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MANICOL : A SESQUITERPENOID HYDROXYTROPOLONE FROM DULACIA GUIANENSIS ; A REVISED STRUCTURE (X-RAY ANALYSIS)

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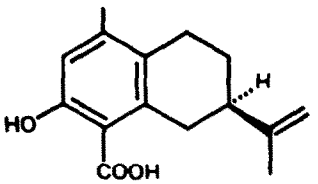
Abstract - Manicol, isolated from Dulacia guianensis and for which structure 1 was previously proposed, was shown to be the sesquiterpenoid hydroxytropolone 5. This revised structure was established by X-ray analysis of manicol and its diacetate 4. Methylation of manicol afforded three dimethyl ethers which were differentiated mainly by ^{13}C nmr spectroscopy including the heteronuclear spin population inversion method. The major methylated product 6 was shown to undergo a LAH rearrangement leading to the benzylic alcohol 9a which was subsequently converted to the methyl ether 10.

Structure 1 was proposed[1] for manicol, $C_{15}H_{18}O_3$, an aromatic sesquiterpene isolated from the root bark of a Guyanan tree Dulacia guianensis (Olacaceae). The structure assignment was based on spectroscopic data (MS, ^1H nmr, ^{13}C nmr) and on comparison of the transformation products obtained from both manicol and the ketol 2 (originally prepared from (+)-dihydrocarvone). Thus, the ketol 2 was converted by standard reactions to the O-methyl ether 3a $C_{16}H_{24}O$. On the other hand, the dimethoxy derivative of manicol (obtained by treatment with CH_2N_2) was reduced by lithium aluminium hydride to a benzylic alcohol which was transformed to an O-methyl ether, $C_{16}H_{24}O$. The tlc, ^1H nmr and $[\alpha]_D$ of the latter were identical with those of the methyl ether 3a, and the compounds were thought to be identical. At this point it should be mentioned that the regioisomer 10 would display these same properties.

Whilst preparing various derivatives of manicol for biological tests, we endeavoured to prepare its monoacetate. All acetylation experiments led to a diacetate, $C_{19}H_{22}O_5$. This unexpected behaviour prompted us to reinvestigate the structure of manicol. The crystalline diacetate was submitted to an X-ray analysis which showed that the compound was a diacetate of a hydroxytropolone, 4. The molecular structure of 4 is shown in Figure 1b.

Diacetate 4, m.p. 89-90°, $[\alpha]_D^{21°}$ +129.1° (c=1.01, chloroform) $C_{19}H_{22}O_5$, UV (EtOH) : λ_{max} 244 (ε 27,600) and 330 nm (ε 6,900), has a molecular ion at m/z 330 with a base peak at m/z 246 (M^+-2 x 42). The 400 MHz ^1H nmr data are presented in Table 1. Under ordinary recording conditions, the room temperature 100.6 MHz ^{13}C nmr spectrum in $CDCl_3$ solution shows the expected signals in the high field region whereas the low field region shows only nine



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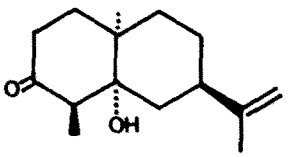

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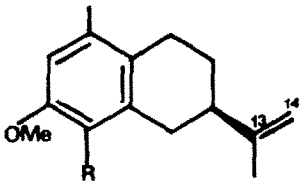
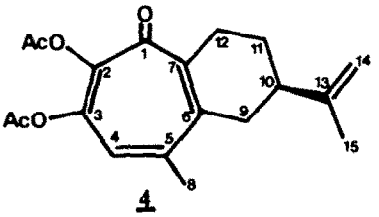
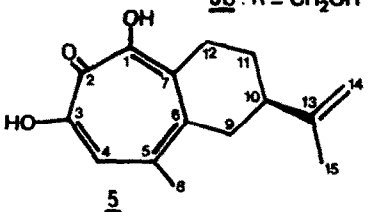


3a : R = Me ; 13,14 dihydro
3b : R = CH_2OH



4



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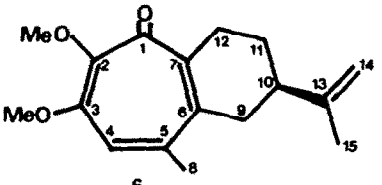

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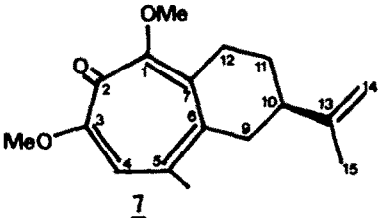

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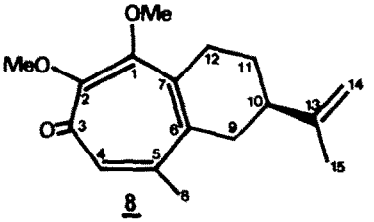

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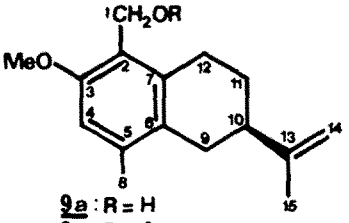
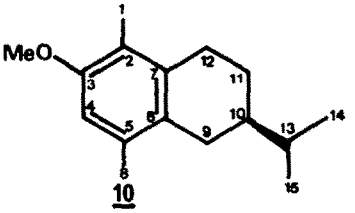


9a : R = H
9b : R = Ac



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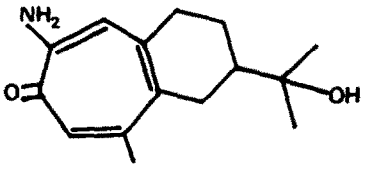

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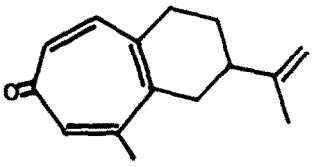


12

instead of the eleven signals for the unsaturated carbon atoms (Table 2). This indicates a fast exchange of the acetyl group between the oxygen atoms on the tropolone ring, a known exchange process of tropolone acetates[2]. The slow exchange spectrum was not observed down to -25°C. This intramolecular acetyl migration is also reflected in the ^{1}H nmr when recorded at 0°C and -25°C where signals, especially the H-4 resonance, are increasingly broadened.

The diacetate 4 on refluxing with methanol gives the starting material. Treatment of 4 with m-chloroperbenzoic acid afforded the 13,14-epoxide, m.p. 114-116°, $C_{19}H_{22}O_6$, (M^+ 346.1426). Its ^{1}H nmr spectrum showed clearly that the oxidation product was a 1:1 mixture of α and β stereoisomeric epoxides. Subsequent hydrolysis with boiling methanol gave a similar mixture of 13,14-epoxides of manicol, m.p. 167-169°, $C_{15}H_{18}O_4$.

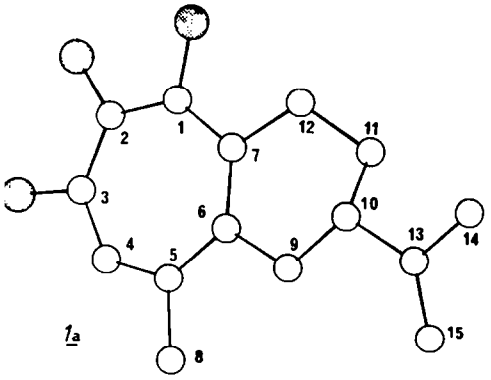
A large thermal disorder prevented a correct refinement of the X-ray structure of the diacetate 4 (vide supra). An X-ray analysis was therefore carried out on manicol itself which proved unambiguously to be the α-hydroxytropolone 5* and not the benzenoid compound 1. The molecular structure of 5 is shown in Figure 1a. Structure 5 accounts for the yellow colouration of manicol, its UV spectrum and for the saturation of four double bonds on catalytic hydrogenation (Pd-C)[1].

In the light of the new structure 5 the reported formation of a benzylic alcohol by LAH reduction of the dimethoxy derivative of manicol had to be reexamined. A detailed study of methylation of manicol was first undertaken.

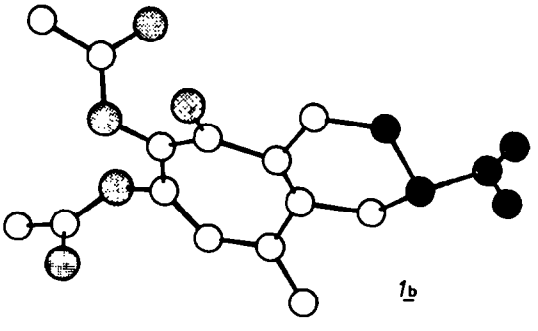
Dimethyl ethers. Treatment of manicol 5 with diazomethane yields three dimethoxy derivatives 6, 7 and 8, $C_{17}H_{22}O_3$, which were isolated as yellow oils by careful silica gel column chromatography in the proportion 6:3:1. The three methyl ethers have close UV spectra : λ_{max} 257 (ε 20,555) 333 nm (ε 5,800). IR spectra, 6 : 1640 (sh), 1610 (sh), 1550, 1450 cm^{-1} ; 8 : 1640 (sh), 1605, 1545, 1440 cm^{-1} ; 7 : 1630 (sh), 1570cm^{-1}.

Bagli et al[3] have shown the usefulness of ^{13}C nmr spectroscopy to distinguish between various isomers in the 2-methoxytropone family and reported on the additivity of substituent effects on the chemical shifts for a number of dimethoxytropone derivatives. This approach was applied to distinguish the three regioisomers 6, 7 and 8. In addition, the heteronuclear spin population inversion technique (SPI)[4],

*For convenience the numbering of the tropolone ring is as for the acetate 4.



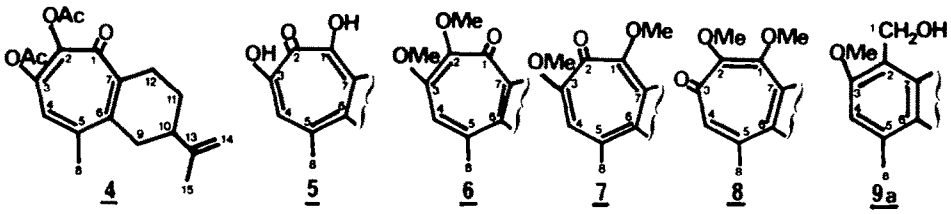
1a



1b

Fig. 1a : Molecular structure of manicol 5. Fig. 1b : Molecular structure of the diacetate 4. Dotted circles denote oxygen atoms and the black circles denote the carbon atoms refined in a rigid group.

400 MHz ^{1}H NMR DATA (TABLE 1) and 100.61 MHz ^{13}C NMR SPECTRA (TABLE 2) of COMPOUNDS 4, 5, 6, 7, 8 and 9a



4 5 6 7 8 9a

TABLE 1

Hydrogens	4	5	6	7	8	9a
H-4	6.84	7.42	6.75	6.73	7.02	6.59
$=CH_2$	4.74 4.79	4.76 4.81	4.75 4.80	4.74 4.78	4.74 4.79	4.76 4.79
$-CH_2OH$	-	-	-	-	-	4.69
OMe	-	-	3.81 3.90	3.82 3.90	3.82 3.85	3.81
Ac	2.33 2.33	-	-	-	-	-
Me-8	2.30	2.41	2.30	2.38	2.26	2.22
Me-15	1.78	1.82	1.80	1.80	1.79	1.80

TABLE 2

Carbons								
C-1			156.0[a]	181.8	159.4	155.0	56.4	t
C-2	148.2[a]	s	163.7	149.7[a]	172.9	159.4	124.1	s
C-3	145.6[a]	s	157.7[a]	155.5[a]	160.3	180.5	155.5	s
C-4	128.6	d	123.7	123.2	118.0	136.8	110.4	d
C-5			134.2[b]	140.2[b]	136.1[a]	139.0[a]	137.1	s
C-6	144.5 141.9	s	138.4[b]	142.0[b]	136.7[a]	139.1[a]	127.8	s
C-7			141.4	146.2	141.3	146.0	136.1	s
C-8	26.2	q	26.9	25.9	26.5	25.9	20.1	q
C-9	29.2[b]	t	28.5[c]	29.1[c]	28.2[b]	28.6[b]	27.7[a]	t
C-10	40.3	d	40.7	40.6	40.5	40.4	41.4	d
C-11	26.2	t	26.1	26.6	26.5	26.6	26.9	t
C-12	36.9[b]	t	37.5[c]	36.1[c]	36.4[b]	36.3[b]	32.3[a]	t
C-13	148.2	s	148.5	148.6	148.8	148.3	149.7	s
C-14	110.0	t	109.8	109.5	109.5	109.6	109.0	t
C-15	20.5	q	20.9	20.6	20.7	20.6	20.7	q
OCH_3				59.1 58.3	56.0 56.0	60.8 59.2	55.5	q
$CH_3\underline{CO}$	167.8 167.5	s						
$\underline{CH_3}CO$	20.7 20.6	q						

[a-c] Signals within any vertical column may be reversed.

which enables to observe long range ^{13}C-^{1}H couplings, was utilised for the assignment of several resonances. It has been shown[5,6,7] that the $^{4}J(\underline{C}CCC\underline{H})$ couplings are very small with respect to the $^{3}J(\underline{C}CC\underline{H})$ and $^{2}J(\underline{C}C\underline{H})$ couplings found for certain carbon atoms of this type of compounds.

The ^{13}C nmr spectra of the three dimethyl ethers are given in Table 2. The assignments of the resonances due to the carbonyl and to the carbon atoms C-4, C-8, C-10, C-11, C-13, C-14 and C-15 are straightforward and further confirmed as shown below. Comparison of the chemical shifts with those reported[3] for 2,3-dimethoxy (X) and 2,7-dimethoxytropone (Y)* was most informative. The structure 7 was assigned because of the upfield carbonyl resonance which resembled that of 2,7-dimethoxytropone (173.7 ppm). The chemical shift of the carbon α to the methoxyl in the latter is also similar to that of C-4 in 7. Furthermore, the C-4 resonances in 6 and 8 are in the same range as the values quoted for the related carbon atoms in the reference compound (X) (127.8 ppm and 140.5 ppm).

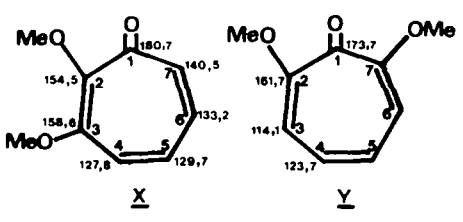
The SPI technique afforded the following information : the two methyl groups in the three dimethyl ethers were readily differentiated. Individual selective proton irradiation of the C-8 and C-15 methyl groups showed long range coupling $^{3}J(\underline{C}CC\underline{H})$ with H-4 in the former case only, whereas a $^{2}J(\underline{C}C\underline{H})$ coupling with C-13 was seen with the latter, thus confirming the assignment of the C-13 resonance.

Selective irradiation at H-4 perturbs, as expected, the C-8 methyl group and modifies the CO resonance in compounds 7 and 8 but not in the dimethyl ether 6 ; this fact proves the assigned structure 6 for the predominant isomer. Also, only structure 6 has both methoxyl resonances modified by irradiation of H-4. The observed long range coupling with H-4 allows also to distinguish between the two methoxyls in compounds 7 and 8. Out of the three quaternary carbons (C-5, C-6 and C-7) on the tropolone ring only one resonance is not modified by selective irradiation of H-4 or of 8-CH_3 and therefore is attributed to C-7. The resonances of C-5 and C-6 can be interchanged.

The 400 MHz ^{1}H nmr data of the regioisomers 6, 7 and 8 are presented in Table 1.

Lithium aluminium hydride rearrangement : Treatment of the major dimethyl ether 6 with LAH afforded, in 68% yield, the crystalline benzylic alcohol 9a. Its structure was established on the following evidence :

The molecular formula was found to be $C_{15}H_{22}O_2$. IR ($CHCl_3$) : ν_{max} 3590 (OH), 1640, 1595, 1578 cm^{-1}. The alcohol 9a showed a benzenoid-type UV spectrum [end absorption 210 nm, λ_{max} 284 (ε 1936), 292 nm (ε 2056)]. The 400 MHz ^{1}H nmr spectrum (Table 1) reveals two methyl groups, a $-\underline{C}(=CH_2)$ group, one aromatic hydrogen, only one methoxyl and a singlet (δ 4.69, 2H) due to a primary alcohol function. Acetylation affords a crystalline monoacetate 9b $C_{18}H_{24}O_3$, the ^{1}H nmr of which shows a



X Y

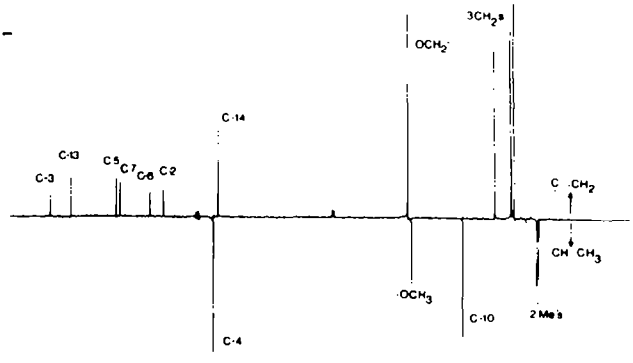
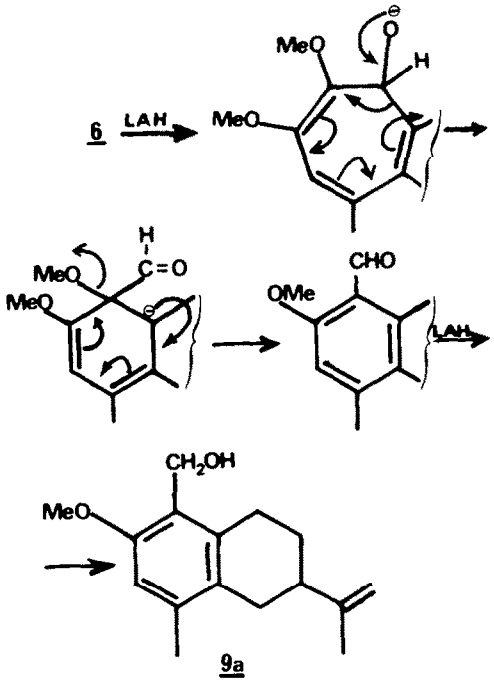


Fig. 2 : J-modulated spin echo ^{13}C nmr spectrum of 9a.

significant downfield shift for the $-CH_2O$ group. The ^{13}C nmr spectrum confirms fully structure 9a for the benzylic alcohol. The J-modulated spin echo ^{13}C nmr spectrum[8] of 9a in which the quaternary and methylene carbons appear as positive peaks, whereas the methine and methyl carbons appear as negative peaks, is presented in Figure 2. The chemical shifts are given in Table 2 and are in agreement with the calculated values[5,9] (using tetrahydronaphtalene as reference) for a 3-methoxy or a 4-methoxybenzylic alcohol. The SPI procedure proves that the methoxyl is, in fact, located at C-3 since selective proton irradiation of $-CH_2OH$ shows a long range coupling with the carbon C-OMe (155.5 ppm) and does not perturb the C-4 resonance (110.4 ppm).

The formation of the benzylic alcohol 9a from the dimethoxy derivative 6 by LAH reduction may be explained by the following mechanism :



9a

Lithium aluminium hydride rearrangements of tropolone methyl ethers leading to benzenoid compounds have been reported previously ; benzaldehyde was obtained from tropolone methyl ether[10] whilst 3-methyltropolone methyl ether gave m-tolualdehyde and 3-methylbenzyl alcohol[11].

Hydrogenation of compound 9a over Pd-C caused reduction of the side chain double bond and hydrogenolysis of the $-CH_2OH$ group to yield the methyl ether 10 as an oil $[\alpha]_D^{21°}$ +55.0° (c=0.35, chloroform), $C_{16}H_{24}O$. Its ^1H nmr spectrum (EXPERIMENTAL) is consistent with structure 10 and discloses, in particular, two distinct aromatic methyl signals (δ_H 2.01 and 2.15)*.

The specific rotation of the methyl ether 10 is comparable to that of 3a ($[\alpha]_D$ +48.2°) which leads one to assume that the configuration at C-10 of manicol 5 is similar to (+)-dihydrocarvone.

X-Ray analysis

A crystal of the diacetate 4 was grown from a mixture of ethyl acetate and hexane. The system is monoclinic, space group $P2_1$ with two molecules in the asymmetric unit (Z=4). The X-ray data are given in Table 4 (see EXPERIMENTAL). The structure was solved by direct methods[12] which led to the straightforward identification of the tropolone ring. During the refinement procedure a large thermal disorder was observed in the six membered ring and in the associated isopropylidene lateral chain and all their atoms were kept in a rigid block in the final steps. The R factor converged to a 16% value. All attempts to include different conformations with variable occupencies did not improve this value. A difference Fourier map showed only peaks below the 0.5 e^- level.

An X-ray analysis was then carried out on manicol 5 itself, since it was expected to display a better stabilization by hydrogen bonding of the free hydroxyl groups. A crystal of manicol 5, obtained from ethyl acetate, is also monoclinic, space group $P2_1$ with Z=4 (see Table 4). The structural problem

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* The methyl ether and the benzylic alcohol obtained from manicol, previously reported[1] as having structures 3a and 3b respectively, are now assigned structures 10 and 9a.

was solved using a Patterson search program[13] with the coordinates (16 atoms) from the diacetate 4 X-ray structure. The complete structure of manicol was readily developed by Fourier recycling procedures. The atomic positional and anisotropic thermal parameters were refined to $R=\Sigma||Fo|-|Fc||/\Sigma|Fo|=6.7\%$; all hydrogen atoms except those of one methyl group (CH_3-8), have been located on difference Fourier maps and were included in the final calculations with an isotropic thermal factor equal to that of the bonded carbons. They were not refined. The two molecules in the asymmetric unit differ only by an up and down orientation of the isopropylidene chain. The most relevant bond distances in manicol 5 are given in Figure 3. The e.s.d.'s on bond length are 0.003 Å.

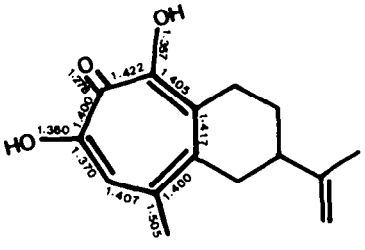


Figure 3

The carbonyl group in manicol is clearly located between the two hydroxyl functions, as indicated by the distinct C-O bond lengths[14]. Positional parameters ($x10^4$) and anisotropic thermal parameters ($x10^4$) for manicol 5 are given in Table 3.

A limited number of tropolones have been found in nature and α-hydroxytropolone derivatives are exceedingly rare[15]. It is of interest that manicoline A, the α-aminotropone 11, was isolated from the same tree[16]. The biogenetic precursor of manicol 5 might be, as proposed for the tropone 11, 1,10-cyclopropanoeudesmol which upon ring expansion would lead via the intermediate 12 to 5.

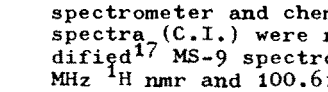
TABLE 3 : Fractional atomic coordinates and anisotropic thermal factors ($x10^4$) for manicol 5 given in the form : $\exp(-2\pi^2 \Sigma U_{ij} \cdot \vec{a}_i^* \cdot \vec{a}_j^* \cdot h_i \cdot h_j)$

	X	Y	Z	U11	U22	U33	U23	U13	U12
C 1	1684	-580	-1148	521	527	446	-51	225	29
C 2	1799	209	-2370	435	437	416	-74	111	-49
C 3	1154	935	-2355	518	455	407	77	209	-26
C 4	398	1230	-1185	597	404	544	130	189	36
C 5	-43	911	272	445	374	438	-25	193	-8
C 6	174	154	890	402	404	525	-11	170	-21
C 7	911	-444	200	493	526	396	-14	146	-9
C 8	-805	1471	1245	671	554	696	-12	385	149
C 9	-462	-16	2500	531	397	410	11	247	-38
C 10	-123	-789	3375	582	508	459	10	244	-54
C 11	-187	-1410	1983	941	512	574	-6	365	-92
C 12	960	-1247	931	977	549	545	27	382	-1
C 13	-1058	-976	4722	694	496	499	40	248	-182
C 14	-2245	-544	4996	1076	712	730	145	666	132
C 15	-675	-1701	5693	995	518	659	111	459	-89
O 1	2431	-1015	-1461	856	520	701	-40	424	197
O 2	2553	48	-3505	594	522	451	-30	318	-10
O 3	1442	1421	-3650	842	516	597	236	339	48
C 1'	3659	1773	-8658	555	421	458	-57	177	4
C 2'	3494	1159	-7541	491	482	391	-68	225	-45
C 3'	4102	429	-6512	529	450	406	-4	196	-28
C 4'	4671	134	-7312	551	583	495	-5	265	30
C 5'	5272	462	-8129	387	477	463	-4	162	5
C 6'	5082	1215	-9264	402	358	399	-23	123	-27
C 7'	4321	1808	-9943	451	395	461	-39	238	50
C 8'	6074	-126	-11158	642	414	572	34	292	112
C 9'	5740	1397	-12327	531	453	464	38	251	0
C10'	5921	2216	-12778	775	426	603	11	407	-2
C11'	4455	2640	-12736	620	675	742	195	366	91
C12'	4184	2606	-9079	984	489	708	123	520	201
C13'	6386	2347	-4472	667	471	497	-19	279	-122
C14'	7181	1745	-5081	1451	914	884	3	651	65
C15'	6044	3022	-5479	1399	676	858	278	476	21
O 1'	2933	2409	-8507	1049	524	781	54	559	191
O 2'	2786	1316	-3736	742	542	495	-12	365	-7
O 3'	3901	-60	-4225	851	522	598	111	432	59

EXPERIMENTAL

M.p.s. were determined using a Kofler hot-stage microscope and are uncorrected. Optical rotations were determined on a Roussel-Jouan Quick polarimeter. IR spectra were recorded with a Perkin-Elmer model 297 spectrometer. The UV spectra were measured with a spectrometer Duospec 203 (Jobin-Yvon). Electron-impact mass spectra (E.I.) were taken on an MS 50-AEI spectrometer and chemical ionisation spectra (C.I.) were recorded on a modified[17] MS-9 spectrometer. The 400 MHz ^1H nmr and 100.61 MHz ^{13}C nmr spectra were recorded with a Bruker WM-400 in $CDCl_3$ solution ; absorptions are given in δ units (p.p.m.).

SPI irradiation sequence :



^1H : π soft pulse = 143 ms
T_R : relaxation delay

Crystallographic Measurements

Crystals were mounted on a PHILIPS PW1100 computer controlled four-circle diffractometer, using the CuKα radiation (λ=1.5418 Å) monochromatized by graphite. The reflections were scanned in the $\theta/2\theta$ mode with a speed of $0.05°.s^{-1}$ over a range of 1.2°. The background was obtained from a stationary count of 10s on both sides of the scanned reflections. Three standard reflections were also scanned each two hours in order to check a possible decay in the data. No decomposition was observed. The intensities were corrected from Lorentz polarization but not from absorption. All calculations were performed on a CII-Mini-6 using locally modified versions of MULTAN 80 and SHELX programs.

Table 4 : Crystal data

	Diacetate 4	Manicol 5
Space group	$P2_1$ (Z=4)	$P2_1$ (Z=4)
Parameters (Å)		
a=	13.510	9.448
b=	12.768	17.349
c=	10.378	7.860
β=	96.01°	101.40°
Volume $(Å)^3$=	1780.3	1262.9
Reflections with $I \geqslant 2\sigma(I)$	2573	1929
Range of data collections	$2° \leqslant \theta \leqslant 55°$	$2° \leqslant \theta \leqslant 62°$
R %	16*	6.7

* Thermal factors in the tropolone ring are anisotropic and in the six membered ring & isopropylidene chain are kept isotropic.

Diacetate 4 : Manicol 5 (1 g) was treated with acetic anhydride (10 ml) and pyridine (1 ml) and retained at 20°C for 12 h. The reaction mixture was poured into ice-HCl and extracted with ether. The ether extract was worked up in the usual manner. Evaporation of the solvent and purification of the residue by column chromatography (Kieselgel 7736) gave the diacetate 4 (467 mg) which crystallised from a mixture of ethyl acetate and hexane as rectangles. MS (C.I., isobutane) : $(M+H)^+$ at m/z 331. Found : C, 69.11 ; H, 6.51 ; $C_{19}H_{22}O_5$ requires C 69.07 ; H, 6.71%.

Diacetate 4 (50 mg) was refluxed in methanol (20 ml) for 3 h. Evaporation of the solvent and recrystallisation from ethyl acetate gave manicol 5 (identity of m.p., MS, ^1H nmr and ^{13}C nmr).

Epoxidation of diacetate 4 : To a solution of diacetate 4 (650 mg) in CH_2Cl_2 (25 ml) was added with stirring at 0° m-chloroperbenzoic acid (344 mg) in CH_2Cl_2 (25 ml). After 12 h at room temperature the reaction mixture was washed with $NaHCO_3$ (5%), water, dried and evaporated. The resultant residue crystallised from ethyl acetate to give a mixture of α- and β-13,14-epoxides of the diacetate. m.p. 114-115° ; $[\alpha]_D^{20°}$ = +100° (c=0.25 ; $CHCl_3$). MS : M^+ at m/z 346.1426. Found : C, 65.61 ; H, 6.36 ; $C_{19}H_{22}O_6$ requires C, 65,58 ; H, 6.4%. ^1H nmr (80 MHz) ; δ 6.83 (s, 1H, H-4), 2.33 (s, 3H, Me-8), 2.27, 2.30 (s, 3H each, CH_3CO) and 1.33, 1.34 (2s, 3H, Me-15).

Refluxing this mixture in methanol afforded α- and β-13,14-epoxides of manicol which crystallised from ethyl acetate. m.p. 167-169°. MS : M^+ at m/z 262. Found : C, 68.54 ; H, 7.20 ; $C_{15}H_{18}O_4$ requires C, 68.68 ; H, 6.92%. ^1H nmr (400 MHz) : 7.42 (s, 1H, H-4), 2.45, 2.44 (2s, 3H, Me-8) and 1.37, 1.36 (2s, 3H, Me-15).

Dimethyl ethers 6, 7 and 8 : Manicol (1 g) dissolved in a 1:1 mixture of ether and chloroform was treated with an excess of ethereal diazomethane. After 6 h at room temperature, the solvents were evaporated and the residue dissolved in ether was treated again with CH_2N_2 in ether. Removal of the solvent after 24 h yielded a mixture of dimethyl ethers which were separated by flash chromatography (Kieselgel 7736). Hexane containing 15% acetone eluted successively dimethyl ether 6 (630 mg), 8 (100 mg) and 7 (290 mg) as yellow oils. MS : M^+ at m/z 274. TLC (system : hexane + acetone, 7:3, two runs) : R_f for 6 : 0.59 ; 8 : 0.48 and 7 : 0.26.

Benzylic alcohol 9a : To the dimethyl ether 6 (310 mg) in ether (70 ml) was added lithium aluminium hydride (333 mg) and the mixture was stirred at 20°C for 3 h. The excess of hydride was destroyed by the addition of ethyl acetate

to the cooled solution. Brine was then added, and the reaction mixture was extracted several times with ether. The organic phase was separated, washed with water, and dried (Na_2SO_4). The solvent was evaporated and the resulting oil (268 mg) was purified by flash chromatography (Kieselgel 7736) using chloroform as eluent to give colourless, crystalline (low melting) alcohol 9a (190 mg ; 68%). $C_{16}H_{22}O_2$, MS : M^+ at m/z 246.

The alcohol 9a (23 mg) was treated with acetic anhydride (1 ml) and pyridine (0.3 ml) and retained at room temperature for 12 h. After the usual work-up, the product was purified by column chromatography (eluent : benzene / ethyl acetate, 9:1) to give the acetate 9b, which crystallised from hexane, m.p. 79-80°. ^1H nmr (60 MHz) : δ 6.71 (s, 1H, H-4), 5.22 (br. s, 2H, CH_2OAc), 4.8 (br. s, 2H, $CH_2=$), 3.81 (s, 3H, OMe), 2.24 (s, 3H, Me-8), 2.05 (s, 3H, CH_3CO), 1.82 (s, 3H, Me-15).

Methylether 10 : The benzylic alcohol 9a (80 mg) was dissolved in ethanol (10 ml) and hydrogenated over palladium (10% on C, 15 mg) for 18 h. The catalyst was filtered off and the solvent evaporated to yield the reduced methyl ether 10 as a colourless oil. $C_{16}H_{24}O$, MS : M^+ at m/z 232. IR ($CHCl_3$) : ν_{max} 1640, 1600, 1580 cm^{-1}. ^1H nmr (400 MHz) : δ 6.55 (s, 1H, H-4), 3.72 (s, 3H, OMe), 2.15 and 2.01 (2s, 3H each, Me-1 and Me-8), 0.9 and 0.88 (2d, 3H each, Me-15 and Me-14). ^{13}C nmr (100.61 MHz)* : δ 10,9 (Me-1), 121.8 (C-2), 155.0 (C-3), 110,4 (C-4), 136.7[b] (C-5), 128.0 (C-6), 134.2[b] (C-7), 19.9 (Me-8), 28.3[a] (C-9), 40.6 (C-10), 26.4 (C-11), 30.7[a] (C-12), 32.5 (C-13), 19.9 (Me-14), 19.8 (Me-15), 55.8 (OMe).

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* The multiplicities were determined by the J-modulated spin echo technique[8].

[a,b] Signals may be reversed.

REFERENCES

1 J. POLONSKY, Z. VARON, H. JACQUEMIN, D.M.X. DONNELLY and M.J. MEEGAN, J. Chem. Soc. Perkin I 2065 (1980).

2 D. MENARD, M. St-JACQUES and J.F. BAGLI, Can. J. Chem. 60, 231 (1982) and references therein.

3 J.F. BAGLI, T. BOGRI, B. PALAMETA and M. St-JACQUES, Can. J. Chem. 57, 1949 (1979).

4 K.G.R. PACHLER and P.L. WESSELS, J. Magn. Reson., 28, 53 (1977).

5 WEHRLI and T. WIRTHLIN "Interpretation of Carbon-13 NMR Spectra", Heyden, London, 1978.

6 S. BRAWN and T. KINKELDEI, Tetrahedron 33, 3127 (1977).

7 J.-Y. LALLEMAND and M. DUTEIL, Org. Magn. Reson. 9, 179 (1977).

8 C. LE COCQ and J.-Y. LALLEMAND, J.C.S. Chem. Comm. 150 (1981).

9 J.B. STOTHERS, "Carbon-13 NMR Spectroscopy", Acad. Press, London, 1972.

10 J.W. COOK, R.A. RAPHAEL and A.I. SCOTT, J. Chem. Soc. 4416 (1952).

11 P. AKROYD, R.D. HAWORTH and P.R. JEFFERIES, J. Chem. Soc. 286 (1954).

12 P. MAIN, S. FISKE, S. HULL, L. LESSINGER, G. GERMAIN, J.P. DECLERCQ and M.M. WOOLFSON, MULTAN 80. A System of Computing Programs for the Automatic Solution of Crystal Structures, Department of Physics, Univ. of York, England and Louvain, Belgium.

13 B.P. BRAUN, J. HORNSTRA and J.L. LEENHOUTS, Philips Research Report, 24, 85 (1969).

14 J.P. SHAEFER and L.L. REED, J. Am. Chem. Soc., 93, 3902 (1971).

15 P.L. PAUSON, Chem. Rev. 55, 9 (1955).

16 J. POLONSKY, J. VARENNE, T. PRANGÉ, C. PASCARD, H. JACQUEMIN and A. FOURNET, J. Chem. Soc. Chem. Comm. 731 (1981).

17 P. VARENNE, B. BARDEY, P. LONGEVIALLE et B.C. DAS, Bull. Soc. Chim. Fr., 886 (1977).