Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

A π-stacked chain of hydrogen-bonded dimers in 3-*tert*-butyl-1-(4-chlorophenyl)-4-phenylindeno[1,2-*b*]pyrazolo[4,3-e]pyridin-5(1*H*)-one and a π-stacked sheet of hydrogen-bonded chains in 3-*tert*-butyl-1-(4-chlorophenyl)-4-(4-methoxyphenyl)indeno[1,2-*b*]pyrazolo[4,3-e]pyridin-5(1*H*)-one

Jaime Portilla,[a] Carolina Lizarazo,[a] Justo Cobo[b] and Christopher Glidewell[c]*

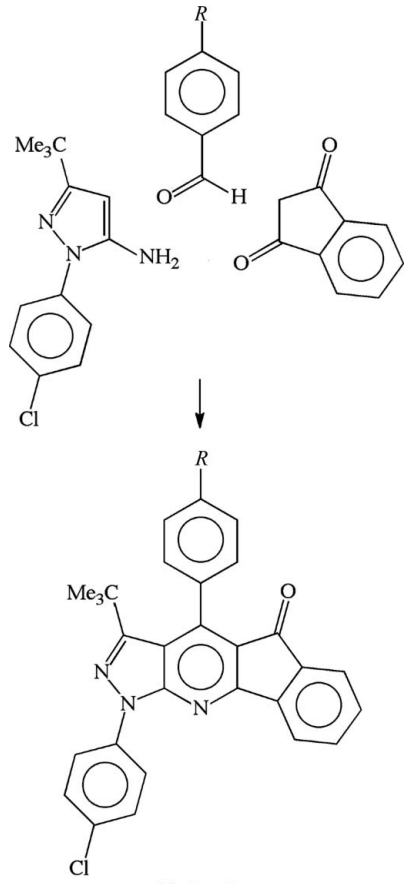
[a]Grupo de Investigación en Compuestos Bio-orgánicos, Departamento de Química, Universidad de los Andes, Cra. 1E No. 18A-10, Edificio H, A.A. 4976, Bogotá D.C., Colombia, [b]Departamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071 Jaén, Spain, and [c]School of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland
Correspondence e-mail: cg@st-andrews.ac.uk

Received 24 October 2011
Accepted 27 October 2011
Online 5 November 2011

In 3-*tert*-butyl-1-(4-chlorophenyl)-4-phenylindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(1*H*)-one, $C_{29}H_{22}ClN_3O$, (I), inversion-related pairs of molecules are linked by C—H···O hydrogen bonds to form $R_2^2(18)$ dimers, which are themselves linked into a chain by a π–π stacking interaction between inversion-related pairs of molecules. In 3-*tert*-butyl-1-(4-chlorophenyl)-4-(4-methoxyphenyl)indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(1*H*)-one, $C_{30}H_{24}ClN_3O_2$, (II), which crystallizes in the space group $P\overline{1}$, with $Z' = 2$ and with different orientations for the methoxy groups in the two independent molecules, a combination of C—H···O and C—H···π(arene) hydrogen bonds links the molecules into chains of rings, which are further linked into sheets by a π–π stacking interaction.

Comment

Pyrazolo[3,4-*b*]pyridines are fused heterocyclic compounds of considerable interest for drug development because of the wide range of biological activities that they exhibit (Quiroga *et al.*, 2005, 2007). Independently, indenopyridine compounds have shown potential activity as antioxidant, antihistamine and antidepressant agents (de Almeida *et al.*, 1976; Strunz & Findlay, 1985; Earl *et al.*, 1998; Padwa *et al.*, 2000; Peters *et al.*, 2004; Evdokimov *et al.*, 2011). As part of a programme to prepare new heterocyclic derivatives combining both these fused ring systems, we report here the structure of 3-*tert*-butyl-1-(4-chlorophenyl)-4-phenylindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(1*H*)-one, (I), and the 4-(4-methoxyphenyl) derivative, (II) (Figs. 1 and 2), which were prepared in good yield by means of a tricomponent reaction between indan-1,3-dione, the corresponding substituted benzaldehyde and 5-amino-3-*tert*-butyl-1-(4-chlorophenyl)-1*H*-pyrazole (see Scheme), which was induced by smooth microwave irradiation using water as solvent and triethylamine as catalyst.



(I) R = H
(II) R = OMe

Compounds (I) and (II) both crystallize in the space group $P\overline{1}$, but with Z' values of 1 and 2, respectively (Figs. 1 and 2); in (II) it will be convenient to refer to the molecules having $x = 1$ and 2 as type 1 and type 2 molecules, respectively. For each of the independent molecules, the conformations can be defined in terms of the orientations of the *tert*-butyl group and of the two pendent aryl substituents relative to the fused ring system, along with the orientation of the methoxy groups in (II).

None of the molecules exhibits any internal symmetry and hence they are all conformationally chiral; however, in each compound the centrosymmetric space group accommodates equal numbers of both conformational enantiomers. In each of the independent molecules, the fused ring system is essentially planar. In compound (I), the maximum deviations from the mean plane through the fused ring system are 0.060 (2) Å for atom C3 and 0.045 (2) Å for atom C5*A*, displaced to opposite sides of the plane; for the type 1 molecule in compound (II),

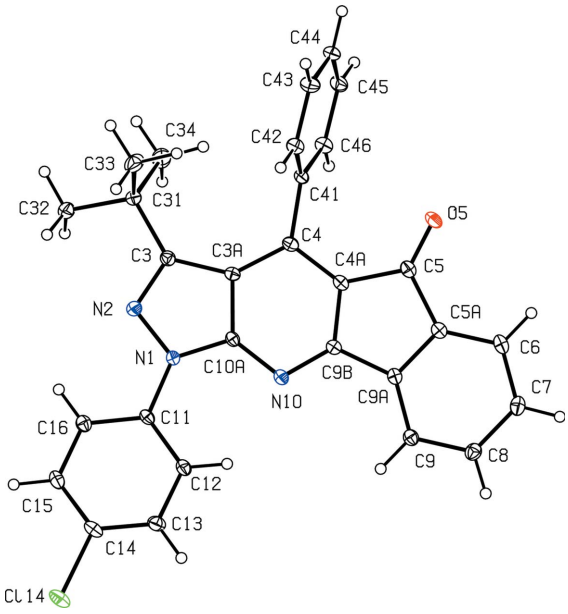


Figure 1
The molecular structure of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

the maximum deviations are 0.118 (2) Å for atom C17 and 0.086 (2) Å for atom C19*B*, again displaced to opposite sides of the plane; and in the type 2 molecule of compound (II), the maximum deviations are 0.086 (2) Å for atom C23 and 0.057 (2) Å for atom C28, this time with both displaced to the same side of the mean plane. Amongst the three independent molecules, no obvious pattern for these displacements can be recognized, so that the displacements are not regarded as chemically or structurally significant.

The corresponding bond distances within the fused ring systems are very similar, and they are consistent with aromatic delocalization in the fused aryl ring, and with delocalization in the pyridine ring accompanied by strong bond fixation in the pyrazole ring, as typically observed in pyrazolopyridine derivatives (Low *et al.*, 2007; Quiroga *et al.*, 2009, 2010; Insuasty *et al.*, 2010).

The key torsion angles (Table 1) confirm that the two independent molecules within the selected asymmetric unit of compound (II) have the same conformation, which is the same as that for the selected asymmetric unit in compound (I). The corresponding values for each of the torsion angles amongst the three independent molecular species are remarkably similar. In each case, one of the methyl C atoms of the *tert*-butyl group, designated C32 in compound (I) and C132 and C232 in the two independent molecules of compound (II) (Figs. 1 and 2), lies close to, but not exactly in, the plane of the adjacent pyrazole ring. The deviations of this atom from the pyrazole plane are 0.388 (2) Å for atom C32 in compound (I), and 0.210 (2) and 0.386 (2) Å for atoms C132 and C232, respectively, in compound (II). Curiously, however, the two independent molecules in compound (II) exhibit different orientations for their methoxy groups (Table 1 and Fig. 2), and this alone suffices to preclude the possibility of any additional crystallographic symmetry.

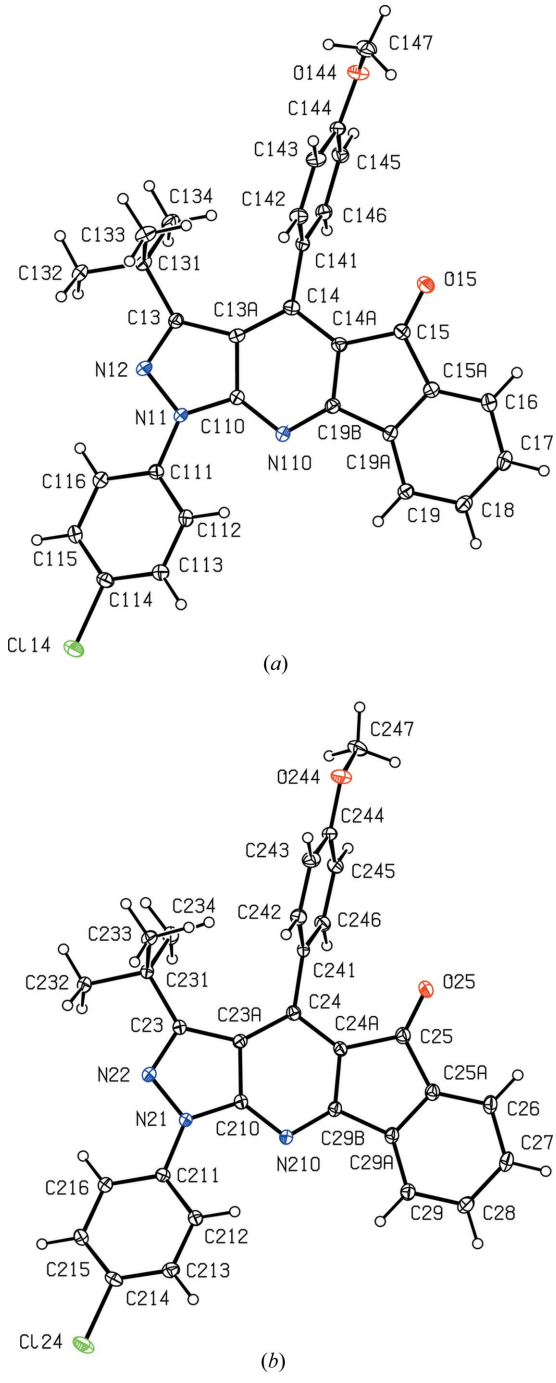


Figure 2
The structures of the two independent molecules of compound (II), showing the atom-labelling scheme for (*a*) a type 1 molecule and (*b*) a type 2 molecule. Displacement ellipsoids are drawn at the 30% probability level.

Despite their close similarity in both constitution and conformation, the molecules of compounds (I) and (II) show different patterns of supramolecular aggregation, leading to arrays which are one- and two-dimensional, respectively.

In the crystal structure of (I), inversion-related pairs of molecules are linked by rather long and weak C—H···O hydrogen bonds (Table 2) into centrosymmetric $R_2^2(18)$ (Bernstein *et al.*, 1995) dimers, and these hydrogen-bonded

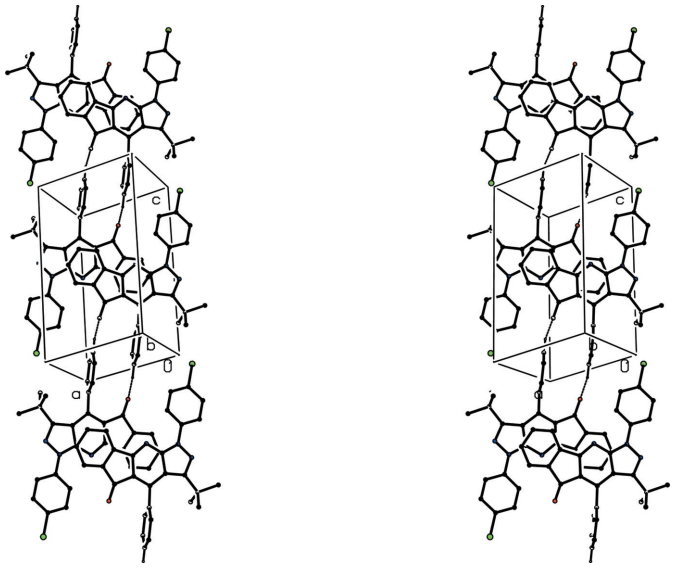


Figure 3
A stereoview of part of the crystal structure of compound (I), showing the formation of a π-stacked chain of hydrogen-bonded dimers along [001]. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

dimers are linked into chains by a single π–π stacking interaction. The planes of the pyridine ring in the molecule at (x, y, z) and the fused aryl ring in the molecule at ($-x+1$, $-y+1$, $-z+1$) make a dihedral angle of only 1.2 (2)°; the corresponding ring-centroid separation is 3.573 (2) Å and the interplanar spacing is *ca* 3.36 Å, giving a ring-centroid offset of *ca* 1.22 Å. The effect of this π-stacking interaction is to link the hydrogen-bonded dimers into a chain running parallel to the [001] direction, with the hydrogen-bonded rings centred at ($\frac{1}{2}$, $\frac{1}{2}$, n), where n represents an integer, alternating with the π-stacking interactions across ($\frac{1}{2}$, $\frac{1}{2}$, $n+\frac{1}{2}$), where n again represents an integer (Fig. 3). It is notable that neither of the pendent aryl rings, *viz.* C11–C16 and C41–C46, participates in any π–π stacking interactions and that, despite the number of aromatic rings present, there are no C—H$\cdots\pi$ hydrogen bonds in the structure of (I).

The direction-specific intermolecular interactions in the crystal structure of compound (II) differ from those in the structure of compound (I) in several respects: firstly, $Z'=2$ in compound (II); secondly, there is a C—H$\cdots\pi$(arene) hydrogen bond present; and thirdly, this hydrogen bond involves both types of pendent aryl ring, with the 4-methoxyphenyl ring in the type 1 molecule providing the donor and the 4-chlorophenyl ring in the type 2 molecule acting as the acceptor.

The single, fairly short, C—H$\cdots\pi$(arene) hydrogen bond (Table 2) links the two independent molecules in the selected asymmetric unit. Two independent C—H$\cdots$O hydrogen bonds, each linking inversion-related pairs of molecules into $R_2^2(14)$ rings, thus generate, in combination with the C—H$\cdots\pi$(arene) hydrogen bond, a chain of rings running parallel to the [110] direction (Fig. 4). There are two independent π–π stacking interactions present in the structure of compound (II). The first of these occurs within the selected asymmetric

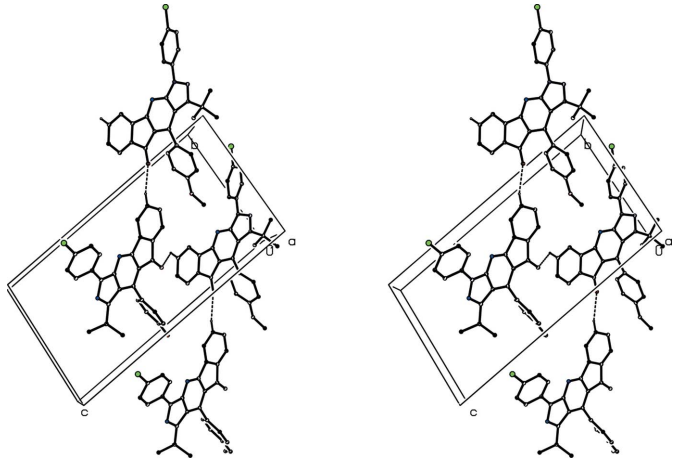


Figure 4
A stereoview of part of the crystal structure of compound (II), showing the formation of one of the hydrogen-bonded $C_2^2(14)$ chains along [110]. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

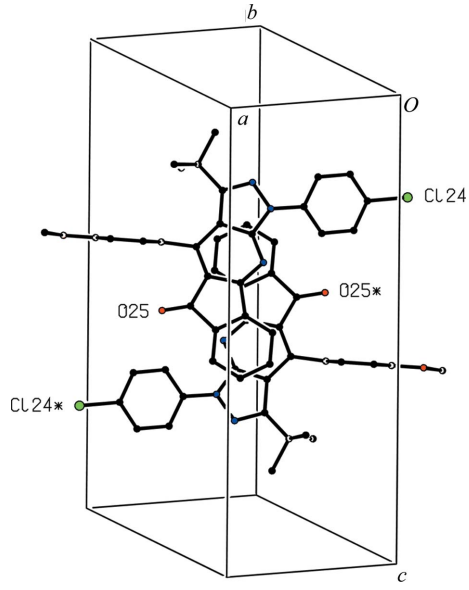


Figure 5
Part of the crystal structure of compound (II), showing the π–π stacking interaction between pairs of type 2 molecules. For the sake of clarity, all H atoms have been omitted. Atoms marked with an asterisk (*) are at the symmetry position ($-x+1$, $-y+1$, $-z+1$).

unit, where the fused aryl ring of the type 1 molecule and the pyridine ring of the type 2 molecule make a dihedral angle of 2.5 (2)°; the ring-centroid separation is 3.701 (2) Å and the interplanar separation is *ca* 3.53 Å, corresponding to a ring-centroid offset of *ca* 1.11 Å. Hence this interaction provides some modest reinforcement to the action of the C—H$\cdots\pi$(arene) hydrogen bond.

Only type 2 molecules of compound (II) are involved in the second type of stacking interaction. The pyridine ring of the type 2 molecule at (x, y, z) and the fused aryl ring of the type 2 molecule at ($-x+1$, $-y+1$, $-z+1$) make a dihedral angle of 2.2 (2)°, with a ring-centroid separation of 3.743 (2) Å, an

interplanar spacing of *ca* 3.56 Å, and a ring-centroid offset of *ca* 1.16 Å (Fig. 5). The effect of this interaction is to link the hydrogen-bonded chains into a sheet parallel to (001). It may be noted here that the overall behaviour of this π-stacking interaction of the type 2 molecules of compound (II) closely corresponds to the π-stacking interaction in compound (I), although the metrics of the two interactions differ somewhat, not surprisingly in view of the presence of an additional molecular type in compound (II).

Experimental

For the synthesis of compounds (I) and (II), equimolar quantities (1 mmol of each component) of indan-1,3-dione, 4-*R*-benzaldehyde, where *R* = H for compound (I) and *R* = OMe for compound (II), and 5-amino-3-*tert*-butyl-1-(4-chlorophenyl)-1*H*-pyrazole were added to a mixture of water and triethylamine (3 ml, 15:1 *v*/*v*), and then subjected to microwave irradiation at 353 K with a maximum power of 80 W for 10 min. The reaction mixture was allowed to cool to ambient temperature and it was then extracted with dichloromethane (3 × 15 ml). The combined extracts were dried over sodium sulfate, filtered and concentrated to give a red solid. The products were recrystallized from ethanol, at ambient temperature and in air, to give light-yellow crystals suitable for single-crystal X-ray diffraction. Compound (I) (*R* = H): yield 77%, m.p. 510–511 K; MS (70 eV) *m*/*z* (%) 465/463 (25/71, *M* + 2/*M*), 450/448 (36/100), 435/433 (9/26), 422/420 (7/20); HRMS *m*/*z* found 463.1469, $C_{29}H_{22}ClN_3O$ requires *m*/*z* = 463.1451. Compound (II) (*R* = OMe), yield 75%, m.p. 503–504 K; MS (70 eV) *m*/*z* (%) 495/493 (28/80, *M* + 2/*M*), 480/478 (30/100), 465/463 (11/37), 452/450 (10/29); HRMS *m*/*z* found 493.1544, $C_{30}H_{24}ClN_3O_2$ requires *m*/*z* = 493.1557.

Compound (I)

Crystal data

$C_{29}H_{22}ClN_3O$
M_r = 463.95
Triclinic, $P\overline{1}$
a = 8.1014 (5) Å
b = 11.3554 (10) Å
c = 13.5762 (11) Å
α = 102.755 (7)°
β = 90.013 (8)°
γ = 108.268 (7)°
V = 1153.47 (16) Å^3
Z = 2
Mo *K*α radiation
μ = 0.19 mm^{-1}
T = 120 K
0.43 × 0.22 × 0.16 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.921, T_{max} = 0.970
29371 measured reflections
5310 independent reflections
4065 reflections with $I > 2\sigma(I)$
R_{int} = 0.045

Table 1
Selected torsion angles (°) for compounds (I) and (II).

	(I) *x* = null	(II) *x* = 1	(II) *x* = 2
N*x*2—N*x*1—C*x*11—C*x*12	−170.54 (14)	−156.56 (19)	−155.80 (18)
N*x*2—C*x*3—C*x*31—C*x*32	−12.9 (2)	−10.7 (2)	−12.8 (2)
N*x*2—C*x*3—C*x*31—C*x*33	105.68 (17)	108.3 (2)	106.2 (2)
N*x*2—C*x*3—C*x*31—C*x*34	−131.81 (16)	−129.98 (19)	−131.46 (19)
C*x*3*A*—C*x*4—C*x*41—C*x*42	78.8 (2)	84.6 (3)	76.8 (3)
C*x*43—C*x*44—O*x*44—C*x*47		10.7 (3)	−177.08 (19)

Table 2
Hydrogen-bond parameters (Å, °) for compounds (I) and (II).

Cg represents the centroid of the C211–C216 ring.

Compound	*D*—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
(I)	C44—H44···O5^{i}	0.95	2.59	3.232 (2)	125
(II)	C146—H146···*Cg*	0.95	2.71	3.655 (2)	172
	C18—H18···O25^{ii}	0.95	2.50	3.151 (3)	126
	C28—H28···O15^{iii}	0.95	2.46	3.226 (3)	138

Symmetry codes: (i) −*x* + 1, −*y* + 1, −*z* + 2; (ii) −*x* + 2, −*y* + 1, −*z* + 1; (iii) −*x* + 1, −*y*, −*z* + 1.

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.098
S = 1.06
5310 reflections
310 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.39 e Å^{-3}

Compound (II)

Crystal data

$C_{30}H_{24}ClN_3O_2$
M_r = 493.97
Triclinic, $P\overline{1}$
a = 11.1911 (9) Å
b = 11.4258 (8) Å
c = 20.095 (2) Å
α = 97.411 (6)°
β = 93.272 (7)°
γ = 107.635 (6)°
V = 2415.7 (4) Å^3
Z = 4
Mo *K*α radiation
μ = 0.19 mm^{-1}
T = 120 K
0.42 × 0.30 × 0.29 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.924, T_{max} = 0.946
63410 measured reflections
11085 independent reflections
7328 reflections with $I > 2\sigma(I)$
R_{int} = 0.061

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.115
S = 1.06
11085 reflections
657 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.37 e Å^{-3}

All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H distances of 0.95 (aromatic) or 0.98 Å (methyl), and with U_{iso}(H) = kU_{eq}(C), where *k* = 1.5 for the methyl groups, which were permitted to rotate but not to tilt, and 1.2 otherwise.

For both compounds, data collection: *COLLECT* (Hooft, 1999); cell refinement: *DIRAX*/*LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

The authors thank 'Centro de Instrumentación Científico-Técnica of Universidad de Jaén' and the staff for data collection. JP and CL thank COLCIENCIAS and Universidad de los Andes for financial support. JC thanks the Consejería de Innovación, Ciencia y Empresa (Junta de Andalucía, Spain) and the Universidad de Jaén for financial support.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG3236). Services for accessing these data are described at the back of the journal.

References

Almeida, M. E. L. de, Braz, F. R., von Bulow, M. V., Gottlieb, O. R. & Maia, J. G. S. (1976). *Phytochemistry*, **1976**, 1186–1187.

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.

Burla, M. C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G. L., De Caro, L., Giacovazzo, C., Polidori, G. & Spagna, R. (2005). *J. Appl. Cryst.* **38**, 381–388.

Duisenberg, A. J. M., Hooft, R. W. W., Schreurs, A. M. M. & Kroon, J. (2000). *J. Appl. Cryst.* **33**, 893–898.

Duisenberg, A. J. M., Kroon-Batenburg, L. M. J. & Schreurs, A. M. M. (2003). *J. Appl. Cryst.* **36**, 220–229.

Earl, R. A., Zaczek, R., Teleha, C. A., Fisher, B. N., Maciag, C. M., Marynowski, M. E., Logue, A. R., Tam, S. W., Tinker, W. J., Huang, S.-M. & Chorvat, R. J. (1998). *J. Med. Chem.* **41**, 4615–4622.

Evdokimov, N. M. *et al.* (2011). *J. Med. Chem.* **54**, 2012–2021.

Hooft, R. W. W. (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.

Insuasty, H., Castro, E., Sánchez, E., Cobo, J. & Glidewell, C. (2010). *Acta Cryst.* C**66**, o141–o146.

Low, J. N., Cobo, J., Sánchez, A., Trilleras, J. & Glidewell, C. (2007). *Acta Cryst.* C**63**, o287–o291.

Padwa, A., Heidelbaugh, T. M. & Kuethe, J. T. (2000). *J. Org. Chem.* **65**, 2368–2378.

Peters, J.-U., Weber, S., Kritter, S., Weiss, P., Wallier, A., Zimmerli, D., Boehringer, M., Steger, M. & Loeffler, B.-M. (2004). *Bioorg. Med. Chem. Lett.* **14**, 3579–3580.

Quiroga, J., Portilla, J., Insuasty, B., Abonía, R., Nogueras, M., Sortino, M. & Zacchino, S. (2005). *J. Heterocycl. Chem.* **42**, 61–66.

Quiroga, J., Portilla, J., Serrano, H., Abonía, R., Insuasty, B., Nogueras, M. & Cobo, J. (2007). *Tetrahedron Lett.* **48**, 1987–1990.

Quiroga, J., Sánchez, A., Cobo, J. & Glidewell, C. (2009). *Acta Cryst.* C**65**, o374–o376.

Quiroga, J., Trilleras, J., Hursthouse, M. B., Cobo, J. & Glidewell, C. (2010). *Acta Cryst.* C**66**, o163–o167.

Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.

Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.

Strunz, G. M. & Findlay, J. A. (1985). *The Alkaloids*, Vol. 26. New York: Academic Press.