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# (1*S*)-(*Z*)-2-Benzyloxy-*N*-(3-methyl-1-butylidene)-1-phenylethylamine *N*-oxide

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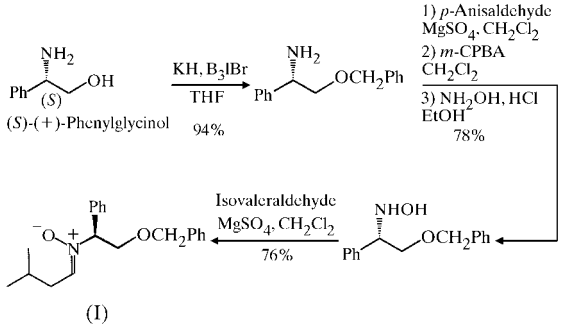
The preparation and crystal structure of the title compound, $C_{20}H_{25}NO_2$, are described. The N atom substituent of the nitrone function adopts a conformation which minimizes the 1,3-allylic strain.

## Comment

The use of nitrones as intermediates in organic synthesis has elicited a great deal of interest over the years (Breuer, 1982; Hamer & Macaluso, 1964). Nitrones undergo 1,3-dipolar cycloaddition reactions with alkenes or alkynes to yield isoxazolidines or isoxazolines, which are easily converted to the corresponding aminoalcohols by N—O bond reduction (Gothelf & Jorgensen, 1998). Two other interesting features of nitrones are their greater stability and greater electrophilicity compared with the corresponding imines. Due to these characteristics, it has been established that nitrones could be used




as precursors for the preparation of hydroxylamines and amines through nucleophilic additions onto the C═N bond (Enders & Reinhold, 1997; Bloch, 1998; Lombardo & Trombini, 2000). Nitrones are also well known as radical spin-trapping agents (Janzen *et al.*, 1978), and their use as potential drugs, antioxidants (Thomas *et al.*, 1994) and enzyme inhibitors (Lee & Kim, 1998) is currently under investigation. Although many nitrones are recorded in the Cambridge Structural Database (2000), very few are homochiral aldonitrones bearing a stereogenic center contiguous to the N atom (Huber *et al.*, 1985; Baskaran *et al.*, 1998; Dhavale *et al.*, 1997). Such nitrones are of interest as potential precursors for the stereoselective synthesis of amine derivatives. Consequently, information regarding the favoured conformation of these homochiral species is needed to help predict and explain the diastereoselectivity of their reactions. In this paper, we describe the preparation of (1*S*)-(*Z*)-2-benzyloxy-*N*-(3-methyl-1-butylidene)-1-phenylethylamine *N*-oxide, (I), from (*S*)-(+)-phenylglycinol and its crystal structure analysis.

X-ray analysis confirmed the *Z* stereochemistry, commonly observed for aldonitrones. A dihedral angle of 11.16 (2)° is observed between the C5/N1/C6 and N1/C6/H11 planes; the H atom of the nitrone function and the benzylic H atom being almost eclipsed. This particular conformation results in a minimization of the 1,3-allylic strain (Hoffmann, 1989). Indeed, the H11—C5—N1—O1—C6—H10 frame is nearly planar, with a mean deviation from the plane of 0.036 Å and a largest deviation for C6 of 0.073 Å. It can be reasonably expected for such a conformation to be adopted in an apolar solution and, consequently, this information could be used to explain the stereoselectivity of nucleophilic additions and cycloadditions onto this nitrone. If we focus on the nitrone function, it is of interest to compare some structural features of the title compound with similar compounds found in the Cambridge Structural Database (2000). There are three bonds originating from the N atom: one to an O atom, another to a C$sp^2$ and a last one to a C$sp^3$ atom. In our case, these distances are 1.303 (2), 1.278 (2) and 1.486 (2) Å, respectively, compared to respective values in other structures of 1.309, 1.288 and 1.490 Å (Huber *et al.*, 1985), 1.308, 1.302 and 1.492 Å (Baskaran *et al.*, 1998), and 1.289, 1.288 and 1.496 Å (Dhavale *et al.*, 1997). If we consider the H atom set on the C$sp^3$ atom, we can define a dihedral angle between the two planes defined by C$sp^2$/N/C$sp^3$ and N/C$sp^3$/H. From the above results, we see that in our case, the angle value is 11.16 (2)°. From the reported examples, we obtain the following values:

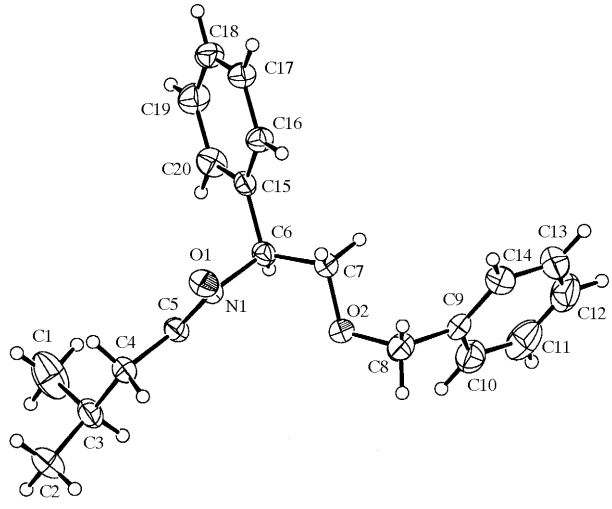



**Figure 1**
*ORTEP*II (Johnson, 1976) molecular diagram of the title compound. Ellipsoids are shown at the 30% probability level.

8.67 (Huber *et al.*, 1985), 3.26 (Baskaran *et al.*, 1998) and 6.43° (Dhavale *et al.*, 1997). Thus, there is a correlation between the dihedral angle value and the C$sp^2$—N length, *i.e.* the longer the C$sp^2$—N bond, the smaller the dihedral angle. This result could be useful when examining stereoselective additions onto nitrones, since facial selectivity should be closely related to the spatial arrangement of the chain set on the N atom.

## Experimental

(*S*)-(+)-Phenylglycinol was selectively *O*-benzylated using potassium hydride and benzyl bromide in tetrahydrofuran (Meyers *et al.*, 1978) in a yield of 94%. The resultant amine was then oxidized by a three-step sequence involving the formation of an imine with *p*-anisaldehyde, oxidation to the corresponding oxaziridine with *meta*-chloroperoxybenzoic acid, and subsequent hydrolysis (Wovkulich & Uskokovic, 1985) to yield *O*-benzylphenylglycinol *N*-hydroxylamine in an overall yield of 78%. The hydroxylamine was then reacted with isovaleraldehyde in the presence of magnesium sulfate as dehydrating agent (Dondoni *et al.*, 1994), to yield the title nitrone as a yellow oil in a non-optimized yield of 76%, according to the following procedure: to a stirred solution of (*S*)-*N*-hydroxy-2-benzyloxy-1-phenylethanamine (2.46 g, 10.1 mmol) in dichloromethane (30 ml) placed under an inert atmosphere were added isovaleraldehyde (869 mg, 10.1 mmol) and anhydrous magnesium sulfate (50 g). Stirring was continued for a period of 12 h, after which the mixture was filtered over celite and the filtrate concentrated under vacuum to yield the crude product. The latter was chromatographed on silica gel using a mixture of pentane/ethyl acetate (1:1) as eluent to afford 2.37 g of the pure nitrone which crystallized upon standing at 279 K (m.p. 321–322 K). $^1$H NMR (300 MHz, $CDCl_3$, p.p.m.): $\delta$ 0.92 (*d*, $J$ = 6.0 Hz, 3H), 0.94 (*d*, $J$ = 6.0 Hz, 3H), 1.89 (*m*, 1H), 2.41 (*m*, 2H), 3.75 (*dd*, $J$ = 4.9, 10.1 Hz, 1H), 4.48 (*t*, $J$ = 10.1 Hz, 1H), 4.53 (*d*, $J$ = 12.1 Hz, 1H), 4.68 (*d*, $J$ = 12.1 Hz, 1H), 4.95 (*dd*, $J$ = 4.9, 10.1 Hz, 1H), 6.85 (*t*, $J$ = 6.0 Hz, 1H), 7.32 (*m*, 8H), 7.48 (*m*, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$, p.p.m.): $\delta$ 22.4, 25.9, 35.3, 69.5, 73.5, 77.9, 127.6, 127.8, 128.3, 128.5, 128.8, 134.7–137.9, 138.9 p.p.m.; analysis calculated for $C_{20}H_{25}NO_2$: C 77.14, H 8.09, N 4.50%; found: C 76.74, H 8.14, N 4.4%.

*Crystal data*

$C_{20}H_{25}NO_2$
$M_r$ = 311.42
Orthorhombic, $P2_12_12_1$
$a$ = 5.639 (3) Å
$b$ = 15.073 (8) Å
$c$ = 21.113 (7) Å
$V$ = 1794 (1) Å$^3$
$Z$ = 4
$D_x$ = 1.153 Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta$ = 10.1–11.6°
$\mu$ = 0.07 mm$^{-1}$
$T$ = 293 K
Orthorhombic prism, yellow
0.28 × 0.25 × 0.22 mm

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| O1—N1 | 1.303 (2) | C4—C5 | 1.482 (2) |
| N1—C5 | 1.278 (2) | C6—C7 | 1.509 (2) |
| N1—C6 | 1.486 (2) | C6—C15 | 1.510 (2) |
| | | | |
| O1—N1—C5 | 123.6 (1) | N1—C6—C7 | 109.3 (1) |
| O1—N1—C6 | 115.8 (1) | N1—C6—C15 | 111.0 (1) |
| C5—N1—C6 | 120.6 (1) | C7—C6—C15 | 114.0 (1) |
| N1—C5—C4 | 122.3 (2) | | |

*Data collection*

Enraf–Nonius CAD-4 diffractometer
$\omega$–2$\theta$ scans
6039 measured reflections
2991 independent reflections
2072 reflections with $I > \sigma(I)$
$R_{int}$ = 0.048
$\theta_{max}$ = 30.0°
$h = -7 \rightarrow 7$
$k = 0 \rightarrow 21$
$l = 0 \rightarrow 29$
2 standard reflections every 120 reflections
intensity decay: 4.0%

*Refinement*

Refinement on $F$
$R$ = 0.056
$wR$ = 0.040
$S$ = 2.00
2072 reflections
208 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o) + 0.00004|F_o|^2]$
$(\Delta/\sigma)_{max}$ = 0.028
$\Delta\rho_{max}$ = 0.21 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.20 e Å$^{-3}$

The absolute configuration of the reported structure was chosen on the basis of the originating (*S*)-(+)-phenylglycinol. The H atoms were placed geometrically and their $U_{iso}$ values set to 1.2 of the $U_{eq}$ value of the parent atom.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1992–1997); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1993); program(s) used to refine structure: *TEXSAN*; software used to prepare material for publication: *TEXSAN*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1479). Services for accessing these data are described at the back of the journal.

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