C2—C1—C6	122.0 (3)	C6—C5—C4	111.2 (2)
C1—C2—C3	124.6 (3)	C8—O3—C5	117.2 (3)
O1—C3—C2	107.4 (3)	O4—C8—O3	122.8 (4)
O1—C3—C4	109.3 (3)	O4—C8—C9	126.2 (4)
C2—C3—C4	112.7 (3)	O3—C8—C9	111.0 (4)
O2—C4—C7	110.2 (2)	O5—C6—C1	109.4 (3)
O2—C4—C5	103.2 (2)	O5—C6—C5	108.7 (2)
C7—C4—C5	110.6 (2)	C1—C6—C5	112.8 (3)
O2—C4—C3	109.2 (2)	C10—O5—C6	115.9 (3)
C7—C4—C3	112.6 (3)	O6—C10—O5	122.7 (3)
C5—C4—C3	110.7 (2)	O6—C10—C11	125.2 (4)
O3—C5—C6	108.8 (3)	O5—C10—C11	112.1 (3)
O3—C5—C4	106.7 (2)		

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1*A*···O2^{i}	0.82	2.02	2.793 (4)	157
O2—H2*A*···O1	0.82	2.33	2.707 (4)	110
O2—H2*A*···O6^{i}	0.82	2.24	2.873 (4)	135

Symmetry code: (i) $1-x, y-\frac{1}{2}, 1-z$.

The H atoms were placed at geometrically suitable positions and refined with fixed isotropic displacement parameters $U_{iso} = 1.2U_{eq}$ of the parent atom, except those belonging to O1, O2, C9 and C11, which were refined with $U_{iso} = 1.5U_{eq}$. The absolute stereochemistry could not be determined from refinement of the Flack parameter because intensities from Friedel mates were not measured. The reported stereochemistry of the structure is consistent with the stereochemistry of the starting material and with spectroscopic studies (Brovetto *et al.*, 1999).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1993). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *MSC/AFC Diffractometer Control Software*. Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997). Molecular graphics: *ZORTEP* (Zsolnai & Pritzkow, 1995). Software used to prepare material for publication: *PLATON*98 (Spek, 1990).

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References

Brovetto, M., Schapiro, V., Cavalli, G., Padilla, P., Sierra, A., Seoane, G., Suescun, L. & Mariezcurrena, R. (1999). *New J. Chem.* **23**, 549.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Hudlicky, T., Luna, H., Barbieri, G. & Kwart, L. (1988). *J. Am. Chem. Soc.* **110**, 4735–4741.
Jeffrey, G. A., Maluszynska, H. & Mitra, J. (1985). *Int. J. Biol. Macromol.* **7**, 336–348.
Molecular Structure Corporation (1993). *MSC/AFC Diffractometer Control Software*. Version 5.1.0. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1997). *SHELXL*97. *Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
Spek, A. L. (1990). *PLATON*98. *Program for the Automated Analysis of Molecular Geometry*. University of Utrecht, The Netherlands.
Zsolnai, L. & Pritzkow, H. (1995). *ZORTEP. An Interactive ORTEP Program*. University of Heidelberg, Germany.

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3,4,5,6-Tetrahydro-2*H*-naphtho[1,2-*b*]-pyran-2-spiro-2′-1′,2′,3′,4′-tetrahydronaphthalene-1′-one

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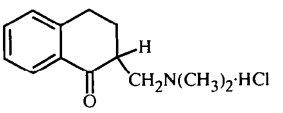
Abstract

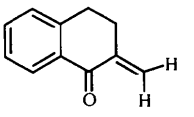
The title compound, $C_{22}H_{20}O_2$, was unexpectedly obtained in an attempt to synthesize 2-methylene-3,4-dihydronaphthalen-1(2*H*)-one, a candidate cytotoxic and anticancer agent, and is a dimer of the expected product.

Comment

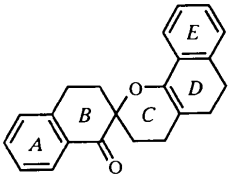
Recently, the cytotoxic evaluation of the Mannich base (1) revealed that its IC_{50} figure towards murine P388 leukaemia cells was 2.3 μ*M* (Dimmock *et al.*, 1998). Since Mannich bases are highly susceptible to deamination, liberating the corresponding α,β-unsaturated ketones (Carey & Sundberg, 1977), the preparation and bioevaluation of (2) was planned, with the aim of understanding whether (1) or its putative breakdown product (2) was principally responsible for cytotoxicity. After heating an aqueous solution of (1) with a slight molar excess of potassium carbonate, a product was obtained whose mass spectrum indicated a molecular ion of 316, *i.e.* twice the value of (2). A survey of the literature revealed that a dimer of (2) had been reported previously (Brugidou & Christol, 1966), for which structure (3) had been proposed (Mühlstädt & Gensrich, 1966; Brugidou *et al.*, 1967).



(1)



(2)



(3)

The objective of the present study was to determine the structure of the 'dimer' in order to evaluate the structure proposed and also to examine the shape of the molecule. The 'dimer' was active not only towards P388 cells (IC_{50} = 17 μM), but also to human K-562 and SR leukaemic cell lines, the IC_{50} values being 19 and 9.5 μM, respectively. Thus, a knowledge of the structure and shape of the molecule may afford some indication as to the contributions of different groups to bioactivity.

The structure of the title compound, (3), is confirmed to be the same as that proposed previously (Mühlstädt & Gensrich, 1966; Brugidou *et al.*, 1967) and is presumably formed by a Diels–Alder-like reaction. The 'dimer' can be viewed as two approximately planar components joined by a spiro-C atom. The two components are both systems of fused six-membered rings, each component containing a phenyl ring. The two phenyl rings are nearly perpendicular to one another [75.95 (5)°].

The features of the molecule that may influence its cytotoxicity are a ketonic-O atom, an ether-O atom and the two phenyl rings. The O atoms can interact with proton-donor groups on proteins or DNA, and the phenyl rings can have stacking interactions with aromatic systems on proteins or DNA. In addition, the phenyl rings can fit into major and minor grooves of DNA helices. The geometric relationship between these features may determine how this molecule interacts with a given binding site.

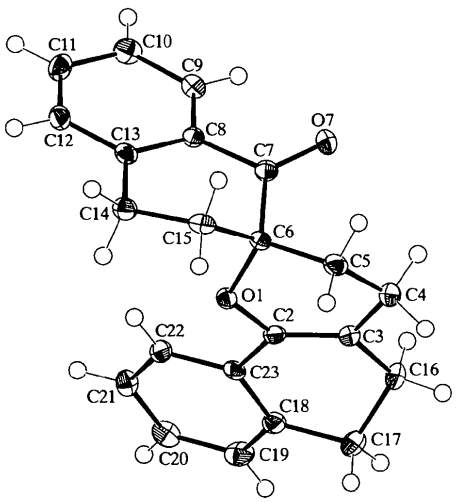


Fig. 1. A general *ORTEP* view (*Xtal*3.5; Hall *et al.*, 1997) of the title compound with non-H-atom displacement ellipsoids drawn at the 50% probability level. For clarity, the H atoms are drawn as small spheres of arbitrary size.

Experimental

A solution of potassium carbonate (0.01 mol) in water (10 ml) was added slowly to a solution of (1) (0.008 mol) in water (20 ml). The mixture was heated under reflux for 24 h and after cooling, was extracted three times with chloroform. The combined organic extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the solvent gave a product which on recrystallization from diethyl ether/methanol gave (3) in 38% yield; m.p. 383 K (literature: 379–380 K; Mühlstädt & Gensrich, 1966). Analysis calculated for $C_{22}H_{20}O_2$: C 83.51, H 6.37%; found: C 83.27, H 6.33%. The cytotoxic evaluation of (1) and the 'dimer' against murine P388 D1 cells was undertaken according to a literature procedure (Phillips *et al.*, 1989) and examination against human leukaemic cells was performed according to a reported protocol (Boyd & Paull, 1995).

Crystal data

$C_{22}H_{20}O_2$
M_r = 316.399
Monoclinic
$P2_1/c$
a = 8.0204 (5) Å
b = 9.0398 (10) Å
c = 22.5974 (15) Å
β = 96.362 (6)°
V = 1628.3 (2) Å^3
Z = 4
D_x = 1.2907 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 10.38–18.17°
μ = 0.081 mm^{-1}
T = 123 (2) K
Block
0.47 × 0.25 × 0.20 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.936, T_{max} = 1.000
3762 measured reflections
3286 independent reflections
2825 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 26.28°
$h = -9 \rightarrow 9$
$k = 0 \rightarrow 11$
$l = 0 \rightarrow 28$
3 standard reflections
every 200 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.199
S = 1.047
3286 reflections
218 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0491P)^2 + 0.6387P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.315 e Å^{-3}
$\Delta\rho_{min}$ = −0.197 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0072 (13)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1992). Cell refinement: *CAD-4 EXPRESS*. Data reduction: *Xtal*3.5 (Hall *et al.*, 1997). Program(s) used to solve structure: *Xtal*3.5. Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997). Molecular graphics: *Xtal*3.5. Software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1069). Services for accessing these data are described at the back of the journal.

References

Boyd, M. R. & Paull, K. D. (1995). *Drug Dev. Res.* **34**, 91–109.
Brugidou, J. & Christol, H. (1966). *Bull. Soc. Chim. Fr.* pp. 1693–1698.
Brugidou, J., Christol, H. & Sachetto, J. P. (1967). *Bull. Soc. Chim. Fr.* pp. 2579–2584.
Carey, F. A. & Sundberg, R. J. (1977). *Advanced Organic Chemistry*, Part B, p. 46. New York: Plenum Press.
Dimmock, J. R., Pandeya, S. N., Allen, T. M. & Kao, G. Y. (1998). *Pharmazie*, **53**, 201–202.
Enraf–Nonius (1992). *CAD-4 EXPRESS*. Version 1.1. Enraf–Nonius, Delft, The Netherlands.
Hall, S. R., King, G. S. D. & Stewart, J. M. (1997). Editors. *Xtal3.5 User's Manual*. University of Western Australia, Australia.
Mühlstädt, M. & Gensrich, H. J. (1966). *J. Prakt. Chem.* **34**, 139–144.
North, A. C. T., Phillips, D. C. & Mathews, F. C. (1968). *Acta Cryst.* A**24**, 351–359.
Phillips, O. A., Nelson, L. A., Knaus, E. E., Allen, T. M. & Fathi-Afshar, R. (1989). *Drug Des. Deliv.* **4**, 121.
Sheldrick, G. M. (1997). *SHELXL97. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

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(*S*)-2,2′-Bis(methoxymethoxy)[1,1′-binaphthyl]-3,3′-dicarbaldehyde

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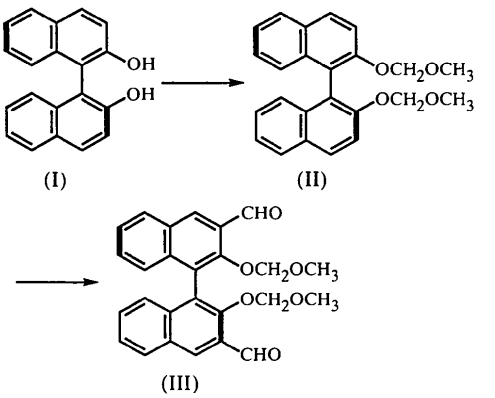
Abstract

The two naphthalene rings of the title compound, $C_{26}H_{22}O_6$, are in a *transoid* conformation. The dihedral angle between the mean planes of the naphthalene rings is large at 107.1 (3)°.

Comment

Optically active 1,1′-binaphthalene derivatives have been widely used in asymmetric reaction as chiral auxiliaries (Rosini *et al.*, 1992; Noyori, 1994). One of their advantages is that the dihedral angles between the two naphthalene ring systems have enough flexibility and adapt to the complexation with various metal ions. To some extent, the molecules can avoid possible steric repulsion by varying their dihedral angles. Their conformation has been analysed in solution using circular dichroism (Hanazaki & Akimoto, 1972; Mason *et al.*, 1974), and in the solid state by X-ray diffraction (Akimoto & Iitaka, 1969; Kerr & Robertson, 1969; Harata & Tanaka, 1973; Kuroda & Mason, 1981; Pauptit & Trotter, 1981, 1983; Franzini *et al.*, 1991).

We herein report the crystal structure of an optically active (*S*)-binaphthalene derivative having 2,2′-bis(methoxymethoxy) and 3,3′-dicarbaldehyde groups. The title compound, (III), was prepared in two steps as shown in the scheme from commercially available (*S*)-1,1′-bi-2-naphthol, (I). [A methoxymethoxy (MOM) group is a flexible chain of moderate length, and synthetically useful both for chelating to metal ions and for protecting an hydroxyl group. A formyl group is also a versatile functional group in organic synthesis.]



(I) (II) (III)

The two naphthalene rings are almost planar with mean deviations of 0.017 (3) and 0.039 (3) Å. The dihedral angle between the least-squares planes of the two rings is 107.1 (3)°. To the best of our knowledge, it is one of the largest values ever reported in the crystal structure of 1,1′-binaphthalene derivatives [*cf.* 103.1 for (*R*)-1,1′-binaphthyl (Kuroda & Mason, 1981) and 111° for 2,2′-dimethoxy-1,1′-binaphthyl (Gridunova *et al.*, 1983)]. Interestingly, the crystals of these three compounds belong to the same space group, $P4_12_12$. Crystal packing of (*R*)-1,1′-binaphthyl was discussed in detail in comparison with that of racemic 1,1′-binaphthyl whose crystal belongs to the *C*2/*c* group (Kuroda & Mason, 1981). This packing is relatively loose, thus causing a larger volume per molecule. It