

## Geometric changes around an N atom due to a urethane-type bis(*tert*-butoxycarbonyl) substituent

Dominika Wojewska, Alicja Kluczyk\* and Katarzyna Ślepokura

Faculty of Chemistry, University of Wrocław, 14 Joliot-Curie Street, 50-383 Wrocław, Poland

Correspondence e-mail: alicja.kluczyk@chem.uni.wroc.pl

Received 3 August 2012

Accepted 28 November 2012

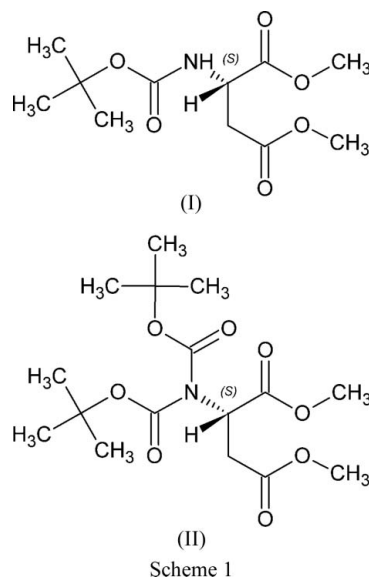
Online 13 December 2012

Two crystal structures of urethane-protected derivatives of aspartic acid dimethyl ester are presented, namely dimethyl (2*S*)-2-[(*tert*-butoxycarbonyl)amino]butanedioate, C<sub>11</sub>H<sub>19</sub>NO<sub>6</sub>, and dimethyl (2*S*)-2-[bis[(*tert*-butoxycarbonyl)amino]butanedioate, C<sub>16</sub>H<sub>27</sub>NO<sub>8</sub>. The geometry at the N atom is discussed and compared with similar structures. The analysis of singly and doubly N-substituted derivatives reveals an elongation of all bonds involving the N atom and conformational changes of the amino acid side chain due to steric interactions with two bulky substituents on the amino group.

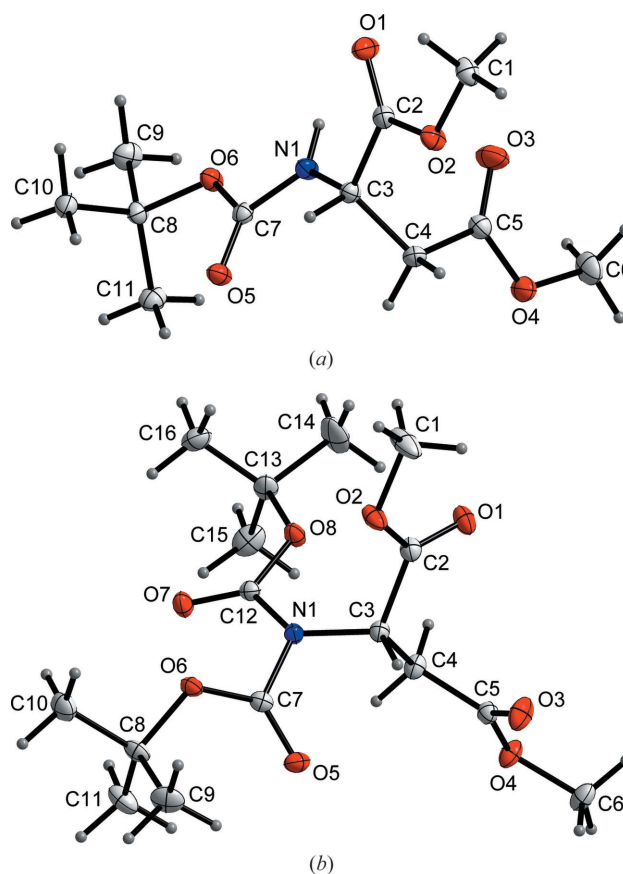
### Comment

Selective protection of functional groups is one of the main issues in organic chemistry (Greene & Wuts, 1999). The strategy of protection is vital in peptide synthesis, especially when peptides are used as scaffolds for complex bioconjugates (*e.g.* Alkhader *et al.*, 2010). The *tert*-butoxycarbonyl (Boc) and bis(*tert*-butoxycarbonyl) (bis-Boc) groups are frequently used to protect amino groups. While Boc-protected organic structures are fairly well represented (452 hits) in the Cambridge Structural Database (CSD, Version 5.33; Allen, 2002), to the best of our knowledge only nine organic structures with bis-Boc protection on the N atom have been deposited to date, and the structures of only two sets of compounds with Boc and bis-Boc protection are available in the CSD [CSD refcodes MUTTOK and MUTTUQ (Macleod *et al.*, 2003), and XUDQUJ and XUDQOD (Ikonen *et al.*, 2009)]. During the synthesis of some novel nonproteinaceous amino acids, we obtained two derivatives of aspartic acid, and their structures form a third pair of this type. We thus present here the crystal structures of dimethyl (2*S*)-2-[(*tert*-butoxycarbonyl)amino]butanedioate, (I), and dimethyl (2*S*)-2-[bis[(*tert*-butoxycarbonyl)amino]butanedioate, (II). We compare the geometry at the N atom in each structure, as well as in the other two Boc-protected pairs mentioned above and in structures

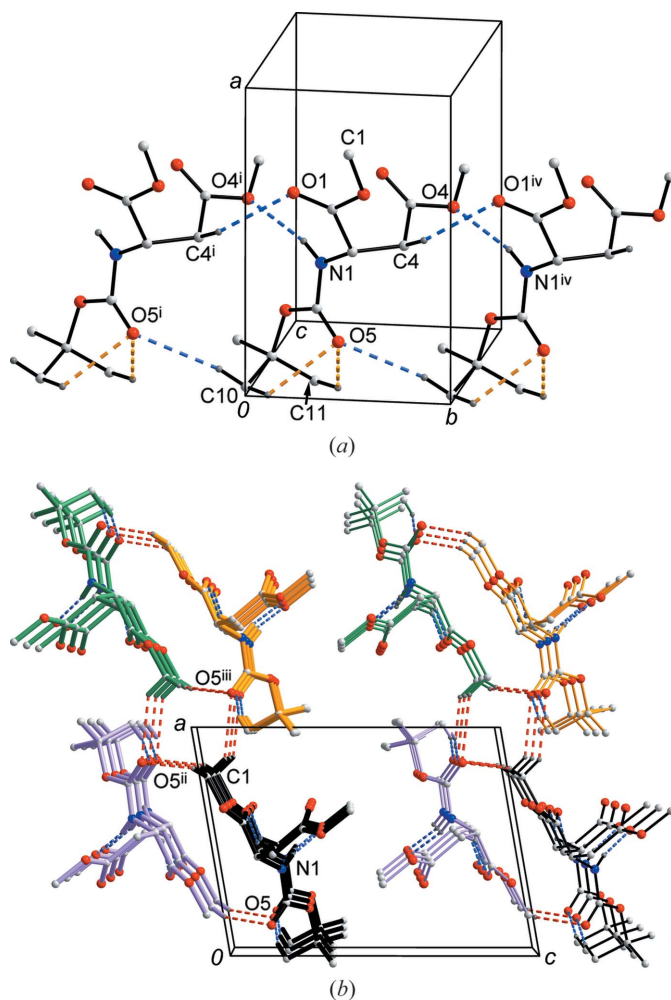
protected by related groups. It is worth noting that (II) is the first chiral and second non-aromatic example of a bis-Boc compound, opening the possibility of observing the arrangement of bulky substituents.



The asymmetric units of (I) and (II) are shown in Fig. 1. The absolute configuration at atom C3 is *S* in both structures, as

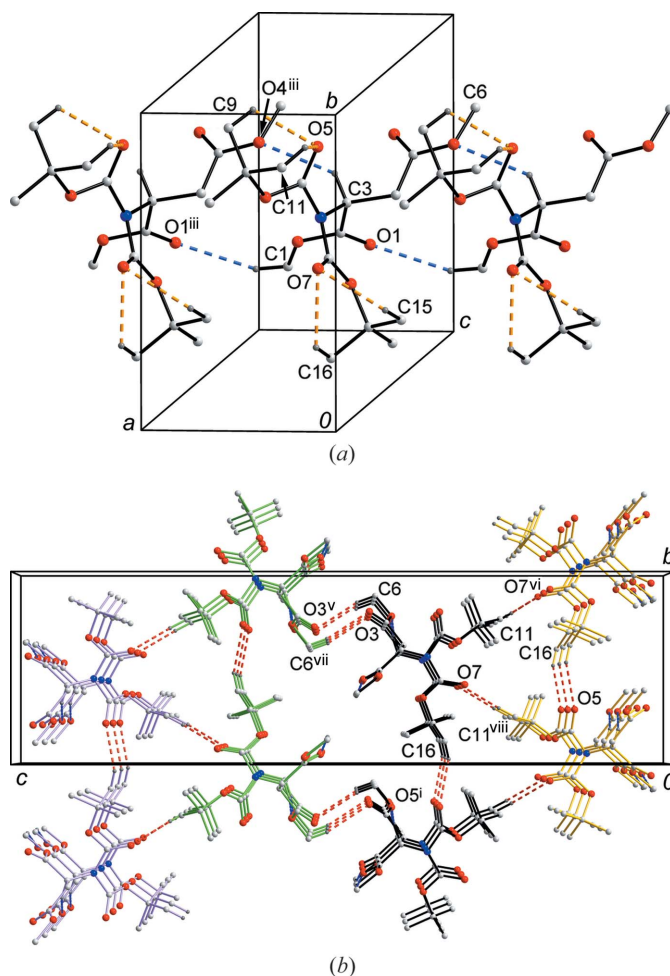


**Figure 1**  
The structure and atom-numbering of (a) (I) and (b) (II). Displacement ellipsoids are drawn at the 50% probability level.



**Figure 2**  
The arrangement of molecules of (I) in the crystal structure. (a) The chains along the *b* axis, with hydrogen-bond contacts shown as dashed lines (in the electronic version of the paper, intramolecular contacts are shown in orange and intermolecular contacts are shown in blue). (b) Layers parallel to the (001) plane, formed by adjacent chains linked *via* C–H...O contacts (red dashed lines). H atoms not involved in hydrogen bonding have been omitted for clarity. [Symmetry codes: (i)  $x, y - 1, z$ ; (ii)  $-x + 1, y + \frac{1}{2}, -z$ ; (iii)  $x + 1, y, z$ ; (iv)  $x, y + 1, z$ .]

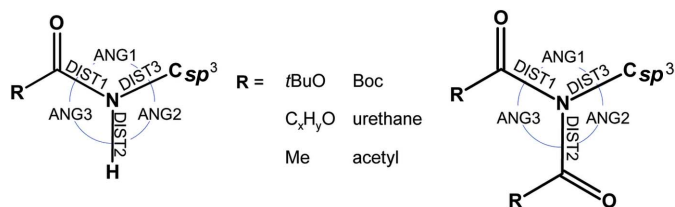
the applied synthetic procedure preserves the configuration of the substrate. All bond lengths and angles are typical, except for those in the urethane group, which will be discussed in detail (Tables 1 and 3). In (I), the orientation of the carbonyl O atom in the Boc substituent is antiperiplanar relative to atom H1N [torsion angle O5–C7–N1–H1N =  $-175.9(14)^\circ$ ], stabilized by two very weak intramolecular hydrogen-bond contacts of C–H...O type (C10–H10B...O5 and C11–H11A...O5; Table 2). Therefore, rotation around the C8–O6 single bond is most probably hindered. In (II), carbonyl atom O5 is synperiplanar to atom C3 and carbonyl atom O7 is antiperiplanar to atom C3. In the other two bis-Boc compounds, the carbonyl O atoms are oriented in the same direction, both antiperiplanar to the C–N bond, but these structures are much less crowded (Macleod *et al.*, 2003; Ikonen *et al.*, 2009). Four very weak intramolecular hydrogen-bond contacts of C–H...O type (C9–H9A...O5, C11–



**Figure 3**  
The arrangement of molecules of (II) in the crystal structure. (a) The chains along the *a* axis, with hydrogen-bond contacts shown as dashed lines (in the electronic version of the paper, intramolecular contacts are shown in orange and intermolecular contacts are shown in blue). (b) The three-dimensional architecture formed by C–H...O contacts (red dashed lines) linking adjacent chains. H atoms not involved in hydrogen bonding have been omitted for clarity. [Symmetry codes: (i)  $x, y - 1, z$ ; (iii)  $x + 1, y, z$ ; (v)  $x - \frac{1}{2}, -y + \frac{3}{2}, -z + 1$ ; (vi)  $-x + 1, y + \frac{1}{2}, -z + \frac{1}{2}$ ; (vii)  $x + \frac{1}{2}, -y + \frac{3}{2}, -z + 1$ ; (viii)  $-x + 1, y - \frac{1}{2}, -z + \frac{1}{2}$ .]

H11C...O5, C15–H15C...O7 and C16–H16A...O7; Table 4) stabilize the conformation of both Boc groups in (II) (Fig. 3a) by hindering rotation around the C8–O6 and C13–O8 single bonds.

In (I), intermolecular hydrogen bonds, utilizing mainly the NH group and both ester groups, stabilize infinite chains running along the *b* axis (Fig. 2a). Two adjacent chains (related by a  $2_1$  symmetry operation) are joined to each other *via* C1–H1C...O5<sup>ii</sup> hydrogen bonds to form helical ribbons down the *b* axis (Fig. 2b and Table 2; symmetry code as in Table 2). The same atom C1 and urethane atom O5 are involved in weaker C1–H1B...O5<sup>iii</sup> contacts, giving rise to layers parallel to the (001) plane (Table 2). In contrast, the crystal structure of (II) has a three-dimensional architecture, although chains of molecules (related by a direct *a*-axis translation), joined *via* C1–H1B...O1<sup>iii</sup> and C3–H3...O4<sup>iii</sup> hydrogen bonds, may be distinguished (Fig. 3a and Table 4; symmetry code in Table 4).



**Figure 4**  
Definitions of the geometric parameters presented in Table 5.

Nonetheless, each chain interacts with five others (related by a *b*-axis translation and symmetries of two  $2_1$  axes), utilizing ester, *tert*-butyl and urethane groups to give a three-dimensional network of hydrogen bonds, as shown in Fig. 3(b).

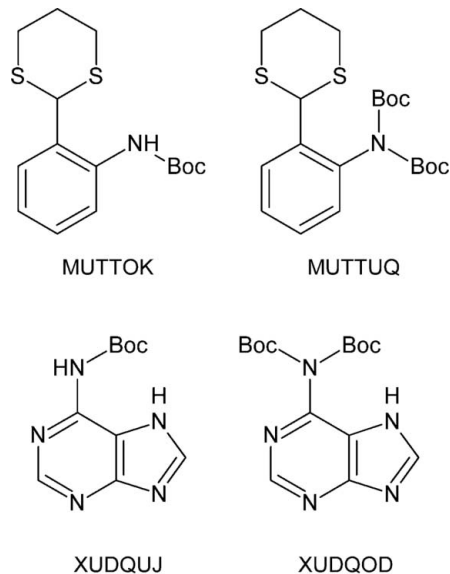
The limited data available on mono- and bis-Boc substituted compounds prompted us to take a closer look at the N-atom geometry. We found almost no information on the values of C–N bond lengths in such urethane-type structures in *International Tables for Crystallography*, Vol. C (Prince, 2004). The only available structural information is the H–N distance in  $X_2$ –N–H of 1.01 Å (Prince, 2004) and the  $Csp^3$ – $Nsp^3$  distance in  $C^*$ –NH–C=O (acyclic amides) of 1.45 Å (Prince, 2004), which is the best available representation of a urethane group. We found 874 urethane-type organic structures in the CSD [*tert*-butoxycarbonyl-, benzyloxycarbonyl-, ethoxycarbonyl-, methoxycarbonyl-, (9*H*-fluoren-9-ylmethoxy)carbonyl-, and others] and only 11 bis-urethane structures. The mean values of selected geometric parameters, defined in Fig. 4, are presented in Table 5 for comparison with (I) and (II), and with acetyl-substituted compounds (non-urethane derivatives).

All bonds at the N atom in (II) are longer than those in (I) due to the introduction of a second bulky *tert*-butoxycarbonyl substituent. Elongation of these bonds should be expected from resonance theory, as the introduction of a second substituent provides a decrease in the double-bond character of the N–C bonds, while the elongation of the N1–C3 bond (DIST3) from 1.4438 (16) to 1.4669 (13) Å seems to be caused by steric effects. It is worth noting that the C=O and C–O bonds in the Boc substituent in (II) are shorter [C=O = 1.2067 (14) and 1.2057 (13) Å, and C–O = 1.3241 (13) and 1.3312 (13) Å] than the respective bonds in (I) [C=O = 1.2169 (14) Å and C–O = 1.3455 (15) Å]. The same is true for the other two sets of Boc and bis-Boc structures (Macleod *et al.*, 2003; Ikonen *et al.*, 2009).

The hybridization of atom N1 in both structures is  $sp^2$ , with angles tending towards 120°. The urethane group in (I) is almost planar and atom N1 is out-of-plane by 0.031 (2) Å. In (II), atom N1 is out of the plane of the neighbouring atoms (C3, C7 and C12) by 0.184 (2) Å, suggesting a partial  $sp^3$  character. The shift of electron density around atoms C7 and C12 towards the O atoms in (II) may be a consequence of this change, probably related to the limited delocalization of electrons in a bis-protected amino acid derivative. It is also possible that the steric repulsion between two bulky Boc substituents also affects the N1 out-of-plane distance. In (II), the C7–N1–C3 angle (ANG1) is much smaller than the

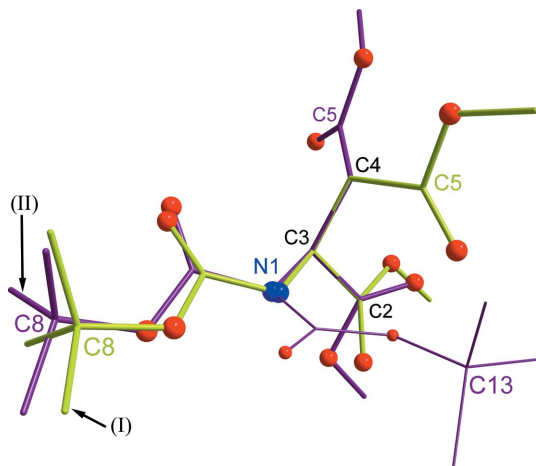
C12–N1–C3 angle (ANG2). As atoms C7 and C12 should create the same chemical environment, this is the effect of stereochemistry and resulting steric correlations with the  $C_\alpha$ –C(O)OMe group of aspartic acid. Only a single H atom (H3) points towards atom C7 (of the Boc group), while the rest of the amino acid chain points towards atom C12 from the other Boc group and therefore decreases the value of ANG1, as the result of steric repulsion between two bulky Boc groups and the side chain. It is of interest that the side-chain ester group has dramatically changed its conformation, as shown in Fig. 5. It seems that this effect was forced by the introduction of the second Boc group and provides the best spatial location of the substituents on the N atom: two Boc groups and the ester side chain of aspartic acid.

The elongation of bonds in (II) is similar to two other Boc and bis-Boc structures (see Scheme 2), as shown in Table 5. The N-atom out-of-plane value is much greater in (II) than in XUDQOD or MUTTUQ. In (II), DIST3 is longer than in the two bis-Boc aromatic structures, while the other two distances (DIST1 and DIST2) are similar. The differences in the angle values are greater in the two aromatic CSD structures than in (II), as the Boc substituents are rotated out of the plane of the aromatic ring, whereas in (II) the side chain of the aspartic acid limits the available space, even with the conformational change of the ester side chain (C2–C3–C4–C5 torsion angle).



Scheme 2

The interatomic distances in (I) and (II) are within the range of other *tert*-butoxycarbonyl- and bis(*tert*-butoxycarbonyl) structures, and those of general urethane and bis-urethane structures. They are also close to those in acyl-substituted species. Resonance theory allows the participation of the second noncarbonyl O atom in resonance structures. Urethane groups are known for their racemization-protecting properties during peptide synthesis, as the resonance of the urethane group lowers the rate of cyclic transient product



**Figure 5**  
Superposition of (I) (green in the electronic version of the paper) and (II) (violet), showing the significant changes in conformation of the aspartic acid side chain. The common reference points are C2, C3 and C4.

formation, which is associated with decreased acidity of urethane NH ( $R-O-CO-NH$ ) compared with amide NH ( $R-CO-NH$ ) (Sewald & Jakubke, 2002; Goodman, 2004). As can be estimated from the Boc and acetyl derivatives, the difference in bond length is rather insignificant, which supports the theory of acidity.

In conclusion, we have observed the elongation of all bonds formed by the N atom in bis-substituted urethane organic compounds. This is probably caused by steric repulsion of bulky substituents and is enhanced by delocalization of the electron pair of the N atom. The nature of the changes depends on the structure of the main part of the molecule and leads to the optimum spatial accommodation of the Boc substituents.

## Experimental

Dimethyl (2*S*)-2-aminobutanedioate hydrochloride was obtained as a colourless oil according to a modified procedure (Schröder & Lübke, 1965) from L-aspartic acid (Reanal). The oil was diluted with MeCN, neutralized with *N,N,N*-triethylamine (Ubichem Ltd) and subjected to further reaction with di-*tert*-butyl dicarbonate ( $Boc_2O$ , GL Biochem) for 9 h, according to Bodanszky & Bodanszky (1994). The resulting oil was treated with *n*-hexane (oil-*n*-hexane 1:6 v/v), yielding long colourless block-shaped crystals of (I) (yield 89%; m.p. 335.7–337.1 K).  $^1H$  NMR (500 MHz,  $CD_3OD$ ):  $\delta$  4.55 (*t*,  $J_1 = 6.0$  Hz, 1H), 3.77 (*s*, 3H), 3.73 (*s*, 3H), 2.89 (*dd*,  $J_1 = 6.0$  Hz,  $J_2 = 16.5$  Hz, 1H), 2.81 (*dd*,  $J_1 = 6.0$  Hz,  $J_2 = 16.5$  Hz, 1H), 1.48 (*s*, 9H). MS (ESI),  $m/z$ , calculated for  $C_{11}H_{20}NO_6$  [ $M + H$ ] $^+$ : 262.128; found: 262.129.

Compound (II) was obtained from (I) according to a modified method (Englund *et al.*, 2004) by overnight reaction with  $Boc_2O$  in MeCN in the presence of 4-(dimethylamino)pyridine (Fluka) at room temperature. Thin colourless needle-shaped crystals of (II) (yield 88%; 325.2–326.0 K) were obtained by slow evaporation of AcOEt.  $^1H$  NMR (500 MHz,  $CD_3OD$ ):  $\delta$  5.44 (*t*,  $J_1 = 6.5$  Hz, 1H), 3.77 (*s*, 3H), 3.73 (*s*, 3H), 3.21 (*dd*,  $J_1 = 6.5$  Hz,  $J_2 = 16.3$  Hz, 1H), 2.83 (*dd*,  $J_1 = 6.5$  Hz,  $J_2 = 16.3$  Hz, 1H), 1.54 (*s*, 18H). MS (ESI),  $m/z$ , calculated for  $C_{16}H_{27}NNaO_8$  [ $M + Na$ ] $^+$ : 384.163; found: 384.163.

**Table 1**  
Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ ) for (I).

N1–C3	1.4438 (16)	N1–H1N	0.87 (2)
N1–C7	1.3568 (16)		
C7–N1–C3	120.10 (10)	C7–N1–H1N	119.1 (13)
C3–N1–H1N	120.6 (12)		
C7–N1–C3–C2	–149.02 (10)	C3–N1–C7–O5	–1.19 (18)
C7–N1–C3–C4	84.01 (12)	C3–N1–C7–O6	179.01 (10)
C2–C3–C4–C5	–61.75 (13)	O5–C7–N1–H1N	–175.9 (14)

**Table 2**  
Hydrogen-bond geometry ( $\text{\AA}$ ,  $^\circ$ ) for (I).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N1–H1N $\cdots$ O4 $^i$	0.87 (2)	2.29 (2)	3.1388 (16)	166.6 (17)
C1–H1C $\cdots$ O5 $^{ii}$	0.98	2.54	3.4775 (19)	160
C1–H1B $\cdots$ O5 $^{iii}$	0.98	2.63	3.4368 (18)	140
C4–H4A $\cdots$ O1 $^{iv}$	0.99	2.53	3.3869 (19)	144
C10–H10B $\cdots$ O5	0.98	2.51	3.0875 (19)	118
C10–H10A $\cdots$ O5 $^i$	0.98	2.62	3.5407 (19)	157
C11–H11A $\cdots$ O5	0.98	2.39	3.0045 (18)	120

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

## Compound (I)

### Crystal data

$C_{11}H_{19}NO_6$	$V = 647.9$ (4) $\text{\AA}^3$
$M_r = 261.27$	$Z = 2$
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
$a = 9.219$ (3) $\text{\AA}$	$\mu = 0.11$ $\text{mm}^{-1}$
$b = 5.815$ (2) $\text{\AA}$	$T = 100$ K
$c = 12.263$ (4) $\text{\AA}$	$0.46 \times 0.16 \times 0.12$ mm
$\beta = 99.74$ (3) $^\circ$	

### Data collection

Oxford Xcalibur PX $\kappa$ -geometry diffractometer with Onyx CCD camera	7321 measured reflections 2437 independent reflections 2219 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan ( <i>CrysAlis RED</i> ; Oxford Diffraction, 2009)	$R_{int} = 0.025$
$T_{min} = 0.942$ , $T_{max} = 1.000$	

### Refinement

$R[F^2 > 2\sigma(F^2)] = 0.030$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.078$	$\Delta\rho_{max} = 0.25$ e $\text{\AA}^{-3}$
$S = 1.07$	$\Delta\rho_{min} = -0.18$ e $\text{\AA}^{-3}$
2437 reflections	Absolute structure: known from the synthesis
172 parameters	
1 restraint	

## Compound (II)

### Crystal data

$C_{16}H_{27}NO_8$	$V = 1884.4$ (9) $\text{\AA}^3$
$M_r = 361.39$	$Z = 4$
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation
$a = 5.922$ (2) $\text{\AA}$	$\mu = 0.10$ $\text{mm}^{-1}$
$b = 9.635$ (2) $\text{\AA}$	$T = 100$ K
$c = 33.026$ (8) $\text{\AA}$	$0.58 \times 0.18 \times 0.13$ mm

**Table 3**  
Selected geometric parameters (Å, °) for (II).

N1—C3	1.4669 (13)	N1—C12	1.3996 (14)
N1—C7	1.4168 (14)		
C7—N1—C3	115.23 (9)	C12—N1—C7	119.14 (8)
C12—N1—C3	120.73 (9)		
C7—N1—C3—C2	−141.94 (9)	C12—N1—C7—O6	−51.38 (12)
C12—N1—C3—C2	63.05 (12)	C3—N1—C7—O6	153.18 (8)
C7—N1—C3—C4	89.45 (12)	C3—N1—C12—O7	159.03 (11)
C12—N1—C3—C4	−65.56 (13)	C7—N1—C12—O7	4.97 (16)
C2—C3—C4—C5	91.04 (12)	C3—N1—C12—O8	−19.26 (13)
C3—N1—C7—O5	−24.65 (14)	C7—N1—C12—O8	−173.32 (9)
C12—N1—C7—O5	130.78 (11)		

**Table 4**  
Hydrogen-bond geometry (Å, °) for (II).

D—H...A	D—H	H...A	D...A	D—H...A
C1—H1B...O1 <sup>iii</sup>	0.98	2.56	3.479 (2)	156
C3—H3...O3	1.00	2.37	2.8121 (15)	106
C3—H3...O4 <sup>iii</sup>	1.00	2.49	3.2767 (16)	135
C6—H6A...O3 <sup>v</sup>	0.98	2.55	3.5079 (18)	167
C9—H9A...O5	0.98	2.44	3.0261 (17)	118
C11—H11C...O5	0.98	2.52	3.0769 (17)	116
C11—H11B...O7 <sup>vi</sup>	0.98	2.58	3.5412 (16)	168
C15—H15C...O7	0.98	2.42	2.9871 (17)	116
C16—H16A...O7	0.98	2.42	2.9897 (17)	117
C16—H16B...O5 <sup>i</sup>	0.98	2.54	3.2780 (17)	132

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

#### Data collection

Oxford Xcalibur PX  $\kappa$ -geometry diffractometer with Onyx CCD camera  
Absorption correction: multi-scan (*CrysAlis RED*; Oxford)

Diffraction, 2009)  
 $T_{\min} = 0.915, T_{\max} = 1.000$   
19441 measured reflections  
4374 independent reflections  
3766 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.026$

#### Refinement

$R[F^2 > 2\sigma(F^2)] = 0.033$   
 $wR(F^2) = 0.084$   
 $S = 1.06$   
4374 reflections  
234 parameters

H-atom parameters constrained  
 $\Delta\rho_{\max} = 0.33 \text{ e \AA}^{-3}$   
 $\Delta\rho_{\min} = -0.21 \text{ e \AA}^{-3}$   
Absolute structure: known from the synthesis

All H atoms were found in difference Fourier maps. In the final refinement cycles, C-bonded H atoms were positioned geometrically and treated as riding atoms, with C—H = 0.98–1.00 Å and  $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{CH})$  and  $1.5U_{\text{eq}}(\text{CH}_2)$  or  $1.5U_{\text{eq}}(\text{CH}_3)$ . Atom H1N in (I) was refined isotropically.

For both compounds, data collection: *CrysAlis CCD* (Oxford Diffraction, 2009); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2009); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *DIAMOND* (Brandenburg, 2012); software used to prepare material for publication: *SHELXL97*.

The authors thank Professors Tadeusz Lis and Zbigniew Szewczuk from the Faculty of Chemistry, University of Wrocław, for their technical support and helpful discussions.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: QS3019). Services for accessing these data are described at the back of the journal.

#### References

- Alkhader, S., Ezra, A., Kasparikova, J., Brabec, V. & Yavin, E. (2010). *Bioconjugate Chem.* **21**, 1425–1431.  
Allen, F. H. (2002). *Acta Cryst.* **B58**, 380–388.  
Bodanszky, M. & Bodanszky, A. (1994). In *The Practice of Peptide Synthesis*. Heidelberg: Springer.  
Brandenburg, K. (2012). *DIAMOND*. Crystal Impact GbR, Bonn, Germany.  
Englund, A. E., Gopi, H. N. & Appella, D. H. (2004). *Org. Lett.* **6**, 213–215.  
Goodman, M. (2004). Editor. In *Synthesis of Peptides and Peptidomimetics*. Stuttgart: Georg Thieme.  
Greene, T. W. & Wuts, P. G. M. (1999). In *Protective Groups in Organic Synthesis*, 3rd ed. New York: Wiley.  
Ikonen, S., Valkonen, A. & Kolehmainen, E. (2009). *J. Mol. Struct.* **930**, 147–156.  
Macleod, C., McKiernan, G. J., Guthrie, E. J., Farrugia, L. J., Hamprecht, D. W., Macritchie, J. & Hartley, R. C. (2003). *J. Org. Chem.* **68**, 387–401.  
Oxford Diffraction (2009). *CrysAlis CCD* and *CrysAlis RED* in *Xcalibur PX Software*. Oxford Diffraction Ltd, Yarnton, Oxfordshire, England.  
Prince, E. (2004). Editor. *International Tables For Crystallography*, Vol. C. Heidelberg: Springer.  
Schröder, E. & Lübke, K. (1965). In *The Peptides*. New York: Academic Press.  
Sewald, N. & Jakubke, H.-D. (2002). In *Peptides: Chemistry and Biology*. Weinheim: Wiley.  
Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.

**Table 5**  
Selected bond lengths and angles (Å, °) for structures (I) and (II) compared with average values obtained from the CSD (Allen, 2002).

Boc/bis-Boc pairs	DIST1	DIST2	DIST3	ANG1	ANG2	ANG3	DIST4†
(I)	1.357 (2)	0.87 (2)	1.444 (2)	120.10 (10)	121 (2)	119 (2)	0.031 (2)
(II)	1.417 (2)	1.400 (2)	1.467 (2)	115.23 (9)	120.73 (9)	119.14 (8)	0.184 (2)
MUTTOK	1.366 (3)	‡	1.419 (3)	125.0 (2)	118 (2)	117 (2)	0.005 (2)
MUTTUQ, fragment 1	1.406 (2)	1.413 (2)	1.451 (2)	120.5 (1)	119.6 (1)	119.9 (1)	0.013 (1)
MUTTUQ, fragment 2	1.408 (2)	1.408 (2)	1.448 (2)	119.5 (1)	119.9 (1)	120.6 (1)	0.012 (1)
XUDQUJ, fragment 1	1.373 (3)	‡	1.390 (2)	125.9 (2)	115 (2)	117 (2)	0.090 (2)
XUDQUJ, fragment 2	1.372 (2)	‡	1.386 (3)	127.2 (2)	115 (2)	118 (2)	0.015 (2)
XUDQOD	1.420 (2)	1.405 (2)	1.431 (2)	118.5 (1)	120.8 (1)	120.6 (1)	0.037 (2)
Protecting groups							
Boc	1.35	‡	1.45	122	119	119	0.04
Bis-Boc	1.41	1.41	1.44	118	119	123	0.04
Urethane	1.35	‡	1.44	123	118	118	0.04
Bis-urethane	1.41	1.41	1.44	119	118	122	0.05
Acetyl	1.35	‡	1.43	125	117	118	0.03
Bis-acetyl	1.41	1.41	1.45	119	117	125	0.03

† DIST4 is the distance between the N atom and the plane defined by the neighbouring atoms; other definitions are given in Fig. 4 ‡ DIST2 in monosubstituted species is not given, as the H atoms were treated in different ways. References: (I) and (II): this work; MUTTOK and MUTTUQ: Macleod *et al.* (2003); XUDQUJ and XUDQOD: Ikonen *et al.* (2009).

## supplementary materials

*Acta Cryst.* (2013). C69, 82-86 [doi:10.1107/S0108270112048846]

## Geometric changes around an N atom due to a urethane-type bis(*tert*-butoxy-carbonyl) substituent

Dominika Wojewska, Alicja Kluczyk and Katarzyna Ślepokura

### (I) Dimethyl (2*S*)-2-[(*tert*-butoxycarbonyl)amino]butanedioate

#### Crystal data

C<sub>11</sub>H<sub>19</sub>NO<sub>6</sub>

$M_r = 261.27$

Monoclinic,  $P2_1$

Hall symbol: P 2yb

$a = 9.219$  (3) Å

$b = 5.815$  (2) Å

$c = 12.263$  (4) Å

$\beta = 99.74$  (3)°

$V = 647.9$  (4) Å<sup>3</sup>

$Z = 2$

$F(000) = 280$

$D_x = 1.339$  Mg m<sup>-3</sup>

Melting point: 335.7 K

Mo  $K\alpha$  radiation,  $\lambda = 0.71073$  Å

Cell parameters from 5074 reflections

$\theta = 5.0$ – $38.6$ °

$\mu = 0.11$  mm<sup>-1</sup>

$T = 100$  K

Block, colourless

$0.46 \times 0.16 \times 0.12$  mm

#### Data collection

Oxford Xcalibur PX  $\kappa$ -geometry

diffractometer with Onyx CCD camera

Radiation source: Enhance (Mo) X-ray Source

Graphite monochromator

$\omega$  and  $\varphi$  scans

Absorption correction: multi-scan

(*CrysAlis RED*; Oxford Diffraction, 2009)

$T_{\min} = 0.942$ ,  $T_{\max} = 1.000$

7321 measured reflections

2437 independent reflections

2219 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.025$

$\theta_{\max} = 33.0$ °,  $\theta_{\min} = 4.9$ °

$h = -13 \rightarrow 13$

$k = -6 \rightarrow 8$

$l = -18 \rightarrow 9$

#### Refinement

Refinement on  $F^2$

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.030$

$wR(F^2) = 0.078$

$S = 1.07$

2437 reflections

172 parameters

1 restraint

Primary atom site location: structure-invariant

direct methods

Secondary atom site location: difference Fourier map

Hydrogen site location: difference Fourier map

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0502P)^2 + 0.0009P]$

where  $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.25$  e Å<sup>-3</sup>

$\Delta\rho_{\min} = -0.18$  e Å<sup>-3</sup>

Absolute structure: known absolute configuration

*Special details*

**Experimental.** <sup>1</sup>HNMR (CD<sub>3</sub>OD):  $\delta$  = 4.55 (t,  $J_1$  = 6.0 Hz, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 2.89 (dd,  $J_1$  = 6.0 Hz,  $J_2$  = 16.5 Hz, 1H), 2.81 (dd,  $J_1$  = 6.0 Hz,  $J_2$  = 16.5 Hz, 1H), 1.48 (s, 9H)

MS (ESI),  $[M+H]^+$ <sub>obsd</sub> ( $[M+H]^+$ <sub>calcd</sub>),  $[M+Na]^+$ <sub>obsd</sub> ( $[M+Na]^+$ <sub>calcd</sub>) Da: 262.129 (262.128), 284.110 (284.110)

Melting point range 335.7–337.1 K

**Geometry.** All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

**Refinement.** Refinement of  $F^2$  against ALL reflections. The weighted  $R$ -factor  $wR$  and goodness of fit  $S$  are based on  $F^2$ , conventional  $R$ -factors  $R$  are based on  $F$ , with  $F$  set to zero for negative  $F^2$ . The threshold expression of  $F^2 > \sigma(F^2)$  is used only for calculating  $R$ -factors(gt) *etc.* and is not relevant to the choice of reflections for refinement.  $R$ -factors based on  $F^2$  are statistically about twice as large as those based on  $F$ , and  $R$ -factors based on ALL data will be even larger.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ( $\text{\AA}^2$ )*

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.63269 (10)	0.20152 (18)	0.13353 (8)	0.0217 (2)
O2	0.65256 (9)	0.55942 (17)	0.06905 (7)	0.01841 (19)
O3	0.65512 (12)	0.5827 (2)	0.34131 (8)	0.0310 (3)
O4	0.54946 (10)	0.92255 (18)	0.36528 (7)	0.0212 (2)
O5	0.14865 (9)	0.41478 (17)	0.15578 (7)	0.01748 (18)
O6	0.21240 (9)	0.12764 (17)	0.28274 (7)	0.01610 (18)
N1	0.38691 (11)	0.31665 (19)	0.21778 (8)	0.0154 (2)
H1N	0.445 (2)	0.220 (4)	0.2574 (13)	0.027 (4)*
C1	0.78864 (13)	0.4954 (3)	0.03299 (10)	0.0190 (2)
H1A	0.7709	0.3642	−0.0177	0.029*
H1B	0.8619	0.4530	0.0974	0.029*
H1C	0.8253	0.6257	−0.0052	0.029*
C2	0.58746 (12)	0.3950 (2)	0.11908 (9)	0.0150 (2)
C3	0.44432 (12)	0.4842 (2)	0.14933 (9)	0.0139 (2)
H3	0.3720	0.4966	0.0790	0.017*
C4	0.45833 (12)	0.7232 (2)	0.20160 (9)	0.0151 (2)
H4A	0.4909	0.8330	0.1490	0.018*
H4B	0.3605	0.7737	0.2154	0.018*
C5	0.56600 (12)	0.7290 (2)	0.30909 (9)	0.0174 (2)
C6	0.64810 (15)	0.9499 (3)	0.46926 (10)	0.0273 (3)
H6A	0.7501	0.9389	0.4569	0.041*
H6B	0.6291	0.8286	0.5206	0.041*
H6C	0.6320	1.1006	0.5009	0.041*
C7	0.23948 (12)	0.2960 (2)	0.21367 (9)	0.0137 (2)
C8	0.05995 (12)	0.0577 (2)	0.29009 (9)	0.0155 (2)
C9	0.08611 (15)	−0.1302 (3)	0.37752 (11)	0.0227 (3)
H9A	0.1402	−0.0663	0.4465	0.034*
H9B	0.1437	−0.2546	0.3518	0.034*
H9C	−0.0087	−0.1908	0.3905	0.034*
C10	−0.01501 (14)	−0.0408 (2)	0.17988 (10)	0.0191 (2)
H10A	0.0444	−0.1671	0.1581	0.029*
H10B	−0.0250	0.0798	0.1233	0.029*
H10C	−0.1127	−0.0986	0.1873	0.029*

C11	-0.02366 (14)	0.2580 (3)	0.32932 (10)	0.0199 (2)
H11A	-0.0303	0.3834	0.2753	0.030*
H11B	0.0283	0.3121	0.4011	0.030*
H11C	-0.1229	0.2077	0.3369	0.030*

Atomic displacement parameters ( $\text{\AA}^2$ )

	$U^{11}$	$U^{22}$	$U^{33}$	$U^{12}$	$U^{13}$	$U^{23}$
O1	0.0194 (4)	0.0158 (5)	0.0316 (4)	0.0010 (3)	0.0090 (4)	0.0010 (4)
O2	0.0151 (4)	0.0200 (5)	0.0213 (4)	-0.0004 (3)	0.0065 (3)	0.0040 (4)
O3	0.0294 (5)	0.0296 (6)	0.0296 (4)	0.0128 (5)	-0.0079 (4)	-0.0053 (5)
O4	0.0208 (4)	0.0217 (5)	0.0194 (4)	0.0025 (4)	-0.0015 (3)	-0.0048 (4)
O5	0.0146 (4)	0.0169 (4)	0.0210 (4)	0.0025 (3)	0.0031 (3)	0.0033 (3)
O6	0.0134 (3)	0.0162 (4)	0.0190 (4)	0.0000 (3)	0.0037 (3)	0.0043 (3)
N1	0.0135 (4)	0.0139 (5)	0.0189 (4)	0.0004 (4)	0.0027 (3)	0.0053 (4)
C1	0.0145 (5)	0.0260 (7)	0.0175 (5)	-0.0022 (5)	0.0052 (4)	-0.0010 (5)
C2	0.0138 (4)	0.0162 (5)	0.0149 (4)	-0.0014 (4)	0.0019 (4)	-0.0008 (4)
C3	0.0137 (4)	0.0127 (5)	0.0157 (4)	-0.0002 (4)	0.0034 (4)	0.0018 (4)
C4	0.0152 (4)	0.0131 (5)	0.0169 (4)	0.0012 (4)	0.0020 (4)	0.0005 (4)
C5	0.0150 (5)	0.0193 (6)	0.0178 (4)	0.0002 (5)	0.0027 (4)	-0.0002 (5)
C6	0.0236 (6)	0.0367 (9)	0.0197 (5)	0.0000 (6)	-0.0019 (4)	-0.0090 (6)
C7	0.0145 (4)	0.0132 (5)	0.0140 (4)	-0.0006 (4)	0.0039 (4)	-0.0017 (4)
C8	0.0137 (4)	0.0148 (6)	0.0191 (5)	-0.0014 (4)	0.0059 (4)	0.0000 (4)
C9	0.0241 (6)	0.0203 (7)	0.0252 (5)	-0.0008 (5)	0.0088 (5)	0.0070 (5)
C10	0.0177 (5)	0.0174 (6)	0.0224 (5)	-0.0022 (4)	0.0045 (4)	-0.0042 (5)
C11	0.0207 (5)	0.0194 (6)	0.0213 (5)	0.0007 (5)	0.0081 (4)	-0.0021 (5)

Geometric parameters ( $\text{\AA}$ ,  $^\circ$ )

O1—C2	1.2026 (17)	C4—C5	1.5104 (16)
O2—C2	1.3324 (16)	C4—H4A	0.99
O2—C1	1.4476 (15)	C4—H4B	0.99
O3—C5	1.2021 (17)	C6—H6A	0.98
O4—C5	1.3416 (17)	C6—H6B	0.98
O4—C6	1.4443 (15)	C6—H6C	0.98
O5—C7	1.2169 (14)	C8—C11	1.5188 (19)
O6—C7	1.3455 (15)	C8—C9	1.5214 (19)
O6—C8	1.4804 (15)	C8—C10	1.5220 (17)
N1—C3	1.4438 (16)	C9—H9A	0.98
N1—C7	1.3568 (16)	C9—H9B	0.98
N1—H1N	0.87 (2)	C9—H9C	0.98
C1—H1A	0.98	C10—H10A	0.98
C1—H1B	0.98	C10—H10B	0.98
C1—H1C	0.98	C10—H10C	0.98
C2—C3	1.5211 (17)	C11—H11A	0.98
C3—C4	1.5264 (18)	C11—H11B	0.98
C3—H3	1.00	C11—H11C	0.98
C2—O2—C1	115.93 (11)	H6A—C6—H6B	109.5
C5—O4—C6	115.87 (11)	O4—C6—H6C	109.5



C7—O6—C8	121.15 (9)	H6A—C6—H6C	109.5
C7—N1—C3	120.10 (10)	H6B—C6—H6C	109.5
C3—N1—H1N	120.6 (12)	O5—C7—O6	126.69 (11)
C7—N1—H1N	119.1 (13)	O5—C7—N1	123.90 (11)
O2—C1—H1A	109.5	O6—C7—N1	109.41 (10)
O2—C1—H1B	109.5	O6—C8—C11	110.29 (10)
H1A—C1—H1B	109.5	O6—C8—C9	101.61 (10)
O2—C1—H1C	109.5	C11—C8—C9	110.85 (11)
H1A—C1—H1C	109.5	O6—C8—C10	110.03 (10)
H1B—C1—H1C	109.5	C11—C8—C10	113.04 (10)
O1—C2—O2	124.55 (12)	C9—C8—C10	110.45 (12)
O1—C2—C3	125.22 (12)	C8—C9—H9A	109.5
O2—C2—C3	110.15 (11)	C8—C9—H9B	109.5
N1—C3—C2	109.27 (10)	H9A—C9—H9B	109.5
N1—C3—C4	112.56 (10)	C8—C9—H9C	109.5
C2—C3—C4	113.43 (10)	H9A—C9—H9C	109.5
N1—C3—H3	107.1	H9B—C9—H9C	109.5
C2—C3—H3	107.1	C8—C10—H10A	109.5
C4—C3—H3	107.1	C8—C10—H10B	109.5
C5—C4—C3	112.54 (10)	H10A—C10—H10B	109.5
C5—C4—H4A	109.1	C8—C10—H10C	109.5
C3—C4—H4A	109.1	H10A—C10—H10C	109.5
C5—C4—H4B	109.1	H10B—C10—H10C	109.5
C3—C4—H4B	109.1	C8—C11—H11A	109.5
H4A—C4—H4B	107.8	C8—C11—H11B	109.5
O3—C5—O4	123.75 (11)	H11A—C11—H11B	109.5
O3—C5—C4	125.63 (12)	C8—C11—H11C	109.5
O4—C5—C4	110.62 (10)	H11A—C11—H11C	109.5
O4—C6—H6A	109.5	H11B—C11—H11C	109.5
O4—C6—H6B	109.5		
<hr/>			
C1—O2—C2—O1	-1.44 (16)	C6—O4—C5—C4	-179.15 (11)
C1—O2—C2—C3	-178.41 (8)	C3—C4—C5—O3	15.03 (19)
C7—N1—C3—C2	-149.02 (10)	C3—C4—C5—O4	-165.07 (10)
C7—N1—C3—C4	84.01 (12)	C8—O6—C7—O5	3.94 (17)
O1—C2—C3—N1	11.62 (15)	C8—O6—C7—N1	-176.27 (10)
O2—C2—C3—N1	-171.43 (9)	C3—N1—C7—O5	-1.19 (18)
O1—C2—C3—C4	138.10 (12)	C3—N1—C7—O6	179.01 (10)
O2—C2—C3—C4	-44.96 (12)	C7—O6—C8—C11	-61.77 (13)
N1—C3—C4—C5	62.96 (13)	C7—O6—C8—C9	-179.37 (10)
C2—C3—C4—C5	-61.75 (13)	C7—O6—C8—C10	63.61 (14)
C6—O4—C5—O3	0.76 (19)	O5—C7—N1—H1N	-175.9 (14)

Hydrogen-bond geometry ( $\text{\AA}$ ,  $^\circ$ )

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N1—H1N $\cdots$ O4 <sup>i</sup>	0.87 (2)	2.29 (2)	3.1388 (16)	166.6 (17)
C1—H1C $\cdots$ O5 <sup>ii</sup>	0.98	2.54	3.4775 (19)	160
C1—H1B $\cdots$ O5 <sup>iii</sup>	0.98	2.63	3.4368 (18)	140

C4—H4A···O1 <sup>iv</sup>	0.99	2.53	3.3869 (19)	144
C10—H10B···O5	0.98	2.51	3.0875 (19)	118
C10—H10A···O5 <sup>i</sup>	0.98	2.62	3.5407 (19)	157
C11—H11A···O5	0.98	2.39	3.0045 (18)	120

Symmetry codes: (i)  $x, y-1, z$ ; (ii)  $-x+1, y+1/2, -z$ ; (iii)  $x+1, y, z$ ; (iv)  $x, y+1, z$ .

## (II) Dimethyl (2S)-2-[bis[(*tert*-butoxycarbonyl)amino]butanedioate

### Crystal data

C <sub>16</sub> H <sub>27</sub> NO <sub>8</sub>	$D_x = 1.274 \text{ Mg m}^{-3}$
$M_r = 361.39$	Melting point: 325.2 K
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
Hall symbol: P 2ac 2ab	Cell parameters from 9210 reflections
$a = 5.922 (2) \text{ \AA}$	$\theta = 2.8\text{--}35.0^\circ$
$b = 9.635 (2) \text{ \AA}$	$\mu = 0.10 \text{ mm}^{-1}$
$c = 33.026 (8) \text{ \AA}$	$T = 100 \text{ K}$
$V = 1884.4 (9) \text{ \AA}^3$	Needle, colourless
$Z = 4$	$0.58 \times 0.18 \times 0.13 \text{ mm}$
$F(000) = 776$	

### Data collection

Oxford Xcalibur PX $\kappa$ -geometry	19441 measured reflections
diffractometer with Onyx CCD camera	4374 independent reflections
Radiation source: Enhance (Mo) X-ray Source	3766 reflections with $I > 2\sigma(I)$
Graphite monochromator	$R_{\text{int}} = 0.026$
$\omega$ and $\varphi$ scans	$\theta_{\text{max}} = 35.1^\circ$ , $\theta_{\text{min}} = 2.8^\circ$
Absorption correction: multi-scan	$h = -7 \rightarrow 9$
( <i>CrysAlis RED</i> ; Oxford Diffraction, 2009)	$k = -13 \rightarrow 14$
$T_{\text{min}} = 0.915$ , $T_{\text{max}} = 1.000$	$l = -52 \rightarrow 49$

### Refinement

Refinement on $F^2$	Secondary atom site location: difference Fourier map
Least-squares matrix: full	map
$R[F^2 > 2\sigma(F^2)] = 0.033$	Hydrogen site location: difference Fourier map
$wR(F^2) = 0.084$	H-atom parameters constrained
$S = 1.06$	$w = 1/[\sigma^2(F_o^2) + (0.0513P)^2]$
4374 reflections	where $P = (F_o^2 + 2F_c^2)/3$
234 parameters	$(\Delta/\sigma)_{\text{max}} = 0.001$
0 restraints	$\Delta\rho_{\text{max}} = 0.33 \text{ e \AA}^{-3}$
Primary atom site location: structure-invariant	$\Delta\rho_{\text{min}} = -0.21 \text{ e \AA}^{-3}$
direct methods	Absolute structure: known absolute configuration

### Special details

**Experimental.** <sup>1</sup>HNMR (CD<sub>3</sub>OD):  $\delta = 5.44$  (t,  $J_1 = 6.5 \text{ Hz}$ , 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.21 (dd,  $J_1 = 6.5 \text{ Hz}$ ,  $J_2 = 16.3 \text{ Hz}$ , 1H), 2.83 (dd,  $J_1 = 6.5 \text{ Hz}$ ,  $J_2 = 16.3 \text{ Hz}$ , 1H), 1.54 (s, 18H)

MS (ESI),  $[M+\text{Na}]^+_{\text{obsd}}$  ( $[M+\text{Na}]^+_{\text{calcd}}$ ),  $[M+\text{K}]^+_{\text{obsd}}$  ( $[M+\text{K}]^+_{\text{calcd}}$ ), Da: 384.163(384.163), 400.137(400.137)

Melting point range 325.2–326.0 K

**Geometry.** All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

**Refinement.** Refinement of  $F^2$  against ALL reflections. The weighted  $R$ -factor  $wR$  and goodness of fit  $S$  are based on  $F^2$ , conventional  $R$ -factors  $R$  are based on  $F$ , with  $F$  set to zero for negative  $F^2$ . The threshold expression of  $F^2 > \sigma(F^2)$  is used only for calculating  $R$ -factors(gt) *etc.* and is not relevant to the choice of reflections for refinement.  $R$ -factors based on  $F^2$  are statistically about twice as large as those based on  $F$ , and  $R$ -factors based on ALL data will be even larger.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ( $\text{\AA}^2$ )*

	$x$	$y$	$z$	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.10714 (14)	0.44229 (11)	0.46790 (2)	0.02093 (18)
O2	0.46447 (14)	0.45633 (11)	0.44508 (2)	0.02078 (18)
O3	-0.02379 (14)	0.79384 (11)	0.45873 (3)	0.02407 (19)
O4	-0.34966 (13)	0.77487 (10)	0.42441 (2)	0.01899 (17)
O5	0.30700 (15)	0.78565 (9)	0.35433 (3)	0.01948 (17)
O6	0.55821 (13)	0.63292 (9)	0.32733 (2)	0.01469 (15)
O7	0.28257 (14)	0.41338 (9)	0.31658 (2)	0.01874 (17)
O8	0.15137 (15)	0.34646 (9)	0.37807 (2)	0.01785 (16)
N1	0.30205 (15)	0.55636 (10)	0.37260 (3)	0.01333 (16)
C1	0.5351 (2)	0.36784 (19)	0.47807 (4)	0.0337 (3)
H1A	0.4874	0.4089	0.5038	0.051*
H1B	0.6999	0.3586	0.4777	0.051*
H1C	0.4659	0.2761	0.4750	0.051*
C2	0.24361 (18)	0.48566 (13)	0.44408 (3)	0.0159 (2)
C3	0.19056 (17)	0.59140 (12)	0.41093 (3)	0.01350 (18)
H3	0.2590	0.6810	0.4201	0.016*
C4	-0.06274 (18)	0.61855 (13)	0.40689 (3)	0.0157 (2)
H4A	-0.0989	0.6397	0.3783	0.019*
H4B	-0.1470	0.5339	0.4147	0.019*
C5	-0.13714 (18)	0.73779 (12)	0.43324 (3)	0.01488 (19)
C6	-0.4464 (2)	0.88285 (14)	0.44944 (4)	0.0221 (2)
H6A	-0.4633	0.8486	0.4772	0.033*
H6B	-0.5948	0.9090	0.4387	0.033*
H6C	-0.3468	0.9640	0.4493	0.033*
C7	0.38586 (18)	0.67098 (12)	0.35033 (3)	0.01373 (19)
C8	0.63469 (18)	0.72188 (13)	0.29332 (3)	0.0171 (2)
C9	0.7367 (2)	0.85604 (15)	0.30919 (4)	0.0263 (3)
H9A	0.6195	0.9106	0.3228	0.039*
H9B	0.7988	0.9096	0.2865	0.039*
H9C	0.8575	0.8344	0.3285	0.039*
C10	0.8129 (2)	0.63109 (16)	0.27350 (4)	0.0245 (3)
H10A	0.9330	0.6112	0.2931	0.037*
H10B	0.8767	0.6796	0.2501	0.037*
H10C	0.7438	0.5439	0.2646	0.037*
C11	0.4374 (2)	0.74738 (16)	0.26484 (4)	0.0254 (3)
H11A	0.3671	0.6586	0.2577	0.038*
H11B	0.4918	0.7931	0.2402	0.038*
H11C	0.3259	0.8069	0.2782	0.038*
C12	0.24901 (18)	0.43346 (12)	0.35211 (3)	0.01332 (18)
C13	0.0502 (2)	0.21508 (13)	0.36310 (3)	0.0196 (2)
C14	-0.0482 (3)	0.15313 (18)	0.40150 (4)	0.0401 (4)
H14A	0.0718	0.1417	0.4217	0.060*

H14B	-0.1152	0.0625	0.3954	0.060*
H14C	-0.1648	0.2152	0.4123	0.060*
C15	-0.1346 (2)	0.24836 (15)	0.33290 (4)	0.0270 (3)
H15A	-0.2384	0.3165	0.3447	0.040*
H15B	-0.2178	0.1634	0.3263	0.040*
H15C	-0.0673	0.2867	0.3082	0.040*
C16	0.2339 (2)	0.12174 (14)	0.34624 (4)	0.0250 (3)
H16A	0.2960	0.1632	0.3215	0.037*
H16B	0.1701	0.0304	0.3399	0.037*
H16C	0.3543	0.1113	0.3664	0.037*

Atomic displacement parameters ( $\text{\AA}^2$ )

	$U^{11}$	$U^{22}$	$U^{33}$	$U^{12}$	$U^{13}$	$U^{23}$
O1	0.0171 (3)	0.0299 (5)	0.0157 (3)	-0.0009 (3)	0.0034 (3)	0.0026 (3)
O2	0.0141 (3)	0.0311 (5)	0.0172 (3)	0.0045 (4)	0.0009 (3)	0.0094 (3)
O3	0.0191 (4)	0.0300 (5)	0.0230 (4)	0.0032 (4)	-0.0045 (3)	-0.0109 (4)
O4	0.0139 (3)	0.0206 (4)	0.0225 (4)	0.0038 (3)	-0.0018 (3)	-0.0067 (3)
O5	0.0221 (4)	0.0137 (4)	0.0226 (4)	0.0026 (3)	0.0003 (3)	0.0024 (3)
O6	0.0141 (3)	0.0146 (4)	0.0154 (3)	-0.0006 (3)	0.0017 (3)	0.0042 (3)
O7	0.0246 (4)	0.0180 (4)	0.0136 (3)	-0.0037 (3)	0.0040 (3)	-0.0022 (3)
O8	0.0260 (4)	0.0135 (4)	0.0141 (3)	-0.0059 (3)	0.0042 (3)	-0.0004 (3)
N1	0.0152 (4)	0.0127 (4)	0.0121 (3)	-0.0010 (3)	0.0017 (3)	-0.0005 (3)
C1	0.0215 (5)	0.0537 (10)	0.0259 (6)	0.0102 (6)	0.0022 (5)	0.0215 (6)
C2	0.0137 (4)	0.0203 (5)	0.0138 (4)	0.0009 (4)	-0.0001 (3)	-0.0005 (4)
C3	0.0125 (4)	0.0156 (5)	0.0124 (4)	0.0012 (4)	-0.0002 (3)	-0.0014 (3)
C4	0.0129 (4)	0.0187 (5)	0.0156 (4)	0.0014 (4)	-0.0015 (3)	-0.0035 (4)
C5	0.0134 (4)	0.0170 (5)	0.0142 (4)	0.0014 (4)	0.0009 (3)	0.0004 (4)
C6	0.0181 (5)	0.0198 (6)	0.0285 (5)	0.0026 (5)	0.0046 (4)	-0.0060 (5)
C7	0.0131 (4)	0.0138 (5)	0.0143 (4)	-0.0015 (4)	-0.0022 (3)	0.0014 (4)
C8	0.0151 (4)	0.0187 (5)	0.0175 (4)	-0.0043 (4)	0.0004 (4)	0.0061 (4)
C9	0.0252 (6)	0.0201 (6)	0.0335 (6)	-0.0089 (5)	0.0001 (5)	0.0042 (5)
C10	0.0210 (5)	0.0295 (7)	0.0229 (5)	-0.0006 (5)	0.0064 (4)	0.0046 (5)
C11	0.0205 (5)	0.0351 (8)	0.0206 (5)	-0.0029 (5)	-0.0027 (4)	0.0111 (5)
C12	0.0125 (4)	0.0125 (5)	0.0150 (4)	0.0004 (4)	0.0005 (3)	0.0013 (4)
C13	0.0240 (5)	0.0136 (5)	0.0211 (5)	-0.0065 (5)	0.0053 (4)	-0.0014 (4)
C14	0.0623 (11)	0.0284 (8)	0.0296 (6)	-0.0220 (8)	0.0186 (7)	0.0001 (6)
C15	0.0183 (5)	0.0242 (7)	0.0384 (7)	-0.0037 (5)	-0.0019 (5)	-0.0062 (5)
C16	0.0281 (6)	0.0150 (5)	0.0318 (6)	0.0024 (5)	0.0008 (5)	-0.0001 (5)

Geometric parameters ( $\text{\AA}$ ,  $^\circ$ )

O1—C2	1.2026 (14)	C6—H6C	0.98
O2—C2	1.3385 (14)	C8—C10	1.5188 (18)
O2—C1	1.4453 (15)	C8—C9	1.5201 (18)
O3—C5	1.2045 (13)	C8—C11	1.5202 (17)
O4—C5	1.3404 (14)	C9—H9A	0.98
O4—C6	1.4471 (14)	C9—H9B	0.98
O5—C7	1.2067 (14)	C9—H9C	0.98
O6—C7	1.3241 (13)	C10—H10A	0.98

O6—C8	1.4836 (13)	C10—H10B	0.98
O7—C12	1.2057 (13)	C10—H10C	0.98
O8—C12	1.3312 (13)	C11—H11A	0.9800
O8—C13	1.4851 (14)	C11—H11B	0.9800
N1—C3	1.4669 (13)	C11—H11C	0.9800
N1—C7	1.4168 (14)	C13—C15	1.5154 (19)
N1—C12	1.3996 (14)	C13—C16	1.5174 (18)
C1—H1A	0.98	C13—C14	1.5180 (17)
C1—H1B	0.98	C14—H14A	0.98
C1—H1C	0.98	C14—H14B	0.98
C2—C3	1.5283 (16)	C14—H14C	0.98
C3—C4	1.5285 (15)	C15—H15A	0.98
C3—H3	1.0000	C15—H15B	0.98
C4—C5	1.5071 (16)	C15—H15C	0.98
C4—H4A	0.99	C16—H16A	0.98
C4—H4B	0.99	C16—H16B	0.98
C6—H6A	0.98	C16—H16C	0.98
C6—H6B	0.98		
C2—O2—C1	115.20 (10)	C8—C9—H9A	109.5
C5—O4—C6	116.05 (9)	C8—C9—H9B	109.5
C7—O6—C8	120.64 (9)	H9A—C9—H9B	109.5
C12—O8—C13	119.84 (8)	C8—C9—H9C	109.5
C7—N1—C3	115.23 (9)	H9A—C9—H9C	109.5
C12—N1—C3	120.73 (9)	H9B—C9—H9C	109.5
C12—N1—C7	119.14 (8)	C8—C10—H10A	109.5
O2—C1—H1A	109.5	C8—C10—H10B	109.5
O2—C1—H1B	109.5	H10A—C10—H10B	109.5
H1A—C1—H1B	109.5	C8—C10—H10C	109.5
O2—C1—H1C	109.5	H10A—C10—H10C	109.5
H1A—C1—H1C	109.5	H10B—C10—H10C	109.5
H1B—C1—H1C	109.5	C8—C11—H11A	109.5
O1—C2—O2	124.56 (11)	C8—C11—H11B	109.5
O1—C2—C3	124.20 (10)	H11A—C11—H11B	109.5
O2—C2—C3	111.05 (9)	C8—C11—H11C	109.5
N1—C3—C2	111.85 (9)	H11A—C11—H11C	109.5
N1—C3—C4	113.94 (8)	H11B—C11—H11C	109.5
C2—C3—C4	112.23 (9)	O7—C12—O8	126.68 (11)
N1—C3—H3	106.0	O7—C12—N1	124.71 (10)
C2—C3—H3	106.0	O8—C12—N1	108.59 (9)
C4—C3—H3	106.0	O8—C13—C15	109.28 (10)
C5—C4—C3	111.53 (9)	O8—C13—C16	109.76 (10)
C5—C4—H4A	109.3	C15—C13—C16	113.69 (10)
C3—C4—H4A	109.3	O8—C13—C14	102.24 (10)
C5—C4—H4B	109.3	C15—C13—C14	110.84 (12)
C3—C4—H4B	109.3	C16—C13—C14	110.42 (12)
H4A—C4—H4B	108.0	C13—C14—H14A	109.5
O3—C5—O4	123.76 (11)	C13—C14—H14B	109.5
O3—C5—C4	125.62 (10)	H14A—C14—H14B	109.5

O4—C5—C4	110.62 (9)	C13—C14—H14C	109.5
O4—C6—H6A	109.5	H14A—C14—H14C	109.5
O4—C6—H6B	109.5	H14B—C14—H14C	109.5
H6A—C6—H6B	109.5	C13—C15—H15A	109.5
O4—C6—H6C	109.5	C13—C15—H15B	109.5
H6A—C6—H6C	109.5	H15A—C15—H15B	109.5
H6B—C6—H6C	109.5	C13—C15—H15C	109.5
O5—C7—O6	127.93 (10)	H15A—C15—H15C	109.5
O5—C7—N1	121.41 (10)	H15B—C15—H15C	109.5
O6—C7—N1	110.61 (9)	C13—C16—H16A	109.5
O6—C8—C10	101.86 (10)	C13—C16—H16B	109.5
O6—C8—C9	110.58 (9)	H16A—C16—H16B	109.5
C10—C8—C9	111.24 (10)	C13—C16—H16C	109.5
O6—C8—C11	109.09 (9)	H16A—C16—H16C	109.5
C10—C8—C11	111.13 (10)	H16B—C16—H16C	109.5
C9—C8—C11	112.42 (11)		
C1—O2—C2—O1	-1.06 (19)	C8—O6—C7—N1	163.20 (8)
C1—O2—C2—C3	174.06 (11)	C3—N1—C7—O5	-24.65 (14)
C7—N1—C3—C2	-141.94 (9)	C12—N1—C7—O5	130.78 (11)
C12—N1—C3—C2	63.05 (12)	C12—N1—C7—O6	-51.38 (12)
C7—N1—C3—C4	89.45 (12)	C3—N1—C7—O6	153.18 (8)
C12—N1—C3—C4	-65.56 (13)	C7—O6—C8—C10	-174.02 (9)
O1—C2—C3—N1	-138.79 (12)	C7—O6—C8—C9	67.66 (12)
O2—C2—C3—N1	46.07 (13)	C7—O6—C8—C11	-56.47 (13)
O1—C2—C3—C4	-9.28 (16)	C13—O8—C12—O7	-6.33 (18)
O2—C2—C3—C4	175.58 (10)	C13—O8—C12—N1	171.91 (9)
N1—C3—C4—C5	-140.53 (10)	C3—N1—C12—O7	159.03 (11)
C2—C3—C4—C5	91.04 (12)	C7—N1—C12—O7	4.97 (16)
C6—O4—C5—O3	-4.08 (17)	C3—N1—C12—O8	-19.26 (13)
C6—O4—C5—C4	176.22 (10)	C7—N1—C12—O8	-173.32 (9)
C3—C4—C5—O3	-9.91 (16)	C12—O8—C13—C15	-60.14 (13)
C3—C4—C5—O4	169.78 (9)	C12—O8—C13—C16	65.16 (13)
C8—O6—C7—O5	-19.14 (16)	C12—O8—C13—C14	-177.62 (12)

Hydrogen-bond geometry (Å, °)

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
C1—H1 <i>B</i> ...O1 <sup>i</sup>	0.98	2.56	3.479 (2)	156
C3—H3...O3	1.00	2.37	2.8121 (15)	106
C3—H3...O4 <sup>i</sup>	1.00	2.49	3.2767 (16)	135
C6—H6 <i>A</i> ...O3 <sup>ii</sup>	0.98	2.55	3.5079 (18)	167
C9—H9 <i>A</i> ...O5	0.98	2.44	3.0261 (17)	118
C11—H11 <i>C</i> ...O5	0.98	2.52	3.0769 (17)	116
C11—H11 <i>B</i> ...O7 <sup>iii</sup>	0.98	2.58	3.5412 (16)	168
C15—H15 <i>C</i> ...O7	0.98	2.42	2.9871 (17)	116
C16—H16 <i>A</i> ...O7	0.98	2.42	2.9897 (17)	117
C16—H16 <i>B</i> ...O5 <sup>iv</sup>	0.98	2.54	3.2780 (17)	132

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

Selected bond lengths and angles ( $\text{\AA}$ ,  $^\circ$ ) for structures (I) and (II) compared with average values obtained from the CSD (Allen, 2002).

Boc/bis-Boc pairs	DIST1	DIST2	DIST3	ANG1	ANG2	ANG3	DIST4 <sup>a</sup>
(I)	1.357 (2)	0.87 (2)	1.444 (2)	120.10 (10)	121 (2)	119 (2)	0.031 (2)
(II)	1.417 (2)	1.400 (2)	1.467 (2)	115.23 (9)	120.73 (9)	119.14 (8)	0.184 (2)
MUTTOK	1.366 (3)	<i>b</i>	1.419 (3)	125.0 (2)	118 (2)	117 (2)	0.005 (2)
MUTTUQ, fragment 1	1.406 (2)	1.413 (2)	1.451 (2)	120.5 (1)	119.6 (1)	119.9 (1)	0.013 (1)
MUTTUQ, fragment 2	1.408 (2)	1.408 (2)	1.448 (2)	119.5 (1)	119.9 (1)	120.6 (1)	0.012 (1)
XUDQUJ, fragment 1	1.373 (3)	<i>b</i>	1.390 (2)	125.9 (2)	115 (2)	117 (2)	0.090 (2)
XUDQUJ, fragment 2	1.372 (2)	<i>b</i>	1.386 (3)	127.2 (2)	115 (2)	118 (2)	0.015 (2)
XUDQOD	1.420 (2)	1.405 (2)	1.431 (2)	118.5 (1)	120.8 (1)	120.6 (1)	0.037 (2)
Protecting groups							
Boc	1.35	<i>b</i>	1.45	122	119	119	0.04
Bis-Boc	1.41	1.41	1.44	118	119	123	0.04
Urethane	1.35	<i>b</i>	1.44	123	118	118	0.04
Bis-urethane	1.41	1.41	1.44	119	118	122	0.05
Acetyl	1.35	<i>b</i>	1.43	125	117	118	0.03
Bis-acetyl	1.41	1.41	1.45	119	117	125	0.03

Notes: (a) DIST4 is the distance between the N atom and the plane defined by the neighbouring atoms; other definitions are given in Fig. 4; (b) DIST2 in monosubstituted species is not given, as the H atoms were treated in different ways.