# 2(S)-N-*tert*-Butoxycarbonylamino-N-methoxy-N-methylbutanamide

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**Key indicators**

Single-crystal X-ray study
$T = 123$ K
Mean $\sigma$(C–C) = 0.002 Å
$R$ factor = 0.034
$wR$ factor = 0.090
Data-to-parameter ratio = 21.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

In the solid state the title compound, $C_{11}H_{22}N_2O_4$, is in an antiperiplanar conformation. The conformation of the compound shows no similarity with the synclinal conformation of the chelated intermediate formed during nucleophilic attack.

## Comment

*N*-Methoxy-*N*-methylamides have been extensively used as carbonyl cation equivalents (Sibi, 1993). They are easy to prepare by several methods and show few side-reactions during nucleophilic addition or selective reduction to aldehydes. These advantages led us to the decision to use the title compound, (I), as an intermediate in alkylation reactions to prepare derivatives of a naturally occurring lipid, sphingosine. Initially, compound (I) was prepared by Harbeson by a different route (Harbeson *et al.*, 1994). The crystal structure of another *N*-methoxy-*N*-methylamide has been reported by Zheng *et al.* (2000).
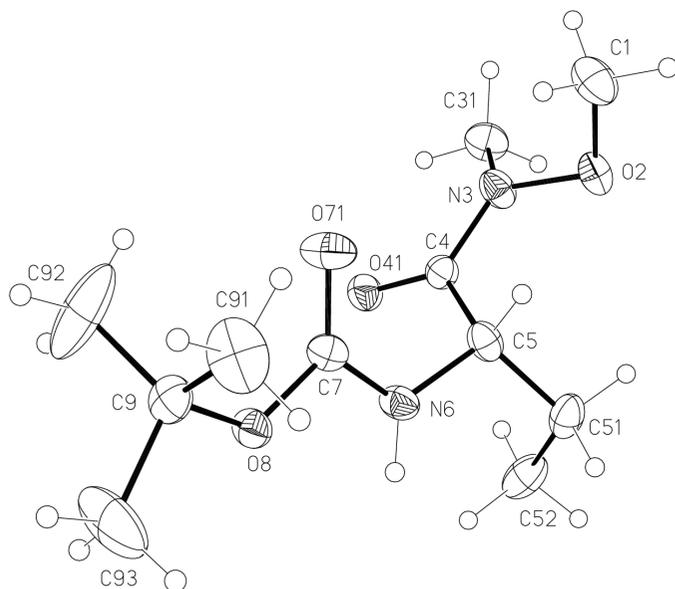


(I)
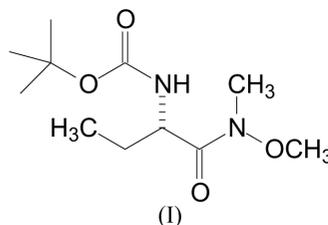
The underlying basis for the usefulness of *N*-methoxy-*N*-methylamides is the formation of a stable chelated tetrahedral intermediate after nucleophilic attack (Fig. 1), which prevents further additions to yield undesired side products (Evans *et al.*, 1991).
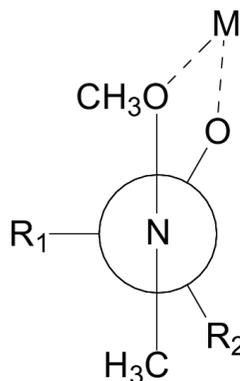


**Figure 1**
The structure of the tetrahedral intermediate.

**Figure 2**
The presumed structure of (I), showing the atom-numbering scheme and displacement ellipsoids at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.

The structure of (I), with the atom numbering, is shown in Fig. 2. Selected geometrical parameters are listed in Table 1. Within the crystal structure five intermolecular hydrogen bonds (Steiner, 2002) were found (Table 2). The four C—H···O hydrogen bonds are weak, whereas the N6—H6···O41 bond is a normal hydrogen bond. With the exception of the C52—H52C···O41 hydrogen bond, in which the deviation from the ideal 180° torsion angle is 30°, all intermolecular hydrogen bonds are almost linear. Within the molecule, the torsion angle O2—N3—C4—O41 is $-172.47\,(10)°$ (nearly ideal antiperiplanar conformation). This torsion angles defines a conformation which has no similarity with the synclinal conformation assumed to occur during nucleophilic attack in the chelated tetrahedral intermediate with a torsion angle of 60°.

## Experimental

Glassware was flame-dried under an argon atmosphere and allowed to cool. (S)-2-Aminobutyric acid (5 g, 48.5 mmol) was dissolved in a cold (273 K) solution of dioxane (50 ml) and 1 M aqueous NaOH (100 ml). To the flask di-*tert*-butyl-dicarbonate (12.8 g, 59.0 mmol) was added in portions, with stirring. After stirring for two days, the solvent was removed by evaporation under reduced pressure. The clear solution was acidified with $1M$ KHSO$_4$ to a pH of 2–3 (white precipitate was formed), and then cold saturated NaHCO$_3$ was added carefully to neutralize the mixture, which was then extracted with ethyl acetate several times. The collected organic phases were dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo* to yield a colourless oil, which was used without further purification. The oil was dissolved in anhydrous dichloromethane (200 ml) and cooled to 250 K. N,O-Dimethylhydroxylamine hydrochloride (4.86 g, 49.8 mmol) and N-methyl morpholine (5.5 ml, 49.8 mmol) were added in one portion. After stirring for 10 min, N-(3-dimethylaminopropyl)-N′-ethyl carbodiimide hydrochloride (9.55 g, 49.8 mmol) was dissolved in the clear solution and stirring continued for 1 h, during which time a white solid precipitated. The aqueous phase was extracted with dichloromethane and the collected organic phases washed with saturated NaHCO$_3$ and then dried over Na$_2$SO$_4$, filtered and evaporated under reduced pressure to yield a colourless solid. The product was purified by flash chromatography on silica gel (cyclohexane/ethyl acetate 2:1) to give colourless crystals (yield: 7.01 g, 58.8%), which were suitable for X-ray analysis.

*Crystal data*

| | |
|---|---|
| C$_{11}$H$_{22}$N$_2$O$_4$ | Mo $K\alpha$ radiation |
| $M_r = 246.31$ | Cell parameters from 19365 |
| Orthorhombic, $P2_12_12_1$ | reflections |
| $a = 6.6315\,(1)$ Å | $\theta = 1–28°$ |
| $b = 9.8478\,(2)$ Å | $\mu = 0.09$ mm$^{-1}$ |
| $c = 20.9769\,(5)$ Å | $T = 123\,(2)$ K |
| $V = 1369.91\,(5)$ Å$^3$ | Prism, colourless |
| $Z = 4$ | $0.40 \times 0.20 \times 0.10$ mm |
| $D_x = 1.194$ Mg m$^{-3}$ | |

*Data collection*

| | |
|---|---|
| Nonius KappaCCD diffractometer | $R_{int} = 0.032$ |
| $\varphi$ and $\omega$ scans | $\theta_{max} = 28.3°$ |
| Absorption correction: none | $h = -8 \rightarrow 8$ |
| 19820 measured reflections | $k = -13 \rightarrow 13$ |
| 3362 independent reflections | $l = -27 \rightarrow 27$ |
| 3020 reflections with $I > 2\sigma(I)$ | |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | $w = 1/[\sigma^2(F_o^2) + (0.0542P)^2$ |
| $R[F^2 > 2\sigma(F^2)] = 0.034$ | $+ 0.0843P]$ |
| $wR(F^2) = 0.090$ | where $P = (F_o^2 + 2F_c^2)/3$ |
| $S = 1.07$ | $(\Delta/\sigma)_{max} = 0.001$ |
| 3362 reflections | $\Delta\rho_{max} = 0.20$ e Å$^{-3}$ |
| 159 parameters | $\Delta\rho_{min} = -0.29$ e Å$^{-3}$ |
| H atoms treated by a mixture of constrained and independent refinement | |

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

| | | | |
|---|---|---|---|
| C5—N6 | 1.4483 (14) | N6—H6 | 0.854 (13) |
| C5—C51 | 1.5319 (17) | | |
| C52—C51—C5 | 114.30 (10) | O71—C7—N6 | 124.15 (11) |
| C5—N6—H6 | 122.2 (11) | | |
| C1—O2—N3—C31 | 93.12 (12) | N6—C5—C51—C52 | 67.04 (13) |
| N3—C4—C5—N6 | 154.95 (10) | C4—C5—N6—C7 | −75.00 (13) |

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

| $D—H\cdots A$ | $D—H$ | $H\cdots A$ | $D\cdots A$ | $D—H\cdots A$ |
|---|---|---|---|---|
| N6—H6···O41$^i$ | 0.854 (13) | 2.156 (14) | 3.0085 (13) | 175.6 (15) |
| C52—H52C···O41$^i$ | 0.98 | 2.45 | 3.3376 (16) | 150 |
| C31—H31B···O71$^{ii}$ | 0.98 | 2.36 | 3.3424 (16) | 177 |
| C1—H1B···O71$^{iii}$ | 0.98 | 2.60 | 3.5589 (16) | 166 |
| C93—H93C···O2$^{iv}$ | 0.98 | 2.56 | 3.5325 (18) | 172 |

Symmetry codes: (i) $x - \frac{1}{2}, \frac{1}{2} - y, 1 - z$; (ii) $\frac{1}{2} + x, \frac{3}{2} - y, 1 - z$; (iii) $x - \frac{1}{2}, \frac{3}{2} - y, 1 - z$; (iv) $\frac{1}{2} - x, 1 - y, z - \frac{1}{2}$.

The absolute configuration of the title compound could not be determined from the X-ray data, but was fixed by the absolute stereochemistry of the starting material, (S)-2-aminobutyric acid; Friedel pairs were averaged in the data set. The position of the amide H atom was determined from a difference Fourier map and its coordinates refined freely, with the isotropic displacement parameter

constrained to $U$(H) = 1.5 $U_{eq}$ (N). All remaining H atoms were treated as riding, with C—H = 0.98–1.00 Å, and $U_{iso}$(H) = 1.2 $U_{eq}$ (CH, CH$_2$) and 1.5 $U_{eq}$ (CH$_3$).

Data collection: *COLLECT* (Nonius, 1997–2000); cell refinement: *HKL SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *HKL DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus* (Sheldrick, 1991); software used to prepare material for publication: *SHELXL*97.

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