$C_{21}H_{24}FNO_3$

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# 4-Cyano-4'-[(4R)-4,5-epoxypentyloxy]biphenyl: a Pseudosymmetry Problem Solved with Synchrotron Data

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## Abstract

The title compound, 4'-[(4R)-4,5-epoxypentyloxy]-4-biphenylcarbonitrile, $C_{18}H_{17}NO_2$, crystallizes in space group $P2_1$ with two independent molecules of identical chirality. The molecules differ significantly only in the conformation of the substituent containing the epoxide ring. With the exception of this ring, the structure approximates closely to the centrosymmetric space group $P2_1/n$, in which refinement can be achieved with the assumption of twofold disorder of orientation of the epoxide ring and a racemic material. The pseudosymmetry is resolved by a weak subset of $h0l$ reflections ($h + l = 2n$), which are found to be significant in a synchrotron data set. The two rings of the biphenyl unit are essentially coplanar, in contrast to most 4-cyano-4'-(alkyloxy)biphenyl compounds.

## Comment

The title compound, (3), was synthesized as part of a study of chiral side-chain liquid crystalline polymers. Only very thin plate crystals could be obtained and no measurable diffraction pattern was found on an Enraf–Nonius FAST diffractometer with Mo $K\alpha$ radiation from a rotating-anode source. Satisfactory data were collected during the commissioning of the new high-flux single-crystal diffraction station 9.8 at CCLRC Daresbury Laboratory Synchrotron Radiation Source (Cernik *et al.*, 1997).

(1)



(2)



(3)
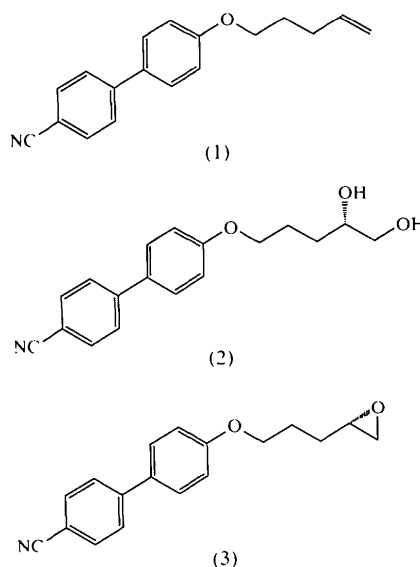
Intensity statistics strongly suggested a centrosymmetric structure, and the presence of a $2_1$ axis was clearly indicated; the mean intensity for $h0l$ reflections with $h + l = 2n + 1$ was only about 10% that of the rest of the data, and they were initially taken to be systematic absences. Structure solution was possible in space group $P2_1/n$ and refinement required a twofold disorder of orientation of the epoxide ring. All other molecular features appeared normal and the final residuals were acceptable, *e.g.* $R$ was approximately 0.07. In this case, the material must be racemic.

The '$n$-glide absences' in the data set, although considerably weaker than the general reflections, were markedly more intense than the absences due to the $2_1$ axis, and the mean $I/\sigma$ ratio was 6.1 for this subset of data (13.4 for the complete data set and 0.4 for the screw-axis absences). There is anecdotal evidence for the overestimation of weak intensities by area-detector systems, but some of the explanations proposed do not apply for synchrotron data collected in this experiment; for example, the second-order harmonic of the selected wavelength (Kirschbaum *et al.*, 1997) is absent, corresponding to the 'forbidden' (in spherical atom terms) 222 reflection of the silicon monochromator, and higher-order harmonics should be rejected by the vertically focusing mirror.

The assumption of space group $P2_1$ led to a solution with two molecules in the asymmetric unit. In this case, apparent disorder of the epoxide rings was due to pseudosymmetry (an approximate inversion centre relating the two molecules), which could be overcome by selection of correct atom sites from the double images initially obtained in electron-density syntheses. On refinement, the second image of each ring disappeared and the molecular geometry was normal, without the need of any constraints or restraints other than the usual con-

strained treatment of H atoms (all of which could be located in a difference synthesis). The weak subset of $h0l$ observed data is matched closely by the calculated data.

Comparison of the two independent molecules in the asymmetric unit (Fig. 1) shows that they have similar bond lengths and angles, which are normal for their respective types. They differ significantly only in the conformation of the substituent containing the epoxide ring. The centroids of the two molecules are separated by 0.5067 (2) and 0.4962 (2) in $x$ and $z$, respectively, and a least-squares fit of one molecule to the inverse of the other (they both have identical chirality) gives an r.m.s. deviation of only 0.032 Å for the non-H atoms, excluding the epoxide ring. Clearly it is essentially only the disposition of this ring, together with the chirality at C17/C35, which breaks the $P2_1/n$ pseudosymmetry; this accounts for the centrosymmetric intensity statistics and the very weak subset of $h0l$ reflections, which are effectively contributed to by only a small fraction of the atoms in the structure.

A search of the most recent release of the Cambridge Structural Database (Allen & Kennard, 1993) revealed 21 other structures of compounds in which the hydroxy H atom of 4'-hydroxy-4-biphenylcarbonitrile is replaced by an alkyl or substituted-alkyl group, some of them determined more than once, usually in the context of liquid-crystal investigations. Bond lengths and angles within the common core of these molecules remain essentially invariant over the range of substituents, but conformations vary, particularly for the degree of planarity of the biphenyl unit. In most cases, the dihedral angle between the mean planes of the two aromatic rings lies between 30 and 48°, maximum conjugation and the possibility of efficient parallel stacking of planar units being insufficient to overcome the steric interference of H atoms *ortho* to the inter-ring bond (Shklover *et al.*, 1987; Walz *et al.*, 1987; Gehring *et al.*, 1991; Malpezzi *et al.*, 1991; Kravers *et al.*, 1992; Zugenmaier & Heiske, 1993; Hori *et al.*, 1993; Hori, Koma *et al.*, 1996; Hori, Kurosaki *et al.*, 1996). In a small number of cases, the dihedral angle is rather smaller: about 23° (Gehring *et al.*, 1991; Zugenmaier & Heiske, 1993; Joachimi *et al.*, 1995) and about 13° (Joachimi *et al.*, 1995). For just two compounds, essentially coplanar rings are found, with a dihedral angle <3° (Mandal & Paul, 1985; Kravers *et al.*, 1992; Hori, Kurosaki *et al.*, 1996). In the two crystallographically independent molecules of the title compound, the dihedral angles are 1.7 (2) and 1.6 (2)°. There is no correlation between this dihedral angle and the size or nature of the substituent on oxygen. Indeed, in some cases, polymorphs of the same compound have quite different conformations and diverse values are found for crystallographically independent molecules within the same structure.

The title compound does not display liquid crystalline phases on heating or cooling and has a melting point of 361.0 K. The analogous cyanobiphenyl compound with a simple $C_5H_{11}$ alkyl group displays an enantiotropic nematic phase between 321 and 341 K. We found it surprising that the introduction of a small oxa substituent not only rendered the compound non-mesogenic, but also quite significantly increased the melting point. It is interesting to note that the intermediate 1,2-diol [compound (2)] does display a stable enantiotropic chiral nematic phase (356.9–407.0 K), which may be attributed to hydrogen bonding between terminal diol groups, causing an effective increase in molecular length. This implies that the incorporation of a terminal lateral substituent does not entirely explain the lack of mesophase formation in epoxide (3). This is a matter for further investigation.
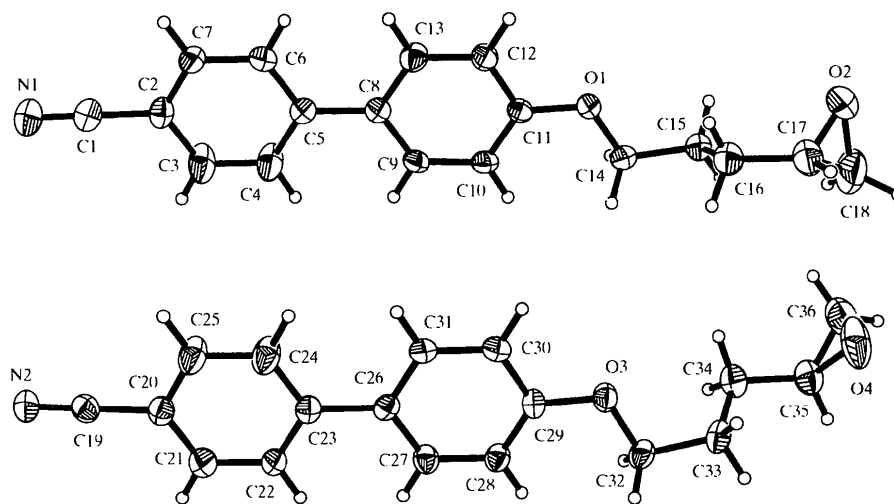


Fig. 1. The structures of both molecules (relative positions and orientations changed to facilitate comparison) with atom labels and 50% probability ellipsoids for non-H atoms.

In the construction and commissioning of a new facility for the collection of data from weakly diffracting single crystals, it is especially satisfying and encouraging to obtain such definitive structural results on the basis of a particularly weak special subset of data, the full set of which is generally of relatively low intensity in any case, and which could not be measured by conventional methods.

## Experimental

The title compound, (3), was synthesized in three steps in 63% overall yield from 4'-hydroxy-4-biphenylcarbonitrile *via* Williamson etherification [to give (1)], followed by asymmetric dihydroxylation [to give (2)] and one-pot epoxidation. 4'-Hydroxy-4-biphenylcarbonitrile (Aldrich, 750 mg, 3.84 mmol) and 1-bromopent-5-ene (687 mg, 4.61 mmol) were refluxed in ethanol (25 ml) with KOH (323 mg, 5.76 mmol) for 20 h. After evaporation of the solvent, the solid residue was dissolved in dichloromethane (25 ml) and the solution washed successively with water, 1 *M* NaOH, 1 *M* NaCl and brine, then dried over MgSO$_4$. Removal of the solvent gave a yellow solid, which was purified by filtration through silica (dichloromethane eluent) to give (1) (929 mg, 69%). Alkene (1) (400 mg) was treated under standard asymmetric dihydroxylation conditions (Kolb *et al.*, 1994) to give 440 mg of diol (2) (97%). This diol (400 mg) was converted to (3) *via* the cyclic *ortho*-ester and acetyl chlorohydrin according to the general procedure of Kolb & Sharpless (1992); yield 357 mg (95%). It was recrystallized from CH$_2$Cl$_2$–EtOH by slow solvent evaporation. All intermediate and final products gave satisfactory microanalysis and NMR spectra (Fallis, 1997).

### Crystal data

$C_{18}H_{17}NO_2$
$M_r = 279.33$
Monoclinic
$P2_1$
$a = 12.698 (3)$ Å
$b = 5.6022 (11)$ Å
$c = 21.041 (4)$ Å
$\beta = 106.387 (4)°$
$V = 1436.0 (5)$ Å$^3$
$Z = 4$
$D_x = 1.292$ Mg m$^{-3}$
$D_m$ not measured

Synchrotron radiation
$\lambda = 0.6956$ Å
Cell parameters from 6753 reflections
$\theta = 1.69–26.30°$
$\mu = 0.084$ mm$^{-1}$
$T = 160 (2)$ K
Plate
$0.25 \times 0.16 \times 0.03$ mm
Colourless

### Data collection

Siemens SMART CCD diffractometer with Oxford Cryosystems Cryostream cooler (Cosier & Glazer, 1986)
$\omega$ rotation scans with narrow frames
Absorption correction: none
9761 measured reflections
4831 independent reflections (including Friedel pairs)

3939 reflections with $I > 2\sigma(I)$
$R_{int} = 0.026$
$\theta_{max} = 25.76°$
$h = -14 \rightarrow 15$
$k = -6 \rightarrow 6$
$l = -26 \rightarrow 25$
Intensity decay: 14%

### Refinement

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.046$
$wR(F^2) = 0.133$
$S = 1.034$
4831 reflections
379 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.0821P)^2 + 0.157P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.003$
$\Delta\rho_{max} = 0.34$ e Å$^{-3}$
$\Delta\rho_{min} = -0.27$ e Å$^{-3}$
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = $-0.4 (15)$

### Table 1. *Selected torsion angles (°)*

| | | | |
|---|---|---|---|
| C11—O1—C14—C15 | -176.84 (19) | C29—O3—C32—C33 | 178.12 (18) |
| O1—C14—C15—C16 | 67.3 (3) | O3—C32—C33—C34 | -69.4 (3) |
| C14—C15—C16—C17 | 172.7 (2) | C32—C33—C34—C35 | -166.3 (2) |
| C15—C16—C17—C18 | -24.6 (4) | C33—C34—C35—O4 | -80.0 (3) |
| C15—C16—C17—O2 | 48.0 (5) | C33—C34—C35—C36 | -151.1 (3) |
| C16—C17—C18—O2 | 105.4 (3) | C34—C35—C36—O4 | 105.7 (3) |
| C16—C17—O2—C18 | -116.7 (4) | C34—C35—O4—C36 | -114.0 (3) |

The data collection nominally covered over a hemisphere of reciprocal space, by a combination of three sets of exposures; each set had a different $\varphi$ angle for the crystal and each exposure covered 0.15° in $\omega$. The intensities were corrected for decay of the synchrotron beam as part of standard inter-frame scaling (Sheldrick, 1997). H atoms were placed geometrically and refined with a riding model and with $U_{iso}$ constrained to be $1.2U_{eq}$ of the carrier atom. For the combination of X-ray wavelength and elements present, anomalous dispersion effects do not permit a determination of the absolute structure.

Data collection: *SMART* (Siemens, 1995). Cell refinement: local programs. Data reduction: *SAINT* (Siemens, 1995). Program(s) used to solve structure: *SHELXTL* (Sheldrick, 1994). Program(s) used to refine structure: *SHELXTL*. Molecular graphics: *SHELXTL*. Software used to prepare material for publication: *SHELXTL* and local programs.

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# 7-(4-Hydroxy-3-methoxyphenyl)-6-hydroxy-methyl-4,10-dimethoxy-2,8-dipropyl-*cis*-6,7-dihydrodibenzo[*b*,*d*]oxepin-11-ol

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## Abstract

The title compound, $C_{30}H_{36}O_7$, has a dibenzoxepine structure formed by acid treatment of a lignin model compound with a dibenzodioxocine structure.

## Comment

Dibenzodioxocines are novel 'neolignans' involving an eight-membered ring system formed in an oxidative coupling reaction of an *o*,*o*′-dihydroxybiphenyl structure with coniferyl alcohol (Karhunen *et al.*, 1995*a*). These structural units have been shown to be present in softwood lignins (Karhunen *et al.*, 1995*b*; Ralph *et al.*, 1997). The elucidation of the chemical behaviour of lignin, especially in degradation procedures, is greatly

facilitated by studying the behaviour of appropriate model compounds under degradative conditions. In order to investigate the reactivity of the dibenzodioxocine structures, hydrolytic reactions have been carried out with compound (I). Under acidic conditions, the main product is observed to have a dibenzoxepine structure, probably formed *via* a benzyl cation (Karhunen *et al.*, 1996). Two isomeric products have been isolated, (II*a*) (major) and (II*b*) (minor). The NMR data of (II*a*) and (II*b*), and the crystal structures of (II*a*) (peracetate) and (III) have been reported previously (Karhunen *et al.*, 1996). We report here the structure of the *cis*-isomer, (II*b*).
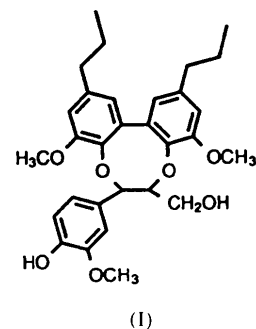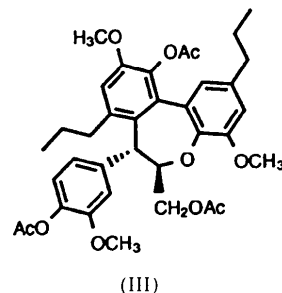


(I)

$H^+$. 323 K
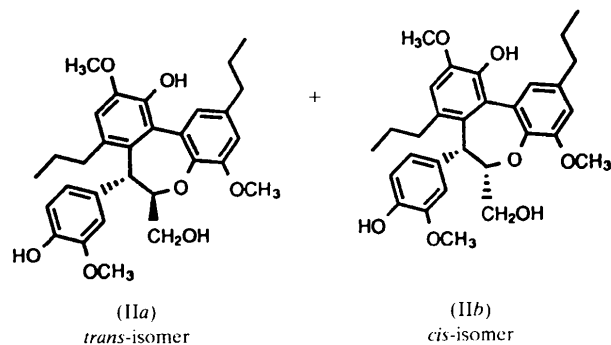


(II*a*)
*trans*-isomer

(II*b*)
*cis*-isomer



(III)

The geometry and numbering scheme of the title molecule are shown in Fig. 1. The most interesting part of the molecule is the seven-membered ring, which is in the boat conformation. Atoms C7, C14 and C19 are above the mean plane defined by atoms C8, C13,