

## ORD AND CD STUDIES ON THE STRUCTURE OF CARBONYL DERIVATIVES OF PENTACYCLIC TRITERPENES

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**Abstract**—A series of mono- and di-carbonyl derivatives of pentacyclic triterpenic alcohols have been investigated by ORD and CD methods. The effect on ORD and CD spectra of backbone type, position of double bond, position of carbonyl groups and position of additional acetoxy groups was determined.

THE RELATIONSHIP between the position of ketone groups in steroids and character of ORD and CD curves is well known.<sup>1, 2, 3, 4, 5</sup>

Pentacyclic triterpenes have been studied less by these methods. Djerassi *et al.*<sup>6</sup> found that molecular amplitudes,  $[\phi]_{\max}$  and  $[\phi]_{\min}$  values, and the sign of the Cotton effect of optical rotation are changed significantly depending on the carbonyl group position (positions 3, 6, 15, 16, 19, 21 and 22 in the oleanane derivatives). It has been suggested<sup>6</sup>, that the method of ORD may find wide application in localization of OH groups (after oxidation to carbonyl groups) in the backbones of pentacyclic triterpenes.

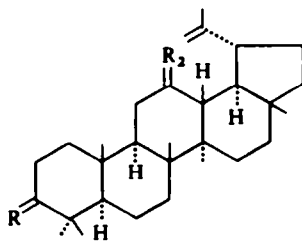
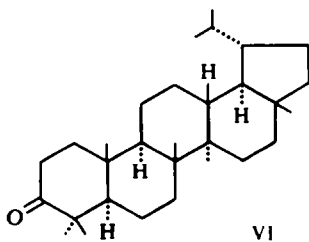
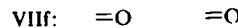
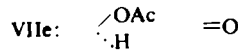
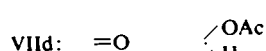
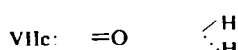
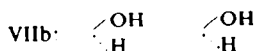
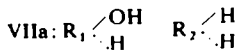
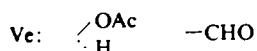
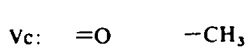
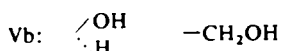
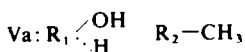
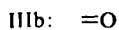
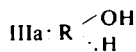
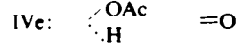
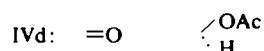
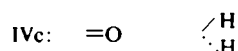
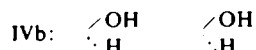
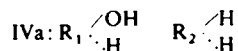
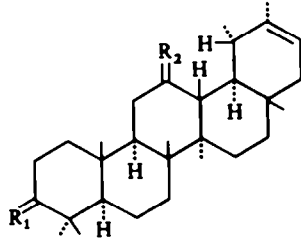
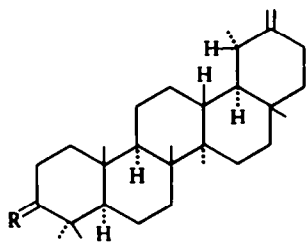
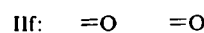
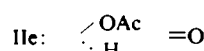
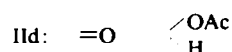
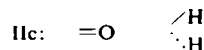
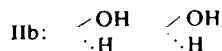
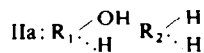
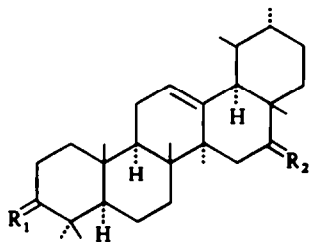
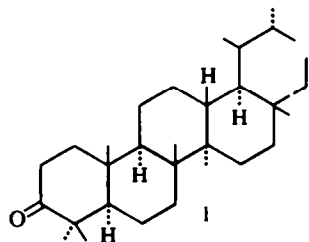
It has been shown<sup>7</sup> in studies on pentacyclic triterpenic alcohols in calendula flowers, that the following compounds are present: 3 $\beta$ -OH-ursa-12-en (IIa), 3 $\beta$ -OH-(18 $\alpha$ , 19 $\beta$ H)-ursa-20(30)-en (IIIa), 3 $\beta$ -OH-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVa), 3 $\beta$ , 16 $\beta$ -di-OH-ursa-12-en (IIb), 3 $\beta$ , 12 $\beta$ -di-OH-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVb), 3 $\beta$ -OH-oleana-12-en (Va), 3 $\beta$ , 28-di-OH-oleana-12-en (Vb), 3 $\beta$ -OH-lupa-20(30)-en (VIIa) and 3 $\beta$ , 12 $\beta$ -di-OH-lupa-20(30)-en (VIIb).

In addition to unidentified compounds in the group of diols, triols and pentacyclic triterpenic tetraols were found. In the present work attempts are made to apply CD and ORD methods to carbonyl derivatives of pentacyclic triterpenic alcohols in order to learn whether, according to a suggestion of Djerassi, these methods may be useful in the determination of the positions of OH groups.

Methods were applied, which allow us to obtain a series of diketone and corresponding monoketone derivatives of pentacyclic triterpenic mono- and dihydroxy-alcohols occurring in calendula.

The following transformations were carried out:

1. monohydroxy alcohols into the corresponding monoketones
2. dihydroxy alcohols into the corresponding diketones and aldehydoketone
3. dihydroxy alcohols into the corresponding monoketone derivatives with a carbonyl group in position 3 or positions 12, 16, 28 of the triterpenic backbone, the second group being acetylated
4. catalytic hydrogenation of 3-oxo-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVc) to 3-oxo-ursane (I) as well as 3-oxo-lupa-(30)-en (VIIc) to 3-oxo-lupane (VI).



FORMULAE

In order to obtain two different monoketone derivatives from a dihydroxy alcohol, acetylation was conducted under such conditions (experimental) as to obtain two monoacetoxyl-monohydroxyl derivatives with a yield of 5–8% (for secondary OH groups), which were then oxidized to ketones. OH groups at position 12 of ursane and lupane backbones were acetylated with the same yield as those at position 3. The OH group at position 16 of the ursane backbone was acetylated with a yield 1/3 lower than the OH group at position 3, this probably being a result of steric hindrance by the Me group at position 17. The primary OH group at position 28 of oleanane was acetylated with a yield 8 times higher than the OH at position 3 of this compound. Monoacetoxyl derivatives were separated by means of TLC and the free OH group oxidized with  $\text{CrO}_3$ . It was not possible to find appropriate conditions for separation of monoketo-monohydroxyl and monoketo-monoacetoxyl derivatives of pentacyclic triterpenic alcohols nor for their diketones.

Further studies were made on the effect of the following structural modifications on the spectra of ORD and CD:

1. type of backbone (localization of Me groups and presence of pentacyclic ring)
2. position of the double bond in the backbone
3. presence of an additional ketone group in the monoketone derivative at various positions of the backbone
4. presence of an additional aldehyde group in the monoketone derivative

It should be emphasized that the solvent used has a considerable effect on the molecular amplitude ( $[\phi]_{\text{max}}$ ,  $[\phi]_{\text{min}}$ ) as well as  $\Delta\epsilon_{\text{max}}$ . According to Crabbé<sup>8</sup> the values of molecular amplitude for compound VI are different in hexane than in MeOH. Different amplitude values,  $[\phi]_{\text{max}}$  and  $[\phi]_{\text{min}}$  were obtained<sup>6</sup> for Vc in dioxane and in MeOH.

The curves obtained in the present work for VI and VIIc differ in their parameters from those described by Djerassi *et al.*<sup>6</sup> This probably results from use of dioxane by these authors, whereas all measurements of ORD and CD were made in this work in MeOH. The differences were also noted with respect to  $\Delta\epsilon_{\text{max}}$  values for IIc, IIIb, Vc and VI in comparison with those obtained in dioxane<sup>9</sup> (the values  $\Delta\epsilon$  for Vc were also measured in MeOH). These differences were accompanied by small shifts in wavelength, at which maxima and minima of CD did occur.

In Table 1 are presented ORD data and m.ps and in Table 2 and Fig. 1–3 CD data of keto derivatives of pentacyclic triterpenes. The backbones of 3-monoketones: I, IIc, IIIb, IVc, Vc, and VIIc belong to three basic types of pentacyclic triterpenes—oleanane, ursane and lupane. The oleanane derivative (Vc) has the most symmetrical structure. A symmetrical structure of ursane derivatives (IIc, IIIb, IVc) is disturbed by a Me group at position 19. The lupane derivatives (VI, VIIc) are least symmetrical, due to the presence of a pentacyclic ring at the terminal position of the molecule. All monoketone derivatives show positive CD (Fig. 1) at the maximum of absorption of the chromophore. However,  $\Delta\epsilon_{\text{max}}$  for Vc is the lowest, and for VIIc the highest. The ursane derivatives show the intermediate values of  $\Delta\epsilon_{\text{max}}$ . These results indicate, that there is a correlation between the symmetry of the molecule and the CD values at the maximum. Analysis of ORD results revealed, that VI and VIIc possess the highest molecular amplitudes and that  $[\phi]_{\text{min}}$  has negative values.

The ketone derivative of the saturated hydrocarbon of the ursane backbone (I) shows positive optical rotation and a positive CD characteristic for the ketone group

TABLE I. CD DATA AND MELTING POINTS OF KETO DERIVATIVES OF PENTACYCLIC TRITERPENIC ALCOHOLS

3-oxo-ursan (I):	250 (0), 260 (+0.08), 270 (+0.18), 280 (+0.28), 290 (+0.33), 300 (+0.28), 310 (+0.15), 320 (0) M.p. 173–176° (rep <sup>12</sup> , 175–176°)
3-oxo-ursa-12-en (IIc):	250 (+0.09), 260 (+0.19), 270 (+0.38), 280 (+0.61), 290 (+0.75), 300 (+0.53), 310 (+0.14), 316 (0), 323 (–0.04), 330 (0) M.p. 123–125° (rep <sup>13</sup> , 125–126°)
3-oxo-(18 $\alpha$ , 19 $\beta$ H)-ursa-20(30)-en (IIIb):	250 (–0.02), 252 (0), 260 (+0.07), 270 (+0.17), 280 (+0.30), 292 (+0.37), 300 (+0.30), 310 (+0.12), 320 (+0.02), 325 (0) M.p. 184–188° (rep <sup>13</sup> , 182–187°)
3-oxo(18 $\alpha$ , 19 $\beta$ 11)-ursa-20-en (IVc):	250 (+0.05), 260 (+0.16), 270 (+0.35), 280 (+0.61), 292 (+0.74), 300 (+0.64), 310 (+0.23), 320 (0) M.p. 169–173° (rep <sup>13</sup> , 166–175°)
3-oxo-oleana-12-en (Vc):	250 (+0.01), 260 (+0.04), 270 (+0.12), 280 (+0.21), 289 (+0.25), 300 (+0.17), 312 (0), 322 (–0.04), 330 (–0.02), 340 (0) M.p. 178–182° (rep <sup>13</sup> , 178–180°)
3-oxo-lupan (VI):	250 (+0.11), 260 (+0.15), 270 (+0.33), 280 (+0.57), 290 (+0.76), 300 (+0.64), 310 (+0.26), 320 (+0.03), 325 (0) M.p. 207–210° (rep <sup>12</sup> , 210°)
3-oxo-lupa-20(30)-en (VIIc):	250 (+0.05), 260 (+0.18), 270 (+0.39), 280 (+0.69), 290 (+0.86), 300 (+0.69), 310 (+0.25), 325 (0) M.p. 167–172° (rep <sup>12</sup> , 163–169°)
3-oxo-16 $\beta$ -acetoxy-ursa-12-en (IIId):	255 (+0.46), 265 (+0.60), 280 (+0.53), 290 (+0.43), 305 (0), 315 (–0.06), 320 (0), 330 (+0.04), 340 (+0.06), 350 (+0.03), 360 (0) M.p. 200–204°
3-oxo-12 $\beta$ -acetoxy-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVd):	250 (+0.31), 257 (+0.21), 270 (+0.40), 280 (+0.65), 290 (+0.75), 300 (+0.56), 310 (+0.17), 318 (0), 325 (–0.02), 335 (0) M.p. 206–210°
3-oxo-28-acetoxy-oleana-12-en (Vd):	250 (+0.29), 260 (+0.56), 270 (+1.18), 280 (+1.88), 289 (+2.14), 300 (+1.51), 310 (+0.40), 316 (0), 320 (–0.05), 330 (0) M.p. 190–195°
3-oxo-12 $\beta$ -acetoxy-lupa-20(30)-en (VIIId):	250 (0), 265 (+0.10), 280 (+0.47), 292 (+0.63), 300 (+0.46), 310 (+0.08), 315 (0), 325 (–0.04), 350 (–0.02), 360 (0) M.p. 211–215°
16-oxo-3 $\beta$ -acetoxy-ursa-12-en (IIe):	250 (0), 260 (–0.18), 270 (–0.58), 280 (–1.13), 290 (–1.87), 298 (–2.13), 306 (–1.84)sh., 310 (–1.37), 320 (–0.50), 330 (–0.05), 335 (0) M.p. 210–213° (rep. <sup>12</sup> , 206–206.5°)
12-oxo-3 $\beta$ -acetoxy-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVe):	250 (–0.06), 260 (–0.24), 270 (–0.65), 280 (–1.30), 292 (–1.80), 300 (–1.54), 310 (–0.69), 320 (–0.13), 330 (0) M.p. 221–226°
12-oxo-3 $\beta$ -acetoxy-lupa-20(30)-en (VIIe):	250 (0), 260 (–0.12), 270 (–0.32), 280 (–0.49), 292 (–0.61), 300 (–0.54), 310 (–0.34), 320 (–0.15), 330 (–0.05), 360 (–0.02) M.p. 238–240°
28-aldehydo-3 $\beta$ -acetoxy-oleana-12-en (Ve):	250 (–0.05), 260 (–0.10), 270 (–0.29), 280 (–0.51), 295 (–0.78), 310 (–0.61), 320 (–0.45), 330 (–0.21), 340 (–0.08), 350 (–0.04), 360 (–0.03) M.p. 223–227° (rep. <sup>13</sup> , 227–229°)
3,16-dioxo-ursa-12-en (IIIf):	250 (+0.11), 257 (0), 270 (–0.43), 280 (–1.16), 290 (–2.06), 298 (–2.52), 307 (–2.32)sh., 310 (–1.81), 320 (–0.78), 335 (0) M.p. 210–213° (rep. <sup>12</sup> , 159–160°)
3,12-dioxo-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVf):	250 (+0.09), 257 (0), 260 (–0.08), 270 (–0.49), 280 (–1.14), 293 (–1.70), 300 (–1.49), 310 (–0.68), 320 (–0.08), 330 (0) M.p. 236–242° (rep. <sup>13</sup> , 249–250°)

TABLE I. CD data and melting points of keto derivatives of pentacyclic triterpenic alcohols—continued

3,12-dioxo-lupa-20(30)-en (VIIf):	250 (0), 260 (+0.03), 270 (+0.12), 286 (+0.29), 300 (+0.15), 308 (0), 318 (-0.15), 330 (-0.08), 360 (-0.02) M.p. 160–163° (rep. <sup>7</sup> , 163°)
3-oxo-28-aldehydo-oleana-12-en (Vf):	250 (-0.05), 260 (-0.04), 267 (0), 275 (+0.05), 284 (+0.08), 294 (0), 300 (-0.09), 314 (-0.28), 330 (-0.17), 345 (0) M.p. 181–184°

at position 3. The derivatives of ursane (IIc, IIIb, IVc) differ only in localization of the double bond in the backbone. The presence of a double bond in the ursane backbone causes an increase in molecular amplitude, increase of  $[\phi]_{\max}$  and  $[\phi]_{\min}$ , of  $\Delta\epsilon_{\max}$  and a slight shift in wavelength, at which extremal optical rotations and CD occur, and for

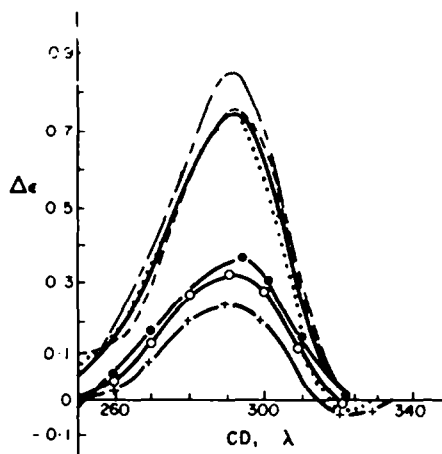


FIG 1. CD curve of I(—○—), IIc(·····), IIIb(—●—), IVc(—), Vc(+ +), VI(---) and VIIc(— · —).

IIc a complex CD curve. The smallest effect on the parameters mentioned above is exerted by the presence of an exocyclic double bond at position 20(30) (IIIb). A more considerable increase in  $[\phi]_{\max}$  and  $[\phi]_{\min}$  values was observed for the derivative of ursane with a double bond at position 20–21 (IVc). The highest values of  $[\phi]_{\max}$  and  $[\phi]_{\min}$  occur when the double bond is at position 12–13 (IIc). In CD curves the presence of an exocyclic double bond at position 20(30) causes a minimal increase in  $\Delta\epsilon_{\max}$  in comparison with the  $\Delta\epsilon_{\max}$  value obtained for the ursane derivative without a double bond (I). Double bonds at positions 12–13 and 20–21 cause a very high increase in  $\Delta\epsilon_{\max}$  (*c.f.* I) almost identical for these two derivatives. The double bond at positions 20–21 and 20(30) causes a bathochromic shift of wavelength corresponding to a maximum of the CD. A similar increase in molecular amplitude,  $[\phi]_{\max}$  and  $[\phi]_{\min}$  values and  $\Delta\epsilon_{\max}$  were observed for the monoketone derivative of lupene (VIIc) with respect to the lupane derivative (VI).

TABLE 2. ORD DATA OF KETO DERIVATIVES OF PENTACYCLIC TRITERPENIC ALCOHOLS

3-oxo-ursan (I):	$[\phi]_{250} + 640^\circ$ , $[\phi]_{260} + 256^\circ$ , $[\phi]_{270} + 128^\circ$ , $[\phi]_{305} + 1345^\circ$ , $[\phi]_{330} + 640^\circ$ , $[\phi]_{360} + 390^\circ$ , $a = +1197^\circ$ .
3-oxo-ursa-12-en (IIc):	$[\phi]_{250} + 6540^\circ$ , $[\phi]_{260} + 4683^\circ$ , $[\phi]_{277} + 3150^\circ$ , $[\phi]_{304} + 4845^\circ$ , $[\phi]_{330} + 2784^\circ$ , $[\phi]_{360} + 2240^\circ$ , $a = +1695^\circ$ .
3-oxo-(18 $\alpha$ , 19 $\beta$ H)-ursa-20(30)-en (IIIb):	$[\phi]_{250} + 1430^\circ$ , $[\phi]_{260} + 986^\circ$ , $[\phi]_{274} + 510^\circ$ , $[\phi]_{305} + 1904^\circ$ , $[\phi]_{330} + 1085^\circ$ , $[\phi]_{360} + 740^\circ$ , $a = +1394^\circ$ .
3-oxo-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVc):	$[\phi]_{250} + 2320^\circ$ , $[\phi]_{260} + 1360^\circ$ , $[\phi]_{274} + 620^\circ$ , $[\phi]_{305} + 3220^\circ$ , $[\phi]_{330} + 1705^\circ$ , $[\phi]_{360} + 1010^\circ$ , $a = +2610^\circ$ .
3-oxo-oleana-12-en (Vc):	$[\phi]_{250} + 5227^\circ$ , $[\phi]_{260} + 4120^\circ$ , $[\phi]_{276} + 2940^\circ$ , $[\phi]_{304} + 4122^\circ$ , $[\phi]_{330} + 2393^\circ$ , $[\phi]_{360} + 1910^\circ$ , $a = +1182^\circ$ .
3-oxo-lupan (VI):	$[\phi]_{250} - 803^\circ$ , $[\phi]_{260} - 1306^\circ$ , $[\phi]_{270} - 1558^\circ$ , $[\phi]_{288} 0^\circ$ , $[\phi]_{306} + 2007^\circ$ , $[\phi]_{330} + 803^\circ$ , $[\phi]_{360} + 520^\circ$ , $a = +3312^\circ$ .
3-oxo-lupa-20(30)-en (VIIc):	$[\phi]_{250} + 2295^\circ$ , $[\phi]_{260} + 867^\circ$ , $[\phi]_{267} 0^\circ$ , $[\phi]_{273} - 153^\circ$ , $[\phi]_{278} 0^\circ$ , $[\phi]_{306} + 4794^\circ$ , $[\phi]_{330} + 2397^\circ$ , $[\phi]_{360} + 1620^\circ$ , $a = +4947^\circ$ .
3-oxo-16 $\beta$ -acetoxy-ursa-12-en (IIId):	$[\phi]_{260} + 6580^\circ$ , $[\phi]_{283} + 3188^\circ$ , $[\phi]_{302} + 3765^\circ$ , $[\phi]_{330} + 1930^\circ$ , $[\phi]_{360} + 1880^\circ$ , $a = +577^\circ$ .
3-oxo-12 $\beta$ -acetoxy-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVd):	$[\phi]_{260} + 1956^\circ$ , $[\phi]_{276} + 1110^\circ$ , $[\phi]_{310} + 3260^\circ$ , $[\phi]_{330} + 1883^\circ$ , $[\phi]_{360} + 1038^\circ$ , $a = +2150^\circ$ .
3-oxo-28-acetoxy-oleana-12-en (Vd):	$[\phi]_{260} + 604^\circ$ , $[\phi]_{274} + 434^\circ$ , $[\phi]_{304} + 758^\circ$ , $[\phi]_{330} + 420^\circ$ , $[\phi]_{360} + 302^\circ$ , $a = +324^\circ$ .
3-oxo-12 $\beta$ -acetoxy-lupa-20(30)-en (VIIId):	$[\phi]_{260} + 1174^\circ$ , $[\phi]_{274} + 613^\circ$ , $[\phi]_{307} + 3284^\circ$ , $[\phi]_{330} + 1798^\circ$ , $[\phi]_{360} + 1180^\circ$ , $a = +2671^\circ$ .
16-oxo-3 $\beta$ -acetoxy-ursa-12-en (IIe):	$[\phi]_{260} + 6980^\circ$ , $[\phi]_{270} + 7390^\circ$ , $[\phi]_{290} + 4420^\circ$ , $[\phi]_{301} 0^\circ$ , $[\phi]_{312-319} - 3236^\circ$ , $[\phi]_{330} - 1570^\circ$ , $[\phi]_{360} - 170^\circ$ , $a = -10626^\circ$ .
12-oxo-3 $\beta$ -acetoxy-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVe):	$[\phi]_{260} + 5748^\circ$ , $[\phi]_{273} + 6496^\circ$ , $[\phi]_{290} + 3140^\circ$ , $[\phi]_{297} 0^\circ$ , $[\phi]_{313} - 4782^\circ$ , $[\phi]_{330} - 1908^\circ$ , $[\phi]_{360} - 652^\circ$ , $a = -11278^\circ$ .
12-oxo-3 $\beta$ -acetoxy-lupa-20(30)-en (VIIe):	$[\phi]_{260} + 5130^\circ$ , $[\phi]_{265} + 5438^\circ$ , $[\phi]_{275} + 4830^\circ$ , $[\phi]_{290} + 2110^\circ$ , $[\phi]_{297} 0^\circ$ , $[\phi]_{307} - 1810^\circ$ , $[\phi]_{335} 0^\circ$ , $[\phi]_{360} + 242^\circ$ , $a = -7248^\circ$ .
28-aldehydo-3 $\beta$ -acetoxy-oleana-12-en (Ve):	$[\phi]_{260} + 4193^\circ$ , $[\phi]_{263} + 4290^\circ$ , $[\phi]_{290} + 2705^\circ$ , $[\phi]_{312} 0^\circ$ , $[\phi]_{327} - 434^\circ$ , $[\phi]_{345} 0^\circ$ , $[\phi]_{360} + 145^\circ$ , $a = -4724^\circ$ .
3,16-dioxo-ursa-12-en (IIIf):	$[\phi]_{260} + 8260^\circ$ , $[\phi]_{273} + 8360^\circ$ , $[\phi]_{290} + 5984^\circ$ , $[\phi]_{305} 0^\circ$ , $[\phi]_{312} - 2706^\circ$ sh., $[\phi]_{315} - 2618^\circ$ , $[\phi]_{320} - 3170^\circ$ , $[\phi]_{330} - 1145^\circ$ , $[\phi]_{352} 0^\circ$ , $[\phi]_{360} + 119^\circ$ , $a = -11830^\circ$ .
3,12-dioxo-(18 $\alpha$ , 19 $\beta$ H)-ursa-20-en (IVf):	$[\phi]_{260} + 5324^\circ$ , $[\phi]_{272} + 5655^\circ$ , $[\phi]_{290} + 3320^\circ$ , $[\phi]_{300} 0^\circ$ , $[\phi]_{314} - 2728^\circ$ , $[\phi]_{330} - 968^\circ$ , $[\phi]_{360} - 132^\circ$ , $a = -8382^\circ$ .
3,12-dioxo-lupa-20(30)-en (VIIf):	$[\phi]_{260} + 338^\circ$ , $[\phi]_{268} + 170^\circ$ , $[\phi]_{300} + 1550^\circ$ , $[\phi]_{330} + 435^\circ$ , $[\phi]_{360} + 290^\circ$ , $a = +1380^\circ$ .
3-oxo-28-aldehydo-oleana-12-en (Vf):	$[\phi]_{260} + 3530^\circ$ , $[\phi]_{277} + 2240^\circ$ , $[\phi]_{297} + 2568^\circ$ , $[\phi]_{334} + 505^\circ$ , $[\phi]_{360} + 724^\circ$ , $a = +328^\circ$ .

Since it was impossible to investigate directly the effect of a double bond at position 12–13 of oleanane on the ORD and CD curves (we had at our disposal only one compound from this group with a double bond at position 12–13, which cannot be catalytically hydrogenated<sup>10</sup>), a comparison was made between compounds IIc and Vc. These compounds have double bonds at position 12–13 and differ only in position of a Me group (position 19 or 20). An additional ORD plain curve with high positive values of  $[\phi]$  in the range 250–350 nm. was obtained by Djerassi<sup>6</sup> for the oleana-12-en hydrocarbon. Superimposition of this strongly positive background originating from the 12–13 bond on the positive Cotton effect of optical rotation connected with the ketone group at position 3 may explain high values of  $[\phi]_{\min}$  obtained for IIc and Vc. Negative  $\Delta\epsilon$  values at wavelengths over 313 nm. were obtained for these derivatives only. Bearing in mind that I differs from IIc by a lack of a double bond in the molecule and does not show this effect, it can be concluded that the complex character of CD curves for IIc and Vc is caused by the presence of a double bond at position 12–13 which is the closest to the ketone group at position 3.

A comparison of 3-monoketo derivatives of the pentacyclic triterpenic diols (with acetylated OH groups in other than the 3 positions: IIId, IVd, V, VIId) with the corresponding 3-monoketones allow us to determine the effect of the presence of an additional OAc group at various positions. In all derivatives studied there is a clear decrease in  $[\phi]_{\max}$  and  $[\phi]_{\min}$  values and in molecular amplitudes with a positive Cotton effect related to the ketone group at position 3. This decrease of  $[\phi]$  value in extremes and a decrease of the amplitude is particularly intense for the derivative with the OAc group at position 28, originating from acetylation of the primary OH group, and thus showing greater possibilities of rotation. This indicates an intramolecular rotatory compensation. At the same time an exceptionally high  $\Delta\epsilon_{\max}$  value is observed for this derivative, indicating that the ketone and OAc groups have synergic action on the increased difference between the absorption coefficients for the levorotatory and dextrorotatory components of the polarized light plane. Hypsochromic shifts of  $[\phi]_{\max}$  are observed for derivatives IIId and Vd and bathochromic shifts for IVd and VIId. For the compounds with OAc groups at the same position (IVd, VIId) similar values of  $[\phi]_{\max}$  and  $\Delta\epsilon_{\max}$  are observed. Negative values of  $\Delta\epsilon$  occur for all analyzed derivatives at a certain range (above 300 nm). The CD curve (Fig. 2) for IIId is difficult to interpret (distinct hypsochromic shift of extremes). The results obtained indicate that although the additional OAc group does not change the general character of ORD and CD curves for 3-monoketones of pentacyclic triterpenes (positive Cotton effect of optical rotation and positive CD) it causes, however, alterations of the molecular amplitudes, extreme values of  $[\phi]$ ,  $\Delta\epsilon$  and hypso- and bathochromic shifts in extremes, as well as the complications of CD curves.

All derivatives with ketone groups at position 12 or 16, an aldehyde group at position 28, and an OAc group at position 3 (IIe, IVe, Ve, VIIe) show a negative Cotton effect of optical rotation and negative CD by contrast to derivatives containing the ketone group at position 3. A comparison of ORD curves of compounds IVe and VIIe with a ketone group at position 12, but with different types of backbones and different double bond localizations, shows that these compounds differ considerably in molecular amplitudes and  $[\phi]$  values at extremes. The wavelength at which the extremes do occur are different for compounds IVe and VIIe, and moreover compound VIIe shows again positive rotation over 340 nm. Great differences in  $\Delta\epsilon_{\max}$

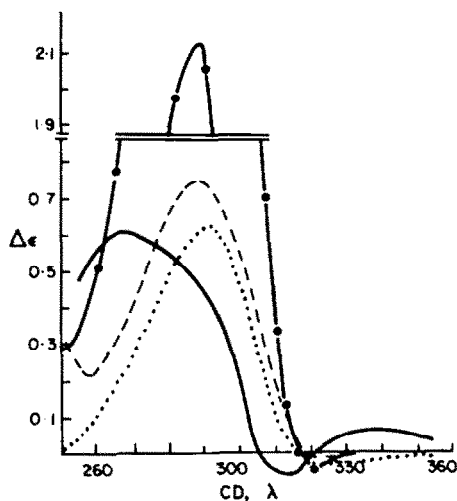


FIG 2. CD curves of IIc(—), IVd(---), Vd(●) and VIId(.....).

values were also observed for these derivatives. More similar are the parameters of ORD and CD curves of compounds IIe and IVe, which are the derivatives with the ketone group at different positions (12 or 16) but with the same type of backbone. This similarity mainly concerns the molecular amplitude (practically identical) and  $[\phi]_{\max}$ ,  $[\phi]_{\min}$  and  $\Delta\epsilon_{\max}$  values. A distinct shift of CD maxima and the extremal points in the Cotton effect of optical rotation were, however, observed for these compounds.

The ORD curve obtained for the compound with an aldehyde group at position 28 of the oleanane backbone (Ve) is similar in its parameters to the Cotton effect of the optical rotation, reported by Djerassi<sup>6</sup> for 3 $\beta$ , 16 $\beta$ -di-OH-28-aldehydo-oleana-12-en. Compound Ve shows negative CD.

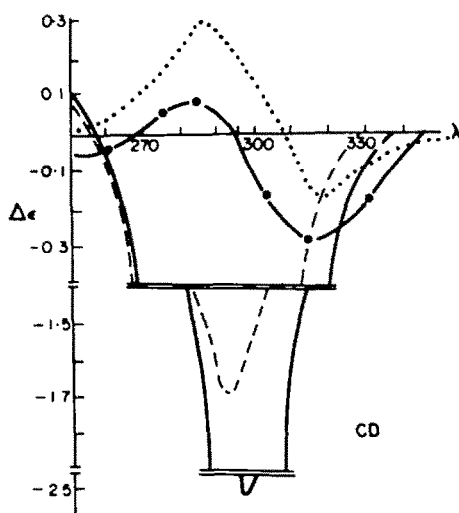


FIG 3. CD curves of IIIf(—), IVf(---), Vf(●) and VIIIf(.....).



ORD and CD curves for the following diketone derivatives of pentacyclic triterpenes—III<sub>f</sub>, IV<sub>f</sub>, VIII<sub>f</sub> and VI<sub>f</sub>, were investigated. A comparison of the curves with the corresponding mono-keto derivatives indicate that in compounds III<sub>f</sub> and IV<sub>f</sub> a decisive effect of general character in the ORD and CD curves is exerted not by the ketone groups in position 3 but by these groups at positions 12 or 16, since the curves for diketones are very similar to ORD and CD curves obtained for corresponding 12 or 16-oxo-3-acetoxy derivatives. The curves obtained for these diketones differ considerably from the curves which are the sum of  $[\phi]$  and  $\Delta\epsilon$  for the corresponding monoketones. There is one earlier example<sup>6</sup> known in which ORD measurements were made for two monoketone derivatives of pentacyclic triterpenes (3-oxo-oleana-12-en and 3 $\beta$ -OH-16-oxo-oleana-12-en) as well as for diketone derivatives with ketone groups at positions 3 and 16 of the oleana-12-en backbone. The Cotton effects obtained for diketones were not the sum of the Cotton effects obtained for two monoketones, (although positions 3 and 16 are not very close), and is in agreement with our findings.

A quite different relationship is observed for ketone derivatives of compound VIII<sub>b</sub>. For VIII<sub>f</sub> the character of the ORD and CD curves is determined by the ketone group at position 3. On the other hand, the results obtained for compounds IV<sub>e</sub> and IV<sub>f</sub> with ketone groups at position 12 show the occurrence of such negative  $[\phi]$  and  $\Delta\epsilon$  values, that the effect of the ketone group at position 3 (positive values of  $[\phi]$  and  $\Delta\epsilon$ ) is masked. This paradox can be explained by accepting an interaction<sup>11</sup> between the oxygen of the ketone group at position 12 and the hydrogens of the double bond 20(30). Such interaction is facilitated by the fact that the D ring of lupene derivatives adopts a boat conformation, causing the ketone group to approach the isopropylidene double bond. The differences in ORD and CD curves for compounds IV<sub>e</sub> and VIII<sub>e</sub> can be explained in terms of formation of a similar hydrogen bond.

Introduction into 3-monoketone V<sub>c</sub> of the aldehyde group at position 28 (VI<sub>f</sub>) results in the occurrence of complex ORD and CD curves. It seems that this is connected with the possibility of rotation of the aldehyde group and interaction of this group with the double bond at position 12–13 as well as with a certain mutual shift of absorption for the ketone and aldehyde group.

The data obtained indicate that the assumption as to the additive character of ORD and CD curves for pentacyclic triterpenic ketones with respect to corresponding monoketones, cannot be accepted. A minimal alteration in the structure of the molecule based on a change of double bond position, change of the localization of a single Me group, and presence of additional OAc group, cause considerable changes in ORD and CD curves. Alterations such as substitution of a six-membered for a five-membered ring, change of localization of ketone group or formation of a hydrogen bond with participation of a ketone group may completely change the character of the Cotton effect. For this reason it seems, that the ORD and CD methods may serve as an auxiliary tool in localization of individual ketone groups in pentacyclic triterpenes with the same type of backbone and double bond position. Presence of a second carbonyl group (ketone or aldehyde) in the molecule causes changes in ORD and CD curves which are difficult to predict, because they depend not only on the distance between these groups (vicinal effect) but also on the structure of the backbone, position of the double bond, localization of Me groups and other elements of the structure which do not show absorption maxima at a given range of the spectrum.

## EXPERIMENTAL

M.ps (uncorrected) were determined by use of a heated microscopic plate.

ORD and CD were measured in MeOH in a JASCO UV/ORD/CD-5 spectrophotometer at concentrations from 2.0 to 5.0 mg/ml at 20° in cuvettes with 1 cm light-path.

Acetylation was carried with Ac<sub>2</sub>O in pyridine at -5° for 30 min. The products were isolated by means of TLC with SiO<sub>2</sub> of Merck in a mixture of hexane:CHCl<sub>3</sub>:MeOH (20:10:1). The chromatographic bands were localized by spraying the plates with water or with 50% H<sub>2</sub>SO<sub>4</sub> and heating.

Oxidation of the OH groups was by CrO<sub>3</sub> in pyridine at room temp for 24 hr (oxidation of monohydroxyl derivatives) or 48 hr (oxidation of dihydroxyl alcohols to diketones). The products were isolated by means of TLC with SiO<sub>2</sub> in hexane:CHCl<sub>3</sub>:MeOH (40:20:1). The compounds separated were crystallized from 70–96% EtOH.

Reduction with H<sub>2</sub> was carried out in the presence of Pd/C in MeOH. The products were isolated by means of TLC with SiO<sub>2</sub> impregnated with 10% AgNO<sub>3</sub> (with respect to the weight of the gel) in CHCl<sub>3</sub>. The chromatographic bands were localized under UV light or after spraying with 50% H<sub>2</sub>SO<sub>4</sub> and heating. The isolated compounds were crystallized as described above.

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