

refined isotropically, all non-H atoms anisotropic. Maximum  $\Delta/\sigma = 0.016$ ;  $\Delta\rho$  excursions = 0.17 to  $-0.16 \text{ e } \text{\AA}^{-3}$ . Scattering factors were obtained from *International Tables for X-ray Crystallography* (1974, Vol. IV) and structure refinement used *SHELX76* (Sheldrick, 1976) as implemented at the University of Manchester Regional Computer Centre.

**Discussion.** The final atomic coordinates are listed in Table 1\* and bond lengths and angles in Table 2. The molecular structure and atomic numbering are shown in Fig. 1; unit-cell contents projected down *c* are represented in Fig. 2.

The structure of the crystalline solid was confirmed to be that of the bicyclic amidine-trifluoroacetate salt. The molecule possesses a twofold axis of symmetry with C(1), C(6), C(13), C(16), C(17), F(1), F(3) and H(12) occupying special positions. The CF<sub>3</sub> group appeared disordered; as a model, five F-atom positions were assigned, all having a variety of occupancy factors < 1. The C(1)—N(2) bond length of 1.316 (3) Å suggests a partial double-bond character [single C—N bond 1.47 Å, double C=N bond 1.27 Å (Stark & Wallace, 1982)] owing to  $\pi$ -electron delocalization about N(2)—C(1)—N(2'). Similarly the C(16)—O(1) bond length of 1.229 (3) Å [single C—O bond 1.48 Å, double C=O bond 1.21 Å (Stark & Wallace, 1982)] also suggests partial double-bond characteristics owing to delocalization of  $\pi$  electrons about the carboxylate. The N(2)—H(1) distance of

0.81 (3) Å implies that covalent bonding exists between these atoms and not a disordered bond between N(2)—H(1)—O(1). The H(1)—O(1) distance of 2.02 (3) Å indicates the existence of a hydrogen bond, further exemplified by the N(2)—H(1)—O(1) bond angle of 175.5 (1)°. A further factor contributing to the stability of the product is the close agreement of several intramolecular distances, namely O(1)⋯O(1') [2.22 (5) Å], H(1)⋯H(1') [2.13 (4) Å] and N(2)⋯N(2') [2.27 (6) Å]. The ability of the base to form a stable salt with carboxylic acids is a direct consequence of similarities between the intramolecular N⋯N distance in the bicyclic amidine and the O⋯O distance of the carboxyl moiety.

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## Structure of *N,N*-Di-*tert*-butyloxycarbonyl-glycine *N'*-Methoxy-*N'*-methanamide

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(Received 23 May 1991; accepted 13 January 1992)

**Abstract.** C<sub>14</sub>H<sub>26</sub>N<sub>2</sub>O<sub>6</sub>, *M<sub>r</sub>* = 318.37, orthorhombic, *Pbca*, *a* = 11.973 (2), *b* = 17.036 (3), *c* = 17.765 (4) Å,

*V* = 3623 (1) Å<sup>3</sup>, *Z* = 8, *D<sub>m</sub>* = 1.17, *D<sub>x</sub>* = 1.163 Mg m<sup>-3</sup>, λ(Cu Kα) = 1.54178 Å, μ = 0.725 mm<sup>-1</sup>, *F*(000) = 1376, room temperature, *R* = 0.041 for 1701 observed reflections. The bond lengths

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and angles do not deviate significantly from standard values. Out-of-plane deformation of the amide group is observed; however, the main chain of glycine is almost planar. The crystalline-phase structure of the molecule and the lowest-energy structure obtained from the *AM1* complete geometry optimization are also compared.

**Introduction.** In recent years variations of amide bond replacements (*surrogates*) in peptides have acquired increasing popularity in an effort to establish structure–bioactivity relationship and develop new analogues with prolonged actions, different patterns of enzymatic degradation or more selective properties (Spatola, 1983).

Replacement of the peptide bond by the  $\text{CH}_2\text{NH}$  group often produces interesting properties in peptide analogues (Martinez *et al.*, 1985; Rodriguez, Bali, Magous, Castro & Martinez, 1986). The  $\psi[\text{CH}_2\text{NH}]$  pseudo-peptide can be obtained directly by the reductive alkylation reaction between *N-tert*-butyloxycarbonylamino aldehyde and an amine (Borch, Bernstein & Durst, 1971). The title compound is the main substrate used to obtain *N,N*-di-*tert*-butyloxycarbonyl-glycinal, a more stable glycinal derivative (Fehrentz & Castro, 1983). Structural investigations of a glycine amide derivative doubly protected with *tert*-butyloxycarbonyl groups are reported in this paper. Several previous papers (Murali, Subramanian & Parthasarathy, 1986; Główska, 1988; Hiyama, Niu, Silvertson, Bavoso & Torchia, 1988) provided only structural information about glycine derivatives mono-substituted with *tert*-butyloxycarbonyl on the amine N atom.

**Experimental.** Crystals were obtained from hot *n*-hexane as colourless prisms; m.p. 350–351 K;  $D_m$  measured by flotation in aqueous KI. The space group was determined from Weissenberg photographs. A crystal  $0.20 \times 0.25 \times 0.25$  mm was used for intensity measurements on a KM-4 diffractometer (Kuma Diffraction, Poland) in the  $\theta$ – $2\theta$ -scan mode. Cell parameters were determined from least-squares treatment of the setting angles of 25 reflections with  $15 \leq 2\theta \leq 60^\circ$ . 2481 reflections with  $2\theta \leq 115^\circ$  in the range  $h\ 0 \rightarrow 13$ ,  $k\ 0 \rightarrow 18$ ,  $l\ 0 \rightarrow 19$ , were measured of which 1701 were observed with  $I \geq 2\sigma(I)$ . Two standard reflections recorded every 100 measurements varied  $\pm 2\%$ . Lorentz and polarization corrections were applied, but absorption effects were ignored. The structure was solved by direct methods using *SHELXS86* (Sheldrick, 1986). Full-matrix least-squares refinement [function minimized:  $\sum w(F_o - F_c)^2$ , with  $w^{-1} = \sigma^2(F_o) + 0.0005F_o^2$ ] of anisotropic non-H atoms was performed. All H atoms were positioned from molecular geometry, treated as riding groups and refined with isotropic

thermal parameters. The refinement included an empirical isotropic extinction parameter,  $x = 0.0065(4)$ ;  $F'_c = F_c[1 + 0.002xF_c^2/\sin(2\theta)]^{-0.25}$ .  $R = 0.041$ ,  $wR = 0.048$ ,  $S = 1.34$ ,  $\Delta/\sigma \leq 0.002$ ,  $\Delta\rho_{\max} = 0.14$ ,  $\Delta\rho_{\min} = -0.12$  e  $\text{\AA}^{-3}$ , 256 parameters refined. Computer programs: *SHELX76* (Sheldrick, 1976), *SHELXS86*, *SHELXS90* (Sheldrick, 1990) and *CRYSRULER* (Rizzoli, Sangermano, Calestani & Andreotti, 1987) package and local programs. Scattering factors used were those stored in *SHELX76* (Sheldrick, 1976). Molecular illustrations were drawn using *ORTEPII* (Johnson, 1976).

**Discussion.** *Crystal structure.* Atomic parameters are given in Table 1,\* and bond lengths and angles in Table 2. The labelling sequence and a view of the molecule are presented in Fig. 1. The differences between the appropriate structural parameters obtained and those reported as standard (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987) fall within the standard deviations. The molecular shape of the compound investigated reminds one of a propeller. The amine N(1) atom is at the centre whereas the *tert*-butyloxycarbonyl and glycine groups form the blades. The amine group is nearly planar [sum of valence angles at central N(1) =  $359.5(6)^\circ$ ]. The best planes calculated for the *tert*-butyloxycarbonyl substituents (H atoms and methyl C atoms excluded) form an angle of  $26.1^\circ$ . The main chain of the glycine amide, terminated by atoms N(1) and C(8), lies approximately in a plane. The mean deviation of atoms from this plane is 0.051 Å. The value of the  $\tau$  angle (Winkler & Dunitz, 1971) indicates the transoidal conformation of the C(2)—O(1) and N(2)—O(4) bonds. Furthermore, the amide group exhibits considerable deviation from planarity (see  $\chi_c$ ,  $\chi_N$ , and  $\tau$  in Table 2). The sum of the valence angles around atom N(2) [ $355.1(6)^\circ$ ] distinctly differs from  $360^\circ$ . The distance between N(2) and the plane through C(2), C(8), O(4) is 0.179 Å.

*Structure of an isolated molecule.* To enable comparison of the solid-state structure of the compound studied with that of the isolated molecule, the conformational analysis was carried out at the level of the semi-empirical *AM1* quantum chemistry method (Dewar, Zoebisch, Healy & Steward, 1985). The first stage was to find different starting geometries of the molecule. In order to do this we have assumed values of four torsion angles [O(2)—C(3)—N(1)—C(3'); C(1)—N(1)—C(3')—O(2'); C(2)—C(1)—N(1)—C(3); N(1)—C(3)—O(2)—C(4)], changing them by  $60^\circ$ ,

\* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55066 (28 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Fractional atomic coordinates and equivalent isotropic thermal parameters (Å<sup>2</sup>)
$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$$

	x	y	z	U <sub>eq</sub>
C(1)	0.1170 (2)	-0.0870 (2)	0.4874 (1)	0.060 (1)
C(2)	0.2344 (2)	-0.1017 (2)	0.5142 (2)	0.059 (1)
O(1)	0.3147 (2)	-0.1012 (2)	0.4726 (1)	0.091 (1)
N(2)	0.2453 (2)	-0.1138 (2)	0.5889 (1)	0.068 (1)
O(4)	0.1470 (2)	-0.1304 (2)	0.6274 (2)	0.074 (1)
C(8)	0.3469 (3)	-0.1417 (2)	0.6245 (2)	0.102 (1)
C(9)	0.1210 (3)	-0.0691 (2)	0.6786 (2)	0.111 (2)
N(1)	0.1148 (2)	-0.0621 (1)	0.4085 (1)	0.057 (1)
C(3)	0.1654 (2)	0.0094 (2)	0.3887 (1)	0.059 (1)
O(2)	0.1736 (1)	0.0534 (1)	0.4503 (1)	0.060 (1)
O(3)	0.1949 (2)	0.0274 (1)	0.3270 (1)	0.090 (1)
C(4)	0.2335 (2)	0.1295 (2)	0.4488 (2)	0.064 (1)
C(5)	0.2253 (3)	0.1547 (2)	0.5306 (2)	0.100 (1)
C(6)	0.1725 (3)	0.1863 (2)	0.3997 (2)	0.107 (2)
C(7)	0.3530 (3)	0.1165 (2)	0.4268 (2)	0.103 (2)
C(3')	0.0731 (2)	-0.1165 (2)	0.3566 (1)	0.059 (1)
O(2')	0.0585 (2)	-0.0840 (1)	0.2899 (1)	0.063 (1)
O(3')	0.0491 (2)	-0.1818 (1)	0.3746 (1)	0.085 (1)
C(4')	0.0095 (2)	-0.1287 (2)	0.2262 (1)	0.067 (1)
C(5')	0.0779 (3)	-0.2001 (2)	0.2098 (2)	0.096 (1)
C(6')	-0.1113 (3)	-0.1475 (2)	0.2442 (2)	0.093 (1)
C(7')	0.0178 (3)	-0.0691 (2)	0.1633 (2)	0.094 (1)

complete geometry optimization at a high level of precision. Four different conformers appeared to have heats of formation between *ca* -853.5 and -805.0 kJ mol<sup>-1</sup>. The lowest energy structure, which we believe corresponds to the global minimum of the molecule, is compared with the structure of

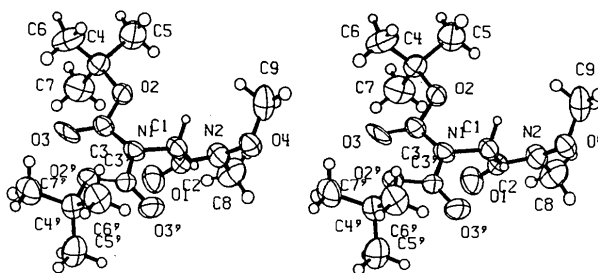


Fig. 1. Stereoview of the molecule with atom numbering. Thermal ellipsoids are drawn at the 40% probability level. H atoms are represented by spheres of arbitrary size.

Table 2. Bond lengths (Å), angles (°) and selected torsion angles (°)

N(1)—C(1)	1.465 (3)	C(4)—C(5)	1.517 (4)
C(1)—C(2)	1.505 (4)	C(4)—C(6)	1.493 (4)
O(1)—C(2)	1.212 (3)	C(4)—C(7)	1.501 (4)
N(2)—C(2)	1.351 (3)	N(1)—C(3)	1.399 (3)
O(4)—N(2)	1.390 (3)	O(3)—C(3')	1.193 (3)
N(2)—C(8)	1.450 (4)	O(2)—C(3)	1.319 (3)
O(4)—C(9)	1.418 (4)	O(2)—C(4')	1.486 (3)
N(1)—C(3)	1.405 (3)	C(4)—C(5')	1.494 (4)
O(3)—C(3)	1.192 (3)	C(4)—C(6')	1.516 (4)
O(2)—C(3)	1.330 (3)	C(4)—C(7')	1.513 (4)
O(2)—C(4)	1.483 (3)		
N(1)—C(1)—C(2)	111.6 (2)	C(5)—C(4)—C(6)	110.2 (2)
C(1)—C(2)—O(1)	123.2 (2)	C(5)—C(4)—C(7)	110.7 (3)
N(2)—C(2)—C(1)	115.3 (2)	C(6)—C(4)—C(7)	114.1 (3)
N(2)—C(2)—O(1)	121.6 (3)	C(1)—N(1)—C(3)	116.4 (2)
O(4)—N(2)—C(2)	115.7 (2)	N(1)—C(3)—O(3')	121.8 (2)
N(2)—O(4)—C(9)	110.7 (2)	O(2)—C(3)—N(1)	111.2 (2)
C(2)—N(2)—C(8)	124.0 (2)	O(2)—C(3)—O(3')	126.9 (2)
O(4)—N(2)—C(8)	115.4 (2)	C(3)—O(2)—C(4')	121.5 (2)
C(3)—N(1)—C(1)	118.8 (2)	O(2)—C(4)—C(5')	110.4 (2)
N(1)—C(3)—O(3)	125.5 (2)	O(2)—C(4)—C(6')	108.9 (2)
O(2)—C(3)—N(1)	108.3 (2)	O(2)—C(4)—C(7')	101.1 (2)
O(2)—C(3)—O(3)	126.2 (2)	C(5)—C(4)—C(6')	113.1 (2)
C(3)—O(2)—C(4)	120.9 (2)	C(7)—C(4)—C(5')	111.6 (2)
O(2)—C(4)—C(5)	101.5 (2)	C(7)—C(4)—C(6')	111.1 (2)
O(2)—C(4)—C(6)	110.0 (2)	C(3)—N(1)—C(3')	124.3 (2)
O(2)—C(4)—C(7)	109.7 (2)		

	Observed	AM1
C(2)—N(2)—O(4)—C(9)	-114.1 (3)	-111.9
C(8)—N(2)—O(4)—C(9)	89.6 (3)	112.4
C(3)—N(1)—C(1)—C(2)	-64.1 (3)	-93.2
C(3')—N(1)—C(1)—C(2)	108.7 (2)	80.4
N(1)—C(1)—C(2)—N(2)	170.9 (2)	124.3
C(1)—C(2)—N(2)—C(8)	169.4 (3)	157.0
O(1)—C(2)—N(2)—O(4)	-166.2 (2)	-160.2
O(1)—C(2)—N(2)—C(8)	-12.1 (4)	-27.0
C(1)—C(2)—N(2)—O(4)	15.3 (3)	23.8
χ <sub>C</sub> = χ[C(1)O(1)]	1.5	4.0
χ <sub>N</sub> = χ[C(8)O(4)]	25.9	46.8
τ	181.6	178.4

The angles ω<sub>b</sub>, χ<sub>C</sub>, χ<sub>N</sub> and τ are appropriate parameters for describing the conformation and out-of-plane deformations of the amide group (Winkler & Dunitz, 1971).

and permitting other parameters to be completely optimized. From 81 primarily constructed molecules only 18 appeared to be thermodynamically stable. These structures were subsequently subjected to

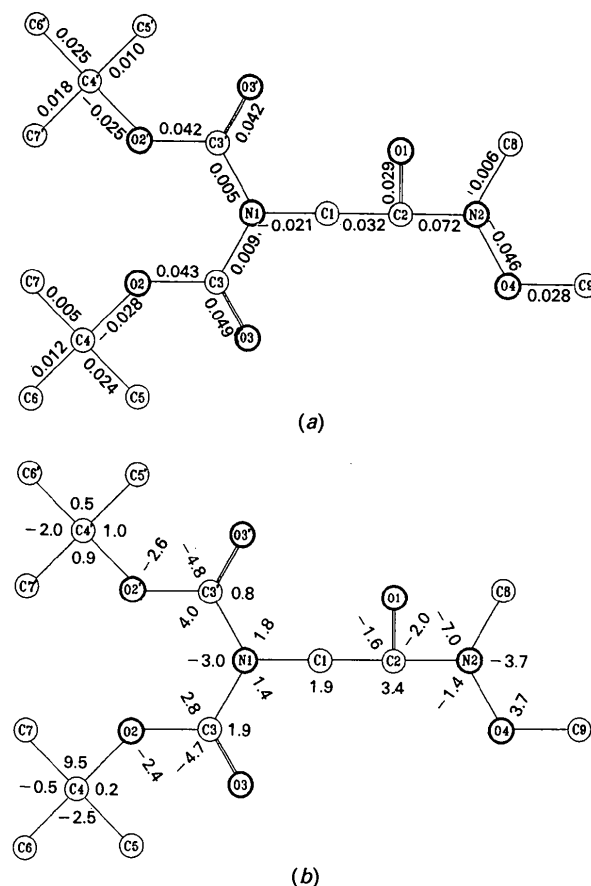


Fig. 2. The differences in (a) corresponding bond lengths (Å) and (b) valence angles (°) of the lowest energy structure from the AM1 calculation and the crystal structure.

the molecule in the crystalline phase in Fig. 2. General comparison shows that almost all bonds (with the exception of some single bonds in which O or N atoms participate) are lengthened in the free molecule. The largest difference was found for the C(2)—N(2) bond. The calculated conformation of the amine group in the isolated molecule is nearly planar. This could be the result of the conjugation of the lone electron pair at N(1) with the two carbonyl bonds. Similarly to the crystal structure, the amide group shows deviations from planarity (see  $\chi_c$ ,  $\chi_N$  and  $\tau$  in Table 2), the C(2)—O(1) and N(2)—O(4) bonds remaining in a transoidal conformation, however.

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## Structure of Ethyl 2-(2-Amino-3-ethoxycarbonyl-4H-chromen-4-yl)-2-cyanoacetate

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**Abstract.**  $C_{17}H_{18}N_2O_5$ ,  $M_r = 330.35$ , monoclinic,  $P2_1/n$ ,  $a = 21.335$  (2),  $b = 8.516$  (1),  $c = 9.273$  (1) Å,  $\beta = 93.645$  (1)°,  $V = 1681.44$  (5) Å<sup>3</sup>,  $Z = 4$ ,  $D_m = 1.330$ ,  $D_x = 1.305$  Mg m<sup>-3</sup>,  $\lambda(\text{Cu } K\alpha) = 1.5418$  Å,  $\mu = 0.77$  mm<sup>-1</sup>,  $F(000) = 696.00$ ,  $T = 300$  K, final  $R = 0.059$  for 3184 observed reflections [ $I > 3\sigma(I)$ ]. The dihydropyran ring makes a dihedral angle of 14.6 (3)° with the benzene ring and is puckered. The ethoxycarbonyl group attached to C(3) makes a dihedral angle of 13.9 (3)° with the chromene ring but the 4-(1-ethoxycarbonyl) group is rotated about C(4) by 81.1 (4)°. The C—C≡N chain is almost

linear and makes a dihedral angle of 48.4 (3)° with the C(4) ethoxycarbonyl group. The molecule exhibits intramolecular hydrogen bonding between the amino group at C(2) and the carbonyl O atom of the C(3) ethoxycarbonyl group. Intermolecular N—H...O bonds link the molecules across the centre of symmetry.

**Introduction.** 4H-Chromene derivatives have been of synthetic (Clarke-Lewis, Ilseley & McGarry, 1976) and structural (Jurd & Waiss, 1968; Bouvier, Andrieux, Cunha & Molho, 1977) interest. They are