal	193 nm 210	3.7 -1.3
2	 $\phi = 100°$ E = 50.0		190	-0.9
3	 $\phi = 40°$ E = 48.4	 $\phi = -140$ E = 49.0	192	-1.0
4	 $\phi = -5°$ E = 40.6	 $\phi = 105°$ E = 40.0	197	2.6
5	 $\phi = 0°$ E = 41	 $\phi = 130°$ E = 40.0	190	-10.0

effect should be:

$$\Delta\epsilon = \sum_i p_i \Delta\epsilon_i = (\eta_0 - \eta_{alkyl}) \sum_i p_i \sin \phi_i.$$

Our results (Table 1) show that there is a linear relationship (Fig. 6) between the observed $\Delta\epsilon_{max}$ and the calculated $\sum_i p_i \sin \phi_i$.

EXPERIMENTAL

Unless otherwise stated, all m.ps were measured on a Kofler hot-stage apparatus and are uncorrected. IR spectra were taken in CCl_4 with a Perkin-Elmer 257 spectrophotometer and NMR spectra in $CDCl_3$ soln with a Jeol C 60 H spectrometer using TMS as internal standard. CD curves were measured in n-hexane at 25° with a Roussel-Jouan CD 185 dichrograph in a 1 mm cell.

17β-Hydroxy-17α-vinyl-5α-androstane 4 was synthesized by lit methods[10] with physical constants in good agreement with those recorded, m.p. 120°–123 from MeOH, (Found: C, 83.30; H, 11.31; $C_{21}H_{34}O$ requires: C, 83.38; H, 11.31%); ν_{max} 3610, 3080, 1645, 1415 and 920 cm⁻¹. δ 6.1 (s, 1H, $-CH{=}C-$), 5.2 (m, 2H, $C{=}CH_2$), 0.8 (s, 18-CH_3) and 0.9 (s, 19-CH_3). $[\alpha]_D + 2°$ (*c* 0.64 $CHCL_3$).

5α-Pregn-trans-17-*en*-21-*al* 6. To a suspension of NaH (1 g of 50% oil dispersion) in anhyd THF (20 ml) was added a soln of diethyl 2-cyclohexyliminoethylphosphonate (6 g) in anhyd THF (40 ml) with stirring and ice cooling under an argon atmosphere while the mixture was stirred for 15 min. A soln of 17-keto-5α-androstane (2 g) in anhyd THF was then added and the mixture was stirred at room temp. overnight. The reaction was followed by TLC. The mixture was poured into ice-water and extracted with ether. The extracts were washed with a sat NaClaq, dried and evaporated *in vacuo* to give the crude aldimine.

The crude aldimine was dissolved in benzene (75 ml). The soln was mixed with 1% oxalic acid soln (200 ml) and stirred overnight at room temp. Working up in the usual way gave a crude *α,β*-unsaturated aldehyde which was purified by silica-gel column chromatography (Elution: petroleum ether-diethyl ether 2:1) to give 1.8 g (82%) m.p. 149–151° (from ether) lit[7] 150–152°. (Found: C, 83.65; H, 10.80. $C_{21}H_{32}$ requires: C, 83.25; H, 10.75%); ν_{max} 2722, 1680 and 1620 cm⁻¹ δ 0.81 and 0.85 (2s, 18 and 19-CH_3), 5.7 (d, J = 8 Hz, $C{=}CH-CHO$), 9.8 (d, J = 8 Hz, $-CHO$).

17α,20-epoxy-5α-pregn-21-al 7. To a stirred mixture of 30% H_2O_2 (5 ml), 1N NaOH (0.5 ml) and MeOH (15 ml) at 40–50° was added dropwise a soln of 6 (0.5 g) in EtOH (10 ml) and benzene (5 ml). The mixture was stirred for 2 hr and the pH was held at 8.5–9.5 (as determined by indicator paper) by addition from time to time of some drops of 1N NaOH. The mixture was then poured in water and extracted 3 times with chloroform. The extracts were combined and washed with sat NaClaq, dried over Na_2SO_4 and evaporated *in vacuo*. The crude material was dissolved in benzene and purified by filtration on Florisil column to give a pure cristalline product, m.p. 110–112°. (Found: C, 79.40; H, 10.44, $C_{21}H_{32}O_2$ requires: C, 79.70; H, 10.19%); ν_{max} 1725 and 1250 cm⁻¹ δ 0.8 and 0.78 (2s, 18 and 19-CH_3) 3.2 (d, J = 6 Hz $\underset{\diagdown\,O\,\diagup}{-C-C}-H$), 9.25 (d, J = 6 Hz $-CHO$). $[\alpha]_D = -40$ (*c*, 0.54 in CHCl3).

17α-Hydroxy-17β-vinyl-5α-androstane 5. To a stirred soln of 7 (300 mg) in MeOH (50 ml) under N_2 was added 98% hydrazine hydrate (0.8 g) in MeOH (5 ml) and AcOH (0.4 ml) in MeOH (4 ml). The mixture was stirred for 18 hr then poured in water and extracted with ether. Washing with water and drying over Na_2SO_4, provided a yellow oil, which was passed in benzene soln through a column of Florisil. The benzene eluted material (120 mg) was crystallized from MeOH to afford 5 as colorless needles, m.p. 102–105°. (Found: C, 83.17; H, 11.30. $C_{21}H_{34}O$ requires: C, 83.38; H, 11.31%); ν_{max} 3610, 3080, 1640, 1415 and 920 cm⁻¹ δ 0.69 and 0.80 (2s, 18 and 19-CH_3), 5.2 (m, $C{=}CH_2$) 6.0 (s, $-CH{=}C\langle$). $[\alpha]_D = -41.6°$ (*c*, 0.49 in CHCl3).

Acknowledgements—We thank Prof. E. von Rudloff, National Research Council, Canada for a sample of 8-epimanoyleoxide and Professor Horeau, Collège de France, Paris for the CD measurements.

REFERENCES

[1] M. Yaris, A. Moscowitz and R. S. Berry, *J. Chem. Phys.* **49**, 3150 (1969); M. B. Robin, H. Basch, N. A. Kuebler, B. E. Kaplan and J. Meinwald, *Ibid.* **48**, 5037 (1968); M. G. Mason and O. Schnepp, *Ibid.* **59**, 1092 (1973).

[2] A. Yogev, D. Amar and Y. Mazur, *Chem. Comm.* 339 (1967); A. W. Burgstahler and R. C. Barkhurst, *J. Am. Chem. Soc.* **92**, 7601 (1970); J. K. Gavronski and M. A. Kielezcski, *Tetrahedron Letters* 2493 (1971); W. Hugand, G. Wagniere, *Tetrahedron* **28**, 1241 (1972).

[3] A. I. Scott and A. D. Wrixon, *Ibid.* **26**, 3695 (1970); **27**, 4787 (1971).

[4a] M. Fetizon and I. Hanna, *Chem. Comm.* 462 (1970); [b] M. Fetizon, I. Hanna, A. I. Scott, A. D. Wrixon and T. K. Devon, *Ibid.* 545 (1971); [c] A. Yogev, J. Sagiv and Y. Mazur, *Ibid.* 411 (1972); [d] M. Fetizon, Y. Lebigot and J. Rens, *Tetrahedron* **28**, 2815 (1973).

[5a] N. H. Anderson, C. R. Costin, D. D. Syrdal and D. P. Svedberg *J. Am. Chem. Soc.* 95, 2049 (1973); [b] N. H. Anderson, C. R. Costin and J. R. Shaw, *Ibid.* 96, 3692 (1974).

[6] N. L. Allinger, M. T. Tripple, M. A. Miller and D. H. Wertz, *Ibid.* 93, 1637 (1971); D. H. Wertz and N. L. Allinger, *Tetrahedron* 30, 1579 (1974).

[7] W. Nagata and Y. Hayase, *J. Chem. Soc.* 460 (1969).

[8] G. B. Payne, *J. Am. Chem. Soc.* 80, 6461 (1958); 81, 4901 (1959); *J. Org. Chem.* 25, 250 (1961).

[9] P. S. Warton and D. H. Dohlen, *J. Org. Chem.* 26, 3615 (1961).

[10] L. F. Fieser and M. Fieser, *Steroids*, p. 625. Reinhold, New York (1959).