Pergamon

Tetrahedron Vol. 51, No. 3, pp. 733-742, 1995

0040-4020/95 $9.50+0.00

0040-4020(94)00974-0

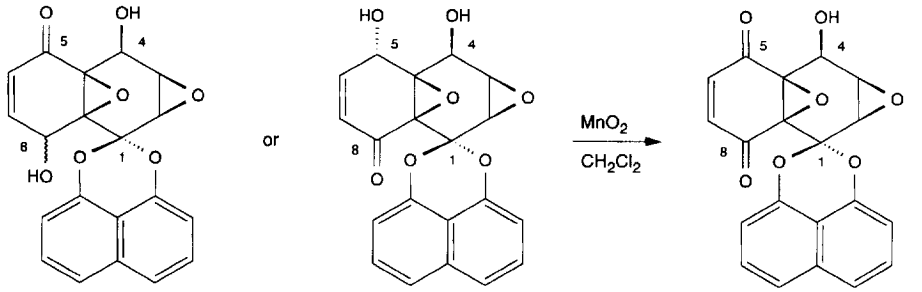
CLADOSPIRONE BISEPOXIDE: DEFINITE STRUCTURE ASSIGNMENT INCLUDING ABSOLUTE CONFIGURATION AND SELECTIVE CHEMICAL TRANSFORMATIONS

Regina Thiergardt, Grety Rihs†, Paul Hug†, Heinrich H. Peter *

Pharmaceutical Research Department, Microbial Chemistry and Central Function Research†
Ciba Geigy Ltd., 4002 Basle, Switzerland

Abstract: The definite structure of cladospirone bisepoxide **1** was determined as **1a** by X-ray analysis. The absolute configuration could be deduced from the X-ray crystallographic structure determination of its ring-opened product **8**. In order to define the structural features responsible for various biological effects of this metabolite, the reactivity of the epoxide and enone functional groups has been explored.

Cladospirone bisepoxide **1** is a novel metabolite isolated from cultures of a saprophytic fungus originally classified as a *Cladosporium chlorocephalum* strain [1]. As a result of a more recent taxonomic investigation, the producing strain F-24707 was reassigned to the *Sphaeropsidales* group, based on the morphological characteristics [2]. The fermentation and isolation procedures for the preparation of this metabolite and its biological activity have been reported in the same publication. The proposed tentative structure **1** was based on comprehensive NMR spectroscopic data and the X-ray crystallographic analysis of the 5,8-dioxo-derivative **2** [1]. In this paper we present (i) the definite structure assignment of cladospirone bisepoxide including the absolute configuration and (ii) selective chemical transformations of the epoxide groups and the enone subunit of **1a** and its 5,8-dioxo-derivative **2**.



1 **1a** **2**

Cladospirone bisepoxide belongs to a rapidly growing family of fungal metabolites containing a spironaphthodioxine substructure as well as a highly substituted decaline diepoxide moiety [3]. Comparison of the physico-chemical data of these compounds suggested that all of the reported structures of this type possess the same C_{20} carbon skeleton and differ only in their oxidation levels and substitution patterns. In

order to conclusively define the structural features of cladospirone bisepoxide, we decided to further scrutinize the tentative structure **1**. The assignment of the enone functional group was mainly based on NOE experiments which excluded a correlation between 4-OH and 5-H. In order to clear up this remaining uncertainty, we planned to corroborate the tentative structure assignment by X-ray structure analysis of the primary fermentation product. The first set of crystals examined turned out to be unsuitable for this purpose. However, by using alcohols, particularly 2-propanol as solvent for recrystallization, single crystals were obtained which could successfully be used for X-ray analysis.

Crystal data of **1a**: $C_{20}H_{14}O_7 \cdot C_3H_8O$, monoclinic, space group $P2_1$, a = 5.752(1) Å, b = 11.426(1) Å, c = 15.558(2) Å, β = 91.61(1)°, Z = 2. An Enraf-Nonius CAD4 diffractometer was used for data collection with graphite monochromated Cu-K_α-radiation. A total of 2246 intensities were measured of which 1513 were classified as observed with $I > 4\sigma(I)$. The structure was solved by direct methods. Hydrogen atom positions were located from difference Fourier maps or calculated assuming normal geometry. The structure was refined using full matrix least-squares calculations with anisotropic displacement parameters for non-hydrogen atoms and fixed ones for hydrogen atoms to a final R-factor of 0.067. The Schakal plot of compound **1a** is shown in figure 1 with the following stereochemistry: C-2/H-2α, C-3/H-3α, C-4/H-4α, C-5/H-5β. The X-ray analysis substantiated the *cis* arrangement of H-2, H-3 and H-4 as well as the *trans* configuration for H-4 and H-5. Both hydroxyl groups are hydrogen bonded to the same cocrystallized 2-propanol molecule.

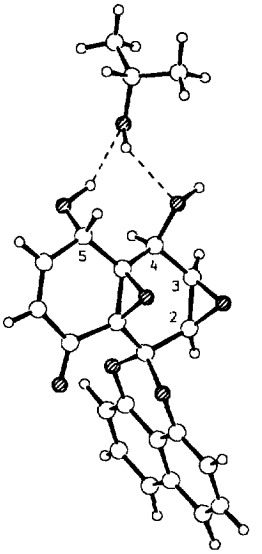


Figure 1: Schakal plot of **1a**

As a result of the X-ray structure analysis of the isopropanol solvate of cladospirone bisepoxide, we now allocate structure **1a** to this metabolite. According to this definite assignment, it turned out to be identical with the structure of compound Sch 49209 which has recently been deduced from the X-ray analysis of the acetate of the triepoxide derivative Sch 50674 [4]. The primary metabolite Sch 49209 is produced in low yields by the fungal strain *Nattrassia mangiferae* ATCC 74078 together with comparable amounts of the dihydro derivative Sch 49210 [5]. Furthermore, structure **1a** is also identical with the structure of diepoxin ζ, a metabolite isolated from an unidentified fungal strain [6]. In all cases the absolute stereochemistry of the compounds remained undefined. In order to address this remaining open question, we set out to find a possibility for the introduction of a heavy atom into the molecule by exploring the reactivity of the main functional groups. In addition, we expected to gain important preliminary information on structure-activity relationships of this prominent representative of the spironaphthodioxine derivatives.

This class of compounds displays a wide spectrum of biological effects [2], such as antimicrobial activity against selected bacteria, yeast and filamentous fungi, inhibition of plant seed germination and interaction with some receptor proteins. In a recent publication on the biological activity of five members of

this class of compounds, the authors reported potent *in vivo* activity against phospholipase D and anti-invasive activity against various tumour cells in the anti-tumour invasion chamber assay [5]. In order to explore the specificity of these inhibitory effects and to evaluate the potential for selectivity of the chemical interactions involved, we investigated the reactivity of the prominent functional groups of cladospirone bisepoxide, e.g. the two epoxide rings and the enone substructure of **1a** and some of its derivatives.

The preliminary analysis of the steric representation of the structure of **1a** (Fig. 2) deduced from the X-ray crystallographic study reveals a pronounced steric hindrance for the backside approach of reagents in case of both epoxide groups. Therefore, we were not surprised by the fact that **1a** turned out to be quite inert towards many reagents routinely used in epoxide ring-opening reactions. On the other hand, the β-position of the enone functional group appears to be easily accessible for nucleophiles used in typical Michael addition reactions.

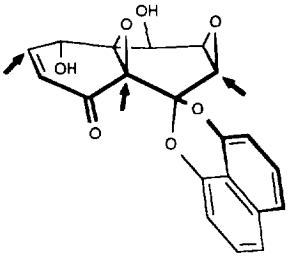
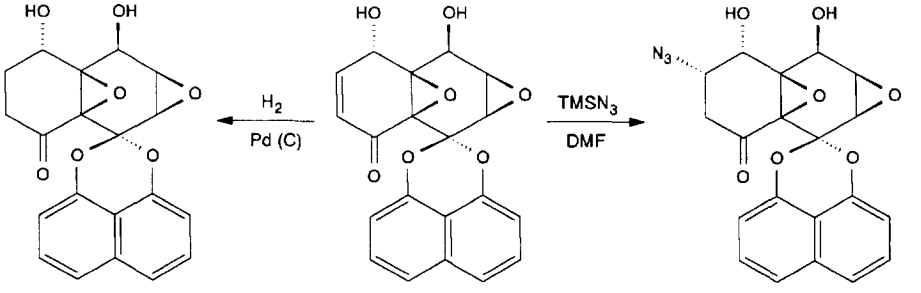


Figure 2

Initially, we hypothesized that a wide spectrum of biological activities of cladospirone bisepoxide could be due to non-specific interactions of the epoxide groups with nucleophiles. Therefore, we tested its reactivity towards a number of common nucleophiles, e.g. NaN_3, Et_2NH, H_2NNH_2, C_6H_5SH. Using various catalysts and solvents under mild conditions, no ring-opening products of the epoxides could be observed. However, more drastic reaction conditions allowed isolation of Michael addition products in good yields.



3 **1a** **4**

In a specific example, stirring of **1a** in DMF with a large excess (13 equiv.) of CH_3OH and $TMSN_3$ (2 h, 70°C) gave the Michael adduct **4** as the main product (67%) after purification by column chromatography (silica gel, CH_2Cl_2/2-propanol 99:1). The structure of **4**, especially the *cis* arrangement of the substituents at C-5 and C-6 and the *trans* configuration of the hydroxyl groups was confirmed by determination of NOEs in CD_3CN (Fig. 3). The hydrogenated derivative **3** was isolated as a minor by-product (19%) presumably originating as an impurity of the starting material.

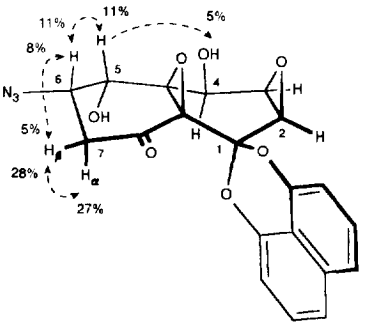
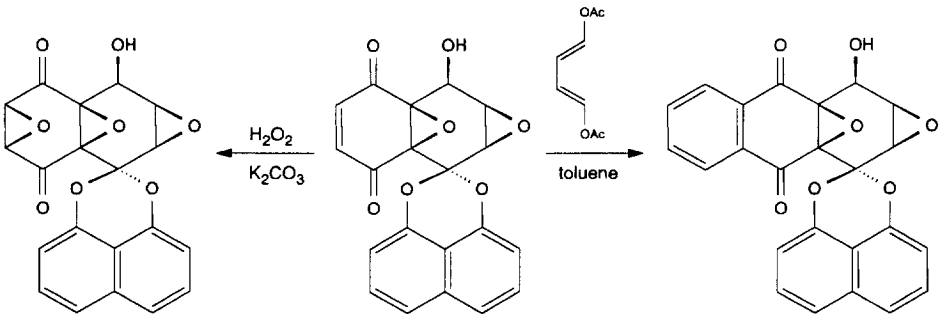


Figure 3

Considerably larger amounts of **3** were formed by the producing strain F-24707 if the cultivation conditions are not tightly controlled as described [2]. The primary metabolite **1a** could be converted to **3** in preparative amounts by a clean hydrogenation (94%) of the enone double bond using palladium on carbon as a catalyst. The products **3** and **4** were characterized by standard spectroscopic techniques (IR, NMR, MS).

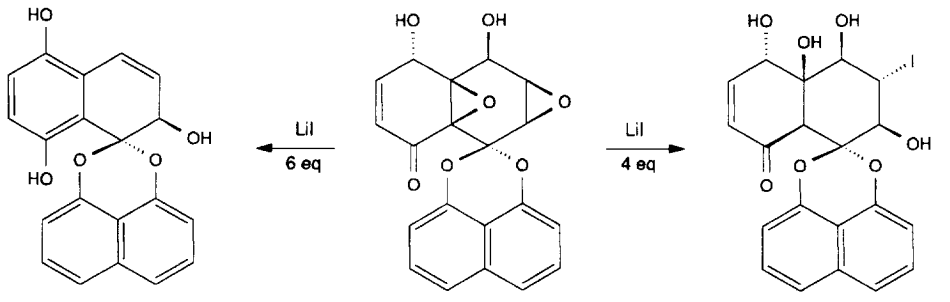
Moreover, the double bond of the enedione **2** could be oxidized to the triepoxide **5** by stirring a suspension of **2**, 1 equivalent of K_2CO_3 and 2 equivalents of a 30% aq. solution of H_2O_2 during 2 h at rt. After extractive work-up and preparative chromatography (silica gel, CH_2Cl_2/2-propanol 95:5) the triepoxide **5** was obtained in form of colourless crystals in 31% yield.



5 **2** **6**

The enedione function of **2** also turned out to be an excellent substrate for Diels-Alder reactions. A very clean addition reaction resulted when ketone **2** was treated with 1 equivalent of diacetoxybutadiene in toluene under Argon in a pressure-proof ampoule at 120°C. After 2 d of stirring reaction product **6** was isolated after column chromatography (silica gel, CH_2Cl_2/2-propanol 95:5) as pale yellow crystals (88%).

As a result of the steric hindrance, both epoxide groups in **1a** proved to be quite inert against various nucleophiles. Ring-opening of the epoxide groups of **1a** could eventually be achieved by treating with anhydrous lithium iodide in 1,2-dimethoxyethane (DME). When the reaction was carried out using 4 molar equivalents of LiI during 20 h at 70°C, the iodide **8** was formed as the main product (64%). **8** was purified by preparative chromatography (silica gel, CH_2Cl_2/2-propanol 99:1) and recrystallization from ethyl ether/pentane.



7 **1a** **8**

When the amount of reagent was further increased to 6 equivalents, the hydroquinone derivative **7** was formed as the main product already after a reaction time of 4 h at 70°C. Analytically pure **7** (63%) was obtained by preparative chromatography (silica gel, CH_2Cl_2/2-propanol 99:1) and recrystallization from ethyl ether/pentane. The structures of the new compounds **7** and **8** were corroborated by MS as well as ^1H and ^{13}C NMR spectroscopy. In both compounds the sterically hindered epoxide rings have been opened. We assume that the successful opening reactions are facilitated by preceding complexation of the oxygen atoms of **1a** by lithium iodide with concomitant change of the conformation and of the reactivity of the epoxide groups.

The mass spectrum of **7** showed a molecular ion peak [M^+] at *m/z* 334 (100%) consistent with a molecular formula of $C_{20}H_{14}O_5$. An absorption band in the IR spectrum of **7** indicated the presence of a phenol substructure (3485 cm^{-1}). This finding was confirmed by two signals at 8.26 ppm (s, 1 phenol. OH) and 7.95 (s, 1 phenol. OH) in the ^1H NMR spectrum of **7** (acetone-d_6). Three signals at 4.25 ppm (dd, 2-H; $J_{2,2\text{-}OH}$ = 7.4, $J_{2,3}$ = 5.4 Hz), 5.96 ppm (dd, 3-H; $J_{2,3}$ = 5.4, $J_{3,4}$ = 9.8 Hz) and 7.17 ppm (d, 4-H; $J_{3,4}$ = 9.8 Hz) were classified as an enol unit.

The molecular weight of **8** was determined to be 496 based on FAB-MS data [*m/z* 497 $(M + H)^+$]. The molecular formula $C_{20}H_{17}IO_7$ was confirmed by elementary analysis and ^{13}C NMR spectroscopy (20 carbons). IR absorption bands at 3610, 3550, 3470, 3320 and 1685 cm^{-1} were indicative of 4 OH groups and a conjugated carbonyl group. The ^{13}C NMR spectrum of **8** showed a carbonyl signal at 194.3 ppm and signals for 10 aromatic and 2 vinylic carbons, 8 of which were attached to protons. A quaternary carbon signal at 101.8 ppm (C-1) indicated a ketal carbon. Three doublets at 3.92 (d, 2-H; $J_{2,3}$ = 11.7 Hz), 4.26 (d, 4-H, $J_{3,4}$ = 11.4 Hz) and 4.29 ppm (d, 5-H, $J_{5,6}$ = 5.7 Hz) in the ^1H NMR spectrum were assigned to methine protons of secondary hydroxyl groups.

Chemical shifts δ [ppm] of **8**							
Pos.	**^1H-NMR**	***J* [Hz]**	**^{13}C-NMR**	**Pos.**	**^1H-NMR**	***J* [Hz]**	**^{13}C-NMR**
1	-	-	101.8	1'	-	-	150.1*
2	3.92 (d)	11.7	67.4	2'	7.33 (m)	-	119.8**
3	4.59 (dd)	11.4; 11.7	80.8	3'	6.81 (dd)*	6.6; 2.4	128.0***
4	4.26 (d)	11.4	74.3	4'	7.33 (m)	-	107.5****
5	4.29 (d)	5.7	74.3	5'	7.33 (m)	-	107.0****
6	6.86 (dd)	5.7; 10.5	130.9	6'	6.73 (dd)*	6.6; 2.4	127.9***
7	5.93 (d)	10.5	145.5	7'	7.33 (m)	-	119.7**
8	-	-	194.3	8'	-	-	149.7*
9	3.39 (s)	-	41.5	9'	-	-	112.6
10	-	-	78.0	10'	-	-	135.1

Table 1: NMR-data of **8** in CD_3OD (* = interchangeable; for the sake of easy comparison of the data the numbering system is the same as used for **1a**.)

In addition, NOE experiments on **8** demonstrated a *cis* arrangement for H-2, H-4 and H-9 as well as a *trans* configuration for H-2 and H-3. The most relevant results are listed in table 2.

	2-H	4-H	5-H	6-H	7-H	9-H
2-H	-	15%	-	-	-	6%
3-H	4%	3%	-	-	-	-
4-H	9%	-	-	-	-	2%
5-H	-	-	-	11%	-	-
6-H	-	-	20%	-	30%	-
9-H	13%	10%	-	-	2%	-

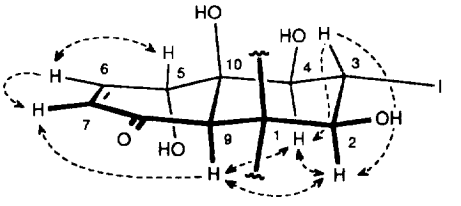


Table 2: Important NOEs of **2** (in CD_3OD)

Compound **8** bearing a heavy atom at position C-3 proved to be a highly suitable derivative to clarify the absolute stereochemistry of the cladospirone bisepoxide family. Tetrol **8** gave suitable crystals from diethyl ether which allowed to establish the absolute configuration as shown in figure 4 with the following stereochemistry: C-2/H-2α, C-3/H-3β, C-4/H-4α, C-5/H-5β, C-9/H-9α. Crystal data of **8**: $C_{20}H_{17}IO_7 \cdot C_4H_{10}O$, monoclinic, space group $P2_1$, a = 10.450(1) Å, b = 11.202(1) Å, c = 19.858(2) Å, β = 90.83(1)°, Z = 4. A Philips PW1100 diffractometer was used for data collection with graphite monochromated Mo-K_α-radiation. A total of 6087 intensities were measured of which 4177 were classified as observed with $I > 2\sigma(I)$. The structure was solved by standard heavy atom methods. Hydrogen atom positions were located from difference Fourier maps or calculated assuming normal geometry.

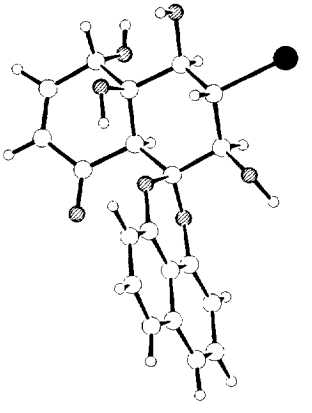


Figure 4: Schakal plot of **8**

The structure was refined using full matrix least-squares calculations with anisotropic displacement parameters for non-hydrogen atoms (hydrogen atoms were not refined) to a final R-factor of 0.043. The asymmetric unit contains two independent, but conformationally similar molecules and two ether molecules. The absolute configuration was determined by an R-factor test (the opposite enantiomer converged to the R-factor of 0.048) and by the measurement of 3140 Bijvoet pairs and refinement of the Flack x-parameter [7]. This parameter gave a value of -0.07(12) for the enantiomer shown in figure 4.

The single crystal structure analysis of cladospirone bisepoxide led to the assignment of the definite structure **1a** to this metabolite. The absolute configuration could be determined by introducing a heavy atom into the molecule, yielding tetrol **8**. Thus, the absolute stereochemistry of all the reported structures of the cladospirone bisepoxide family could be defined. The reactivity of both the enone substructure and the epoxide groups has been explored by selective chemical transformations. The exploratory derivatisation reactions described above have provided us with a valuable insight into the chemical reactivity of the complex natural product **1a**. This information will prove to be very precious for conceiving more systematic investigations of structure-activity relationships in various biological test systems.

Experimental

The NMR spectra were obtained on a Varian VXR-400-S spectrometer. The chemical shifts are reported in ppm downfield from TMS as the internal standard. For the assignment of the NMR signals of compound **7** and **8**, the numbering system used for **1a** and the other cladospirone bisepoxide derivatives is maintained in order to allow direct comparison of the data. IR spectra were recorded on Perkin-Elmer 983b spectrophotometer. Mass measurements were carried out on ZAB-HF (FAB-MS), BIO-ION-TOF (MS) and elemental analysis were performed on a Perkin-Elmer CHN-Automat. Melting points were determined on a Büchi 520 and are uncorrected. All reactions were monitored by employing tlc technique using appropriate solvent systems for the development. Solvents and reagents were purchased from Fluka or Aldrich.

6,7-Dihydrocladospirone bisepoxide (3)

660 mg (1.8 mmol) of **1a** in 30 ml of ethyl acetate was hydrogenated after addition of 100 mg of 5 % Pd/C. The catalyst was removed by suction filtration and after solvent evaporation, the residue was crystallized from methylene chloride/isopropanol (95:5) to give 620 mg (94%) of **3** as colourless crystals, mp 230°C (dec.).-

IR (CH_2Cl_2): 3550 (OH), 3040 (CH), 1750 (C=O), 1620 (C=C), 1430 (C=C), 1280 (aryl-O) cm^{-1}.- ^1H NMR (CD_3OD): δ = 7.55 (d, 2'-H), 7.53 (d, 7'-H), 7.47 (dd, 3'-H), 7.44 (dd, 6'-H), 7.01 (d, 4'-H), 6.94 (d, 5'-H), 4.84 (d, 4-H), 4.70 (dd, 5-H), 3.44 (d, 2-H), 3.42 (dd, 3-H), 2.61-2.51 (m, 7a-H), 2.31 (ddd, 7b-H), 2.08-1.98 (m, 6a-H), 1.81 (dddd, 6b-H).- ^{13}C NMR (CD_3OD): δ = 199.8 (C-8), 147.2 (C-1'), 146.9 (C-8'), 135.6 (C-10'), 128.7 (C-3'), 128.5 (C-6'), 121.8 (C-2'), 121.7 (C-7'), 113.4 (C-9'), 110.2 (C-4'), 109.7 (C-5'), 96.4 (C-1), 70.9 (C-10), 65.2 (C-9), 63.8 (C-4), 62.8 (C-5), 56.6 (C-2), 54.6 (C-3), 33.6 (C-7), 25.4 (C-6).- MS: *m/z* = 366 [M^+].

6-Azidocladospirone bisepoxide (4)

A solution of 500 mg (1.37 mmol) of **1a** in 7.5 ml of dimethylformamide and 710 µl (17.7 mmol) of methanol was treated dropwise with 2.33 ml (17.7 mmol) of trimethylsilyl azide. After stirring at 70°C for 2 h, 5 ml of water was added and the mixture was extracted with methylene chloride. The organic layers were dried (Na_2SO_4), the solvent was evaporated, and the crude reaction product was purified by column chromatography on silica gel [methylene chloride/1% of isopropanol; R_f = 0.24]. Crystallization from diethyl ether/pentane (75:25) yielded 374 mg (67%) of **4**, mp 238°C (dec.) and 95 mg (19%) of **3** as colourless crystals.-

IR (CH_2Cl_2): 3565 (OH), 3060 (CH), 2105 (N_3), 1760 (C=O), 1610 (C=C), 1410 (C=C), 1380 (C=C) cm^{-1}.- ^1H NMR (CD_3CN/C_6D_6): δ = 8.05 (d, 2'-, 7'-H),7.92 (t, 3'-H), 7.89 (t, 6'-H), 7.59 (d, 4'-H), 7.48 (d, 5'-H), 5.62 (dd, 5-H), 5.44 (d, 4-H), 4.89 (d, 5-OH), 4.50 (d, 4-OH), 4.39 (ddd, 6-H), 3.79 (d, 2-H), 3.76 (dd, 3-H), 3.27 (dd, 7α-H), 3.10 (dd, 7β-H); $J_{2,3}$ = 4.2, $J_{3,4}$ = 2.9, $J_{5,6}$ = 2.8, $J_{5,7\beta}$ 0 0.6, $J_{6,7\beta}$ = 5.8, $J_{6,7\alpha}$ = 10.8, $J_{7\alpha,7\beta}$ = 17.8 Hz.- ^{13}C NMR (CD_3CN): δ = 196.4 (C-8), 146.6 (C-1'), 146.3 (C-8'), 135.2 (C-10'), 128.8 (C-3'), 128.6 (C-6'), 121.9 (C-4',-5'), 112.8 (C-9'), 110.2 (C-2'), 109.7 (C-7'), 96.1 (C-1), 70.2 (C-10), 66.1 (C-5), 63.6 (C-9), 62.5 (C-4), 56.1 (C-3), 55.9 (C-2), 54.3 (C-6), 38.5 (C-7).- MS: *m/z* = 377 [M^++1].

6,7-Epoxy-5-oxocladospirone bisepoxide (5)

An ice-cooled mixture of 570 mg (1.57 mmol) of **2**, 40 ml of methylene chloride/methanol (1:1) and 640 ml of hydrogen peroxide was treated with 220 mg (1.57 mmol) of potassium carbonate in portions. After stirring at room temperature for 2 h, 20 ml of water was added and the mixture extracted with methylene chloride. The organic extract was washed with a saturated aqueous solution of sodium hydrogensulphite, dried (Na_2SO_4), and concentrated in vacuum. The crude product was purified by silica gel column chromatography [methylene chloride/isopropanol (95:5); R_f (**5**) = 0.46; R_f (**3**) = 0.41] yielding 185 mg (31 %) of **5**, mp 270°C (dec.) and 328 mg (57%) of **3** as colourless crystrals.-

IR (CH_2Cl_2): 3560 (OH), 3060 (CH), 2935 (CH), 1750 (C=O), 1615 (C=C), 1415 (C=C), 1380 (C=C) cm^{-1}.- ^1H NMR (CD_2Cl_2): δ = 7.62 (d, 2'-H), 7.60 (d, 7'-H), 7.53 (dd, 3'-H), 7.48 (dd, 6'-H), 7.13 (d, 4'-H), 6.94 (d, 5'-H), 5.17 (mc, 4-H), 3.91 (d, 6-H), 3.89 (d, 7-H), 3.51 (d, 2-H), 3.47 (d, 3-H), 2.81 (br., 4-OH); $J_{2,3}$ = 4.1, $J_{6,7}$ = 3.8 Hz.- ^{13}C NMR (CD_2Cl_2): δ = 191.1 (C-5), 185.2 (C-8), 145.1 (C-1'), 143.2 (C-8'), 134.5 (C-10'), 128.2 (C-3'), 127.6 (C-6'), 121.6 (C-2'), 121.5 (C-7'), 112.1 (C-9'), 109.9 (C-4'), 109.2 (C-5'), 96.4 (C-1), 67.2 (C-10)*, 65.2 (C-9)*, 61.9 (C-4), 56.6 (C-6)*, 56.4 (C-7)*, 54.8 (C-2)*, 54.2 (C-3)*.- MS: *m/z* = 380 [M^+].

6,7-Benzo-5-oxocladospirone bisepoxide (6)

A degassed solution of 300 mg (0.824 mmol) of **2**, 140 mg (0.824 mmol) of diacetoxybutadiene and 4 ml of toluene was heated in a sealed vial with expansion valve at 120°C for 48 h. After solvent evaporation, the residue was subjected to silica gel column chromatography [methylene chloride/isopropanol (95:5); R_f = 0.72] affording 302 mg (88%) of **6** as pale yellow crystals, mp 260°C (dec.).-

IR (CH_2Cl_2): 3560 (OH), 3060 (CH), 1710 (C=O), 1610 (C=C), 1415 (C=C), 1380 (C=C), 1275 (aryl-O) cm^{-1}.- ^1H NMR (CD_2Cl_2): δ = 8.05/8.02 (AA'), 7.83 (BB'), 7.63 (d, 2'-H), 7.62 (d, 7'-H), 7.59 (dd, 3'-H), 7.51 (dd, 6'-H), 717 (d, 4'-H), 6.98 (d, 5'-H), 5.35 (dd, 4-H), 3.60 (m, 2-, 3-H), 3.33 (d, 1-OH); $J_{4,4\text{-OH}}$ = 6.7, $J_{3,4}$ = 2.8.- ^{13}C NMR (CD_2Cl_2): δ = 191.1 (C-5), 185.0 (C-8), 145.5 (C-1'), 145.3 (C-8'), 135.6 (A), 135.0 (A'), 134.5 (C-10'), 132.3 (C-7), 139.7 (C-6), 128.1 (B'), 127.9 (B'), 127.7 (C-4'), 127.5 (C-5'), 121.5 (C-3', -6'), 112.0 (C-9'), 109.8 (C-2'), 109.1 (C-7'), 95.1 (C-1), 66.0 (C-9, -10), 62.2 (C-4), 54.9 (C-3), 54.3 (C-2).- MS: *m/z* = 414 [M^+].

1,4,7β-Trihydroxy-8(spirodioxy-1',8'-naphthyl)-7,8-dihydronaphthalene (7)

A solution of 1.0 g (2.75 mmol) of **1a**, 25 ml of dimethoxyethane and 2.2 g (16.50 mmol) of lithium iodide was stirred at 70°C for 4 h. The reaction was carried out under an atmosphere of argon. The mixture was diluted with 25 ml of methylene chloride, washed with 20 ml of a saturated aqueous solution of sodium thiosulphate, dried (Na_2SO_4), and evaporated in vacuum. The residue was subjected to chromatography on silica gel [methylene chloride/1% of isopropanol; R_f (**7**) = 0.21; R_f (**8**) = 0.18]. After crystallisation from diethyl ether/pentane (75:25) 578 mg (63%) of **7** and 284 mg (21%) of **8** were obtained as colourless crystals, mp 112°C (dec.).-

IR (CH_2Cl_2): 3580 (OH), 3485 (OH), 3060 (CH), 1610 (C=C), 1460 (C=C), 1410 (C=C), 1380 (C=C), 1280 (aryl-O) cm^{-1}.- ^1H NMR (CD_3COCD_3): δ = 8.26 (s, 1 phenol. OH), 7.95 (s, 1 phenol. OH), 7.65 (d, 2'-H), 7.59 (d, 7'-H), 7.56 (dd, 3'-H), 7.50 (dd, 6'-H), 7.17 (d, 4-H), 7.02 (d, 4'-H), 6.93 (d, 6-H), 6.89 (d, 4'-H), 6.72 (d, 7-H), 5.96 (dd, 3-H), 4.30 (d, 2-OH), 4.25 (dd, 2-H); $J_{2,2\text{-OH}}$ =7.4, $J_{2,3}$ = 5.4, $J_{3,4}$ = 9.8, $J_{6,7}$ = 8.9.- ^{13}C NMR (actetone-d_6): δ = 151.6 (quat. C), 147.5 (quat. C), 145.3 (quat. C), 144.8 (quat. C), 134.4 (quat. C), 127.6, 127.4, 124.4, 124.0, 122.5, 121.3 (quat. C), 121.1, 120.2, 119.5, 114.2 (quat. C), 113.9 (quat. C), 110.5, 110.0, 104.5 (C-1), 63.4 (C-2).- MS: *m/z* = 334 [M^+].

4α,5β,6β,8β-Tetrahydroxy-7α-iodo-9(spirodioxy-1',8'-naphthyl)2,3-dehydro-1-decalone (8)

A solution of 2.5 g (6.83 mmol) of **1a**, 125 ml of dimethoxyethane and 3.75 g (27.32 mmol) of lithium iodide was stirred at 70°C for 20 h. The reaction was carried out under an atmosphere of argon. The mixture was diluted with 150 ml of methylene chloride, washed with 200 ml of a saturated aqueous solution of sodium thiosulphate, dried (Na_2SO_4), and evaporated in vacuum. The reaction product was purified by column chromatography on silica gel [methylene chloride/1% of isopropanol; R_f (**8**) = 0.18]. Crystallization from diethyl ether provided 2.16 g (64%) of **8** as colourless crystals, mp 180°C (dec.).-

IR (CH_2Cl_2): 3610 (OH), 3550 (OH), 3470 (OH), 3320 (OH), 1685 (C=O), 1610 (C=C), 1425 (C=C), 1280 (aryl-O) cm^{-1}.- ^1H and ^{13}C NMR see table 1.- FAB-MS: *m/z* = 497 [M^+ + 1].- *Anal.* Calcd for $C_{20}H_{17}IO_7$: C, 48.41 %; H, 3.45 %. Found: C, 48.69 %; H, 3.65.

References and Notes

1) Thiergardt, R.; Hug, P.; Rihs, G.; Peter, H.H. *Tetrahedron Lett.* **1994**, *35*, 1043-1046.
2) Petersen, F.; Moerker, T.; Vanzanella, F.; Peter, H.H. *J. Antibiot.*, accepted for publication.
3) A short review of these compounds and the pertinent literature references are summarized in the above mentioned publication manuscript.
4) Chu, M.; Trummees, I.; Patel, M.G.; Gullo, V.P.; Puar, M.S. *J. Org. Chem.* **1994**, *59*, 1222-1223.
5) Chu, M.; Trummees, I.; Patel, M.G.; Gullo, V.P.; Blood, C.; King, I.; Pai, J.-K.; Puar, M.S. *Tetrahedron Lett.* **1994**, *35*, 1343-1346.
6) Schlingmann, G.; West, R. R.; Milne, L.; Pearce, C.J.; Carter, G.T. *Tetrahedron Lett.* **1993**, *34*, 7225-7228.
7) Flack, H.D. *Acta Cryst.* **1983**, *A39*, 876.

Tables of coordinates, bond lengths and angles of both compounds were deposited with the Crystallographic Data Centre, Cambridge, University Chemical Lab, Cambridge CB2 1EW, UK.

Atomic Coordinates of **1a**

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
O(1)	-0.316(1)	-0.6525(6)	-0.2133(4)	O(2)	-0.006(1)	-0.7910(7)	-0.2149(4)
O(3)	-0.334(1)	-0.9295(6)	-0.3358(4)	O(4)	-0.033(1)	-0.7644(6)	-0.4034(4)
O(5)	-0.486(1)	-0.8245(7)	-0.5091(5)	O(6)	-0.412(1)	-0.5528(7)	-0.5192(5)
O(7)	0.115(1)	-0.5523(9)	-0.2544(5)	C(8)	-0.387(2)	-0.8394(9)	-0.2759(6)
C(9)	-0.513(2)	-0.846(1)	-0.3569(6)	C(10)	-0.469(2)	-0.7632(9)	-0.4289(5)
C(11)	-0.238(1)	-0.6974(9)	-0.4232(6)	C(12)	-0.199(2)	-0.6112(9)	-0.4963(6)

C(13)	-0.012(2)	-0.524(1)	-0.4773(7)	C(14)	0.092(2)	-0.508(1)	-0.4012(7)
C(15)	0.043(2)	-0.579(1)	-0.3258(6)	C(16)	-0.112(1)	-0.6834(8)	-0.3385(6)
C(17)	-0.205(2)	-0.7421(9)	-0.2603(6)	C(18)	-0.357(2)	-0.676(1)	-0.1295(6)
C(19)	-0.528(2)	-0.618(1)	-0.0881(7)	C(20)	-0.560(2)	-0.639(1)	-0.0024(8)
C(21)	-0.422(2)	-0.718(1)	0.0440(8)	C(22)	-0.246(2)	-0.782(1)	0.0020(6)
C(23)	-0.097(2)	-0.866(1)	0.0430(8)	C(24)	0.069(2)	-0.921(1)	-0.0027(8)
C(25)	0.099(2)	-0.899(1)	-0.0893(8)	C(26)	-0.038(2)	-0.819(1)	-0.1307(6)
C(27)	-0.214(2)	-0.759(1)	-0.0858(6)	O(28)	-0.699(2)	-0.690(1)	0.3698(6)
C(29)	-0.660(4)	-0.835(2)	0.259(1)	C(30)	-0.731(4)	-0.716(2)	0.281(1)
C(31)	-0.946(6)	-0.665(3)	0.249(2)				

Atomic Coordinates of **8**

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
I(1)	-0.19726(9)	-0.0934(1)	-0.13716(4)	O(2)	-0.3386(6)	-0.5000(6)	-0.0151(3)
O(3)	-0.4995(8)	-0.3487(8)	-0.0092(4)	O(4)	-0.2430(6)	-0.2631(8)	-0.0049(3)
O(5)	-0.4614(8)	-0.1754(7)	-0.2175(4)	O(6)	-0.6207(6)	-0.2952(7)	-0.1303(3)
O(7)	-0.4734(7)	-0.4396(7)	-0.2717(3)	O(8)	-0.5921(7)	-0.5776(9)	-0.0397(4)
C(9)	-0.351(1)	-0.2134(9)	-0.1103(5)	C(10)	-0.409(1)	-0.266(1)	-0.1752(4)
C(11)	-0.5140(9)	-0.3552(9)	-0.1593(5)	C(12)	-0.569(1)	-0.412(1)	-0.2244(5)
C(13)	-0.645(1)	-0.521(1)	-0.2114(6)	C(14)	-0.649(1)	-0.580(1)	-0.1550(6)
C(15)	-0.570(1)	-0.539(1)	-0.0961(6)	C(16)	-0.4649(9)	-0.4535(9)	-0.1110(4)
C(17)	-0.3994(9)	-0.4013(9)	-0.0482(5)	C(18)	-0.2981(9)	-0.3107(9)	-0.0645(4)
C(19)	-0.318(1)	-0.492(1)	0.0539(5)	C(20)	-0.220(1)	-0.558(1)	0.0832(5)
C(21)	-0.208(1)	-0.552(1)	0.1553(6)	C(22)	-0.290(1)	-0.490(1)	0.1927(6)
C(23)	-0.392(1)	-0.423(1)	0.1633(5)	C(24)	-0.482(1)	-0.359(1)	0.1995(6)
C(25)	-0.577(1)	-0.297(1)	0.1670(6)	C(26)	-0.585(1)	-0.293(1)	0.0948(5)
C(27)	-0.498(1)	-0.354(1)	0.0607(5)	C(28)	-0.403(1)	-0.423(1)	0.0915(5)
I(29)	-0.64780(9	-1.2540(1)	-0.63227(4)	O(30)	-0.8518(7)	-0.8955(7)	-0.5343(3)
O(31)	-1.0314(7)	-1.0248(8)	-0.5131(3)	O(32)	-0.7768(7)	-1.1223(7)	-0.5041(3)
O(33)	-0.7511(6)	-1.0632(7)	-0.7460(3)	O(34)	-0.8128(6)	-0.8506(6)	-0.6739(3)
O(35)	-1.0550(7)	-1.0206(8)	-0.7632(3)	O(36)	-1.0974(8)	-0.7986(8)	-0.5599(4)
C(37)	-0.7559(8)	-1.093(1)	-0.6233(4)	C(38)	-0.8313(9)	-1.0656(9)	-0.6885(4)
C(39)	-0.9013(9)	-0.9478(9)	-0.6807(4)	C(40)	-0.978(1)	-0.920(1)	-0.7452(5)
C(41)	-1.065(1)	-0.816(1)	-0.7366(6)	C(42)	-1.106(1)	-0.779(1)	-0.6773(7)
C(43)	-1.068(1)	-0.837(1)	-0.6148(6)	C(44)	-0.9934(9	-0.9535(9)	-0.6223(5)
C(45)	-0.931(1)	-0.995(1)	-0.5559(5)	C(46)	-0.8480(8	-1.104(1)	-0.5649(4)
C(47)	-0.847(1)	-0.865(1)	-0.4665(5)	C(48)	-0.760(1)	-0.783(1)	-0.4463(6)
C(49)	-0.756(1)	-0.750(1)	-0.3777(5)	C(50)	-0.840(1)	-0.795(1)	-0.3328(6)
C(51)	-0.931(1)	-0.884(1)	-0.3531(5)	C(52)	-1.016(1)	-0.941(1)	-0.3108(5)
C(53)	-1.101(1)	-1.022(1)	-0.3343(6)	C(54)	-1.106(1)	-1.054(1)	-0.4025(5)
C(55)	-1.022(1)	-0.999(1)	-0.4451(5)	C(56)	-0.930(1)	-0.916(1)	-0.4232(5)
O(57)	-0.5137(9)	-0.7954(9)	-0.6176(5)	C(58)	-0.553(1)	-0.671(2)	-0.6162(8)
C(59)	-0.444(1)	-0.585(2)	-0.6308(8)	C(60)	-0.441(2)	-0.833(2)	-0.5593(9)
C(61)	-0.407(2)	-0.957(2)	-0.564(1)	O(62)	0.001(1)	-0.558(1)	-0.1049(5)
C(63)	0.039(1)	-0.493(2)	-0.0484(8)	C(64)	0.092(1)	-0.377(2)	-0.0634(8)
C(65)	-0.063(2)	-0.670(2)	-0.097(1)	C(66)	-0.021(2)	-0.764(2)	-0.132(1)

(*Received in Germany* 12 *September* 1994; *accepted* 2 *November* 1994)