References

Allen, F. H., Bellard, S., Brice, M. D., Cartwright, B. A., Doubleday, A., Higgs, H., Hummelink, T., Hummelink-Peters, B. G., Kennard, O., Motherwell, W. D. S., Rodgers, J. R. & Watson, D. G. (1979). *Acta Cryst.* B**35**, 2331–2339.

Allen, F. H., Davies, J. E., Galloy, J. J., Johnson, O., Kennard, O., Macrae, C. F., Mitchell, E. M., Mitchell, G. F., Smith, J. M. & Watson, D. G. (1991). *J. Chem. Inf. Comput. Sci.* **31**, 187–204.

Cyrański, M. & Krygowski, T. M. (1996). *J. Chem. Inf. Comput. Sci.* **36**, 1142–1145.

Guttsait, A. V., Belyakov, S. V., Mishnev, A. F., Bleidelis, Ya. Ya. & Gudrinietse, E. Yu. (1987). *Khim. Geterotsikl. Soedin.* pp. 1233–1237.

Kruszewski, J. & Krygowski, T. M. (1972). *Tetrahedron Lett.* pp. 3839–3942.

Krygowski, T. M. & Cyrański, M. (1996*a*). *Tetrahedron*, **52**, 1713–1722.

Krygowski, T. M. & Cyrański, M. (1996*b*). *Tetrahedron*, **52**, 10255–10264.

Kuma Diffraction (1991). *KM-4 Software*. Version 5.0. Kuma Diffraction, Wrocław, Poland.

Lesher, Y. & Grvet, D. M. (1973). *Fr. Demande*, **138**, 216.

Perez-Medina, L. A., Meriella, R. P. & McElvain, S. M. (1947). *J. Am. Chem. Soc.* **69**, 2574–2579.

Sheldrick, G. M. (1990*a*). *Acta Cryst.* A**46**, 467–473.

Sheldrick, G. M. (1990*b*). *SHELXTL/PC User's Manual*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

Acta Cryst. (1998). C**54**, 1523–1525

O—H···O, C—H···O and C—H···π_{arene} Intermolecular Interactions in (2*R*/2*S*)-2-(1-Oxo-1,3-dihydroisoindol-2-yl)-3-phenylpropanoic Acid

FIONA BRADY, JOHN F. GALLAGHER AND PETER T. M. KENNY

School of Chemical Sciences, Dublin City University, Dublin 9, Ireland. E-mail: gallagherjfg@dcu.ie

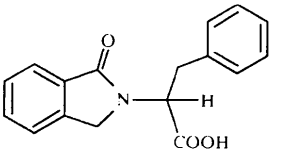
(*Received 30 January 1998; accepted 20 April 1998*)

Abstract

The title compound, $C_{17}H_{15}NO_3$, forms a hydrogen-bonded network in the solid state consisting of O—H···O=C, C_{arene}—H···O=C and C_{arene}—H···π_{arene} intermolecular interactions, with shortest O···O, C···O and C···C distances of 2.625 (2), 3.281 (3) and 3.652 (3) Å, respectively. The interplanar angle between the five- and six-membered rings of the isoindole system is 1.07 (14)°, with the carbonyl O atom 0.110 (3) Å from the C_4N ring plane.

Comment

The study of biologically active molecules is of primary importance in medicinal chemistry. Processes such as hormone processing, viral replication and cancer cell invasion are critically dependent on protease enzymes which have recently become attractive target molecules in drug design (Testa *et al.*, 1993). Many inhibitors are based on modified amino acids which incorporate the basic structural features determining normal enzyme–substrate interactions. Phthalimidine (isoindolin-1-one) derivatives often display biological activity as potential anti-inflammatory agents and antipsychotics. The majority of structurally determined phthalimidine systems are either *N*-substituted or have a hydroxy substituent at the 3-position (McNab *et al.*, 1997). The title compound, (I), synthesized as a racemic mixture from DL-phenylalanine, is part of an ongoing study of hydrogen-bonding interactions in amino acid derivatives.



(I)

A view of molecule (I) (*S* configuration) with the atomic numbering scheme is given in Fig. 1 and selected dimensions are given in Table 1. The bond lengths and angles in the heterocyclic ring are similar to those reported previously (McNab *et al.*, 1997) and in agreement with expected values (Orpen *et al.*, 1994). The angle between the five- and six-membered rings of the isoindole system is 1.07 (14)° and the maximum deviation from planarity for an atom in either ring plane is 0.021 (1) Å for C3, with the carbonyl O3 atom 0.110 (3) Å from the C_4N ring plane. This ring is almost perpendicular to both the carboxylic acid CO_2 plane [84.74 (15)°] and the 3-phenyl ring plane

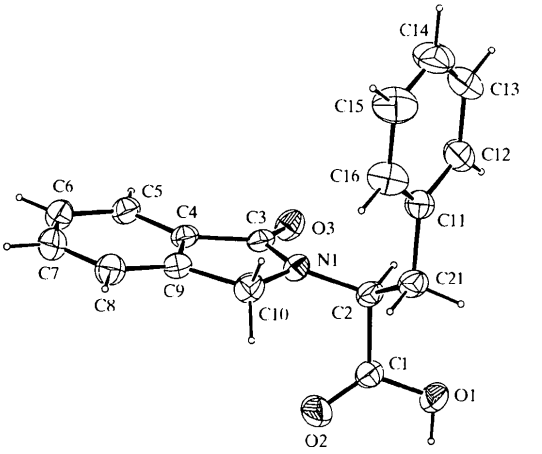


Fig. 1. A view of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

[84.78 (6)°]. Examination of (I) with *PLATON* (Spek, 1997*a*) revealed voids in the crystal lattice of volume 16 Å^3, which is too small a volume for a solvent molecule to occupy.

The hydrogen bonding in (I) is dominated by O—H···O=C, C_{arene}—H···O=C and C_{arene}—H···π_{arene} intermolecular interactions (Table 2 and Fig. 2). Conventional carboxylic acid O—H···O hydrogen bonding between pairs of carboxylic acid groups with graph set $R_2^2(8)$ (Ferguson *et al.*, 1995) is not observed. Hydrogen-bonded rings with graph set $R_2^2(9)$ are formed from the combination of (i) carboxylic acid O1—H1···O3^i interactions with the heterocyclic ring C=O group [O1···O3^i 2.625 (2) Å; symmetry code: (i) $\frac{1}{2}-x$, $\frac{1}{2}+y$, z] and (ii) phenyl ring C5—H5···O2^{ii} contacts with the carboxylic acid C=O moiety [O2···C5^{ii} 3.281 (3) Å; symmetry code: (ii) $\frac{1}{2}-x$, $y-\frac{1}{2}$, z]. Association of (I) about inversion centres as *R*/*S* hydrogen-bonded pairs arises through C—H···π_{arene} interactions [C6···*Cg*2^{iii} 3.623 (2) Å, with a corresponding shortest C···C distance of 3.652 (3) Å; *Cg*2 is the ring centroid of the 3-phenyl ring; symmetry code: (iii) $-x$, $-1-y$, $1-z$]. The dimers are linked by C—H···π_{arene} interactions [C16···*Cg*1^{iv} 3.739 (2) Å; *Cg*1 is the ring centroid of the isoindolinone phenyl ring; symmetry code: (iv) $x-\frac{1}{2}$, $-\frac{1}{2}-y$, $1-z$].

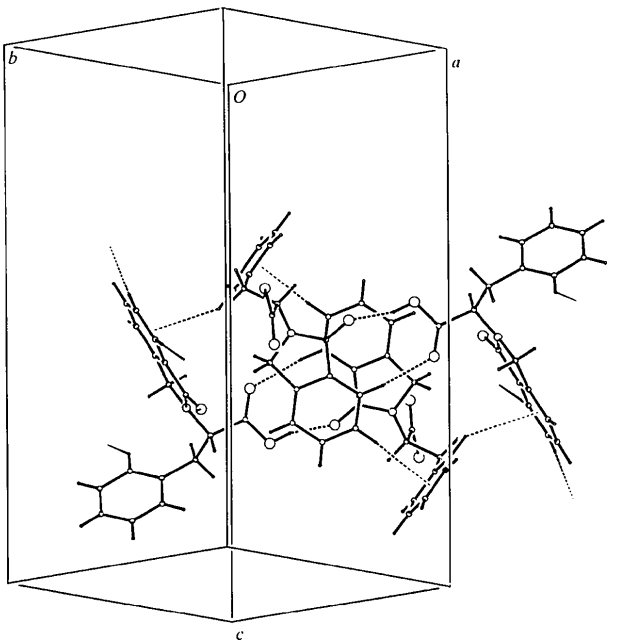


Fig. 2. A view of the hydrogen-bonding interactions in the crystal structure of (I).

The presence of C—H···O and C—H···π_{arene} interactions with stronger hydrogen bonds, *e.g.* O—H···O, has been commented on previously (Steiner, 1997). The formation of one-dimensional molecular zippers in calixarenes has been attributed to result from the intramolecular O—H···O hydrogen bonds pairing off to define the calixarene molecular cavity with cooperative intermolecular C—H···π_{arene} interactions determining the polymeric self-inclusion process (Böhmer *et al.*, 1994; Gallagher *et al.*, 1994). Further studies are in progress on interactions in related amino acid derivatives.

Experimental

The title compound was prepared by the overnight reaction of DL-phenylalanine and *o*-phthalaldehyde in refluxing CH_3CN under N_2 (Allin *et al.*, 1996). Filtration of the hot solution and subsequent slow cooling of the filtrate allowed the isolation of large colourless crystals [m.p. 469–470 K (uncorrected)].

Crystal data

$C_{17}H_{15}NO_3$
M_r = 281.30
Orthorhombic
Pbca
a = 11.4712 (8) Å
b = 12.3457 (8) Å
c = 20.582 (2) Å
V = 2914.9 (4) Å^3
Z = 8
D_x = 1.282 Mg m^{-3}
D_m not measured
Mo $K\alpha$ radiation
λ = 0.7107 Å
Cell parameters from 25 reflections
θ = 9.55–19.33°
μ = 0.088 mm^{-1}
T = 294 (1) K
Block
0.43 × 0.38 × 0.15 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: none
5641 measured reflections
2558 independent reflections
1620 reflections with $I > 2\sigma(I)$
R_{int} = 0.013
θ_{max} = 25°
h = 0 → 13
k = 0 → 14
l = −24 → 24
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.098
S = 1.013
2558 reflections
191 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.0436P)^2 + 0.3708P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.138 e Å^{-3}
$\Delta\rho_{min}$ = −0.128 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0040 (6)
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

O1—C1	1.314 (2)	C1—C2	1.519 (2)
O2—C1	1.194 (2)	C2—C21	1.531 (3)
O3—C3	1.239 (2)	C3—C4	1.469 (2)
N1—C2	1.452 (2)	C9—C10	1.491 (3)
N1—C3	1.354 (2)	C11—C21	1.511 (3)
N1—C10	1.458 (2)		
C2—N1—C3	121.55 (14)	C1—C2—C21	112.07 (14)
C2—N1—C10	123.06 (14)	O3—C3—N1	123.78 (16)
C3—N1—C10	112.94 (14)	O3—C3—C4	129.44 (16)

O1—C1—O2	124.00 (18)	N1—C3—C4	106.75 (16)
O1—C1—C2	112.05 (16)	C3—C4—C5	129.84 (18)
O2—C1—C2	123.95 (18)	C8—C9—C10	129.88 (18)
N1—C2—C1	109.24 (15)	N1—C10—C9	102.20 (14)
N1—C2—C21	112.79 (15)		

Table 2. *Hydrogen-bonding geometry (Å, °)*

*Cg*1 is the ring centroid of the isoindolinone phenyl ring and *Cg*2 is the ring centroid of the 3-phenyl ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O3^{i}	0.87	1.78	2.625 (2)	163
C5—H5···O2^{ii}	0.93	2.36	3.281 (3)	171
C6—H6···*Cg*2^{iii}	0.93	2.69	3.623 (2)	176
C16—H16···*Cg*1^{iv}	0.93	2.97	3.739 (2)	141

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

H atoms were allowed for as riding atoms with C—H distances in the range 0.93–0.98 Å; the coordinates of the carboxylic acid H atom were located in a difference Fourier map in the latter stages of refinement and included in the structure-factor calculations with O—H 0.87 Å and C—O—H 110°.

Data collection: *CAD-4-PC Software* (Enraf–Nonius, 1992). Cell refinement: *SET*4 and *CELDIM* in *CAD-4-PC Software*. Data reduction: *DATRD*2 in *NRCVAX*96 (Gabe *et al.*, 1989). Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*a*). Program(s) used to refine structure: *NRCVAX*96 and *SHELXL*97 (Sheldrick, 1997*b*). Molecular graphics: *NRCVAX*96, *ORTEP*II (Johnson, 1976) and *PLUTON* (Spek, 1997*b*). Software used to prepare material for publication: *NRCVAX*96, *SHELXL*97 and *WordPerfect* macro *PRPCIF*97 (Ferguson, 1997).

JFG thanks the Research and Postgraduate Committee of Dublin City University, the Royal Irish Academy and Forbairt for the generous funding of a research visit to the University of Guelph (June–August, 1997), and especially Professor George Ferguson for use of his diffractometer and computer system.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: CF1250). Services for accessing these data are described at the back of the journal.

References

Allin, S. M., Hodkinson, C. C. & Taj, N. (1996). *Synlett*, pp. 781–782.
Böhmer, V., Kraft, D., Vogt, W., Ferguson, G. & Gallagher, J. F. (1994). *J. Chem. Soc. Perkin Trans.* 1, pp. 1221–1230.
Enraf–Nonius (1992). *CAD-4-PC Software*. Version 1.1. Enraf–Nonius, Delft, The Netherlands.
Ferguson, G. (1997). *PRPCIF*97. *A WordPerfect*-5.1 *Macro to Merge and Polish CIF Format Files from NRCVAX and SHELXL*97 *Programs*. University of Guelph, Canada.
Ferguson, G., Gallagher, J. F. & McAlees, A. J. (1995). *Acta Cryst.* C**51**, 454–458.
Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384–387.
Gallagher, J. F., Ferguson, G., Böhmer, V. & Kraft, D. (1994). *Acta Cryst.* C**50**, 73–77.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
McNab, H., Parsons, S. & Shannon, D. A. (1997). *Acta Cryst.* C**53**, 1098–1099.
Orpen, A. G., Brammer, L., Allen, F. H., Kennard, O., Watson, D. G. & Taylor, R. (1994). *Structure Correlation*, Vol. 2. edited by H.-B. Bürgi & J. D. Dunitz, Appendix A. Weinheim: VCH Publishers.
Sheldrick, G. M. (1997*a*). *SHELXS*97. *Program for the Solution of Crystal Structures*. University of Göttingen, Germany.
Sheldrick, G. M. (1997*b*). *SHELXL*97. *Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
Spek, A. L. (1997*a*). *PLATON. Molecular Geometry Program*. Version of May 1997. University of Utrecht, The Netherlands.
Spek, A. L. (1997*b*). *PLUTON. Molecular Graphics Program*. Version of May 1997. University of Utrecht, The Netherlands.
Steiner, T. (1997). *J. Chem. Soc. Chem. Commun.* pp. 727–734.
Testa, B., Kyburz, E., Fuhrer, W. & Giger, R. (1993). Editors. *Perspectives in Medicinal Chemistry*. Basel: Verlag Helvetica Chimica Acta.

Acta Cryst. (1998). C**54**, 1525–1527

6-(4-Chlorophenyl)-3-methyl-2,4a-diphenyl-5,6-dihydro-1*H*,4a*H*-1,3-oxazino[2,3-*d*][1,5]-benzothiazepin-1-one

JIAXI XU,[a] SHENG JIN,[a] ZEYING ZHANG[b] AND THOMAS C. W. MAK[b]

[a]*College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, People's Republic of China, and* [b]*Department of Chemistry, The Chinese University of Hong Kong, Shatin, NT, Hong Kong. E-mail: jxxu@chemms.chem.pku.edu.cn*

(Received 5 January 1998; accepted 16 April 1998)

Abstract

The title compound, $C_{31}H_{24}ClNO_2S$, has a *cis*-ring-fusion tricyclic structure, which is formed from a benzene ring, a seven-membered heterocyclic thiazepine ring and a 1,3-oxazinone ring. The 1,5-thiazepine ring has a slightly distorted boat-like conformation, whereas the 1,3-oxazinone ring adopts a half-chair conformation.

Comment

Benzothiazepines, especially those with a fused heterocyclic ring, are potential pharmaceutical agents (Corral *et al.*, 1985; Bock *et al.*, 1989; Xu & Jin, 1994). 5,6-Dihydro-1*H*,4a*H*-1,3-oxazino[2,3-*d*][1,5]benzothiazepin-1-one derivatives with potential anxiolytic and hypnotic activities (Sternbach, 1979; Xu & Jin, 1992) were synthesized by the Diels–Alder reaction of 2,4-diaryl-2,3-dihydro-1,5-benzothiazepine derivatives and α-diazo-β-diketone (Capuano & Gartner, 1981; Capuano & Wamprecht, 1986). When an asymmetric α-diazo-β-diketone, such as 2-diazo-1-phenyl-1,3-butanedione, is