Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

The diastereoisomers methyl 5-(*S*)-[2-(*R*)/(*S*)-methoxycarbonyl)-2,3,4,5-tetrahydropyrrol-1-ylcarbonyl]-1-(4-methylphenyl)-4,5-dihydropyrazole-3-carboxylate

Tullio Pilati* and Gianluigi Casalone

CNR–Centro per lo Studio delle Relazioni fra Struttura e Reattività Chimica, c/o Dipartimento di Chimica–Fisica ed Elettrochimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano, Italy
Correspondence e-mail: pila@csrsrc.mi.cnr.it

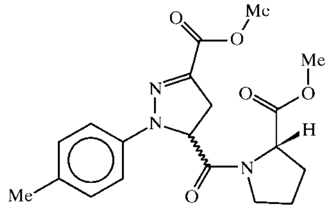
Received 9 November 2001
Accepted 17 December 2001
Online 28 February 2002

The title diastereoisomers, methyl 5-(*S*)-[2-(*S*)-methoxycarbonyl)-2,3,4,5-tetrahydropyrrol-1-ylcarbonyl]-1-(4-methylphenyl)-4,5-dihydropyrazole-3-carboxylate and methyl 5-(*S*)-[2-(*R*)-methoxycarbonyl)-2,3,4,5-tetrahydropyrrol-1-ylcarbonyl]-1-(4-methylphenyl)-4,5-dihydropyrazole-3-carboxylate, both $C_{19}H_{23}N_3O_5$, have been studied in two crystalline forms. The first form, methyl 5-(*S*)-[2-(*S*)-methoxycarbonyl)-2,3,4,5-tetrahydropyrrol-1-ylcarbonyl]-1-(4-methylphenyl)-4,5-dihydropyrazole-3-carboxylate–methyl 5-(*S*)-[2-(*R*)-methoxycarbonyl)-2,3,4,5-tetrahydropyrrol-1-ylcarbonyl]-1-(4-methylphenyl)-4,5-dihydropyrazole-3-carboxylate (1/1), 2(*S*),5(*S*)-$C_{19}H_{23}N_3O_5$·2(*R*),5(*S*)-$C_{19}H_{23}N_3O_5$, contains both *S*,*S* and *S*,*R* isomers, while the second, methyl 5-(*S*)-[2-(*S*)-methoxycarbonyl)-2,3,4,5-tetrahydropyrrol-1-ylcarbonyl]-1-(4-methylphenyl)-4,5-dihydropyrazole-3-carboxylate, 2(*S*),5(*S*)-$C_{19}H_{23}N_3O_5$, is the pure *S*,*S* isomer. The *S*,*S* isomers in the two structures show very similar geometries, the maximum difference being about 15° on one torsion angle. The differences between the *S*,*S* and *S*,*R* isomers, apart from those due to the inversion of one chiral centre, are more remarkable, and are partially due to a possible rotational disorder of the 2-(methoxycarbonyl)tetrahydropyrrole group.

Comment

The title diastereoisomers were synthesized (Garanti & Molteni, 2002) by 1,3-dipolar cycloaddition of *N*-4-methylphenyl-*C*-methoxycarbonylnitrilimine to 1-(1-oxoprop-2-enyl)-2-(*S*)-methoxycarbonyl-2,3,4,5-tetrahydropyrazole. A 67:33 ratio of the diastereoisomers was observed by NMR spectroscopy, and a crystal structure determination was suggested in order to establish the configuration of the major component.

Since separation of the isomers by standard chromatographic methods failed, an attempt was made to crystallize the mixture directly by diffusion of hexane into a CH_2Cl_2 solution at 297–298 K. Initially, small amorphous or microcrystalline spheres (about 1 mm in diameter) were obtained, while in the end, good crystals were obtained in the form of long thin blades suitable for X-ray analysis. Quite surprisingly, the structure of these blades [hereinafter (I)] shows the presence of both isomers, *i.e.* the *S*,*S* compound (molecule *A*) and the *S*,*R* compound (molecule *B*). Molecule *A* is ordered, while the 2-methoxycarbonyltetrahydropyrrole group of *B* shows quite large displacement parameters, indicating a partial rotational disorder. For this reason, we may deduce that, in solution, a pre-organized *AB* adduct exists which is more soluble than the single diastereoisomer *A*. This is quite unusual since, to our knowledge, very few cocrystallized diastereoisomers have been reported in the crystallographic literature, especially ones which are ordered and in a 1:1 ratio. Two rare examples are given by Soriano-García *et al.* (1990) and Bligh *et al.* (1993).



(I)

The microspheres obtained from the first crystallization were separated by hand from the crystals containing both diastereoisomers. The material of these microspheres was shown by NMR spectroscopy to be the pure major component of the mixture. It was recrystallized using the same solvents but at a lower temperature (292 K) in an air-conditioned

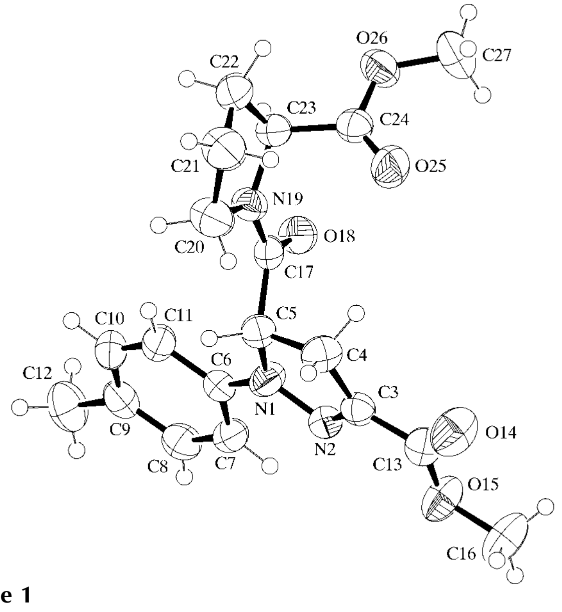


Figure 1
A view of the pure *S*,*S* isomer from (II) (molecule *C*) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

DOI: 10.1107/S0108270101021552

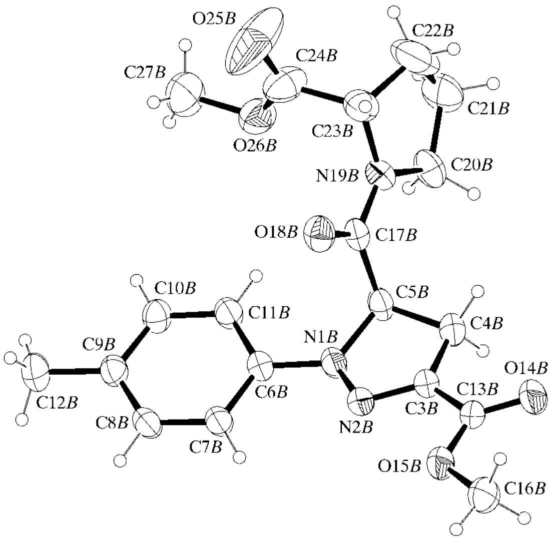


Figure 2
A view of molecule *B* (the *S*,*R* isomer) from (I) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. The large anisotropy of the ellipsoids of the methoxycarbonylpyrrole group indicates a possible rotational disorder. Atom H5*B* is wholly obscured behind C5*B*.

room. The crystals obtained were, in general, multiply twinned, but sufficiently large to allow a wedge large enough for X-ray analysis to be cut. This material, (II) (molecule *C*, Fig. 1), is the *S*,*S* molecule.

The chemically equivalent bond distances in molecules *A* and *C* do not differ by more than 3 s.u.'s from their mean values, while equivalent angles in some cases reach this limit, the largest difference occurring for N19—C23—C24 [110.5 (2) and 108.3 (3)° for molecules *C* and *A*, respectively]. The differences in the torsion angles are sometimes greater than 10°, in particular around the bonds N1—C6, N1—C5 and C23—C24, the maximum difference being for the torsion angle C5—N1—C6—C7 [168.5 (3) and −176.7 (2)° in molecules *A* and *C*, respectively]. In consequence, the conformation of the pyrazole ring is more planar in molecule *C* than in molecule *A*, with the total puckering coordinates q_2 being 0.036 (3) and 0.133 (3) Å, respectively [Cremer & Pople (1975), calculated after Nardelli (1983)].

Apart from the different configuration at C5, with obvious changes in the torsion angles around all bonds to C5, molecules *A* and *B* show greater deviations of other chemically equivalent parameters. For example, the configuration of the pyrazole ring is more deformed in *B*, with q_2 = 0.219 (7) Å, but with opposite phase [φ_2 is 136 (2) and −40 (2)° in *A* and *B*, respectively].

The possible partial disorder affecting molecule *B* is reflected not only in the large displacement parameters of the 2-methoxycarbonyltetrahydropyrrole group of molecule *B* (Fig. 2), but also in the apparent shortening of some distances, such as C20—C21 [1.458 (7) and 1.509 (6) Å in *B* and *A*, respectively], C21—C22 [1.467 (9) and 1.510 (7) Å], C22—C23 [1.488 (7) and 1.523 (5) Å], C24—O25 [1.148 (6) and 1.177 (4) Å] and in the short contact C13*B*···O25*B*($-x, y-\frac{1}{2}, -z$) [2.946 (6) Å].

The packing of (I) is characterized by the antiparallel coupling of the 1-(4-methylphenyl)dihydropyrazole moieties of molecules *A* and *B*; the angle between the lines joining N1*A* to C12*A* and N1*B* to C12*B* is 164.1 (1)°, while the angle between the mean planes through the ring atoms N1/C6–C12 in molecules *A* and *B* is 157.5 (1)°.

Three weak and approximately linear C—H···O hydrogen bonds help to stabilize the crystal of (I), together with other, less linear, hydrogen bonds. In the packing of (II), molecules are linked by a C—H···O hydrogen bond.

Experimental

The title diastereoisomers were synthesized according to the method of Garanti & Molteni (2002) by 1,3-dipolar cycloaddition of *N*-4-methylphenyl-*C*-methoxycarbonylnitrilimine to 1-(1-oxoprop-2-enyl)-2-(*S*)-methoxycarbonyl-2,3,4,5-tetrahydropyrazole. A ratio of 67:33 the diastereoisomers was observed by NMR spectroscopy. Crystals were obtained by diffusion of hexane into a CH_2Cl_2 solution at 297–298 K.

Compound (I)

Crystal data

$C_{19}H_{23}N_3O_5{\cdot}C_{19}H_{23}N_3O_5$
M_r = 746.81
Monoclinic, $P2_1$
a = 12.5056 (14) Å
b = 13.3082 (16) Å
c = 12.9491 (14) Å
β = 117.695 (2)°
V = 1908.2 (4) Å^3
Z = 2

D_x = 1.300 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4420 reflections
θ = 2.3–20.7°
μ = 0.10 mm^{-1}
T = 293 (2) K
Rhombic prism, yellow
0.42 × 0.34 × 0.12 mm

Data collection

Bruker SMART CCD area-detector diffractometer
ω and φ scans
21 406 measured reflections
3524 independent reflections
2789 reflections with $I > 2\sigma(I)$

$R_{\rm int}$ = 0.034
$\theta_{\rm max}$ = 25°
$h = -14 \rightarrow 14$
$k = -15 \rightarrow 15$
$l = -15 \rightarrow 15$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.101
S = 0.94
3524 reflections
503 parameters

H-atoms parameters constrained
$w = 1/\sigma^2(F_o^2)$
$(\Delta/\sigma)_{\rm max}$ = 0.001
$\Delta\rho_{\rm max}$ = 0.20 e Å^{-3}
$\Delta\rho_{\rm min}$ = −0.12 e Å^{-3}

Compound (II)

Crystal data

$C_{19}H_{23}N_3O_5$
M_r = 373.40
Monoclinic, $P2_1$
a = 6.9782 (9) Å
b = 17.56 (2) Å
c = 7.7576 (10) Å
β = 103.884 (5)°
V = 922.7 (11) Å^3
Z = 2

D_x = 1.344 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5921 reflections
θ = 2.3–26.5°
μ = 0.10 mm^{-1}
T = 293 (2) K
Wedge, yellow
0.40 × 0.30 × 0.22 mm

Data collection

Bruker SMART CCD area-detector diffractometer	$R_{\rm int} = 0.028$
ω and φ scans	$\theta_{\rm max} = 27.5°$
21 391 measured reflections	$h = -9 \rightarrow 9$
2188 independent reflections	$k = -22 \rightarrow 22$
1649 reflections with $I > 2\sigma(I)$	$l = -10 \rightarrow 10$

Refinement

Refinement on F^2	H-atoms parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.029$	$w = 1/[\sigma^2(F_o^2) + (0.0161P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.061$	$(\Delta/\sigma)_{\rm max} = 0.002$
$S = 0.84$	$\Delta\rho_{\rm max} = 0.12$ e Å^{-3}
2188 reflections	$\Delta\rho_{\rm min} = -0.11$ e Å^{-3}
300 parameters	

Due to the insignificant degree of anomalous scattering, Friedel pairs were merged for both structures and the handedness of the structure was assigned from the known configuration at C23. The H atoms of methyl groups attached to sp^2 and sp^3 centres were located from difference Fourier syntheses and were refined as part of a rigid rotating group, with C—H = 0.96 Å and $U_{\rm iso}$(H) = $1.5U_{\rm eq}$(C) for both structures. For (II), all other H atoms were refined isotropically. Due to the low ratio of observations to parameters for (I), all H atoms in this structure were introduced at calculated positions as riding atoms, with C—H = 0.93 (CH) or 0.97 Å (CH_2) and $U_{\rm iso}$(H) = $1.2U_{\rm eq}$(C). Because it converged to a meaningless value for both structures, no extinction parameter was refined in the final least-squares cycles.

For both compounds, data collection: *SMART* (Bruker, 1999); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1999); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXL*97.

We thank Professor L. Garanti and Dr G. Molteni for suggesting this study, and for the gift of suitable crystals.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1481). Services for accessing these data are described at the back of the journal.

References

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.

Bligh, S. W. A., Choi, N., Cummins, W. J., Evagorou, E. G., Kelly, J. D. & McPartlin, M. (1993). *J. Chem. Soc. Dalton Trans.* pp. 3829–3831.

Bruker (1999). *SMART* and *SAINT*. Bruker AXS Inc., Madison, Wisconsin, USA.

Burnett, M. N. & Johnson, C. K. (1996). *ORTEP*III. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Garanti, L. & Molteni, G. (2002). In preparation.

Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.

Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.

Soriano-García, M., Walls, F., Yuste, F., Sánchez-Obregón, R., Ortíz, B., Díaz, E., Toscano, R. A. & Barrios, H. (1990). *Acta Cryst.* C**46**, 1860–1863.