Table 2. *Cremer & Pople* puckering parameters (Å, °) of the rings A–E*

	Size	Q, q_2	Φ, φ_2	θ	Type†
A	6	0.546 (8)	89 (4)	10.9 (8)	*c*
B	6	0.547 (7)	215.2 (9)	50.3 (7)	*h*
C	6	0.520 (7)	171 (3)	14.4 (8)	*c*
D	5	0.111 (7)	144 (3)	—	*e*
E	5	0.189 (7)	52 (2)	—	*t*

* Cremer & Pople (1975); Luger & Bülow (1983). † Type: *c* = chair; *h* = half-chair; *t* = twist; *e* = envelope.

Data collection: Stoe software. Cell refinement: Stoe software. Data reduction: in-house program. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *SCHAKAL*88 (Keller, 1988). Software used to prepare material for publication: *SHELXL*93.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: JZ1101). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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3-(1-Naphthyloxy)-1,2-benzisothiazole 1,1-Dioxide: Electronic Effects of Conjugation

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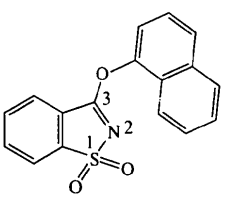
Abstract

The conjugation of oxygen with an aromatic ring, as in 1-naphthol, results in a C—O bond length of 1.35 Å and a C—O—C bond angle of almost 120°, whereas the C—O bond length in an aliphatic ether is about 1.45 Å, with a C—O—C angle of about 110°. The pseudo-saccharyl ether of 1-naphthol, $C_{17}H_{11}NO_3S$, changes the phenolic C—O bond length to 1.422 (7) Å, while maintaining the C—O—C angle. The result implies that the original naphtholic O atom is no longer π-conjugated with the naphthalene ring system, but only with the saccharyl system.

Comment

Derivatives of saccharin are known for their biological activity (Strupczewski *et al.*, 1995). The saccharyl system has also been used as a cheap and effective leaving group in important chemical transformations such as the derivatization of phenols prior to their conversion into arenes by transfer hydrogenolysis (Brigas & Johnstone, 1990) and for cross-coupling C—C bond formation with zinc and tin organometallic reagents (Brigas & Johnstone, 1994). Phenolic saccharyl ethers such as the title compound, 3-(1-naphthyloxy)-1,2-benzisothiazole 1,1-dioxide, (1), are easily prepared in high yield.



(1)

The effect of the saccharyl system on the conjugation of oxygen into an aryl ring has been discussed in a previous paper (Brigas & Johnstone, 1996). Briefly, for a simple benzene compound (the *O*-saccharyl ether of 4-methoxyphenol), it was shown that the original C—O

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phenolic bond was lengthened on formation of the ether, but that the methoxy C—O bond remained unchanged. This lengthening of the C—O bond is a factor in facilitating C—O bond catalytic hydrogenolysis.

In the present work, the structure of a saccharyl ether, (1), of the more extensively aromatic naphthalene (10 coplanar π electrons) is compared with that of the smaller aromatic benzene (six coplanar π electrons). There are two molecules in the unit cell, but the structure of only one of them is given as they are identical to within three times the error limits.

The investigation of (1) reveals several important points. Firstly, the geometry of the naphthalene skeleton is very similar to that of naphthalene itself (Mitchell & Cross, 1958); the same holds for the saccharyl ether compared with saccharin (Dart, 1968). In (1), the central C—O—C linkage (C1—O1—C8) is much shorter on the saccharyl side [C1—O1 1.316 (7) Å] than on the naphthyl side [C8—O1 1.422 (7) Å] and, with a bond angle of 117.5 (4)°, is near the 120° required for an sp^2 hybrid. These values, coupled with the sp^2 nature of the oxygen (O1) indicate very clearly that this atom is conjugated strongly with the saccharyl ring system but not at all with that of the naphthalene. The C8 atom is also sp^2 so that the C8—O1 bond could be expected to be about 1.32 Å for an sp^2—sp^2 connection, but instead, the value of 1.422 (7) Å for this bond is very similar to that for a single C—O bond (sp^3—sp^3). This long bond could be considered to be due to the fact that, in the crystal, the plane of the naphthyl ring is at right angles to that of the saccharyl ring system. If O1 conjugates with C1 through an sp^2 hybrid then it cannot also conjugate with C8 and, although C8—O1 might be longer than expected for simple sp^2—sp^2 conjugation, it should not be as long as a simple sp^3—sp^3 hybrid bond.

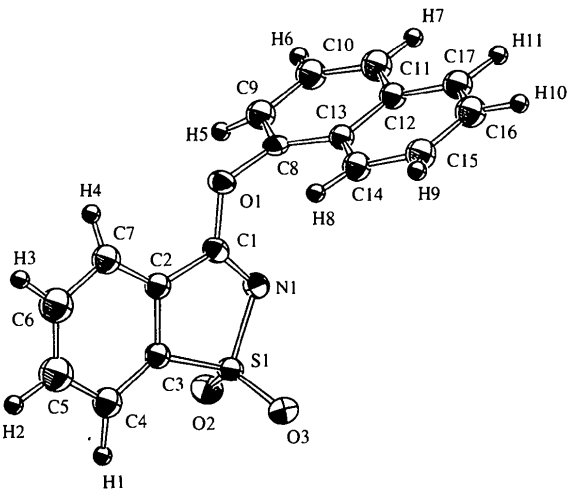

Fig. 1. Perspective view of the title compound showing 50% probability displacement ellipsoids. The atomic numbering system does not follow normal rules of chemical nomenclature. H atoms have been assigned arbitrary radii.

Similar conclusions concerning less highly conjugated ethers were reached in a survey of C—O bond lengths taken from the Cambridge Structural Database (Allen & Kirby, 1984).

The above results imply that the C8—O1 bond must have stretched and become more ionic. A simple calculation of percentage ionic character in a bond (Pauling, 1939) suggests that the C8—O1 bond is behaving as though the oxygen (O1) is much more electronegative than in most ethers. This finding would be entirely consistent with the strongly electron-withdrawing nature of the attached saccharyl ring system. Some verification for this increase in effective electronegativity of O1 can be gleaned from a comparison of the ^{1}H NMR spectra of various saccharyl ethers of phenols with those of the phenols themselves; there is a change in chemical shift for all protons in the phenol from their normal positions near δ 6.8 to a value near δ 7.2–7.3 p.p.m., which is typical of an electron-withdrawing substituent.

If the C8—O1 bond is closer to a single bond, it would be expected that the original naphtholic conjugated C—O bond strength would fall by about 70 kJ mol^{-1}, becoming more like that of an aliphatic C—O bond (Weast, 1976). This change is undoubtedly one important reason for making the saccharyl system a good leaving group for catalytic hydrogenolysis and cross-coupling, but it is not the only reason because simple alkyl saccharyl ethers are unreactive under reaction conditions similar to those giving rapid easy hydrogenolysis of aromatic saccharyl ethers (Brigas & Johnstone, 1994).

Experimental

A mixture of pseudo-saccharyl chloride (7.6 g, 0.026 mol), triethylamine (3.4 g, 0.034 mol) and 1-naphthol (3.7 g, 0.026 mol) in toluene (100 ml) was stirred under reflux for 2 h. The precipitate of triethylamine hydrochloride was filtered off and the filtrate was washed with 0.5 *M* HCl, aqueous $NaHCO_3$ and water before being dried (Na_2SO_4). After filtration and evaporation of the solvent, the residual solid was recrystallized from toluene as colourless crystals (m.p. 474–475 K, 85% yield). Elemental analysis: calculated for $C_{17}H_{11}NO_3S$ C 66.0, H 3.6, N 4.5%; found C 66.1, H 3.5, N 4.3%. ^{1}H NMR [$(CD_3)_2SO$, 295 K]: 8.20–8.31 (*m*, 4H, ArH), 7.89–8.15 p.p.m. (*m*, 7H, ArH). IR (ν_{max}): 1615, 1555, 1378, 1325, 1173, 1157, 772 cm^{-1}. MS: *m/z* 309 (M^+).

Crystal data

$C_{17}H_{11}NO_3S$
M_r = 309.34
Orthorhombic
$Pca2_1$
a = 15.875 (9) Å
b = 13.09 (1) Å
c = 13.771 (8) Å
V = 2861 (5) Å^3
Z = 8
D_x = 1.436 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.7107 Å
Cell parameters from 20 reflections
θ = 3.34–5.57°
μ = 0.1133 mm^{-1}
T = 153 K
Plate
0.40 × 0.35 × 0.15 mm
Colourless

Data collection

Rigaku AFC-6*S* diffractometer	$\theta_{max} = 24.97°$
$\omega/2\theta$ scans	$h = 0 \rightarrow 19$
Absorption correction: none	$k = 0 \rightarrow 16$
2850 measured reflections	$l = 0 \rightarrow 16$
2850 independent reflections	3 standard reflections monitored every 150 reflections
2020 observed reflections $[I > 3\sigma(I)]$	intensity decay: 1.10%

Refinement

Refinement on F	$w = 4F_o^2/\sigma^2(F_o^2)$
$R = 0.0449$	$(\Delta/\sigma)_{max} = 0.014$
$wR = 0.0491$	$\Delta\rho_{max} = 0.32$ e Å^{-3}
$S = 1.586$	$\Delta\rho_{min} = -0.30$ e Å^{-3}
2018 reflections	Extinction correction: none
246 parameters	Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)
H-atom positions were found from ΔF synthesis and included with $U_{iso}(H) = 1.2U_{eq}(C)$	Absolute configuration: not established

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	U_{eq}
S1	0.08324 (9)	0.41793 (10)	0.3682	0.0247 (7)
S2	0.25715 (9)	0.01417 (10)	0.1303 (2)	0.0254 (7)
O1	0.0654 (3)	0.6548 (3)	0.2240 (3)	0.027 (2)
O2	0.1614 (3)	0.3964 (3)	0.4146 (3)	0.033 (2)
O3	0.0084 (3)	0.3798 (3)	0.4120 (3)	0.032 (2)
O4	0.4164 (2)	−0.1396 (3)	0.2606 (3)	0.029 (2)
O5	0.2251 (3)	−0.0289 (3)	0.0426 (3)	0.037 (3)
O6	0.2020 (3)	0.0795 (3)	0.1836 (3)	0.036 (2)
N1	0.0734 (3)	0.5437 (3)	0.3523 (4)	0.025 (3)
N2	0.2896 (3)	−0.0791 (4)	0.2022 (4)	0.029 (3)
C1	0.0722 (3)	0.5627 (4)	0.2616 (4)	0.023 (3)
C2	0.0795 (4)	0.4772 (4)	0.1919 (4)	0.025 (1)
C3	0.0886 (4)	0.3870 (4)	0.2426 (4)	0.023 (1)
C4	0.1017 (4)	0.2943 (5)	0.1979 (5)	0.032 (2)
C5	0.1046 (5)	0.2969 (5)	0.0967 (6)	0.046 (2)
C6	0.0945 (4)	0.3852 (5)	0.0457 (5)	0.044 (2)
C7	0.0823 (4)	0.4778 (5)	0.0912 (5)	0.031 (2)
C8	0.0607 (4)	0.7386 (4)	0.2894 (4)	0.025 (3)
C9	0.1321 (4)	0.7882 (5)	0.3126 (5)	0.031 (2)
C10	0.1291 (4)	0.8757 (4)	0.3700 (5)	0.034 (1)
C11	0.0521 (4)	0.9115 (5)	0.4024 (5)	0.036 (2)
C12	−0.0232 (3)	0.8619 (4)	0.3767 (5)	0.027 (1)
C13	−0.0200 (3)	0.7725 (4)	0.3186 (4)	0.023 (1)
C14	−0.0961 (4)	0.7243 (5)	0.2895 (5)	0.029 (1)
C15	−0.1722 (4)	0.7638 (5)	0.3179 (5)	0.034 (2)
C16	−0.1756 (4)	0.8529 (4)	0.3730 (6)	0.036 (2)
C17	−0.1036 (4)	0.8998 (4)	0.4027 (5)	0.031 (2)
C18	0.3702 (3)	−0.0740 (4)	0.2090 (5)	0.024 (3)
C19	0.4158 (4)	0.0088 (4)	0.1585 (4)	0.024 (1)
C20	0.3581 (3)	0.0696 (4)	0.1107 (4)	0.021 (1)
C21	0.3806 (4)	0.1536 (5)	0.0584 (5)	0.030 (1)
C22	0.4676 (4)	0.1747 (5)	0.0545 (5)	0.032 (2)
C23	0.5258 (4)	0.1136 (4)	0.0998 (5)	0.027 (1)
C24	0.5010 (4)	0.0286 (4)	0.1523 (4)	0.026 (1)
C25	0.3717 (4)	−0.2222 (4)	0.3053 (5)	0.029 (3)
C26	0.3491 (4)	−0.2130 (4)	0.3988 (4)	0.025 (1)
C27	0.3099 (4)	−0.2961 (5)	0.4464 (5)	0.034 (2)
C28	0.2953 (4)	−0.3845 (4)	0.3948 (5)	0.031 (2)
C29	0.3184 (4)	−0.3934 (4)	0.2962 (5)	0.027 (1)
C30	0.3584 (4)	−0.3093 (4)	0.2487 (4)	0.023 (1)
C31	0.3798 (4)	−0.3182 (5)	0.1488 (5)	0.033 (2)
C32	0.3622 (4)	−0.4066 (5)	0.1008 (5)	0.042 (2)
C33	0.3229 (4)	−0.4882 (5)	0.1462 (5)	0.043 (2)
C34	0.3011 (4)	−0.4819 (5)	0.2411 (5)	0.036 (2)

Table 2. *Selected geometric parameters (Å, °)*

S1—O2	1.424 (4)	O1—C8	1.422 (7)
S1—O3	1.423 (4)	N1—C1	1.274 (7)
S1—N1	1.668 (5)	C1—C2	1.480 (8)
S1—C3	1.778 (6)	C2—C3	1.379 (8)
O1—C1	1.316 (7)		
O2—S1—O3	117.9 (2)	O1—C1—C2	116.4 (5)
O2—S1—N1	109.6 (2)	N1—C1—C2	119.1 (5)
O2—S1—C3	110.4 (3)	C1—C2—C3	109.2 (5)
O3—S1—N1	108.8 (3)	C1—C2—C7	130.3 (6)
O3—S1—C3	111.9 (3)	S1—C3—C2	107.0 (4)
N1—S1—C3	95.8 (3)	O1—C8—C9	118.6 (5)
C1—O1—C8	117.5 (4)	O1—C8—C13	118.0 (5)
S1—N1—C1	108.9 (4)	C9—C8—C13	123.0 (5)
O1—C1—N1	124.5 (6)		
S1—N1—C1—O1	−179.7 (4)	O2—S1—N1—C1	115.4 (4)
S1—N1—C1—C2	−0.3 (7)	O2—S1—C3—C2	−115.5 (4)
S1—C3—C2—C1	2.0 (6)	N1—S1—C3—C2	−2.0 (5)
O1—C1—C2—C3	178.2 (5)	N1—C1—O1—C8	1.2 (8)
O1—C1—C2—C7	2 (1)	N1—C1—C2—C3	−1.2 (8)
O1—C8—C9—C10	174.7 (5)	C1—O1—C8—C9	94.3 (6)
O1—C8—C13—C12	−174.4 (5)	C1—N1—S1—C3	1.3 (5)
O1—C8—C13—C14	2.9 (8)	C2—C1—O1—C8	−178.2 (5)

Determination of the absolute structure by refinement of the η parameter (Rogers, 1981) was not available within our *TEXSAN* software (Molecular Structure Corporation, 1993). When the structure of opposite polarity was refined there were no significant differences either in the residuals or in the molecular geometry parameters. Although, it was therefore impossible to determine the polarity of the structure, we are confident that this indeterminacy will not significantly affect the structure.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN PROCESS*. Program(s) used to refine structure: *TEXSAN LS*. Software used to prepare material for publication: *TEXSAN FINISH*.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry, along with a view of the two molecules in the unit cell, have been deposited with the IUCr (Reference: BM1049). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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A Key Intermediate in the Synthesis of (+)-Hernandulcin

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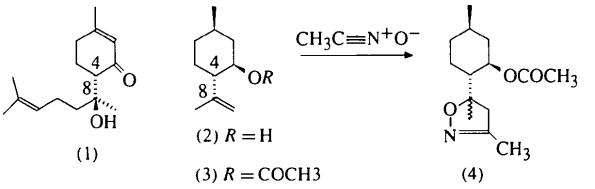
Abstract

(5*R*)-3,5-Dimethyl-5-[(1′*R*,2′*R*,4′*R*)-2′-acetoxy-4′-methylcyclohexyl]-Δ^2-isoxazoline ($C_{14}H_{23}NO_3$) is a key intermediate in the reaction pathway aiming at the synthesis of (+)-hernandulcin. The five-membered heterocycle ring is in a twist conformation and the cyclohexane ring is in a chair conformation. The molecular packing involves C—H···O intermolecular contacts.

Comment

The naturally occurring bisabolane sesquiterpene (+)-hernandulcin, (1), isolated from the central american herb *Lippia dulcis*, has been shown to be *ca* 1000 times sweeter than sucrose while being non-mutagenic and non-toxic (Compadre, Raouf, de Compadre, Pezzuto & Kinghorn, 1987). The relative and absolute configurations of (+)-(4*S*,8*S*)-hernandulcin, (1), were proposed as shown in the scheme, based on its synthesis from (*R*)-(−)-limonene (Mori & Kato, 1986).



Our synthetic endeavours towards natural (+)-hernandulcin, (1), are based upon stereoselective cycloaddition reactions of suitable nitrile oxides and (−)-isopulegol, (2), and derivatives. The absolute configuration of (2) is the same as (+)-hernandulcin at C4, and thus the synthetic strategy depends upon the correct diastereoselection at C8 in the cycloaddition reaction. The cycloaddition reaction was carried out on isopulegyl acetate, (3), with acetonitrile oxide, using conditions developed recently in our laboratory, and led in good yield to the cycloadduct isoxazoline, (4), which could be crystallized. The definition of the new stereogenic centre at C8, created in the cycloaddition reaction, is not amenable to the usual spectroscopic methods, including high-field NMR. In order to determine unambiguously its configuration, which will be of aid in the prediction of the steric course of subsequent reactions, a crystal-structure determination of (4) was undertaken.

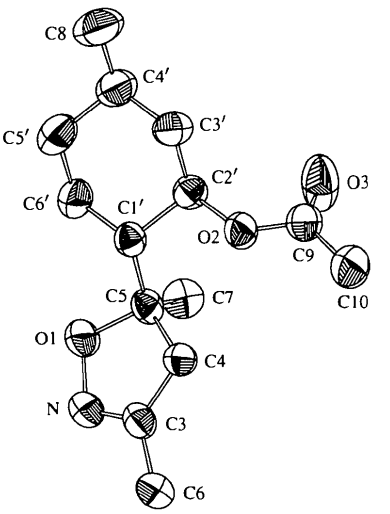


Fig. 1. Projection of $C_{14}H_{23}NO_3$ showing the atom labelling. 50% probability displacement ellipsoids are shown for non-H atoms.

The coplanar relationship between the two rings, which are joined by one single bond, forces the quaternary methyl group into an orthogonal axis. The isoxazoline ring is in a twist conformation and the six-membered carbocycle ring is in a chair conformation, as shown by the Cremer & Pople (1975) puckering parameters of q_2 = 0.258 (4) Å, Φ_2 = 51 (1)° and Q = 0.579 (5) Å, θ = 175.5 (5), Φ = 187 (7)°, respectively. The molecular packing involves intermolecular C—H···O interactions: C4···N^{i} =