Tetrahedron. Vol. 24, pp. 3273 to 3283. Pergamon Press. 1968. Printed in Great Britain

CITRUS BITTER PRINCIPLES—VIII[1]

APPLICATION OF ORD AND CD TO STEREOCHEMICAL PROBLEMS

D. L. DREYER*

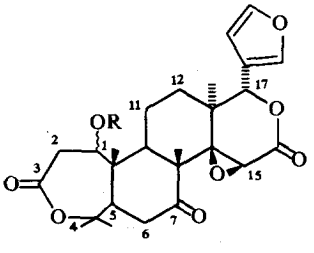
Fruit and Vegetable Chemistry Laboratory,† 263 South Chester Avenue, Pasadena, California 91106

(*Received in USA* 2 *October* 1967; *accepted for publication* 4 *November* 1967)

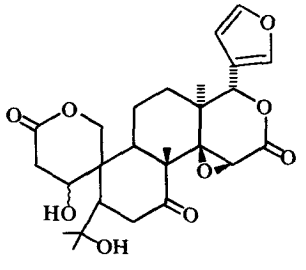
Abstract—A systematic CD and ORD study of limonoids is reported. The data obtained have been used to define completely the relative stereochemistry at the 13- and 17-positions and absolute stereochemistry of odoratin as well as that at C-17 in obacunone and congeners. The role of C-1 stereochemistry in the conversion of ichangin to limonin is discussed.

ALTHOUGH scattered data have been published, no systematic ORD or CD treatment of limonoids has yet appeared. It is the purpose of this study to determine the possible use of ORD and CD in exploring the fine structure of limonoids and in solving some of the remaining stereochemical problems in this series of degraded triterpenes. Among these are the determination of stereochemistry at C-17 in nomilin (**1**) and obacunone (**2**) and at C-1 in nomilin (**1**), deacetylnomilin (**3**) and ichangin (**4**). Such a study of known limonoids might form a basis for the more extensive use of ORD and CD as tools in solving structural and stereochemical problems on unknown limonoids.[1,2]

Two Cotton effects are readily discernable in most limonoids with a 7-keto group. The Cotton effect in the range 290–320 mμ dominates the ORD curves of these limonoids in the most accessible region of the spectrum (Table 1). The position and sign of this Cotton effect, due to the $n \rightarrow \pi^*$ transition of the 7-keto group, is similar to the relatively weak negative Cotton effect exhibited by 7-keto-5α-steroids (**6**), for example, 3β-acetoxycholestan-7-one,[3] and is predicted by the octant rule.[4]



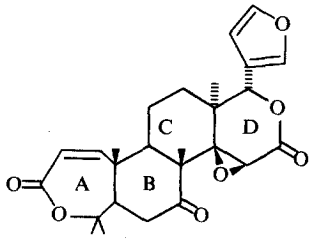
1: R = Ac
3: R = H
27: R = PhCOCO
28: R = PhCO



4

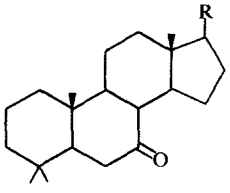
* Present address: Dept. of Chemistry, San Francisco State College, San Francisco, Calif.

† A laboratory of the Western Utilization Research and Development Division, Agricultural Research Service, U.S. Department of Agriculture.



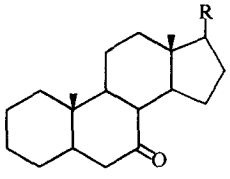
2

The 4β-Me group of the corresponding 4,4-dimethyl-7-keto-5α-steroids (**5**) projects into a positive octant causing a decrease in amplitude of the Cotton effect relative to those of 7-ketocholestane derivatives (**6**)[5,*] In a similar manner, the 4β-Me group in 7-keto limonoids also projects into a positive octant. However, quantitatively, 7-keto limonoids differ in two important respects from 7-keto-5α-steroids. Firstly, the axial C-8 Me of limonoids projects into the lower negative octant contributing to an increase in amplitude of the negative Cotton effect. Secondly, the D-ring occupies both upper and lower front octants but only the lower front octant in the steroid case.[7]



5

	Δ_ε
R = H	−0·39
R = C_8H_{17}	−0·39



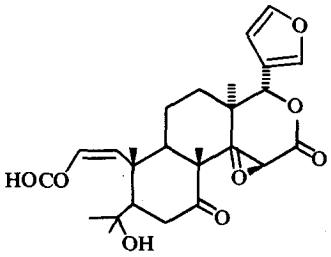
6

	Δ_ε
R = H	−0·63
R = C_8H_{17}	−0·59

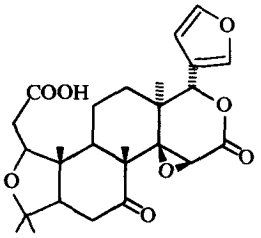
The differences in amplitudes for the negative Cotton effects of many simple limonin derivatives can be explained by twisting of the *gem*-dimethyl group in different positions to accommodate the various A-rings. For the various A-rings there will then be slight changes in position of the 4,4-dimethyl group relative to the 7-keto group leading to slight differences in amplitude (Table 1). The higher amplitude in obacunone (**2**) appears due to the partial overlap of the negative keto and A-ring lactone Cotton effects and this is reflected in the ORD curve as well. The ORD curve of obacunone (**2**) differs considerably from the curves of most 7-ketolimonoids. On the other hand the ORD curve of the closely related obacunoic acid (**7**) is very similar to that of limonin (**8**), isoobacunoic acid (**11**), nomilin (**1**) and its derivatives **3** (Experimental).

The keto chromophore in limonilic acid (**12**) and its deoxy derivative (**13**) shows both negative and positive CD components with a shift to lower energies caused by the presence of the axial ether bridge. Since the B-ring is rigid and conformationally

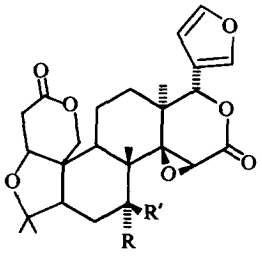
* The Cotton effect is completely reversed in 6,6-dimethyl-7-keto-5α-steroids (positive Cotton effect) due to warping of the B-ring as a result of 1,3-diaxial methyl-methyl interactions.[6]



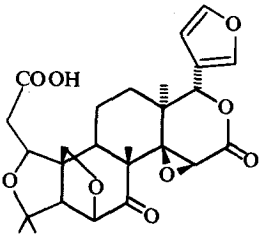
7



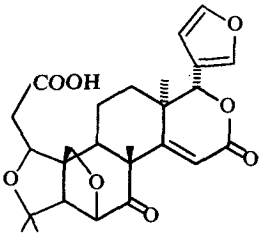
11



8: R,R′ = O
9: R = OH, R′ = H
10: R = H, R′ = OH



12



13

TABLE 1. SUMMARY OF CD DATA AND AMPLITUDES (*a*) FOR LIMONIN AND CONGENERS

	Δε Keto	Δε Lactone	*a* (Keto)
Limonin (**8**)	−2·50 (293)	−4·21 (233)	−90
Tetrahydrolimonin	−2·42 (292)		−92
Isoobacunoic acid (**11**)	−1·90 (296)	−3·69 (235)	−81
Ichangin (**4**)			−56
Nomilin (**1**)	−2·21 (291)	−4·83 (232)	−65
Deacetylnomilin (**3**)	−2·10 (291)	−4·30 (236)	−70
Deacetylnomilin benzoate (**28**)	−2·10 (291)		−75!
Obacunone (**2**)	−3·00 (291)	−3·66 (247)	−123
Obacunoic acid (**7**)	−2·99 (291)	−3·73 (238)	−91
7-Deacetoxy-7-oxogedunin (**26**)	−2·72 (291)	−2·47 (247)	
Limonol (**10**)		−2·23 (233)	
Epilimonol (**9**)		−2·22 (236)	

fixed, the positive component is due to unsymmetrical solvation of the keto group and not to a conformational equilibrium.[8,*]

Limonoids show a second negative Cotton effect in the range 233–240 mμ which

* The low amplitude of the Cotton effect is consistent with unsymmetrical solvation.[8]

is assigned to the n → π* transition of the D-ring lactone group (Table 1). Saturated lactones normally show a Cotton effect in the ORD with the first extremum at about 220–230 mμ.[9, 10,] † The shift to lower energies of this extremum for the D-ring lactone is presumably caused by the α, β-epoxy group.[12] Limonol (**9**) and epilimonol (**10**) both show only this lactone Cotton effect. Tetrahydrolimonin (**8**, furan ring saturated) and isoobacunoic acid (**11**) both give curves almost identical to that of limonin (**8**) so that this band cannot be due to other functional groups, in particular, the furan ring or the A-ring lactone. Since the lactone group, C—CO—O—C, is planar,[13] the presence of the α, β-epoxy group will impose further planarity on the D-ring so that it is only slightly puckered and resembles to some extent an envelope conformation. A negative Cotton effect is predicted by application of the sector rule[9, 14] for lactones. Since the equatorial furan ring lies close to the sector planes, it presumably makes very little contribution to the Cotton effect. There is only limited ORD data in the literature on α-substituted lactones,[15] but apparently the presence of an α, β-epoxy group does not cause reversal of sign of the Cotton effect[9] as is the case in ketones.[16]

The furan ring is an optically active chromophore and shows a Cotton effect centered near 220 mμ.[17] This is below the range routinely covered in this study. Moreover, the close similarity between the ORD curves of limonin (**8**) and tetrahydrolimonin (**8** with furan ring saturated) indicates that the furan ring is contributing very little to the curves above 235 mμ.

The negative D-ring Cotton effect is strongly positive in the corresponding deoxy compounds (**13**, **14**, **15**). The interpretation of the ORD curve for citrolin (**16**) is more difficult because the lactone Cotton effects are superimposed.‡ Reichstein *et al.*[19] have reported ORD data on an extended number of α, β-unsaturated lactones and found that the two extrema occurred at about 260 and 228 mμ. No effort at a general emperical correlation of the ORD for α,β-unsaturated lactones appears to have been reported. The D-ring lactone Cotton effect in obacunone (**2**) is partly obscured by the negative Cotton effect from the A-ring α,β-unsaturated lactone.

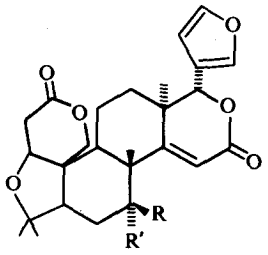
The position and intensity of the ene lactone band in deoxylimonin (**14**) compares well with CD data reported by Chan *et al.*[20] for the ene lactone group in odoratin (**17**); 264 mμ ($\Delta\varepsilon = +7{\cdot}0$). As deoxylimonin (**14**) is a good model for such a D-ring, this completely defines the stereochemistry at the 13- and 17-positions in odoratin (**17**) and indicates the absolute configuration of odoratin (**17**) is the same as the other C_{26} limonoids. This stereochemistry provides strong circumstantial support for the proposed biogenesis of odoratin (**17**).[20] Other stereochemical elements in **17** have been defined by previously published data.[20, 21]

The identity of the ORD and CD curves of nomilin (**1**), limonin (**8**) and deacetylnomilin (**3**) especially in the 250 mμ region also confirms identical stereochemistry at C-17. Previous interconversion of obacunone **2** (which has been related to nomilin **1**)[22] with limonin (**8**)[23] was not unambiguous on this point.

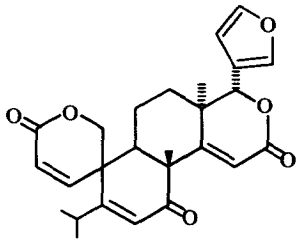
Snatzke[24] has reported CD data on cedrelone (**18**) and some of its derivatives (Table 2). These compounds show an intense negative Cotton effect centered at about

† The Cotton effect is centered at about 215–220 mμ.[11]

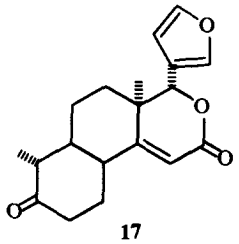
‡ The negative Cotton effect shown by the α,β-unsaturated keto system in citrolin (**16**) is similar to that of Δ^5-7-ketotriterpenes and quite unlike that of Δ^5-7-ketosteroids.[18]



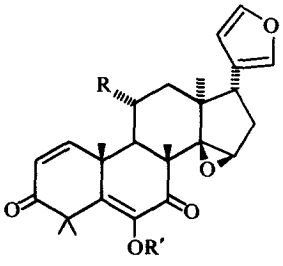
14: R,R′ = O
15: R = OH, R′ = H



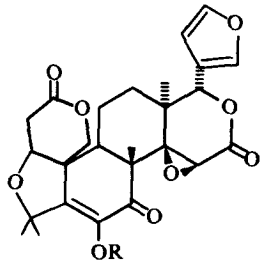
16



17



18: R = H R′ = H
19: R = AcO R′ = H
21: R = H R′ = Me
22: R = H R′ = Ac
24: R = AcO R′ = Ac



20: R = H
23: R = Ac

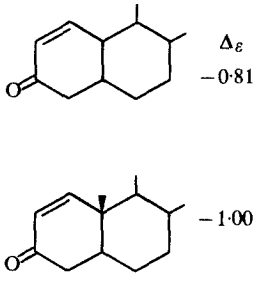
316 mμ which is due to the diosphenol chromophore. Snatzke has suggested[24] that this group might best be considered as an inherently dissymmetric chromophore to account for the large amplitude of the Cotton effect. Limonoids investigated in this study with the diosphenol group (anthothecol **19** and limonin diosphenol **20**) also showed an exceptionally intense negative Cotton effect at 320 mμ (Table 2) accompanied by an intense positive Cotton effect at 274–280 mμ. The latter Cotton effect appears due to the $\pi \rightarrow \pi^*$ transition of the diosphenol chromophore. Limonin diosphenol acetate (**23**) and anthothecol acetate (**24**) both showed Cotton effects of lower amplitudes and a shift to lower energies compared to the parent diosphenols (cf. cedrelone **18** and cedrelone acetate **22**[24]). Moreover, the CD data of anthothecol (**19**) and limonin diosphenol (**20**) are comparable with that reported by Snatzke[24] for cedrelone **18** (Table 2).

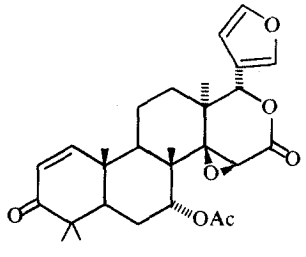
TABLE 2. SUMMARY OF CD DATA FOR DIOSPHENOL LIMONOIDS

	Δε
Cedrelone (**18**)[24]	−12·82 (316)
Dihydrocedrelone[24]	−2·57 (314)
Cedrelone methyl ether (**21**)[24]	−5·66 (335)
Cedrelone acetate (**22**)[24]	−6·00 (330)
Anthothecol (**19**)	−10·8 (320) + 18·9 (280)
Anthothecol acetate (**24**)	−5·39 (331)
Limonin diosphenol (**20**)	−8·3 (320) + 15·7 (274)
Limonin diosphenol acetate (**23**)	−3·08 (330)

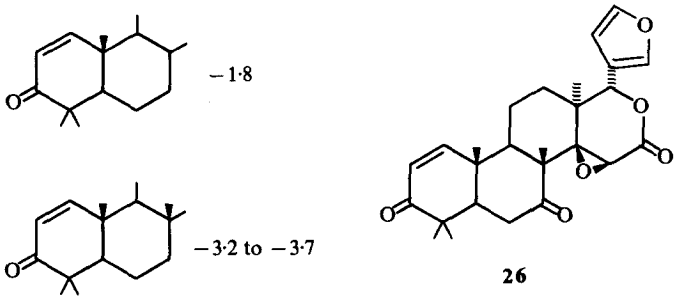
Limonoids containing a Δ^1ene-3-one A-ring show a number of unexpected chemical properties. For example, the 3-keto group in cedrelone (**18**) is resistant to oxime formation and instead gives a Michael addition product with hydroxylamine.[25] Cedrelone (**18**) gives only a dihydrocedrelone (**18** with A-ring saturated) with borohydride[25] whereas dihydrogedunin (**25** with A-ring saturated) is reduced normally by borohydride.[26] Dihydrocedrelone fails to form an oxime[25] and anthothecol (**19**) and dihydroanthothecol (**19** with A-ring saturated) fail to form 2,4-DNP's.[27] 3-Ketotriterpenes normally undergo both oxime formation and reduction with borohydride. It has been proposed[25] that the A-ring in cedrelone and presumably anthothecol and derivatives is in a boat conformation so that eclipsed interactions between the 6-substituent and the 4α-Me group of a chair A-ring are avoided. Reactions in which C-3 becomes tetrahedral cause unfavorable 1,4-flagpole interactions. These explanations are supported by the X-ray crystallographic structure determination of cedrelone iodoacetate which shows that the A-ring exists in a boat conformation in the crystal.[28]

A/B *Trans* Δ^1-3-keto steroids and triterpenes form a regular series whose CD curves show increasing amplitude with an increasing number of 1,3-diaxial methyl-methyl interactions. This has been explained[29] by the increasing crowding of the axial Me groups and warping of the A-ring to relieve this crowding. These Δ^1en-3-ones are good examples of the dependence of Δε on the amount of twist in a ring system. Snatzke[24] has analyzed the CD data for this chromophore in gedunin (**25**) and some cedrelone derivatives and interpreted the results in terms of warping of the A-ring. Gedunin (**25**) and 7-deacetoxy-7-oxogedunin (**26**) do not fall neatly into the accepted divisions. Comparison of this Cotton effect in **25** and **26** with that of the A-ring of cedrelone (**18**) is complicated by the presence of the intense negative Cotton effect of the diosphenol chromophore in the latter.



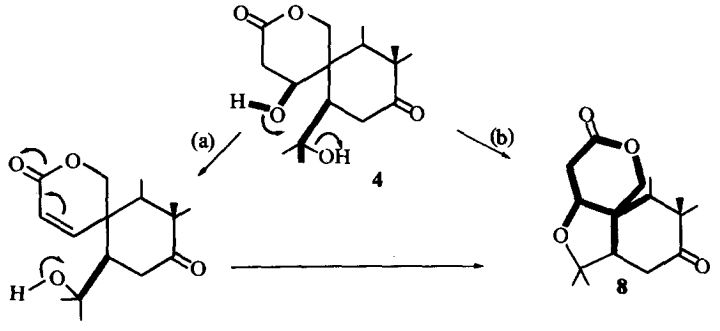


25



26

The natural cooccurrance and close structural similarity of nomilin (**1**), deacetylnomilin (**3**) and ichangin (**4**) suggests identical stereochemistry at C-1 in all three limonoids.* The stereochemistry at C-1 in these limonoids has an important bearing on the biogenetic formation of limonin (**8**). The acid-catalyzed conversion of ichangin (**4**) to limonin (**8**) has previously been reported.[31] This ring closure could occur by two different mechanisms. These are: (a) elimination of the 1-OH group and a Michael type addition of the 4-OH group across the resulting α,β-unsaturated lactone system (as in the conversion of obacunoic acid to isoobacunoic acid[32]) or (b) displacement of the tertiary OH at C-4 by the 1-OH. In process (a) there are no stereochemical requirements for the 1-OH, in (b) the 1-OH group must be positioned on the same side (α-configuration in deacetylnomilin **3**) as the isopropyl group in order to effect ring closure of the ether bridge. In mechanism (a) the oxygen bridge results from the 4-OH group, in (b) the bridge results from the 1-OH group. Similar considerations apply to the biogenetic conversion of obacunone (**2**), deacetylnomilin (**3**) or ichangin (**4**) to limonin (**8**).



4 8

Previous attempts[33] to assign stereochemistry at C-1 in nomilin (**1**) involving consideration of the NMR-coupling constants for H-1 were not unambiguous. This approach suffers from uncertainty of the A-ring conformations. Because of the obvious importance of C-1 stereochemistry in the biogenetic relationships of limonoids, more direct evidence on this point was desirable.

Attempts to determine the stereochemistry at C-1 by Horeau's method[34,35] failed because of the low reactivity of deacetylnomilin (**3**) with α-phenylbutyric anhydride, even with heating. Most of the deacetylnomilin was recovered unchanged even though it is acetylated without difficulty at room temperature.[30] 11β-Hydroxy-

* Acetylation of deacetylnomilin gives nomilin showing in these two cases identical stereochemistry at C-1.[30]

steroids also fail to react in the Horeau method.[34] Application of the Prelog method[36] to deacetylnomilin phenylglyoxylate (**27**) was also unsuccessful.

With a view of applying Brewster's benzoate rule,[37] deacetylnomilin (**3**) was converted to its benzoate (**28**). Deacetylnomilin benzoate (**28**) and phenylglyoxylate (**27**) both showed one C-Me resonance relatively far upfield (at δ 0·68) compared with nomilin (**1**) and deacetylnomilin (**3**).[33] The acyl group is not responsible for the upfield shift since the shift is not present in nomilin (**1**). Inspection of models indicates two conformations of the A-ring are reasonable which account for the observed spectra. These are a twist chair form for nomilin (**1**) and deacetylnomilin (**3**) and a twist boat form for the benzoate (**28**) and phenylglyoxylate (**29**) even though it occurs at the expense of twisting the lactone group. A normal boat and chair conformation is unlikely because of the severe eclipsed interactions. In the boat form the C-19 Me falls in the shielding region of the lactone CO group causing an upfield shift of the C-19 resonance. The twist boat form avoids severe interference of the more bulky 1-α-acyl group of **28** and **29** with the 11-α-proton. This A-ring conformational difference between nomilin or deacetylnomilin (**3**) and its benzoate (**28**) invalidates application of Brewster's benzoate rule.[37] The different conformations of the A-ring in the various deacetylnomilin derivatives is also reflected qualitatively in the ORD and CD curves. Thus, the negative Cotton effect for the 7-keto group is the same in the 300 mμ region but whereas nomilin (**1**) and its deacetyl derivative **3** are nearly identical and negative in the 250 mμ region, the benzoate **28** is positive. The region below 250 mμ was inaccessible in the benzoate **28** due to the intense adsorption.

Deacetylnomilin phenylglyoxylate (**27**) showed a weak negative Cotton effect at 351 mμ. Such a Cotton effect in the phenyl glyoxylate of an optically active secondary alcohol has previously been reported.[38] With proper models such derivatives may be of value for determination of absolute configuration of optically active alcohols.

At 60 Mc. the resonance for H-1 in deacetylnomilin benzoate (**28**) and phenylglyoxylate (**27**) was partly overlapped by the 17-resonance. At 100 Mc, H-1 in each case was a clearly resolved *doublet* of $J \doteq 5$. Thus, the coupling of H-1 with one of the 2-protons must be zero. Using the Karplus relationship[39] the observed coupling in **1**,[33] **3**, **28** and **29** would require that the 1-OH be in the α-position.

In spite of these arguments, more decisive evidence bearing on the conformation at C-1 would still be desirable. Accepting the 1α-OH configuration and stereochemical homogeneity between deacetylnomilin (**3**) and inchangin (**4**), ichangin (**4**) can be converted to limonin (**8**) by either mechanism (a) or (b) above. Grandifolione,[40] its acetate (khayanthone),[41] khivorin,[42] 3-,[43] and 7-deacetylkhivorin,[42] 7-deacetoxy-7-oxokhivorin,[42] salannin,[44] and methyl angolensate[45] are naturally occurring limonoids isolated from plants of the family Meliaceae and all possess a hydroxyl or acyloxy group at the 1-position. The biogenetically related limonoids fissinolide,[46] swietenine,[47] swietenolide,[48] and khyasin[49] occurring in plants of the same family also have identical stereochemistry at the 1-position.[50] With the exception of methyl angolensate, the stereochemistry at the 1-position in the former group has been assigned the α-configuration in all cases on the basis of the half-line widths of H-1 in the NMR. These limonoids from the Meliaceae thus have the same configuration at C-1 as those occurring in the Rutaceae.

EXPERIMENTAL

All ORD and CD data are given in dioxane solvent unless noted otherwise. For CD notation, see Ref. 24.

Limonin (**8**). CD (*c*, 0·003): 340 (0), 312i (−1·53), 300i (−2·44), 293 (−2·50), 233 (−4·21); ORD (*c*, 0·15): $[\alpha]_{600}$ −110°, $[\alpha]_{317}$ −1810°, $[\alpha]_{309}$ −1600° (sh), $[\alpha]_{298}$ −860° (sh), $[\alpha]_{288}$ −120° (sh), $[\alpha]_{280}$ +120°, $[\alpha]_{251}$ −1370°, $[\alpha]_{229}$ +1370° (last reading).

Tetrahydrolimonin.[51] CD (*c*, 0·002): 340 (0), 312i (−1·73), 301 (−2·36), 293 (−2·64), 235 (−3·78) (last reading); ORD (*c*, 0·18): $[\alpha]_{600}$ −116°, $[\alpha]_{315}$ −1830°, $[\alpha]_{309}$ −1600°, $[\alpha]_{305}$ −1630°, $[\alpha]_{297}$ −835° (sh), $[\alpha]_{288}$ −158° (sh), $[\alpha]_{278}$ +110°, $[\alpha]_{248}$ −1350°, $[\alpha]_{230}$ +340° (last reading).

Nomilin (**1**).* CD (*c*, 0·007): 330 (0), 310i (−1·25), 299 (−2·08), 291 (−2·21), 232 (−4·83); ORD (*c*, 0·22): $[\alpha]_{600}$ −91°, $[\alpha]_{315}$ −1410°, $[\alpha]_{310}$ −1270°, $[\alpha]_{306}$ −1320°, $[\alpha]_{297}$ −770° (sh), $[\alpha]_{287}$ −730° (sh), $[\alpha]_{279}$ −136°, $[\alpha]_{270}$ −273° (last reading); ORD† in 95% EtOH (*c*, 0·1): $[\alpha]_{600}$ −94°, $[\alpha]_{314}$ −1290°, $[\alpha]_{309}$ −1250°, $[\alpha]_{305}$ −1290°, $[\alpha]_{297}$ −934° (sh), $[\alpha]_{287}$ −334° (sh), $[\alpha]_{277}$ −83°, $[\alpha]_{248}$ −1400°, $[\alpha]_{224}$ +1350°, $[\alpha]_{215}$ +940° (last reading).

Deacetylnomilin (**3**).[30] CD (*c*, 0·004): 330 (0), 308i (−1·12), 298 (−2·00), 291 (−2·10), 236 (−4·30); ORD (*c*, 0·17): $[\alpha]_{600}$ −112°, $[\alpha]_{314}$ −1530°, $[\alpha]_{309}$ −1365°, $[\alpha]_{305}$ −1436°, $[\alpha]_{296}$ −895° (sh), $[\alpha]_{286}$ −353° (sh), $[\alpha]_{278}$ −200°, $[\alpha]_{270}$ −435° (last reading); ORD† in 95% EtOH (*c*, 0·06): $[\alpha]_{600}$ −120°, $[\alpha]_{314}$ −1524°, $[\alpha]_{310}$ −1500°, $[\alpha]_{306}$ −1524°, $[\alpha]_{297}$ −1050° (sh), $[\alpha]_{287}$ −510° (sh), $[\alpha]_{277}$ −160°, $[\alpha]_{247}$ −1680°, $[\alpha]_{225}$ +1600°, $[\alpha]_{215}$ −950° (last reading).

Deacetylnomilin benzoate (**28**). CD (*c*, 0·003): 330 (0), 310i (−1·1), 299 (−1·96), 291 (−2·10), 260 (0); ORD (*c*, 0·26): $[\alpha]_{600}$ −10°, $[\alpha]_{314}$ −1270°, $[\alpha]_{308}$ −1080°, $[\alpha]_{304}$ −1100°, $[\alpha]_{295}$ −410° (sh), $[\alpha]_{289}$ 0° (sh), $[\alpha]_{287}$ +10° (last reading); ORD† in 95% EtOH (*c*, 0·2): $[\alpha]_{600}$ −66°, $[\alpha]_{313}$ −1109°, $[\alpha]_{310}$ −1095°, $[\alpha]_{306}$ −1115°, $[\alpha]_{297}$ −530° (sh), $[\alpha]_{287}$ +94° (sh), $[\alpha]_{268}$ +1130°, $[\alpha]_{233}$ −3540°, $[\alpha]_{222}$ 0° (last reading).

Deacetylnomilin phenylglyoxylate (**27**). CD (*c*, 0·003): 400 (0), 363i (−0·24), 351 (−0·31), 340i (−0·24); ORD (*c*, 0·18): $[\alpha]_{600}$ −53°, $[\alpha]_{373}$ −383°, $[\alpha]_{360}$ −287° (sh), $[\alpha]_{344}$ −138°, $[\alpha]_{339}$ −145°, $[\alpha]_{332}$ −112°, $[\alpha]_{314}$ −410° (last reading).

Isoobacunoic acid (**11**).[52] CD (*c*, 0·005): 336 (0), 309i (−1·20), 300 (−1·90), 292 (−1·90), 235 (−3·69); ORD (*c*, 0·2): $[\alpha]_{600}$ −60°, $[\alpha]_{316}$ −1170°, $[\alpha]_{308}$ −966° (sh), $[\alpha]_{286}$ +380° (sh), $[\alpha]_{278}$ +550°, $[\alpha]_{252}$ −600°, $[\alpha]_{230}$ +2260° (last reading).

Obacunone (**2**). CD (*c*, 0·002): 326 (0), 308i (−1·47), 299i (−2·53), 291 (−3·00), 281 (−3·00), 247 (−3·67); ORD (*c*, 0·6): $[\alpha]_{600}$ −88°, $[\alpha]_{314}$ −1770°, $[\alpha]_{308}$ −1540°, $[\alpha]_{303}$ −1625°, $[\alpha]_{296}$ −1000° (sh), $[\alpha]_{288}$ −350° (sh), $[\alpha]_{270}$ +950° (sh), $[\alpha]_{242}$ +5800° (last reading).

Obacunoic acid (**7**).[52] CD (*c*, 0·007): 320 (0), 308i (−1·56), 299 (−2·60), 291 (−2·99), 238 (−3·73); ORD (*c*, 0·3): $[\alpha]_{600}$ −125°, $[\alpha]_{313}$ −1810°, $[\alpha]_{308}$ −1690°. $[\alpha]_{305}$ −1720°, $[\alpha]_{296}$ −1060° (sh), $[\alpha]_{286}$ −440° (sh), $[\alpha]_{276}$ +125°, $[\alpha]_{250}$ −1125°, $[\alpha]_{238}$ +310° (last reading).

Limonol (**9**).[53] CD (*c*, 0·003): 270 (0), 233 (−2·23); ORD (*c*, 0·14): $[\alpha]_{600}$ −84°, $[\alpha]_{252}$ −2170°, $[\alpha]_{228}$ +1120° (last reading).

Epilimonol (**10**).[53] CD (*c*, 0·002): 270 (0), 236 (−2·22); ORD (*c*, 0·07): $[\alpha]_{600}$ −21°, $[\alpha]_{252}$ −1630°, $[\alpha]_{226}$ +2340° (last reading).

Citrolin (**16**).[54] CD (*c*, 0·002): 354 (0), 375i (−0·96), 361 (−2·00), 347 (−2·17), 336i (−1·76), 274 (+4·77) (last reading); ORD§ (*c*, 0·1): $[\alpha]_{600}$ −113°, $[\alpha]_{383}$ −1304°, $[\alpha]_{373}$ −1153°, $[\alpha]_{367}$ −1228°, $[\alpha]_{352}$ −380° (sh), $[\alpha]_{339}$ +435° (sh), $[\alpha]_{324}$ +890° (sh), $[\alpha]_{295}$ +1285°, $[\alpha]_{256}$ −12,095°, $[\alpha]_{248}$ −6800° (last reading).

Deoxylimonin (**14**).[52] CD (*c*, 0·0005): 330 (0), 302 (−2·61), 267 (+5·84), 238 (−13·00); ORD (*c*, 0·25), $[\alpha]_{600}$ −60°, $[\alpha]_{325}$ −800°, $[\alpha]_{285}$ +1900°, $[\alpha]_{251}$ −5000°, $[\alpha]_{232}$ +7150° (last reading).

Deoxyepilimonol (**15**).[52] CD (*c*, 0·0007): 310 (0), 264 (+6·05); ORD (*c*, 0·17): $[\alpha]_{600}$ +70°, $[\alpha]_{285}$ +2230°, $[\alpha]_{252}$ −5000° (last reading).

Deoxylimonilic acid (**13**).[52] CD (*c*, 0·002): 350 (0), 343 (+0·02), 326i (−0·45), 313 (−0·90), 270 (+5·40), 245 (−7·20) (last reading); ORD (*c*, 0·1): $[\alpha]_{600}$ +80°, $[\alpha]_{350}$ +150°, $[\alpha]_{332}$ 0°, $[\alpha]_{286}$ +2800°, $[\alpha]_{252}$ −6060°, $[\alpha]_{227}$ +12,400°, $[\alpha]_{224}$ +11,000° (last reading).

* The ORD data on nomilin in Ref. 30 is in error.

† The author is indebted to Dr. William Gaffield for this determination.

§ The author is indebted to Prof. P. Crabbé for this determination.

Limonilic acid (**12**)[51] CD (*c*, 0·002): 350 (0), 337 (+0·18), 323i (−0·24), 306 (−0·60), 236 (−4·64); ORD (*c*, 0·2): $[\alpha]_{600}$ +90°, $[\alpha]_{348}$ +157°, $[\alpha]_{328}$ −157°, $[\alpha]_{319}$ −110° (sh), $[\alpha]_{289}$ +370°, $[\alpha]_{256}$ −900°, $[\alpha]_{226}$ +2700° (last reading).

Limonin diosphenol (**20**).[52] CD (*c*, 0·0007): 370 (0), 320 (−8·3), 274 (+15·7); ORD (*c*, 0·03): $[\alpha]_{600}$ −210°, $[\alpha]_{345}$ −2650°, $[\alpha]_{298}$ +9650° (last reading).

Limonin diosphenol acetate (**23**).[52] CD (*c*, 0·0008): 390 (0), 344i (−2·64), 330 (−3·36), 320i (+2·16), 260 (+2·96) (last reading); ORD (*c*, 0·04): $[\alpha]_{600}$ −100°, $[\alpha]_{365}$ −1250° (sh), $[\alpha]_{353}$ −1350°, $[\alpha]_{290}$ +1750° (sh), $[\alpha]_{260}$ +2750° (last reading).

Anthothecol (**19**).[27] CD (*c*, 0·0004): 380 (0), 320 (−10·8), 280 (+18·9); ORD (*c*, 0·09): $[\alpha]_{600}$ −80°, $[\alpha]_{356}$ −2600°, $[\alpha]_{298}$ +14,500°, $[\alpha]_{290}$ +11,100° (last reading).

Anthothecol acetate (**24**).[27] CD (*c*, 0·002): 380 (0), 331 (−5·95), 285i (−0·34), 271 (+4·02) (last reading); ORD (*c*, 0·08): $[\alpha]_{600}$ −63°, $[\alpha]_{361}$ −1770°, $[\alpha]_{302}$ +4100° (sh), $[\alpha]_{272}$ +8400° (last reading).

7-Deacetoxy-7-oxogedunin (**26**).[55] CD (*c*, 0·002): 396 (0), 372i (−0·85), 358i (−1·92), 347 (−2·12), 336i (−1·79), 308i (−1·96), 299 (−2·77), 291 (−2·72), 247 (−1·83); ORD (*c*, 0·1): $[\alpha]_{600}$ −46°, $[\alpha]_{383}$ −1020°, $[\alpha]_{376}$ −950°, $[\alpha]_{368}$ −1020°, $[\alpha]_{354}$ −340° (sh), $[\alpha]_{338}$ +410° (sh), $[\alpha]_{329}$ +580°, $[\alpha]_{314}$ 0°, $[\alpha]_{308}$ +272°, $[\alpha]_{304}$ +204°, $[\alpha]_{295}$ +1090° (sh), $[\alpha]_{285}$ +2040° (sh), $[\alpha]_{274}$ +2500°, $[\alpha]_{261}$ +2380°, $[\alpha]_{243}$ +4750° (last reading).

Gedunin (**25**).[26] CD (*c*, 0·005): 396 (0), 364i (−0·84), 357i (−1·96), 347 (−2·15), 250 (−1·42) (last reading); ORD (*c*, 0·3): $[\alpha]_{600}$ +38°, $[\alpha]_{382}$ −700°, $[\alpha]_{373}$ −600°, $[\alpha]_{367}$ −655°, $[\alpha]_{351}$ +280° (sh), $[\alpha]_{335}$ +1180° (sh), $[\alpha]_{315}$ +1575°, $[\alpha]_{290}$ +1460°, $[\alpha]_{270}$ +1550° (sh), $[\alpha]_{256}$ +1875° (last reading).

Deacetylnomilin benzoate (**28**). Deacetylnomilin was allowed to stand overnight with excess benzoyl chloride-pyridine. The reaction mixture was decomposed with water and extracted with $CHCl_3$. The $CHCl_3$ extracts were washed, dried and concentrated. The soln was filtered through a short column of acid-washed alumina and after removal of solvent the residue was crystallized from EtOH, m.p. 213–215°; ν 1744, 1713 (CO), 1600, 1584 (aromatic), 1502, 882 (β-substituted furan) cm^{-1} (Nujol); NMR δ 7·27 (J = 1) α-furan; 6·12 (J = 1) β-furan; 5·32 H-17; 5·25 (d, J = 5) H-1; 3·75 H-15; 1·55, 1·48, 1·35, 1·15, 0·69 (C-Me's) ppm ($CDCl_3$). (Found: C, 68·7; 68·6; H, 6·43, 6·27. $C_{33}H_{36}O_9$ requires: C, 68·73; H, 6·29%).

Deacetylnomilin phenylglyoxylate (**27**). This material was prepared from deacetylnomilin and phenylglyoxyloyl chloride as described above for the benzoate. The product showed m.p. 245–246°, from $CHCl_3$–EtOH; ν 1728, 1704, 1678 (CO), 1592 (aromatic), 1502, 883 (β-substituted furan) cm^{-1} (Nujol); NMR δ 7·27 (d, J = 1) α-furan; 6·12 (d, J = 1) β-furan; 5·32 (s) H-17; 5·25 (d, J = 5) H-1; 3·75 (s) H-15; 1·57, 1·52, 1·37, 1·15, 0·68 (C-Me's) ppm ($CDCl_3$). (Found: C, 67·8; H, 6·03. $C_{34}H_{36}O_{10}$ requires: C, 67·54; H, 6·00%).

Acknowledgement—The author is indebted to Dr. W. R. Chan, University of the West Indies, for a sample of 7-deacetyl-7-oxogedunin, to Dr. D. J. Bertelli, University of California, Santa Barbara for 100 Mc NMR spectra, and to Dr. W. E. Thiessen, University of California, Davis, for making ORD/CD facilities available and helpful discussions.

REFERENCES

[1] Part VII, D. L. Dreyer, *J. Org. Chem.* **23**, 3442 (1967).
[2] D. L. Dreyer, unpublished results.
[3] C. Djerassi and W. Closson, *J. Am. Chem. Soc.* **78**, 3761 (1956).
[4] W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, *Ibid.* **83**, 4013 (1961); C. Djerassi and W. Klyne, *J. Chem. Soc.* 2390 (1963).
[5] M. Fétizon and M. Golfier, *Bull. Soc. Chim. Fr.* 859 (1966).
[6] F. Lederer and G. Ourisson, *Bull. Soc. Chim. Fr.* 1298 (1965).
[7] cf. G. Wagniere, *J. Am. Chem. Soc.* **88**, 3937 (1966).
[8] K. M. Wellman, P. H. A. Laur, W. S. Briggs, A. Moscowitz and C. Djerassi, *J. Am. Chem. Soc.* **87**, 66 (1965).
[9] J. P. Jennings, W. Klyne and P. M. Scopes, *J. Chem. Soc.* 7211 (1965).
[10] H. Wolf, *Tetrahedron Letters* 1075 (1965).
[11] See, for example, K. Takeda, M. Iwasake, A. Shimaoka and H. Minato, *Tetrahedron Suppl.* **8**, 123 (1966).
[12] See also, S. D. Levine, *J. Org. Chem.* **31**, 3189 (1966).
[13] K. K. Cheung, K. H. Overton and G. A. Sim, *Chem. Comm.* 634 (1965) and Refs cited therein.

[14] H. Wolf, *Tetrahedron Letters* 5151 (1966); G. Snatzke, H. Ripperger, Chr. Horstmann and K. Schreiber, *Tetrahedron* **22**, 3103 (1966); M. Legrand and R. Bucourt, *Bull. Soc. Chim. Fr.* 2241 (1967).
[15] T. Okuda, S. Marigaya and A. Kiyomoto, *Chem. and Pharm. Bull. Japan* **12**, 504 (1964); W. Gaffield, A. C. Waiss and J. Corse, *J. Chem. Soc.* (C) 1885 (1966).
[16] K. Schaffner and G. Snatzke, *Helv. Chim. Acta* **48**, 247 (1965); C. Djerassi, W. Klyne, T. Norin, G. Ohloff and E. Klein, *Tetrahedron* **21**, 163 (1965).
[17] L. Verbit, E. Pfeil and W. Becker, *Tetrahedron Letters* 2169 (1967); see also, P. Crabbé, *Ind. Chim. Belge* **31**, 131 (1966); M. Ogama and Y. Hirose, *J. Chem. Soc. Japan* **86**, 1335 (1965).
[18] C. Djerassi, O. Halpern, V. Halpern and B. Riniker, *J. Am. Chem. Soc.* **80**, 4001 (1958).
[19] F. Burkhardt, W. Meier, A. Fuerst and T. Reichstein, *Helv. Chim. Acta* **50**, 607 (1967); See also, U. Weiss and H. Ziffer, *J. Org. Chem.* **28**, 1248 (1963); D. Arigoni, W. Jon Daehne, W. O. Godtfredsen, A. Melera and S. Vangedal, *Experientia* **20**, 344 (1964).
[20] W. R. Chan, D. R. Taylor and R. T. Alpin, *Chem. Comm.* 576 (1966).
[21] P. Crabbé, *Optical Rotatory dispersion and Circular Dichroism in Organic Chemistry*, p. 95. Holden Day, San Francisco, Calif. (1965).
[22] O. H. Emerson, *J. Am. Chem. Soc.* **73**, 2621 (1951).
[23] T. Kubota, T. Matsuura, T. Tokoroyama, T. Kamikawa and T. Matsumoto, *Tetrahedron Letters* 325 (1961).
[24] G. Snatzke, *Tetrahedron* **21**, 421 (1965).
[25] R. Hodges, S. G. McGeachin and R. A. Raphael, *J. Chem. Soc.* 2515 (1963).
[26] A. Akisanya, C. W. L. Bevan, T. G. Halsall, J. W. Powell and D. A. H. Taylor, *J. Chem. Soc.* 3705 (1961).
[27] C. W. L. Bevan, A. H. Rees and D. A. H. Taylor, *Ibid.* 983 (1963).
[28] I. J. Grant, J. A. Hamilton, R. A. Hamor, J. M. Robertson and G. A. Sim, *Ibid.* 2506 (1963).
[29] P. Witz, H. Herrmann, J. Lehn and G. Ourisson, *Bull. Soc. Chim. Fr.* 1101 (1963).
[30] D. L. Dreyer, *J. Org. Chem.* **30**, 749 (1965).
[31] D. L. Dreyer, *J. Org. Chem.* **31**, 2279 (1966).
[32] T. Kamikawa and T. Kubota, *Tetrahedron* **12**, 262 (1961).
[33] D. L. Dreyer, *Tetrahedron* **21**, 75 (1965).
[34] A. Horeau and H. B. Kagan, *Tetrahedron* **20**, 2431 (1964).
[35] A. Marquet and A. Horeau, *Bull. Soc. Chim. Fr.* 124 (1967)
[36] V. Prelog, *Helv. Chim. Acta* **36**, 308 (1953); V. Prelog and H. L. Meier, *Ibid.* 320 (1953); W. G. Dauben, D. F. Dickel, O. Jeger and V. Prelog, *Ibid.* 325 (1953).
[37] J. H. Brewster, *Tetrahedron* **13**, 106 (1961); see also, M. Miyamoto, K. Morita, Y. Kawamatsu, K. Kawashima and K. Nakanishi, *Tetrahedron* **23**, 411 (1966).
[38] J. C. Danilewicz, D. C. F. Garbutt, A. Horeau and W. Klyne, *J. Chem. Soc.* 2254 (1964).
[39] H. Conroy, *Advances in Organic Chemistry* Vol. 2; p. 311. Interscience, New York (1960).
[40] J. D. Connolly, K. L. Handa, R. McCrindle and K. H. Overton, *Chem. Comm.* 867 (1966).
[41] E. K. Adesogan and D. A. H. Taylor, *Ibid.* 379 (1967).
[42] A. Akisanya, E. O. Arene, C. W. L. Bevan, O. E. U. Ekong, M. N. Nwaji, J. I. Okogun, J. W. Powell and D. A. H. Taylor, *Ibid.* (C) 506 (1966).
[43] E. K. Adesogan, J. W. Powell and D. A. H. Taylor, *Ibid.* (C) 554 (1967).
[44] R. Henderson, R. McCrindle, K. H. Overton and A. Melera, *Tetrahedron Letters* 3969 (1964).
[45] W. R. Chan, K. E. Magnus and B. S. Mootoo, *J. Chem. Soc.* (C) 171 (1967); C. W. L. Bevan, J. W. Powell, D. A. H. Taylor, T. G. Halsall, P. Toft and M. Welford, *Ibid.* 163 (1967).
[46] R. Zelnik and C. M. Rosito, *Tetrahedron Letters* 6441 (1966); E. K. Adesogan and D. A. H. Taylor, *Chem. Comm.* 225 (1967).
[47] J. D. Connolly, R. Henderson, R. McCrindle, K. H. Overton and N. S. Bhacca, *J. Chem. Soc.* 6935 (1965).
[48] J. D. Connolly, R. McCrindle, K. H. Overton and W. D. C. Warnock, *Tetrahedron Letters* 2937 (1965).
[49] E. K. Adesogan, C. W. L. Bevan, J. W. Powell and D. A. H. Taylor, *Chem. Comm.* 27 (1966).
[50] For a review, see G. P. Moss, *Planta Medica Suppl.* 86 (1966).
[51] O. H. Emerson, *J. Am. Chem. Soc.* **74**, 688 (1952).
[52] D. H. R. Barton, S. K. Pradhan, S. Sternhell and J. F. Templeton, *J. Chem. Soc.* 255 (1961).
[53] A. Melera, K. Schaffner, D. Arigoni and O. Jeger, *Helv. Chim. Acta* **40**, 1420 (1957).
[54] T. A. Geissman and V. Tulagin, *J. Org. Chem.* **11**, 760 (1946).
[55] C. W. L. Bevan, J. W. Powell and D. A. H. Taylor, *J. Chem. Soc.* 980 (1963).