

N14	0.6258 (6)	0.3170 (5)	0.7260 (5)	0.043 (2)
N17	0.5202 (6)	0.1872 (6)	0.9257 (5)	0.044 (2)
O1	1.0030 (6)	0.8048 (6)	0.2355 (5)	0.065 (2)
O2	1.1582 (7)	0.9571 (6)	0.4269 (6)	0.073 (3)
O4	0.8089 (5)	0.5812 (5)	0.2452 (4)	0.051 (2)
C2	1.0377 (8)	0.7759 (6)	0.5856 (6)	0.039 (3)
C3	0.9835 (8)	0.7460 (7)	0.4455 (7)	0.042 (3)
C4	0.8605 (7)	0.6169 (7)	0.3722 (6)	0.040 (3)
C5	0.6600 (7)	0.4150 (6)	0.4026 (6)	0.037 (3)
C6	0.6010 (7)	0.3413 (6)	0.4883 (6)	0.037 (2)
C7	0.6777 (7)	0.3818 (6)	0.6327 (6)	0.036 (3)
C9	0.8572 (7)	0.5744 (6)	0.6016 (6)	0.035 (3)
C10	0.7935 (7)	0.5352 (6)	0.4598 (6)	0.036 (2)
C11	1.0541 (8)	0.7313 (7)	0.8130 (6)	0.047 (3)
C12	0.9700 (10)	0.8257 (8)	0.8752 (7)	0.070 (4)
C13	1.0571 (9)	0.8469 (8)	0.3716 (8)	0.052 (3)
C15	0.6902 (9)	0.3871 (8)	0.8681 (7)	0.054 (3)
C16	0.5637 (9)	0.3447 (7)	0.9383 (7)	0.052 (3)
C18	0.4538 (8)	0.1196 (7)	0.7814 (6)	0.045 (3)
C19	0.5779 (8)	0.1571 (6)	0.7116 (7)	0.046 (3)
C20	0.3996 (9)	0.1520 (9)	0.9936 (8)	0.064 (3)

Table 2. Selected geometric parameters (Å, °)

Cl—C6	1.738 (5)	C13—O1	1.341 (9)
N1—C2	1.321 (9)	C13—O2	1.203 (8)
N1—C9	1.379 (7)	N14—C15	1.446 (8)
N1—C11	1.481 (8)	N14—C19	1.486 (7)
C4—O4	1.250 (7)	C16—N17	1.464 (9)
C7—N8	1.345 (7)	N17—C18	1.460 (7)
C7—N14	1.368 (9)	N17—C20	1.466 (11)
N8—C9	1.349 (9)		
C9—N1—C11	119.7 (5)	N1—C11—C12	113.4 (6)
C2—N1—C11	120.7 (5)	C3—C13—O2	124.0 (7)
C2—N1—C9	119.6 (5)	C3—C13—O1	114.6 (7)
N1—C2—C3	124.4 (6)	O1—C13—O2	121.4 (7)
C3—C4—O4	123.5 (6)	C7—N14—C19	122.8 (5)
C10—C4—O4	122.5 (6)	C7—N14—C15	119.2 (5)
Cl—C6—C5	117.2 (5)	C15—N14—C19	111.0 (5)
Cl—C6—C7	122.1 (5)	N14—C15—C16	109.5 (6)
C6—C7—N14	124.6 (5)	C15—C16—N17	110.5 (6)
C6—C7—N8	119.6 (5)	C16—N17—C20	108.6 (6)
N8—C7—N14	115.6 (5)	C16—N17—C18	109.2 (5)
C7—N8—C9	120.3 (5)	C18—N17—C20	110.4 (6)
N1—C9—N8	117.1 (5)	N17—C18—C19	110.3 (5)
N8—C9—C10	122.7 (6)	N14—C19—C18	109.7 (5)
N1—C9—C10	120.2 (6)		
C9—N1—C11—C12	-87.0 (7)	C6—C7—N14—C19	45.7 (9)
C2—N1—C11—C12	89.2 (8)	N8—C7—N14—C15	8.7 (8)
C6—C7—N14—C15	-166.3 (6)	N8—C7—N14—C19	-139.4 (6)

Refinement was by full-matrix least squares methods. Of the 19 H atoms, 18 were calculated and not refined.

Programs used to solve structure: *MULTAN78* (Main *et al.*, 1978). Programs used to refine structure: *SHELX76* (Sheldrick, 1976). Molecular graphics: *ORTEPII* (Johnson, 1976). Software used for geometrical calculations and to prepare material for publication: *PARST* (Nardelli, 1983). All calculations were performed on a Super 32 computer (VECC, Calcutta).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: VJ1004). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Methyl (2*S*,6*S*:2*R*,6*R*)-6-(2-Cyanoethyl)-4,6-dimethyl-2-morpholineacetate

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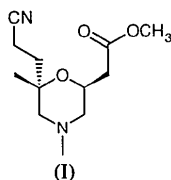
Abstract

The morpholine ring of the title compound, C₁₂H₂₀N₂O₃, adopts a chair conformation with an equatorial (methoxycarbonyl)methyl group. The cyanoethyl and (methoxycarbonyl)methyl groups are *trans* with respect to each other. The global minimum conformation, as computed by *PCMODEL* [Gajewski & Gilbert (1992). *Molecular Modeling Package*. Version 4.0], of the title compound agrees with that observed in the crystal. In the crystal, the torsion angles (N≡C)—CH₂—CH₂—C(O), (N≡C)CH₂—CH₂—C—O, O—CH—CH₂—C(OOCH₃) and (O)CH—CH₂—C(O)—O(CH₃) have values -170.0 (1), -45.9 (2), -71.6 (2) and 142.8 (1)°, respectively.

Comment

As a part of an effort to synthesize the four possible stereoisomers of our reaction-intermediate analogues for carnitine acyltransferases (Gandour, Blackwell, Colucci, Chung, Bieber, Ramsay, Brass & Fronczek, 1992), we prepared the title compound, (I). We undertook the structure determination to assign the relative stereochemistry of this racemate and, by inference, that of the diastereomer. This isomer has a

melting point of 322.0–323.0 K. The morpholine ring is in a chair conformation. The (methoxycarbonyl)methyl group and methyl group on C3 are *cis* to each other and both occupy equatorial positions, as does the *N*-methyl group.



The molecule contains two side chains which each have two freely rotatable bonds: C11—C10 and C10—C3 for the 2-cyanoethyl group and C2—C6 and C6—C7 for the (methoxycarbonyl)methyl group. 81 staggered conformations are possible for this set of torsion angles. We were interested in finding out if the conformation in the crystal was the same as the global minimum obtained from molecule-mechanics calculations.

We used *PCMODEL* (Gajewski & Gilbert, 1992) to calculate the energies of all possible staggered conformations. Each calculation began with idealized values of the torsion angles and was completely minimized. We also used *GMMX* (Serena Software, 1992), a global-minimum search routine. Both methods found the same lowest-energy conformation.

The global minimum has torsion angles C12—C11—C10—C3 179.2, C11—C10—C3—O1 -50.5, O1—C2—C6—C7 -60.0 and C2—C6—C7—O3 140.2°. In the crystal, these torsion angles are -170.0 (1), -45.9 (2), -71.6 (2) and 142.8 (1)°, respectively. We conclude that these are similar conformations. Eight bond distances in the global minimum differ by >0.02 Å from those of the crystal structure; C1—C2, C2—C6 and C3—C4 appear short in the crystal. Six angles differ by >2.0°, C7—O3—C8 being the most disparate. The *PCMODEL* results are included in Table 2.

The Cambridge Structural Database (Allen, Kennard & Taylor, 1983) contains structures for some *N*-oxide and *N,N*-dialkylmorpholinium compounds, but no structure of an *N*-methylmorpholine. All structures have chair conformations. When compared with *meso*-2,6-bis(carboxymethyl)-4,4-dimethylmorpholinium bromide (Colucci, Gandour, Fronczek, Brady & Brady, 1987) and 6-(carboxymethyl)-2-hydroxy-2,4,4-trimethylmorpholinium chloride (Gandour, Blackwell, Colucci, Chung, Bieber, Ramsay, Brass & Fronczek, 1992), both of which adopt chair conformations with equatorial carboxymethyl groups, the title compound exhibits no significant differences in either the O1—C2 and O1—C3 bond distances or the bond angles and torsion angles within the morpholine ring. The

C1—C2 (or C3—C4) and N1—C1, N1—C4 and N1—C5 bond distances in the title compound are about 0.02 and 0.08 Å shorter than those in the two morpholinium compounds, respectively. We assume that the positive charge and the steric crowding of the groups attached to the quaternary N atom increase the bond distances in the morpholinium compounds. The torsion angles O1—C2—C6—C7 [-71.6 (2)°] and C2—C6—C7—O3 [142.8 (1)°] in the title compound are almost the same as those [-68.5 (2) and 153.1 (2)°, respectively] in *meso*-2,6-bis(carboxymethyl)-4,4-dimethylmorpholinium bromide, but different from those [-168.7 (2) and -174.5 (2)°, respectively] in 6-(carboxymethyl)-2-hydroxy-2,4,4-trimethylmorpholinium chloride. Calculations and NMR studies of carnitine and acetylcarnitine (Colucci, Gandour & Mooberry, 1986) indicate only a small difference in energy between *anti* and *gauche*(-) rotamers about the (O)CH—CH₂COO⁻ bond.

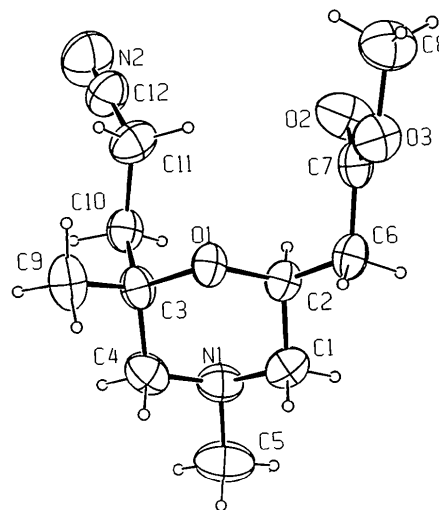


Fig. 1. View of the title compound showing the numbering scheme with displacement ellipsoids drawn at the 40% probability level. H atoms are drawn as circles of arbitrary radii.

Experimental

Crystal data

C₁₂H₂₀N₂O₃
M_r = 240.3
 Triclinic
P $\bar{1}$
a = 5.6057 (4) Å
b = 9.1737 (7) Å
c = 14.1151 (10) Å
 α = 74.430 (7)°
 β = 88.908 (6)°
 γ = 79.302 (6)°
V = 686.7 (1) Å³
Z = 2
D_x = 1.162 Mg m⁻³

Mo *K*α radiation
 λ = 0.71073 Å
 Cell parameters from 25 reflections
 θ = 9–11°
 μ = 0.08 mm⁻¹
T = 297 K
 Lath
 0.55 × 0.28 × 0.08 mm
 Colorless
 Crystal source: crystallized from hexane

Data collection

Enraf-Nonius CAD-4 diffractometer $\theta_{\max} = 25^\circ$
 $h = 0 \rightarrow 6$
 $\omega/2\theta$ scans $k = -10 \rightarrow 10$
 Absorption correction: none $l = -16 \rightarrow 16$
 2409 measured reflections 3 standard reflections
 2409 independent reflections frequency: 166.67 min
 1850 observed reflections intensity decay: 3.8%
 $[I > 2\sigma(I)]$

Refinement

Refinement on F $\Delta\rho_{\max} = 0.17 \text{ e } \text{\AA}^{-3}$
 $R = 0.040$ $\Delta\rho_{\min} = -0.08 \text{ e } \text{\AA}^{-3}$
 $wR = 0.045$ Extinction correction:
 $S = 2.075$ $(1 + gI_c)^{-1}$ applied to F_c
 1850 reflections Extinction coefficient:
 235 parameters $g = 3.6(3) \times 10^{-6}$
 All H-atom parameters re- Atomic scattering factors
 fined from Cromer (1974) and
 $w = 4F_o^2/[\sigma^2(I) + (0.02F_o^2)^2]$ Cromer & Waber (1974)
 $(\Delta/\sigma)_{\max} = 0.01$

C2—O1—C3	115.0 (1)	114.0
C7—O3—C8	116.2 (1)	122.8
C1—N1—C4	108.5 (1)	109.4
C1—N1—C5	112.1 (2)	111.5
C4—N1—C5	111.4 (1)	111.6
N1—C1—C2	109.1 (1)	110.3
O1—C2—C1	110.7 (1)	110.3
C4—C3—C9	110.7 (1)	108.3
C4—C3—C10	110.2 (1)	111.4
C9—C3—C10	111.5 (1)	109.7
N1—C4—C3	112.1 (1)	111.7
C2—C6—C7	112.1 (1)	112.2
O2—C7—O3	121.9 (2)	124.1
O2—C7—C6	125.3 (2)	125.0
O1—C2—C6	105.0 (1)	108.0
C1—C2—C6	113.8 (1)	111.2
O1—C3—C4	109.3 (1)	109.3
O1—C3—C9	104.0 (1)	106.4
O1—C3—C10	111.0 (1)	111.7
O3—C7—C6	112.8 (1)	111.0
C3—C10—C11	113.8 (1)	115.1
C10—C11—C12	111.1 (2)	112.0
N2—C12—C11	178.6 (2)	179.3
O1—C2—C6—C7	-71.6 (2)	-60.0
O1—C3—C10—C11	-45.9 (2)	-50.5
C2—C6—C7—O3	142.8 (1)	140.2
C3—C10—C11—C12	-170.0 (1)	179.2

The *MolEN* programs (Fair, 1990) were used for structure solution and refinement.

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2)

$$B_{\text{eq}} = (8\pi^2/3)\sum_i\sum_j U_{ij}a_i^*a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	B_{eq}
O1	0.1478 (2)	0.3437 (1)	0.77508 (6)	3.84 (2)
O2	0.0572 (2)	0.6770 (1)	0.5993 (1)	6.85 (4)
O3	0.4592 (2)	0.6267 (1)	0.59987 (8)	5.33 (3)
N1	-0.1319 (3)	0.1366 (1)	0.7412 (1)	5.00 (3)
N2	-0.6392 (4)	0.7041 (2)	0.8732 (1)	8.44 (5)
C1	0.0433 (3)	0.1943 (2)	0.6707 (1)	4.97 (4)
C2	0.0703 (3)	0.3509 (2)	0.6780 (1)	3.82 (3)
C3	-0.0015 (3)	0.2750 (2)	0.8525 (1)	4.04 (4)
C4	-0.0398 (3)	0.1219 (2)	0.8395 (1)	5.19 (4)
C5	-0.1843 (4)	-0.0096 (2)	0.7321 (2)	1.71 (6)
C6	0.2589 (3)	0.4188 (2)	0.6118 (1)	4.51 (4)
C7	0.2421 (3)	0.5856 (2)	0.6039 (1)	4.34 (4)
C8	0.4578 (4)	0.7879 (2)	0.5869 (2)	6.75 (5)
C9	0.1474 (4)	0.2508 (2)	0.9463 (1)	5.76 (5)
C10	-0.2458 (3)	0.3815 (2)	0.8519 (1)	4.33 (4)
C11	-0.2261 (3)	0.5475 (2)	0.8417 (1)	5.43 (4)
C12	-0.4585 (4)	0.6373 (2)	0.8589 (1)	5.78 (5)

Table 2. Comparison of geometric parameters (\AA , $^\circ$) obtained from X-ray structure analysis and PCMODEL calculations

	X-ray	PCMODEL
O1—C2	1.427 (2)	1.423
O1—C3	1.444 (2)	1.426
O2—C7	1.197 (2)	1.211
O3—C7	1.335 (2)	1.349
O3—C8	1.439 (2)	1.414
N1—C1	1.453 (2)	1.454
N1—C4	1.453 (2)	1.454
N1—C5	1.463 (3)	1.457
N2—C12	1.127 (3)	1.164
C1—C2	1.502 (2)	1.536
C2—C6	1.508 (2)	1.539
C3—C4	1.517 (3)	1.544
C3—C9	1.521 (2)	1.546
C3—C10	1.526 (2)	1.549
C6—C7	1.489 (2)	1.514
C10—C11	1.515 (2)	1.536
C11—C12	1.460 (2)	1.469

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and torsion angles have been deposited with the IUCr (Reference: CD1050). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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