Comparison of the NMR Coupling Paths in Leucodrin and Conocarpin by Low-temperature X-Ray Structure Analysis

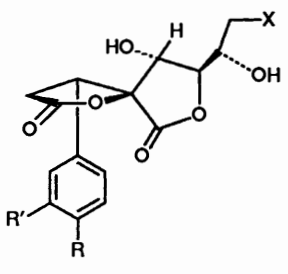
D. G. Billing, J. C. A. Boeyens,* L. Carlton, D. C. Levendis and G. W. Perold
Department of Chemistry, University of the Witwatersrand, P.O. Wits, 2050, Johannesburg, South Africa

Clear $^5J_{3\text{-H},9\text{-H}}$ couplings have been observed for four representatives of the leucodrin series of compounds, and also for their diastereoisomer, conocarpin. The relative degree of co-planarity of the six atoms involved in these couplings is discussed in terms of the detailed geometry of the leucodrin and conocarpin molecules. The importance of favourable transoid dihedral (torsion) angles along the coupling pathway, rather than co-planarity of the nuclei along the chain, is demonstrated. The solid–state ^{13}C NMR characteristics of leucodrin reflect the restricted rotation of the aromatic ring in the molecular packing pattern of the crystal lattice. The crystal structures of the diastereoisomers leucodrin and conocarpin, $C_{15}H_{16}O_8$, have been determined by single-crystal X-ray analysis, the former at both room temperature and liquid nitrogen temperature, the latter only at room temperature. The experimentally determined low-temperature hydrogen positions serve as a starting point from which to rationalize the observed five-bond NMR coupling constants in terms of the torsion angles along the chain.

The characteristic structural feature of the bislactone, leucodrin* (**1a**)[1–3] and of its diastereoisomer, conocarpin (**2**),[4] is the presence of the free spiro union[5] at atom C-5 and this gives rise to a rigid molecular framework for the bislactone portions of these molecules. It was therefore of interest to note[6] that three congeners of leucodrin, *viz.* leudrin (**1b**), its 11-bromo-11-deoxy derivative (**1c**), and its aryldimethyl ether (**1d**), showed five-bond proton–proton couplings of *ca.* 1 Hz for the six-atom chain 3a-H, C-3, C-4, C-5, C-9, 9-H in solution, while no such effect obtained for the similar chain starting from 3b-H. This effect has now been established for leucodrin (**1a**) itself, and also for conocarpin (**2**), where the corresponding value of $^5J_{3b\text{-H},9\text{-H}}$ is reduced to 0.4 Hz.

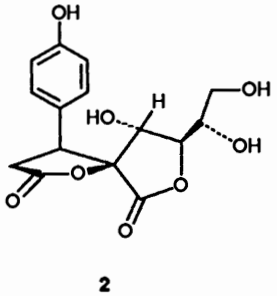
Long-range couplings of this order are well-known for conjugated unsaturated chains, or for chains containing sp^2-carbon atoms or heteroatoms, with planar disposition of the atoms[7] and have also been reported for some polycyclic saturated systems involving cyclopropane rings where planarity of the members of the chain could also be postulated;[8,9] cases of five-bond proton–proton coupling over single bonds are, however, rare.[10] The detailed geometry of these extended coupling paths has now been established for both leucodrin (**1a**) and conocarpin (**2**).† Since hydrogen atomic positions are crucial in the development of the arguments the best experimental determination is desirable. A low-temperature analysis of both structures was therefore planned, but crystals of conocarpin fracture so badly on cooling that only the room-temperature analysis has been possible in this case.

Inspection of Dreiding models of leucodrin and conocarpin molecules shows that a strong degree of puckering of the aryl-substituted lactone ring would be involved in forcing a co-planar arrangement for structure element 3-H, C-3, C-4, C-5, C-9, 9-H of these molecules. The detailed geometry of this chain of six atoms (from the X-ray diffraction data, below) shows the extent to which deviations from the mean planes of these six atoms occur for the cases of 3a-H to 9-H in the crystalline state, and they are compared (Table 1) with the similar cases of the paths from 3b-H to 9-H. Due to the rigid spiro-bislactone cages of these molecules no appreciable changes in these parameters are expected to occur in solution.

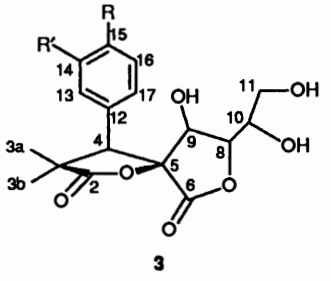


1

a R = OH, R' = H, X = OH
b R = R' = OH, X = OH
c R = R' = OH, X = Br
d R = R' = OMe, X = OH



2



3

The deviations of the six atom positions from their mean planes are rather similar in the two compounds and offer no specific rationale for the coupling effects found. The strikingly different values for the linear separation of 3-H to 9-H found for the two paths suggest conformational differences, discussed below.

The differences in torsion angles along these chains (Table 2) are, however, of direct interest. Coupling interactions over single bonds occur *via* the bonding electrons, and vicinal orbital transmissions are at a maximum when these orbitals are *trans* to each other. In a multinuclear chain the coupling effect is thus largest when these nuclei are in a planar zig-zag array. For the case of a six-atom system, three dihedral (torsion) angles of 180°

* *Systematic name:* 8-(1,2-dihydroxyethyl)-9-hydroxy-4-(*p*-hydroxyphenyl)-1,7-dioxaspiro[4.4]nonane-2,6-dione. The detailed numbering is represented in structure **3**.

† Of the remaining three members of the leucodrin series of compounds under discussion, leudrin[14,15]-dimethyl ether (**1d**) is crystalline, while the other leucodrin compounds **1b** and **1c** are not. Only leucodrin and concocarpin could, however, be obtained as single crystals suitable for X-ray crystallography.

Table 1 Distances from the mean plane for leucodrin and conocargin

	Distance/Å from the mean plane of 3-H, C-3, C-4, C-5, C-9, 9-H						Arithmetic mean	Linear separation/Å
	3-H	C-3	C-4	C-5	C-9	9-H		
Leucodrin								
3a-H	−0.385(7)	−0.362(6)	0.229(6)	−0.526(5)	0.173(5)	0.120(6)	0.30	5.055(1)
3b-H	0.331(7)	−0.509(6)	−0.140(6)	0.307(5)	0.186(5)	−0.251(5)	0.29	5.022(1)
Conocarpin								
3a-H	0.234(4)	−0.361(4)	0.265(4)	−0.308(3)	0.408(3)	−0.232(3)	0.30	3.502(1)
3b-H	0.002(4)	−0.021(4)	−0.225(4)	0.442(3)	−0.355(3)	0.114(3)	0.19	4.729(1)

Table 2 Torsion angles/° for leucodrin and conocarpin

	H(3)–C(3)–C(4)–C(5)	C(3)–C(4)–C(5)–C(9)	C(4)–C(5)–C(9)–H(9)
Leucodrin			
3a-H	144.8(6)	−155.0(5)	135.1(5)
3b-H	−93.3(5)	−155.0(5)	135.1(5)
Conocarpin			
3a-H	85.2(3)	−87.3(2)	127.1(3)
3b-H	−152.6(4)	−87.3(2)	127.1(3)

Table 3 ^{13}C Chemical shifts for leucodrin

	2	3	4	5	6	8	9	10	11	12	13	14	15	16	17
Solution (CD_3CN)[a]	175.53	34.43	42.48	90.82	173.00	81.33	70.92	70.24	62.98	125.36	131.25	116.53	158.08	116.53	131.25
Solid[b]	176	34	43	91	175	84	72	70	60	123	126	115	157	115	134

[a] δ (ppm) from TMS. [b] CP MAS spectrum, with chemical shift of C-3 equated with that of C-3 in the solution spectrum.

along a planar array would therefore offer the most favourable coupling conditions.[11]

In the case of leucodrin (**1a**) the three torsion angles for the chain 3a-H to 9-H under discussion are measured at 145°, −155° and 135° (Table 2), and, by analogy with vicinal proton–proton couplings (the Karplus equation)[12] could allow effective coupling transmission along the chain. In the case of the chain 3b-H to 9-H, the second and third torsion angles are the same as before but the first torsion element (at −94°) shows that the first σ-orbital is aligned orthogonally to the plane of the two other orbitals, so that zero (or minimal) coupling would obtain, as found experimentally.

For conocarpin the corresponding three torsion angles (Table 2) are now (in the same order, for 3b-H) −153° and −87° and 127° and (for 3a-H) 85°, −87° and 127°. These striking results indicate that location of an orthogonal torsion angle at the terminus of the six-atom chain inhibits coupling transmission, while its location midway along the chain has a lesser effect.

The ^1H and ^{13}C NMR data for leucorin and conocarpin in acetonitrile solution are given in Tables 3–5, together with the ^{13}C NMR data obtained for leucodrin in the solid state.

The ^{13}C NMR data (also in Table 3) reveal a further effect of the molecular packing in the crystal lattice in that the two *ortho*-aromatic carbon atoms C-13 and C-17 are here non-identical. The magnetic environments of these two atoms may be assessed by consideration of their spatial environment in terms of the X-ray diffraction data; they are positioned at distances of 3.04 Å (C-13) and 4.41 Å (C-17) from the midpoint of the carbon–oxygen bond of carbonyl [C(6)–O(12)] in such a way as to place C-13 in the diamagnetic shielding zone of this bond. The solid state ^{13}C NMR chemical shifts for C-13 and C-17 are thus found, respectively, to higher and to lower field of their common value in solution [where free rotation about the C(4)–C(12) bond is expected to occur], with their mean shift not significantly different from this value.

Experimental

NMR spectra were recorded on a Bruker AC200 FT spectrometer operating at 200.13 MHz (^1H) and 50.32 MHz (^{13}C). Cross-polarisation magic angle spinning (CP MAS) was carried out using a boron nitride rotor and a spinning speed of 4.1 kHz. Transients (31000) were collected with a 5 μs pulse, contact time 4 ms, acquisition time 0.09 s and recycle delay 2 s.

Leucodrin (**1a**) from *Leucadendron salignum* (ex *adscendens*)[3] crystallised from its solution in warm ethanol (96%) over a period of 3 days as well-developed near cubic crystals (edge *ca.* 0.5 mm) which were suitable for X-ray crystallographic study. Conocarpin (**2**) from *Leucospermum conocarpodendron* (L.) Buek.[4] was recrystallised from butanone overlayered with light petroleum (b.p. 60–90 °C)[13] to afford massive crystals which were suitable for X-ray crystallography.

Crystallography.—Leucodrin and conocarpin are diastereoisomers from various species of the Proteaceae family. The stereochemistry of leucodrin was demonstrated by X-ray analysis[2] of a dibromo derivative, but atomic coordinates were not disclosed. The room temperature structures of both diastereoisomers and of leucodrin at liquid nitrogen temperature, have now been determined independently by X-ray methods.

All measurements were carried out on an Enraf–Nonius CAD4 single-crystal diffractometer equipped with an incident-

Table 4 ^{1}H Chemical shifts (CD_3CN solution)[a] for leucodrin and conocarpin

3a	3b	4	8[b]	9	10[b]	11a	11b	13	14	16	17	9-OH	10-OH	11-OH	15-OH
Leucodrin															
2.83	3.14	4.35	~3.59	4.69	~3.59	3.43	3.31	7.24	6.79	6.79	7.24	~4.5 (broad)	~3.3 (broad)	~3.3 (broad)	~7 (broad)
Conocarpin															
3.44	2.76	3.92	3.23	4.58	(3.5–3.16, broad)[c]			7.21	6.78	6.78	7.21	4.13	3.50–3.16[c]	2.90	7.08

[a] δ (ppm) from TMS. [b] The chemical shifts of 8-H and 10-H lie within a range of 5 Hz, giving a strongly second order coupling pattern. [c] The chemical shifts of 10-H, 11a-H, 11b-H and 10-OH lie within a range of 1.7 ppm giving broad unresolved signals.

Table 5 Proton–proton coupling constants J_{H-H}/Hz [a] for leucodrin and conocarpin

	3a–3b	3a–4	3a–9	3b–9	3b–4	8–9	8–10	10–11a	11–11b	11a–11b
Leucodrin	−17.4	8.8	0.8	—	12.6	8.2	—	6.1	6.6	−11.0
Conocarpin	−16.7	13.2	—	0.4	7.8	8.8	3.0	—	—	—

[a] A dash (—) in Table 5 indicates that the coupling constant could not be measured under the conditions used to obtain the spectrum.

Table 6 Crystal data and details of crystallographic refinement

	Conocarpin	Leucodrin	Leucodrin (100 K)
Formula	$C_{15}H_{16}O_8$	$C_{15}H_{16}O_8$	$C_{15}H_{16}O_8$
M_r	324.29	324.29	324.29
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a/Å	6.0657(5)	6.079(1)	6.0196(8)
b/Å	13.021(1)	9.047(1)	8.9827(9)
c/Å	18.772(1)	25.789(3)	25.645(1)
V/Å^3	1482.64	1418.28	1386.284
D_c/g cm^{-3}	1.453	1.519	1.553
Z	4	4	4
F(000)	680	680	680
Radiation	Mo-Kα	Cu-Kα	Mo-Kα
μ	0.76	9.59	0.81
Scan	ω–2θ	ω–2θ	ω–2θ
Vertical aperture/mm	4	4	4
Horizontal aperture/mm	1.5	1.5	1.3
Max. scan speed/° min^{-1}	5.49	5.49	5.49
Range/°	$3 \leqslant \theta \leqslant 28$	$3 \leqslant \theta \leqslant 65$	$3 \leqslant \theta \leqslant 46$
h	−8 ⟶ 8	0 ⟶ 7	−2 ⟶ 11
k	0 ⟶ 17	0 ⟶ 10	−3 ⟶ 17
l	0 ⟶ 24	0 ⟶ 30	−4 ⟶ 48
Measured data	3494	1434	8691
Observed unique data	3270	1424	7268
$F_o \leqslant n\sigma(F_o)$	4	2	4
LS parameters	221	221	257
Max. $\Delta x/\sigma$	0.89	0.090	0.002
R	0.049	0.051	0.040
R_w, $w\alpha l/\sigma^2(F)$	0.046	0.050	0.039
Residual density/e Å^{-3}			
Max.	0.51	0.33	0.94
Min.	−0.50	−0.30	−0.52

beam graphite crystal monochromator. The low-temperature (*ca.* 100 K) data were obtained by immersion of the crystal in a constant stream of nitrogen gas from boiling nitrogen. The temperature was not monitored for the room-temperature measurements. Cell constants were refined by least-squares on the basis of optimised setting angles of 25 reflections measured at four equivalent positions each. Data reduction consisted of correction for background, Lp factors and absorption, by an empirical method.[14] The structures were solved by direct methods and refined by full-matrix least-squares using the set of SHELX programs[15] for all computations. Numerical detail related to cell data and structure refinement is collated in Table 6. Refined atomic coordinates and selected bond lengths and angles are given in Tables 7–15. Stereoscopic drawings of the molecules are shown in Fig. 1. Absolute structures could not be refined with confidence, but the known stereochemistry in each case gave a somewhat better numerical fit with the measured data, in least-square refinement. Full lists of bond lengths, bond angles, hydrogen atom coordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC).*

The most interesting aspect of the series of analyses is the comparison of the room temperature and low temperature

* For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1991, in the January issue.

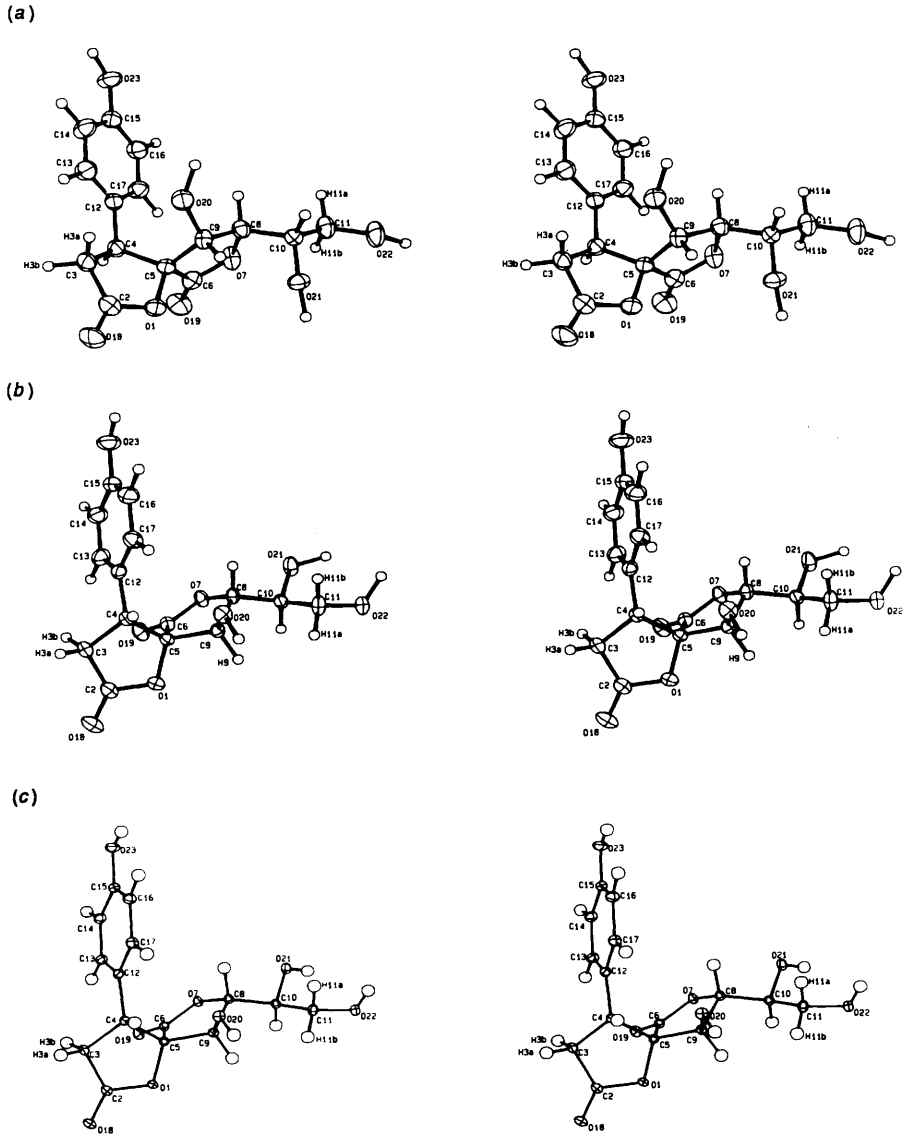


Fig. 1 Stereoscopic diagrams to define the numbering scheme and molecular conformation of (*a*) conocarpin, (*b*) and (*c*) the low temperature leucodrin structure

Table 7 Fractional atomic co-ordinates (× 10^4) for conocarpin

	x/a	*y/b*	*z/c*
O(1)	2503(3)	182(1)	7298(1)
O(7)	5793(3)	2028(2)	7994(1)
O(18)	521(4)	−944(1)	6697(1)
O(19)	7079(3)	678(2)	7391(1)
O(20)	527(3)	2584(1)	7264(1)
O(21)	3085(3)	1648(1)	9157(1)
O(22)	4636(3)	3342(2)	9995(1)
O(23)	3839(4)	5453(1)	5334(1)
C(2)	1341(5)	−104(2)	6724(2)
C(3)	1316(5)	728(2)	6181(1)
C(4)	3332(5)	1362(2)	6389(1)
C(5)	3296(4)	1235(2)	7208(1)
C(6)	5614(5)	1244(2)	7530(1)
C(8)	3705(4)	2584(2)	8079(1)
C(9)	1954(4)	1963(2)	7673(1)
C(10)	3265(5)	2657(2)	8874(1)
C(11)	5059(5)	3264(2)	9246(1)
C(12)	3479(5)	2456(2)	6096(1)
C(13)	1846(5)	2852(2)	5655(2)
C(14)	1996(5)	3853(2)	5400(2)
C(15)	3772(5)	4465(2)	5592(1)
C(16)	5423(5)	4074(2)	6018(2)
C(17)	5274(5)	3072(2)	6266(1)

Table 8 Selected bond lengths/Å for conocarpin

C(2)–O(1)	1.340(3)	C(5)–O(1)	1.464(3)
C(6)–O(7)	1.346(3)	C(8)–O(7)	1.467(3)
C(2)–O(18)	1.202(3)	C(6)–O(19)	1.183(3)
C(9)–O(20)	1.411(3)	C(10)–O(21)	1.422(3)
C(11)–O(22)	1.433(3)	C(15)–O(23)	1.375(3)
C(3)–C(2)	1.487(3)	C(4)–C(3)	1.526(4)
C(5)–C(4)	1.546(3)	C(12)–C(4)	1.530(3)
C(6)–C(5)	1.530(4)	C(9)–C(5)	1.524(3)
C(9)–C(8)	1.537(3)	C(10)–C(8)	1.520(3)
C(11)–C(10)	1.515(3)	C(13)–C(12)	1.390(4)
C(17)–C(12)	1.389(4)	C(14)–C(13)	1.392(4)
C(15)–C(14)	1.387(4)	C(16)–C(15)	1.380(4)
C(17)–C(16)	1.388(3)		

structures of leucodrin. The most convenient comparison is obtained by overlaying transparencies of the structural diagrams of Fig. 1. The overlay is almost exact, and the only obvious differences are in the hydrogen positions of the hydroxy groups. It is noted that these have been determined experimentally in the low-temperature analyses and calculated geometrically for the ambient structure. The measured O–H bond lengths are uniformly shorter than the 1.08 Å assumed in the geometrical calculation, at an average of 0.73(1) Å, whereas

Table 9 Selected bond angles/° for conocarpin

C(5)–O(1)–C(2)	109.9(2)	C(8)–O(7)–C(6)	112.0(2)
O(18)–C(2)–O(1)	120.3(3)	C(3)–C(2)–O(1)	110.7(2)
C(3)–C(2)–O(18)	129.0(3)	C(4)–C(3)–C(2)	102.2(2)
C(5)–C(4)–C(3)	100.7(2)	C(12)–C(4)–C(3)	117.3(2)
C(12)–C(4)–C(5)	117.2(2)	C(4)–C(5)–O(1)	102.7(2)
C(6)–C(5)–O(1)	105.3(2)	C(6)–C(5)–C(4)	112.3(2)
C(9)–C(5)–O(1)	109.9(2)	C(9)–C(5)–C(4)	120.7(2)
C(9)–C(5)–C(6)	105.1(2)	O(19)–C(6)–O(7)	123.6(3)
C(5)–C(6)–O(7)	109.6(2)	C(5)–C(6)–O(19)	126.8(3)
C(9)–C(8)–O(7)	106.4(2)	C(10)–C(8)–O(7)	106.8(2)
C(10)–C(8)–C(9)	113.5(2)	C(5)–C(9)–O(20)	111.9(2)
C(8)–C(9)–O(20)	113.1(2)	C(8)–C(9)–C(5)	104.0(2)
C(8)–C(10)–O(21)	108.8(2)	C(11)–C(10)–O(21)	111.4(2)
C(11)–C(10)–C(8)	111.1(2)	C(10)–C(11)–O(22)	111.2(2)
C(13)–C(12)–C(4)	121.2(3)	C(17)–C(12)–C(4)	120.1(3)
C(17)–C(12)–C(13)	118.8(2)	C(14)–C(13)–C(12)	120.4(3)
C(15)–C(14)–C(13)	119.9(3)	C(14)–C(15)–O(23)	117.9(3)
C(16)–C(15)–O(23)	121.9(3)	C(16)–C(15)–C(14)	120.2(2)
C(17)–C(16)–C(15)	119.6(3)	C(16)–C(17)–C(12)	121.1(3)

Table 10 Fractional atomic co-ordinates (× 10^4) for leucodrin

	x/a	*y/b*	*z/c*
O(1)	−3 536(5)	5 893(3)	8 021(1)
O(7)	1 265(5)	4 155(3)	8 406(1)
O(18)	−5 029(5)	8 141(3)	7 933(1)
O(19)	922(5)	6 569(3)	8 276(1)
O(20)	−4 007(5)	2 682(3)	8 667(1)
O(21)	2 747(5)	1 161(3)	8 289(1)
O(22)	178(6)	−735(3)	7 745(1)
O(23)	2 295(6)	4 492(4)	10 650(1)
C(2)	−4 254(7)	7 217(4)	8 213(2)
C(3)	−3 884(9)	7 275(5)	8 789(2)
C(4)	−3 312(7)	5 664(4)	8 935(1)
C(5)	−2 365(7)	5 075(4)	8 412(1)
C(6)	80(8)	5 386(4)	8 346(2)
C(8)	−168(7)	2 869(4)	8 453(2)
C(9)	−2 510(7)	3 408(4)	8 327(2)
C(10)	686(7)	1 681(4)	8 086(2)
C(11)	−879(8)	382(4)	8 046(2)
C(12)	−1 853(7)	5 426(4)	9 403(2)
C(13)	112(9)	6 202(5)	9 485(2)
C(14)	1 479(9)	5 893(5)	9 903(2)
C(15)	882(8)	4 778(5)	10 249(2)
C(16)	−1 127(9)	4 044(5)	10 193(2)
C(17)	−2 437(8)	4 346(5)	9 767(2)

Table 11 Selected bond lengths/Å for leucodrin

C(2)–O(1)	1.368(5)	C(5)–O(1)	1.439(5)
C(6)–O(7)	1.335(5)	C(8)–O(7)	1.458(4)
C(2)–O(18)	1.201(5)	C(6)–O(19)	1.200(5)
C(9)–O(20)	1.424(5)	C(10)–O(21)	1.437(5)
C(11)–O(22)	1.427(5)	C(15)–O(23)	1.370(5)
C(3)–C(2)	1.503(5)	C(4)–C(3)	1.545(5)
C(5)–C(4)	1.559(5)	C(12)–C(4)	1.515(5)
C(6)–C(5)	1.523(6)	C(9)–C(5)	1.526(5)
C(9)–C(8)	1.540(6)	C(10)–C(8)	1.525(5)
C(11)–C(10)	1.515(6)	C(13)–C(12)	1.401(6)
C(17)–C(12)	1.399(5)	C(14)–C(13)	1.390(6)
C(15)–C(14)	1.395(6)	C(16)–C(15)	1.398(7)
C(17)–C(16)	1.384(6)		

Table 12 Selected bond angles/° for leucodrin

C(5)–O(1)–C(2)	110.8(3)	C(8)–O(7)–C(6)	110.7(3)
O(18)–C(2)–O(1)	121.2(4)	C(3)–C(2)–O(1)	109.9(3)
C(3)–C(2)–O(18)	129.0(4)	C(4)–C(3)–C(2)	104.0(3)
C(5)–C(4)–C(3)	101.3(3)	C(12)–C(4)–C(3)	117.4(3)
C(12)–C(4)–C(5)	115.2(3)	C(4)–C(5)–O(1)	104.3(3)
C(6)–C(5)–O(1)	108.0(3)	C(6)–C(5)–C(4)	113.2(3)
C(9)–C(5)–O(1)	112.2(3)	C(9)–C(5)–C(4)	116.2(3)
C(9)–C(5)–C(6)	102.9(4)	O(19)–C(6)–O(7)	122.1(4)
C(5)–C(6)–O(7)	111.0(3)	C(5)–C(6)–O(19)	126.8(4)
C(9)–C(8)–O(7)	106.4(3)	C(10)–C(8)–O(7)	107.9(3)
C(10)–C(8)–C(9)	114.0(3)	C(5)–C(9)–O(20)	113.8(3)
C(8)–C(9)–O(20)	108.3(3)	C(8)–C(9)–C(5)	103.2(3)
C(8)–C(10)–O(21)	107.5(3)	C(11)–C(10)–O(21)	108.6(3)
C(11)–C(10)–C(8)	112.0(4)	C(10)–C(11)–O(22)	107.6(4)
C(13)–C(12)–C(4)	123.2(4)	C(17)–C(12)–C(4)	119.0(4)
C(17)–C(12)–C(13)	117.8(4)	C(14)–C(13)–C(12)	121.7(4)
C(15)–C(14)–C(13)	119.1(5)	C(14)–C(15)–O(23)	117.2(4)
C(16)–C(15)–O(23)	122.4(4)	C(16)–C(15)–C(14)	120.3(4)
C(17)–C(16)–C(15)	119.4(4)	C(16)–C(17)–C(12)	121.5(4)

Table 13 Fractional atomic co-ordinates (× 10^5) for leucodrin (100 K)

	x/a	*y/b*	*z/c*
O(1)	−35 359(13)	59 653(8)	80 199(3)
O(7)	13 261(12)	42 097(8)	84 063(3)
O(18)	−50 139(14)	82 363(9)	79 364(3)
O(19)	9 770(13)	66 436(8)	82 682(3)
O(20)	−39 747(13)	27 174(9)	86 768(3)
O(21)	27 777(13)	11 411(8)	83 056(3)
O(22)	1 848(15)	−6 967(9)	77 243(3)
O(23)	24 307(16)	44 398(10)	106 475(3)
C(2)	−42 413(17)	72 957(11)	82 168(4)
C(3)	−38 550(20)	73 387(11)	87 979(4)
C(4)	−32 838(17)	57 241(11)	89 399(4)
C(5)	−23 550(17)	51 366(10)	84 128(4)
C(6)	1 292(17)	54 468(11)	83 474(4)
C(8)	−1 124(17)	29 084(10)	84 514(4)
C(9)	−24 963(17)	34 473(11)	83 326(4)
C(10)	7 532(17)	17 078(11)	80 878(4)
C(11)	−8 740(18)	4 209(11)	80 260(4)
C(12)	−18 096(18)	54 605(11)	94 090(4)
C(13)	1 968(19)	62 260(12)	94 883(4)
C(14)	15 857(19)	58 755(13)	99 022(4)
C(15)	9 870(19)	47 567(12)	102 535(4)
C(16)	−10 463(20)	40 402(12)	101 960(4)
C(17)	−24 094(19)	43 811(12)	97 745(4)

Table 14 Selected bond lengths/Å for leucodrin (100 K)

C(2)–O(1)	1.365(1)	C(5)–O(1)	1.440(1)
C(6)–O(7)	1.333(1)	C(8)–O(7)	1.459(1)
C(2)–O(18)	1.203(1)	C(6)–O(19)	1.207(1)
C(9)–O(20)	1.415(1)	C(10)–O(21)	1.434(1)
C(11)–O(22)	1.419(1)	C(15)–O(23)	1.363(1)
C(3)–C(2)	1.509(1)	C(4)–C(3)	1.535(1)
C(5)–C(4)	1.555(1)	C(12)–C(4)	1.514(1)
C(6)–C(5)	1.530(1)	C(9)–C(5)	1.534(1)
C(9)–C(8)	1.545(1)	C(10)–C(8)	1.518(1)
C(11)–C(10)	1.524(1)	C(13)–C(12)	1.405(1)
C(17)–C(12)	1.396(1)	C(14)–C(13)	1.387(1)
C(15)–C(14)	1.397(1)	C(16)–C(15)	1.391(2)
C(17)–C(16)	1.391(1)		

the measured C–O–H angles, on average 107(1)°, are less than the 114° assumed for the calculation. The calculated hydrogen positions of importance with respect to the five-bond coupling of interest, from C(3)–C(9) are therefore not in doubt. Comparison of the room-temperature structures of leucodrin and conocarpin should therefore be sufficiently reliable to account for the differences in observed coupling constants.

The single most important factor that affects the coupling between remote protons is the magnitude of the torsion angles along the connecting chain. The three torsion angles along the H(3a)–H(9) chain for leucodrin and conocarpin, respectively, are 145°, −155°, 135° and 85°, −87°, 127°. Only leucodrin had a measurable coupling constant of 0.8 Hz. On the other hand, a 3b–9 coupling of 0.4 Hz could be measured only in the case of conocarpin, with torsion angles of −153° −87°, 127°, compared to −94°, −155°, 135° for leucodrin. The message is clear: any torsion angle that approaches 90° reduces the

Table 15 Selected bond angles/° for leucodrin (100 K)

C(5)–O(1)–C(2)	110.3(1)	C(8)–O(7)–C(6)	110.9(1)
O(18)–C(2)–O(1)	120.9(1)	C(3)–C(2)–O(1)	109.9(1)
C(3)–C(2)–O(18)	129.2(1)	C(4)–C(3)–C(2)	104.2(1)
C(5)–C(4)–C(3)	101.2(1)	C(12)–C(4)–C(3)	117.9(1)
C(12)–C(4)–C(5)	115.3(1)	C(4)–C(5)–O(1)	104.8(1)
C(6)–C(5)–O(1)	108.1(1)	C(6)–C(5)–C(4)	112.6(1)
C(9)–C(5)–O(1)	113.0(1)	C(9)–C(5)–C(4)	115.6(1)
C(9)–C(5)–C(6)	102.7(1)	O(19)–C(6)–O(7)	122.2(1)
C(5)–C(6)–O(7)	111.3(1)	C(5)–C(6)–O(19)	126.4(1)
C(9)–C(8)–O(7)	106.5(1)	C(10)–C(8)–O(7)	108.5(1)
C(10)–C(8)–C(9)	114.9(1)	C(5)–C(9)–O(20)	114.2(1)
C(8)–C(9)–O(20)	108.4(1)	C(8)–C(9)–C(5)	103.4(1)
C(8)–C(10)–O(21)	107.7(1)	C(11)–C(10)–O(21)	108.5(1)
C(11)–C(10)–C(8)	112.5(1)	C(10)–C(11)–O(22)	107.8(1)
C(13)–C(12)–C(4)	122.9(1)	C(17)–C(12)–C(4)	119.4(1)
C(17)–C(12)–C(13)	117.7(1)	C(14)–C(13)–C(12)	121.2(1)
C(15)–C(14)–C(13)	120.1(1)	C(14)–C(15)–O(23)	117.6(1)
C(16)–C(15)–O(23)	122.9(1)	C(16)–C(15)–C(14)	119.5(1)
C(17)–C(16)–C(15)	120.0(1)	C(16)–C(17)–C(12)	121.5(1)

coupling constant—when it involves one of the protons directly the effect is enhanced and the coupling becomes too small to measure.

It is commonly assumed that the planarity of the coupling path determines the degree of coupling. The calculated mean planes through the fragments of interest in the present case, however, have no rational relationship with the observed coupling constants. In the case of leucodrin the mean atomic deviation from the best plane through the relevant six-atom fragments is identical for 3a–9 and 3b–9 and the linear separation between the end members is 5.0 Å in both cases. The deviations from planarity in conocarpin is of the same order as in leucodrin but the distance between end members, d[H(3a)–H(9)] = 3.5 Å, d[H(3b)–H(9)] = 4.7 Å is noticeably different. This difference is due to conformational differences between corresponding five-membered rings in the two compounds.

Ring conformations are compared quantitatively as linear combination of primitive forms[16] in terms of normalized coefficients and the integers k that identify the phases of contributing forms of N-membered rings as $\varphi = k\pi/2N$. (Evans and Boeyens, 1989.) For five-membered rings the two primitive forms are envelope and twist conformations. In terms of this terminology the central five-membered rings [O(1)–C(2)–C(3)–C(4)–C(5)] have closely related conformations of $29E(16)71T(17)$ and $84E(16)16T(17)$ for leucodrin and conocarpin, respectively, whereas the outside rings [O(7)–C(8)–C(9)–C(5)–C(6)–C(7)] with conformations of $14E(14)86T(15)$ and $44E(4)56T(5)$ are enantiomers, according to the numbering adopted here.

Because of the presence of several hydroxy and carbonyl groups on these molecules a variety of intermolecular hydrogen bonds is expected in the solid state. Several such possibilities are observed, but only in the case of the low temperature leucodrin structure has any attempt been made to identify hydrogen bonds in terms of non-bonded O ··· H contacts. The only contact <2 Å, between O(21) ··· H(20) (d = 1.75 Å) can be so interpreted with confidence. Other possibilities are represented by the contacts d[O(20) ··· H(23)] = 2.00 Å, d[O(19) ··· H(22)] = 2.07 Å.

References

1 G. W. Perold and K. G. R. Pachler, *Proc. Chem. Soc., London*, 1964, 62.
2 R. D. Diamand and D. Rogers, *Proc. Chem. Soc., London*, 1964, 63.
3 G. W. Perold and K. G. R. Pachler, *J. Chem. Soc. C*, 1966, 1918.
4 P. E. J. Kruger and G. W. Perold, *J. Chem. Soc. C*, 1970, 2127.
5 *IUPAC: Nomenclature of Organic Chemistry*, 3rd edn., Butterworths, London, 1971, p. 37.
6 G. W. Perold, L. Carlton, A. S. Howard and J. P. Michael, *J. Chem. Soc., Perkin Trans. 1*, 1988, 881.
7 L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance in Organic Chemistry*, 2nd edn., Pergamon, Oxford, 1969, p. 333.
8 K. Tori and M. Ohtsura, *J. Chem. Soc., Chem. Commun.*, 1966, 886.
9 R. M. Coates and J. L. Kirkpatrick, *J. Am. Chem. Soc.*, 1968, **90**, 4162.
10 L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance in Organic Chemistry*, 2nd edn., Pergamon, Oxford, 1969, p. 342.
11 R. K. Harris, *Nuclear Magnetic Resonance—A Physicochemical View*, Pitman, London, 1983, p. 224.
12 J. W. Akitt, *NMR and Chemistry*, 2nd edn., Chapman and Hall, London, 1983, p. 31.
13 P. G. Jones, *Chem. Br.*, 1981, **17**, 222.
14 A. C. T. North, D. C. Phillips, F. Mathews, *Acta Crystallogr., Sect. A*, 1968, **24**, 351.
15 G. M. Sheldrick in *Crystallographic Computing 3*, eds. G. M. Sheldrick, C. Krüger and R. Goddard, Oxford University Press, 1985.
16 D. G. Evans and J. C. A. Boeyens, *Acta Crystallogr., Sect. B*, 1989, **45**, 581.

Paper 0/04351F
Received 26*th September* 1990
Accepted 4*th December* 1990