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

O1A—C15A	1.197 (4)	O1B —C15B	1.214 (4)
O2A—C16A	1.225 (5)	O2B —C16B	1.204 (5)
C4A—C5A	1.555 (4)	C4B—C5B	1.553 (4)
C5A—C10A	1.549 (4)	C5B—C10B	1.564 (4)
C8A—C9A	1.564 (4)	C8B—C9B	1.546 (4)
C8A—C14A	1.567 (4)	C8B—C14B	1.569 (4)
C9A—C10A	1.576 (4)	C9B—C10B	1.570 (4)
C11A—C12A	1.488 (5)	C11B—C12B	1.473 (5)
C12A—C13A	1.332 (5)	C12B—C13B	1.338 (5)
C13A—C14A	1.514 (4)	C13B—C14B	1.515 (5)
C13A—C16A	1.454 (5)	C13B—C16B	1.452 (5)
C14A—C15A	1.519 (4)	C14B—C15B	1.508 (5)
C5A—C4A—C18A	114.8 (2)	C5B—C4B—C18B	114.1 (2)
C4A—C5A—C10A	117.0 (2)	C4B—C5B—C10B	116.8 (2)
C6A—C7A—C8A	113.9 (2)	C6B—C7B—C8B	113.1 (2)
C9A—C8A—C20A	113.5 (2)	C9B—C8B—C20B	113.6 (2)
C8A—C9A—C10A	115.7 (2)	C8B—C9B—C10B	117.3 (2)
C5A—C10A—C19A	114.1 (2)	C5B—C10B—C19B	113.8 (2)
C11A—C12A—C13A	124.1 (3)	C11B—C12B—C13B	124.5 (3)
C12A —C13A —C14A	122.6 (3)	C12B—C13B—C14B	122.2 (3)
O1A—C15A—C14A	124.3 (3)	O1B—C15B—C14B	122.8 (3)
O2A—C16A—C13A	122.8 (3)	O2B—C16B—C13B	124.3 (3)

C6A—C5A—C10A—C1A	174.9 (2)
C7A—C8A—C9A—C11A	−179.9 (2)
C14A—C8A—C9A—C11A	−63.8 (3)
C16A—C13A—C14A—C15A	43.0 (4)
C12A—C13A—C16A—O2A	−178.1 (3)
C8A—C14A—C15A—O1A	86.2 (4)
C6B—C5B—C10B—C1B	175.3 (2)
C7B—C8B—C9B—C11B	178.8 (2)
C14B—C8B—C9B—C11B	−65.3 (3)
C16B—C13B—C14B—C15B	42.1 (4)
C12B—C13B—C16B—O2B	−177.1 (4)
C8B—C14B—C15B—O1B	94.4 (4)

The structure was solved using the *SIR*92 package (Altomare *et al.*, 1993). H atoms were placed on the basis of geometrical considerations and ΔF map suggestions for methyl groups. All H atoms were included in the final refinement as fixed atoms with B_{iso} set equal to B_{eq} of the parent atom. The anomalous dispersion terms of O and C are small and not sufficient to determine unquestionably the absolute configuration. However, the refined Rogers parameter supports the correctness of the absolute configuration chosen according to that of the scalarane skeleton (Kazlauskas *et al.*, 1980; Cimino, De Rosa *et al.*, 1987). All calculations were performed using *SDP* software (Enraf–Nonius, 1985) on a MicroVAX 3100 computer.

The *MM*2 energy minimization (Allinger, 1977) was performed on a Pentium 166 PC using the *HyperChem* 4.5 software (Hypercube, 1994). The potential-energy curve was computed by incrementing θ in the 360° space in steps of 5°. The convergence criterium was set to an r.m.s. gradient less than 0.2 kJ mol^{-1} Å^{-1}. In order to constrain the θ torsion angle, a high harmonic restoring force (4000 kJ mol^{-1} degree^{-2}) has been introduced at every step of the geometry optimization. The restoring force has been removed during the evaluation of the total energy.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: KA1332). Services for accessing these data are described at the back of the journal.

References

Allinger, N. L. (1997). *J. Am. Chem. Soc.* **99**, 8127–8134.

Altomare, A., Cascarano, G., Giacovazzo, C. & Guagliardi, A. (1993). *J. Appl. Cryst.* **26**, 343–350.

Cambie, R. C., Rickard, C. E. F., Rutledge, P. S. & Yang, X.-S. (1999). *Acta Cryst.* C**55**, 112–114.

Ciavatta, M. L., Gavagnin, M., Puliti, R., Cimino, G., Martinez, E., Ortea, J. & Mattia, C. A. (1997). *Tetrahedron*, **53**, 17343–17350.

Cimino, G., De Rosa, S., De Stefano, S., Puliti, R., Strazzullo, G., Mattia, C. A. & Mazzarella, L. (1987). *Tetrahedron*, **43**, 4777–4784.

Cimino, G., Morrone, R. & Sodano, G. (1982). *Tetrahedron Lett.* **23**, 4139–4142.

Cimino, G., Sodano, G. & Spinella, A. (1987). *Tetrahedron*, **43**, 5401–5410.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1361.

Croft, K. D., Ghisalberti, E. L., Skelton, B. W. & White, A. H. (1983). *J. Chem. Soc. Perkin Trans.* 1, pp. 155–159.

De Rosa, S., Puliti, R., Crispino, A., De Giulio, A., De Sena, C., Iodice, C. & Mattia, C. A. (1995). *Tetrahedron*, **51**, 10731–10736.

De Rosa, S., Puliti, R., Crispino, A., De Giulio, A., Mattia, C. A. & Mazzarella, L. (1994). *J. Nat. Prod.* **57**, 256–262.

Duax, W. L., Weeks, C. M. & Rohrer, D. C. (1976). *Top. Stereochem.* **9**, 271–283.

Enraf–Nonius (1985). *Structure Determination Package. SDP/PDP User's Guide*. Version 3.0. Enraf–Nonius, Delft, The Netherlands.

Faulkner, D. J. (1998). *J. Nat. Prod. Rep.* **15**, 113–158.

Hypercube (1994). *HyperChem Program*. Release 4.5 for Windows. *Molecular Visualization and Simulation*. Hypercube Inc., Ontario, Canada.

Kazlauskas, R., Murphy, P. T., Wells, R. J. & Daly, J. J. (1980). *Aust. J. Chem.* **33**, 1783–1797.

Killean, R. C. G. & Lawrence, J. L. (1969). *Acta Cryst.* B**25**, 1750–1752.

Puliti, R., Gavagnin, M., Cimino, G., Mattia, C. A. & Mazzarella, L. (1992). *Acta Cryst.* C**48**, 2145–2147.

Puliti, R. & Mattia, C. A. (1999). *J. Mol. Struct.* In the press.

Puliti, R., Mattia, C. A. & Mazzarella, L. (1995). *Acta Cryst.* C**51**, 1703–1707.

Rogers, D. (1981). *Acta Cryst.* A**37**, 734–741.

Stout, G. H. & Jensen, L. H. (1968). *X-ray Structure Determination*, pp. 409–412. New York: Macmillan.

Acta Cryst. (1999). C**55**, 2163–2167

2-(2-Fluoro-4-nitroanilinoethyl)benzaldehyde and *N*-(2-fluoro-4-nitrophenyl)-1-methoxy-1,2,3,4-tetrahydroisoquinoline

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Abstract

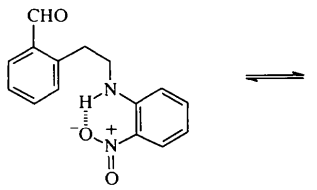
2-(2-Fluoro-4-nitroanilinoethyl)benzaldehyde, $C_{15}H_{13}FN_2O_3$, exists as the aldehyde form with essentially

† Deceased.

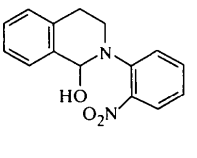
planar and parallel benzaldehyde and nitroaniline fragments, which are linked through an ethylene bridge joining the aniline N atom and an *ortho*-C atom of the benzaldehyde fragment. *N*-(2-Fluoro-4-nitrophenyl)-1-methoxy-1,2,3,4-tetrahydroisoquinoline, $C_{16}H_{15}FN_2O_3$, obtained as a methanolysis product on attempted recrystallization of 2-(2-fluoro-4-nitroanilinoethyl)benzaldehyde from methanol solution, consists of essentially planar nitrobenzene and non-planar tetrahydroquinoline fragments, which are linked directly through the *para*-C atom of the former and the endocyclic N atom of the latter.

Comment

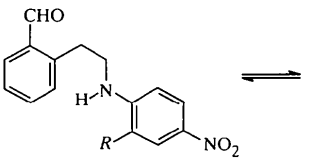
We have shown previously that in compound (1) there is intramolecular hydrogen bonding between the amine substituent and the nitro group (Clegg *et al.*, 1994). This compound can, in principle, exist as the cyclic hemi-aminal (2), but structure (1) is favoured by the hydrogen bonding. In contrast, the isomeric compound (3) can not display intramolecular hydrogen bonding and, in this case, the cyclic hemi-aminal structure (4) is preferred (Steith & Fizet, 1977). We have also prepared compound (5) and shown that this aldehyde structure is preferred over its corresponding hemi-aminal (6) (Hedley & Stanforth, 1992). This result



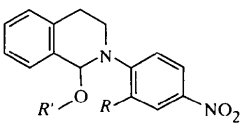
(1)



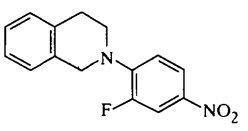
(2)



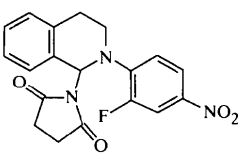
(3) R = H
(5) R = Me
(7) R = F



(4) R = H, R' = H
(6) R = Me, R' = H
(8) R = F, R' = H
(9) R = F, R' = Me



(10)



(11)

was surprising, as the inductive effect of the methyl group was expected to favour the hemi-aminal (6); the exclusive formation of the aldehyde (5) was, therefore, attributed to potentially unfavourable steric interactions between the hydroxy and methyl substituents in (6). In a continuation of our work in this area, we were interested in preparing 2-(2-fluoro-4-nitroanilinoethyl)-benzaldehyde, (7), and investigating the possibility of intramolecular hydrogen bonding between the amine and fluoro substituents. We expected that the presence of an electron-withdrawing substituent would favour aldehyde structure (7) over the hemi-aminal (8), because the electron lone pair in (7) would be less nucleophilic than in the parent derivative (3).

The aldehyde (7) was prepared from *N*-(2-fluoro-4-nitrophenyl)-1,2,3,4-tetrahydroisoquinoline, (10), following the methodology reported earlier by Hedley & Stanforth (1992) for the synthesis of related compounds. When *N*-bromosuccinimide was used to oxidize compound (10), a mixture of the aldehyde (7) and compound (11) was formed. Compound (11) is presumably formed by a reaction of the hemi-aminal tautomer (8) of aldehyde (7) with succinimide. When this mixture of aldehyde (7) and succinimide derivative (11) was treated with acid and water, hydrolysis of compound (11) occurred giving aldehyde (7). Aldehyde (7) can also be prepared by oxidation of compound (10) with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ). ^{1}H NMR spectroscopy and microanalytical data confirmed the structure of (7). When compound (7) was heated in methanol, the methoxy derivative *N*-(2-fluoro-4-nitrophenyl)-1-methoxy-1,2,3,4-tetrahydroisoquinoline, (9), was formed; this compound was formed evidently *via* the hemi-aminal (8). Microanalytical data confirmed the proposed structure (9).

The structure of compound (7) (Fig. 1) is clearly that of the aldehyde form, and consists of essentially planar and parallel benzaldehyde and nitroaniline components; the r.m.s. deviations of the atoms of the two six-membered rings are 0.003 and 0.004 Å, and the dihedral angle between these two mean planes is 11.76 (6)°. These fragments are joined together through an ethylene bridge between the aniline N atom and an *ortho*-C atom of the benzaldehyde fragment. In this respect, the structure of (7) is similar to that of (1) (Clegg *et al.*, 1994). The substituents of each ring (nitro, aldehyde and amino) are essentially coplanar with their respective rings (Table 1), so that all the atoms of the molecule, with the exception of the H atoms of the ethylene bridge, lie almost in two parallel planes. The disparate C9—N1 and C10—N1 distances (Table 1) reflect the essentially single-bond character of the former and some π-bond character in the latter (Eichorn, 1987). The N—O distances of the nitro group are equivalent, unlike those in (1), and are slightly longer than those in (9); they are characteristic of significant delocalized π-bond character. The coplanarity of the N—H bond with the fluoro-substituted ring, and the fact that the F atom lies on the same side of the C10—N1 bond as the amine H atom rather than on the opposite side, means that these H and F atoms are close together (2.315 Å). This probably represents a significant hydrogen-bonding

interaction [N···F 2.675 (4) Å and N—H···F 105°], as we hoped to see in this structure, favouring the aldehyde form (7) over the hemi-aminal (8).

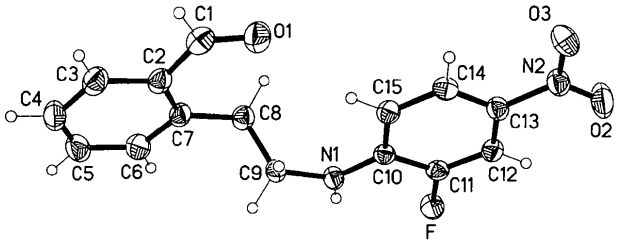


Fig. 1. The molecular structure of (7) with atom labels and 50% probability ellipsoids for non-H atoms.

The molecular structure of (9) (Fig. 2) consists of essentially planar nitrobenzene and non-planar tetrahydroquinoline components, directly linked through the *para*-C1 atom of the former and the heterocyclic N2 atom of the latter. The nitrogen-containing six-membered ring has a boat conformation. The main interest in the geometry of (9) lies with the exocyclic and endocyclic N atoms (Table 2). The N—O distances of the nitro group are equivalent, and the C4—N1 distance is that of a single bond (Eichorn, 1987). The C—N bonds within the tetrahydroquinoline fragment are also effectively single bonds, but the inter-ring C1—N2 bond length shows some π-bond character. The two main fragments of the molecule are twisted relative to each other about the C1—N2 bond (Table 1) to avoid unfavourable steric interactions between the ring substituents.

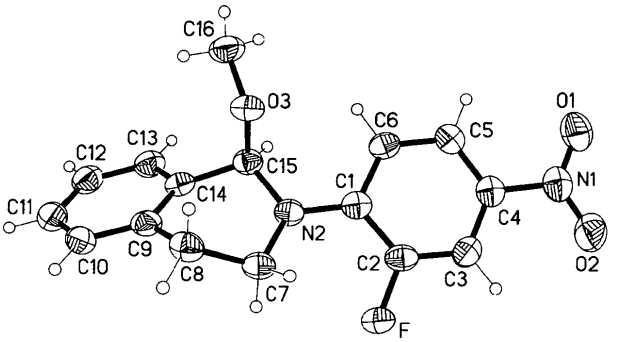


Fig. 2. The molecular structure of (9) with atom labels and 50% probability ellipsoids for non-H atoms. The minor disorder component is not shown.

Experimental

N-(2-Fluoro-4-nitrophenyl)-1,2,3,4-tetrahydroisoquinoline, (10). To a mixture of 1,2-difluoro-4-nitrobenzene (3.2 g, 20 mmol) and potassium carbonate (3.6 g, 26 mmol) in dimethyl sulfoxide (10 ml) was added 1,2,3,4-tetrahydroisoquinoline (2.8 g, 21 mmol) portionwise over a period of 5 min with stirring at room temperature. The resulting yellow mixture was then heated on a steam bath (1 h), allowed to cool to room temperature and diluted with water (100 ml). The mixture was extracted with dichloromethane (2 × 20 ml) and the combined organic extracts were washed with dilute hydrochloric acid (20 ml) and water (2 × 20 ml), and dried ($MgSO_4$) and evaporated giving *N*-(2-fluoro-4-nitrophenyl)-1,2,3,4-tetrahydroisoquinoline, (10) (5.1 g, 93%), as a pale-orange solid (m.p. 384–385 K, from ethanol). Found: C 66.4, H 4.6, N 10.5%; $C_{15}H_{13}FN_2O_2$ requires: C 66.2, H 4.8, N 10.3%; ^{1}H NMR: δ ($CDCl_3$) 7.95 (2H, *m*, ArH), 7.19 (4H, *m*, ArH), 6.96 (1H, *t*, J = 9 Hz, ArH), 4.55 (2H, *s*, CH_2), 3.70 (2H, *t*, J = 6 Hz, $-CH_2CH_2-$) and 3.02 (2H, *t*, J = 6 Hz, $-CH_2CH_2-$).

2-(2-Fluoro-4-nitroanilinoethyl)benzaldehyde, (7). Method 1: to a solution of compound (10) (1.1 g, 4.9 mmol) in dichloromethane (10 ml) at room temperature was added *N*-bromosuccinimide (1.0 g, 5.6 mmol) portionwise over a period of 5 min. The mixture was allowed to stand at room temperature (0.25 h) and was then washed sequentially with dilute sodium hydroxide solution (10 ml) and water (10 ml). The organic layer was dried ($MgSO_4$) and evaporated yielding a yellow solid (1.2 g) which was shown to be a 1:1 mixture of aldehyde (7) and succinimide derivative (11) [δ ($CDCl_3$) 6.99 (1H, *s*, CH), 2.60 (4H, *s*, $-CH_2CH_2-$)] by ^{1}H NMR spectroscopy. This mixture was dissolved in tetrahydrofuran (15 ml) and dilute hydrochloric acid (2 ml) was added. The mixture was heated at reflux (0.5 h), allowed to cool to room temperature, poured into dilute sodium hydroxide solution (50 ml) and extracted with dichloromethane (2 × 20 ml). The combined organic extracts were washed with water (20 ml), dried (K_2CO_3) and evaporated giving compound (7) (0.44 g, 37%) as a yellow solid (m.p. 418–419 K). Found: C 62.75, H 4.6, N 9.75%; $C_{15}H_{13}FN_2O_3$ requires: C 62.5, H 4.55, N 9.7%; ν_{max} (KBr): 3340 and 1695 cm^{-1}; δ ($CDCl_3$) 10.15 (1H, *s*, CHO), 7.98 (1H, *dd*, J = 9 and 1 Hz, ArH), 8.82 (2H, *m*, ArH), 7.55 (2H, *m*, ArH), 7.32 (1H, *d*, J = 7 Hz, ArH), 5.40 (1H, broad *s*, NH), 3.58 (2H, *t*, J = 6 Hz, $-CH_2CH_2-$) and 3.38 (2H, *t*, J = 6 Hz, $-CH_2CH_2-$).

2-(2-Fluoro-4-nitroanilinoethyl)benzaldehyde, (7). Method 2: to a stirred solution of compound (10) (0.22 g, 0.97 mmol) in dichloromethane (10 ml) at room temperature was added 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ; 0.28 g, 1.23 mmol) portionwise over a period of 2 min. The resulting dark mixture was stirred (0.75 h) and then a further portion of DDQ (0.08 g, 0.35 mmol) was added. After stirring (0.25 h), dichloromethane (10 ml) and dilute sodium hydroxide (10 ml) were added to the mixture. The mixture was filtered through a small pad of silica gel, and the organic layer was separated, dried (K_2CO_3) and evaporated giving compound (7) (0.11 g, 46%), identical with an authentic sample.

N-(2-Fluoro-4-nitrophenyl)-1-methoxy-1,2,3,4-tetrahydroisoquinoline, (9). When compound (7) was heated at reflux with methanol (2 h), upon cooling, compound (9) crystallized (m.p. 370–372 K). Found: C 63.65, H 4.95, N 9.2%; $C_{16}H_{15}FN_2O_3$ requires: C 63.6, H 5.0, N 9.3%. When compound (9) was dissolved in $CDCl_3$, the resulting ^{1}H NMR spectrum always showed a 1:2 mixture of aldehyde (7) and methoxy derivative (9) [δ ($CDCl_3$) 5.64 (1H, *s*, CHOMe), 3.35 (3H, *s*, OMe)], presumably due to hydrolysis of compound (9). The microanalytical and X-ray data fully support the proposed structure (9).

Compound (7)

Crystal data

$C_{15}H_{13}FN_2O_3$ — Mo $K\alpha$ radiation
M_r = 288.27 — λ = 0.71073 Å

Monoclinic
$P2_1/n$
a = 8.0570 (14) Å
b = 11.564 (2) Å
c = 14.445 (2) Å
β = 95.225 (4)°
V = 1340.3 (4) Å^3
Z = 4
D_x = 1.429 Mg m^{-3}
D_m not measured

Cell parameters from 5244 reflections
θ = 2.26–28.29°
μ = 0.110 mm^{-1}
T = 160 (2) K
Block
0.62 × 0.60 × 0.44 mm
Yellow

Data collection

Bruker AXS SMART CCD diffractometer
ω rotation with narrow frames
Absorption correction: none
7991 measured reflections
3031 independent reflections

2564 reflections with $I > 2\sigma(I)$
R_{int} = 0.026
θ_{max} = 28.32°
$h = -9 \rightarrow 10$
$k = -13 \rightarrow 15$
$l = -18 \rightarrow 18$
Intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.102
S = 1.041
3031 reflections
191 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0462P)^2 + 0.4257P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Extinction correction: *SHELXTL*
Extinction coefficient: 0.0073 (12)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °) for (7)*

C9—N1	1.4553 (15)	O2—N2	1.2372 (16)
C10—N1	1.3506 (15)	O3—N2	1.2381 (15)
C13—N2	1.4313 (15)		
C10—N1—C9	124.07 (10)	O2—N2—C13	118.92 (11)
O2—N2—O3	122.23 (11)	O3—N2—C13	118.85 (11)
O1—C1—C2—C3	173.04 (14)	C11—C10—N1—C9	172.00 (11)
O1—C1—C2—C7	−8.0 (2)	C8—C9—N1—C10	92.06 (14)
C6—C7—C8—C9	−87.72 (14)	C14—C13—N2—O2	−179.24 (12)
C2—C7—C8—C9	90.08 (14)	C12—C13—N2—O2	−1.02 (18)
C7—C8—C9—N1	176.02 (10)	C14—C13—N2—O3	0.46 (17)
C15—C10—N1—C9	−7.95 (18)	C12—C13—N2—O3	178.68 (11)

Compound (9)

Crystal data

$C_{16}H_{15}FN_2O_3$
M_r = 302.30
Orthorhombic
Pbca
a = 13.534 (3) Å
b = 7.0535 (14) Å
c = 29.526 (8) Å
V = 2818.6 (11) Å^3
Z = 8
D_x = 1.425 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 30 reflections
θ = 12.10–12.37°
μ = 0.108 mm^{-1}
T = 160 (2) K
Plate
0.34 × 0.34 × 0.14 mm
Yellow

Data collection

Stoe–Siemens diffractometer with Cryostream cooler (Cosier & Glazer, 1986)

1650 reflections with $I > 2\sigma(I)$
R_{int} = 0.032
ω/θ scans with on-line profile fitting (Clegg, 1981)
Absorption correction: none
3628 measured reflections
2485 independent reflections

θ_{max} = 25.03°
$h = -16 \rightarrow 16$
$k = -2 \rightarrow 8$
$l = -35 \rightarrow 35$
5 standard reflections
frequency: 60 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.211
S = 1.115
2485 reflections
205 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0447P)^2 + 11.3438P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max}$ = 0.004
$\Delta\rho_{max}$ = 0.40 e Å^{-3}
$\Delta\rho_{min}$ = −0.34 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 2. *Selected geometric parameters (Å, °) for (9)*

C1—N2	1.382 (6)	N1—O2	1.230 (6)
C4—N1	1.466 (6)	N2—C15	1.444 (6)
N1—O1	1.229 (6)	N2—C7	1.480 (6)
O1—N1—O2	124.1 (4)	C1—N2—C15	118.0 (4)
O1—N1—C4	118.4 (4)	C1—N2—C7	121.7 (4)
O2—N1—C4	117.5 (4)	C15—N2—C7	119.1 (4)
C5—C4—N1—O1	5.9 (7)	C2—C1—N2—C15	−161.4 (4)
C3—C4—N1—O1	−177.1 (4)	C6—C1—N2—C15	15.4 (6)
C5—C4—N1—O2	−173.9 (5)	C2—C1—N2—C7	31.1 (7)
C3—C4—N1—O2	3.0 (7)	C6—C1—N2—C7	−152.1 (4)

A minor disorder component was resolved and refined for (9), involving exchange of the F atom on C2 and the H atom on C6; the minor component had an occupancy factor of 0.060 (8), and the F atom for this was refined only isotropically.

Data collection: *SMART* (Siemens, 1995) for (7); *DIF*4 (Stoe & Cie, 1988) for (9). Cell refinement: local programs for (7); *DIF*4 for (9). Data reduction: *SAINT* (Siemens, 1995) for (7); local programs for (9). For both compounds, program(s) used to solve structures: *SHELXTL* (Sheldrick, 1994); program(s) used to refine structures: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL* and local programs.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1367). Services for accessing these data are described at the back of the journal.

References

Clegg, W. (1981). *Acta Cryst.* A**37**, 22–28.
Clegg, W., Stanforth, S. P., Hedley, K. A., Raper, E. S. & Creighton, J. R. (1994). *Acta Cryst.* C**50**, 583–585.
Cosier, J. & Glazer, A. M. (1986). *J. Appl. Cryst.* **19**, 105–107.
Eichorn, K. (1987). *Acta Cryst.* B**43**, 111–112.
Hedley, K. A. & Stanforth, S. P. (1992). *Tetrahedron*, **48**, 743–750.
Sheldrick, G. M. (1994). *SHELXTL*. Version 5. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Siemens (1995). *SMART* and *SAINT*. *Area Detector Control and Integration Software*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Steith, J. & Fizet, C. (1977). *Tetrahedron Lett.* **37**, 3297–3300.
Stoe & Cie (1988). *DIF4. Diffractometer Control Program.* Version 7.04. Stoe & Cie, Darmstadt, Germany.

Acta Cryst. (1999). C**55**, 2167–2169

C—H···π_{arene}, Csp^3—H···O=C and O—H···O intermolecular interactions in (2*R*/2*S*)-3-(3-hydroxyphenyl)-2-(1-oxo-1,3-dihydro-2*H*-isoindol-2-yl)propanoic acid: a *meta*-tyrosine derivative

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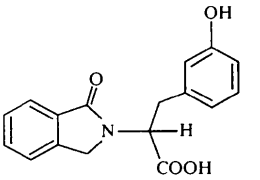
Abstract

The title compound, $C_{17}H_{15}NO_4$, a DL-*meta*-tyrosine derivative forms a hydrogen-bonded network in the solid state which consists of O_{acid}—H···O_{phenyl}—H···O=$C_{isoindole}$ chains [O···O 2.668 (2) and 2.653 (2) Å], Csp^3—H···O=C_{acid} [C···O 3.225 (3) Å] and two C—H···π_{arene} intermolecular interactions. The C_{arene}—H···π_{phenyl} interaction is short, C···*Cg* 3.542 (3) Å, where *Cg* is the phenyl ring centroid (H···*Cg* 2.64 Å and C—H···*Cg* 165°). The interplanar angle between the five- and six-membered rings of the isoindole system is 0.95 (13)° with the carbonyl-O atom 0.096 (3) Å from the C_4N ring plane. π–π stacking involving inversion symmetry-related isoindole groups occurs with *RS* pairs (interplanar distance of 3.43 Å).

Comment

Amino acid derivatives are a major class of chiral compounds with diverse applications in asymmetric synthesis and medicinal chemistry. DL-*meta*-Tyrosine (Byrkjedal *et al.*, 1974) and related compounds have attracted much interest, *e.g.* in biological studies (Kawai *et al.*, 1999), not least due to the close structural relationship with L-dopa (Howard *et al.*, 1995). The title compound, (I), a phthalimidine (isoindolin-1-one) derivative (Allin *et al.*, 1996; McNab *et al.*, 1997) is synthesized as a racemic mixture from DL-*meta*-tyrosine and forms part of a study of the hydrogen-bonding interactions and anion-recognition properties of a series of unnatural amino acid compounds (Dalton *et al.*, 1999; Gallagher *et al.*, 1999*a*,*b*).



(I)

A view of molecule (I) (*S* configuration) with our numbering scheme is given in Fig. 1 and selected dimensions are in Table 1. The bond lengths and angles in the heterocyclic ring are similar to those reported previously (Brady *et al.*, 1998) and in agreement with expected values (Orpen *et al.*, 1994). The angle between the five- and six-membered rings of the isoindole system is 0.95 (13)° and the maximum deviation from planarity for an atom in either ring plane is 0.0179 (12) Å for C3, with the carbonyl O3 atom 0.096 (3) Å from the C_4N ring plane. This ring is almost perpendicular to both the carboxylic acid CCO_2 plane, 83.12 (8)° and the 3-phenyl ring plane, 87.15 (7)°. Stacking arises involving the π–π systems of inversion symmetry-related isoindole groups (*RS* pairs), with an interplanar distance of 3.43 Å [3.35 Å in the DL-phenylalanine derivative (2*R*/2*S*)-2-(1-oxo-1,3-dihydro-2*H*-isoindol-2-yl)-3-phenylpropanoic acid, (II), which has a similar molecular geometry (Brady *et al.*, 1998)]. Examination of (I) with *PLATON* (Spek, 1998) revealed voids in the crystal lattice of volume 7 Å^3 (×4) which are too small to accommodate a solvent molecule.

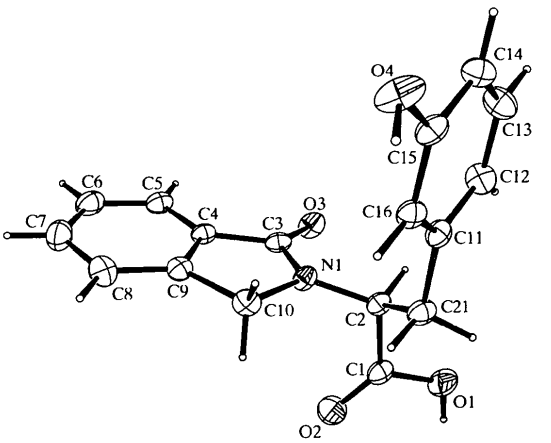


Fig. 1. A view of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

The hydrogen bonding in (I) is dominated by O—H···O, C—H···O and C—H···π_{phenyl} interactions, detailed in Table 2 and depicted in Fig. 2. Conventional carboxylic acid O—H···O hydrogen bonding between pairs of carboxylic acid groups with graph set $R_2^2(8)$ is not observed (Ferguson *et al.*, 1995). Hydrogen bonding arises involving (i) the carboxylic acid O—H, phenolic O—H and phthalimidine carbonyl acceptor as O_{acid}—H···O_{phenyl}—H···O=$C_{isoindole}$ systems with (ii)