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4-Difluoromethyl-1-(2,5-dimethoxyphenyl)-1*H*-1,2,3-triazole

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.002 Å
R factor = 0.042
wR factor = 0.110
Data-to-parameter ratio = 15.0

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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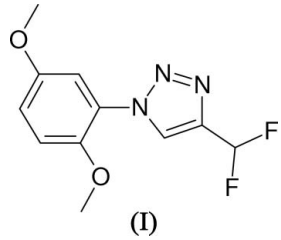
In the title compound, $C_{11}H_{11}F_2N_3O_2$, the aryl and triazole rings are both planar, but at an angle of 45.27 (4)° to each other.

Comment

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains a leading cause of mortality worldwide. The World Health Organization estimates that about one-third of the world's population harbours latent infection of TB. Among such infected individuals, approximately eight million develop active TB, and almost two million of these die from this disease each year. 95% of new TB cases occur in developing countries. The current human immunodeficiency virus (AIDS) pandemic and resistance to the currently available drugs are proving major obstacles to the control of tuberculosis (Tewari *et al.*, 2004; World Health Organization, 2005; Tripathi *et al.*, 2005).

Chemotherapy of TB started in the 1940s. Various drugs have been used against TB, including *para*-aminosalicylic acid, isoniazid, pyrazinamide, cycloserine, ethionamide, rifampicin and ethambutol. However, six decades have passed without any significant development of new chemical treatments of tuberculosis. TB really can be classed as a neglected disease.

In pursuit of new drugs for TB, we have synthesized a new series of 1-aryl-4-difluoromethyl-1,2,3-triazole derivatives and evaluated their inhibitory activities against *M. tuberculosis*. All derivatives exhibited tuberculosis inhibitory activity at high concentrations (MIC > 6.5 g ml^{-1}); a full description of the biological tests will be reported elsewhere (Costa, Boechat, Rangel *et al.*, 2006). The structure of the title compound, (I), which exhibited 74% of inhibition at a concentration of 80.0 μg ml^{-1}, is reported below.



(I)

$C_{11}H_{11}F_2N_3O_2$ (Fig. 1) crystallizes in the space group $P2_1/c$; the geometry of the structure was analysed with the aid of *PLATON* (Spek, 2003). Both the triazole and the aryl rings are planar and the methoxy groups are nearly coplanar with the aryl ring, with torsion angles C8—C7—O7—O71 = 4.7 (2)° and C9—C10—O10—C101 = 6.7 (2)°. The angle between the

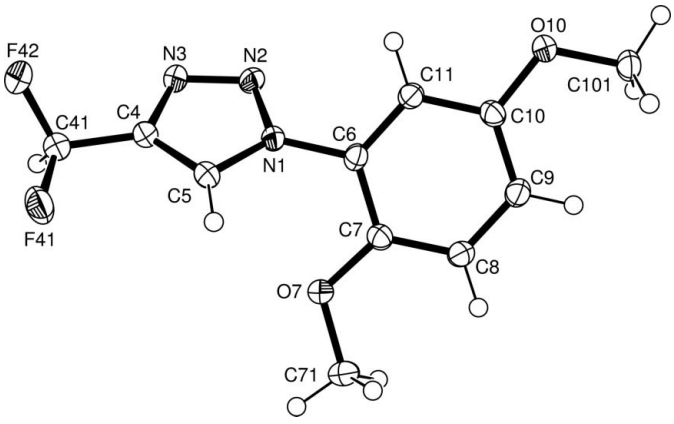


Figure 1
The molecular structure of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown as circles of arbitrary radii.

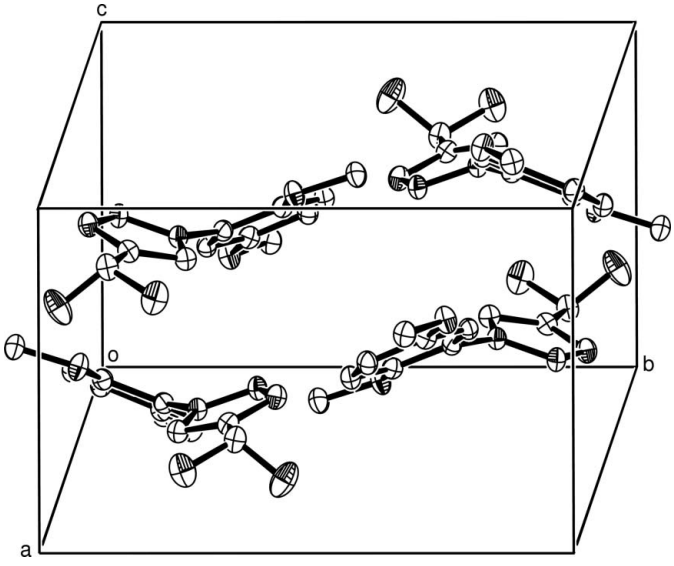


Figure 2
The unit-cell contents, showing the relative orientation of the triazole and aryl groups. Ellipsoids are represented as in Fig. 1. H atoms have been omitted.

planes defined by the triazole and aryl rings is 45.27 (4)° (Fig. 2). Comparison with 1-(4-methylphenyl)-4-difluoromethyl-1*H*-1,2,3-triazole (Costa, Boechat, Ferreira *et al.*, 2006) indicates that the presence of the methoxy groups, *ortho* and *meta* to the triazole, leads to this deviation from coplanarity.

Experimental

A solution of diazomalonaldehyde (5.0 mmol) in water (30 ml) was added dropwise to a stirred solution of 2,5-dimethoxyaniline hydrochloride (4.5 mmol) in water (5 ml). The reaction mixture was stirred for 24 h at room temperature; the solid was collected, washed with cold water and crystallized from aqueous ethanol. The title compound was obtained in 98% yield as a white solid (m.p. 351–352 K). ^{1}H NMR (500 MHz, $CDCl_3$/Me_4Si): δ 3.89 (*s*, 3H, $2OCH_3$), 6.95 (*t*, 1H, CHF_2, J = 55.0 Hz), 7.04 (*dd*, 2H, J = 2.0 e 7.0 Hz, arom.), 7.63 (*dd*, 2H, J = 2.0 e 7.0 Hz, arom.), 8.14 (*sl*, 1H, triazole). ^{19}F NMR (376.0 MHz, $CDCl_3$/$CFCl_3$): δ −112.2 (2F, CHF_2). Full spectroscopic data are given in the CIF. Analysis calculated for $C_{11}H_{11}F_2N_3O_2$: C 51.77, H 4.34, N 16.46%; found: C 51.78, H 4.36, N 16.49%.

Crystal data

$C_{11}H_{11}F_2N_3O_2$
M_r = 255.23
Monoclinic, $P2_1/c$
a = 13.4574 (6) Å
b = 11.4815 (5) Å
c = 7.3719 (2) Å
β = 105.247 (3)°
V = 1098.95 (7) Å^3
Z = 4
D_x = 1.543 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.13 mm^{-1}
T = 120 (2) K
Shard, colourless
0.14 × 0.12 × 0.05 mm

Data collection

Nonius KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.822, T_{max} = 1.000
14882 measured reflections
2510 independent reflections
1975 reflections with $I > 2\sigma(I)$
R_{int} = 0.053
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.110
S = 1.06
2510 reflections
167 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0488P)^2 + 0.501P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.021 (3)

All H atoms were located in difference maps and then treated as riding atoms with C—H distances of 0.95 (aryl), 1.00 (methine), 1.01 (triazole) and 0.98 Å (methyl), and with U_{iso}(H) values of $1.2U_{eq}$(aryl) or $1.5U_{eq}$(methyl); U_{iso} values for the triazole and methine H atoms were freely refined.

Data collection: *COLLECT* (Hooft, 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *OSCAIL* (McArdle, 2003) and *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *OSCAIL* and *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *CIFTAB* (Sheldrick, 1997).

We are indebted to the EPSRC for the use of both the Chemical Database Service at Daresbury, primarily for access to the Cambridge Structural Database (Fletcher *et al.*, 1996), and the X-ray service at the University of Southampton for data collection.

References

Costa, M. S., Boechat, N., Ferreira, V. F., Wardell, S. M. S. V. & Skakle, J. M. S. (2006). *Acta Cryst.* E**62**, o1925–o1927.
Costa, M. S., Boechat, N., Rangel, È. A., Ferreira, V. F., Junior, I. N., Lourenço, M. C. S. & Wardell, S. M. S. V. (2006). *Eur. J. Med. Chem.* In preparation.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Fletcher, D. A., McMeeking, R. F. & Parkin, D. (1996). *J. Chem. Inf. Comput. Sci.* **36**, 746–749.
Hooft, R. W. W. (1998). *COLLECT*. Nonius BV, Delft, The Netherlands.
McArdle, P. (2003). *OSCAIL for Windows*. Version 10. Crystallography Centre, Chemistry Department, NUI Galway, Ireland.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276. *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Sheldrick, G. M. (1997). *SHELXS97*, *SHELXL97* and *CIFTAB*. University of Göttingen, Germany.
Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Tewari, N., Tiwari, V. K., Tipathi, R. P., Chaturvedi, V., Srivastava, A., Srivastava, R., Shukla, P. K., Chaturvedi, A. K., Gaikwad, A., Sinha, S. & Srivastava, B. S. (2004). *Bioorg. Med. Chem. Lett.* **14**, 329–332.
Tripathi, R. P., Tewari, N., Dwivedi, N. & Tiwari, V. K. (2005). *Med. Res. Rev.* **25**, 93–131.
World Health Organization (2005). WHO Report 2005. *Global Tuberculosis Control – Surveillance, Planning, Financing*. WHO/HTM/TB/2005. http://www.who.int/tb.

supporting information

Acta Cryst. (2006). E**62**, o2048–o2050 [https://doi.org/10.1107/S1600536806013924]

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Crystal data

$C_{11}H_{11}F_2N_3O_2$
$M_r = 255.23$
Monoclinic, $P2_1/c$
Hall symbol: -P 2ybc
$a = 13.4574$ (6) Å
$b = 11.4815$ (5) Å
$c = 7.3719$ (2) Å
$\beta = 105.247$ (3)°
$V = 1098.95$ (7) Å^3
$Z = 4$
$F(000) = 528$
$D_x = 1.543$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2600 reflections
$\theta = 2.9$–$27.5°$
$\mu = 0.13$ mm^{-1}
$T = 120$ K
Shard, colourless
0.14 × 0.12 × 0.05 mm

Data collection

Nonius KappaCCD diffractometer
Radiation source: Bruker–Nonius FR591 rotating anode
10 cm confocal mirrors monochromator
Detector resolution: 9.091 pixels mm^{-1}
φ and ω scans
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)
$T_{min} = 0.822$, $T_{max} = 1.000$
14882 measured reflections
2510 independent reflections
1975 reflections with $I > 2\sigma(I)$
$R_{int} = 0.053$
$\theta_{max} = 27.5°$, $\theta_{min} = 3.1°$
$h = -17\rightarrow17$
$k = -14\rightarrow14$
$l = -9\rightarrow9$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.110$
$S = 1.06$
2510 reflections
167 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: difference Fourier map
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0488P)^2 + 0.501P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.26$ e Å^{-3}
$\Delta\rho_{min} = -0.24$ e Å^{-3}
Extinction correction: SHELXL97, $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.021 (3)

Special details

Experimental. IR (KBr) ν_{max} (cm^{-1}) 3169; 1027
^{13}C NMR (125 MHz; $CDCl_3/Me_4Si$): δ 55.9 (3*H*, OCH_3); 56.5 (3*H*, OCH_3); 110.3 (t, CF_2H, J= 230.0 Hz); 113.6; 116.2; 124.4; 121.1; 127.3; 142.3 (t, J = 29.1 Hz) 144.7; 153.9;
EIMS (m/*z*): 255(M^+; 60%); 227(M^+-28; 8%); 226(M^+-29; 5%); 212 (M^+-43; 100%).

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($Å^2$)

	x	*y*	*z*	U_{iso}*/U_{eq}
N1	0.24556 (10)	0.76731 (11)	0.21516 (18)	0.0190 (3)
N2	0.25076 (10)	0.87928 (11)	0.15679 (18)	0.0218 (3)
N3	0.15878 (10)	0.92462 (11)	0.13265 (19)	0.0231 (3)
C4	0.09560 (12)	0.84281 (14)	0.1761 (2)	0.0211 (3)
C41	−0.01440 (13)	0.86907 (14)	0.1624 (2)	0.0258 (4)
H41	−0.0524	0.8858	0.0291	0.035 (5)*
F41	−0.05715 (8)	0.77552 (9)	0.22864 (16)	0.0367 (3)
F42	−0.02215 (8)	0.96095 (10)	0.27463 (17)	0.0414 (3)
C5	0.14916 (12)	0.74227 (14)	0.2272 (2)	0.0213 (3)
H5	0.1350	0.6622	0.2711	0.028 (5)*
C6	0.33404 (12)	0.69383 (13)	0.2450 (2)	0.0193 (3)
C7	0.32268 (12)	0.58104 (14)	0.1701 (2)	0.0200 (3)
O7	0.22486 (9)	0.54727 (9)	0.08105 (16)	0.0247 (3)
C71	0.21121 (14)	0.42979 (14)	0.0163 (2)	0.0260 (4)
H71A	0.2503	0.4168	−0.0769	0.039*
H71B	0.1380	0.4152	−0.0415	0.039*
H71C	0.2360	0.3767	0.1227	0.039*
C8	0.41010 (12)	0.51322 (14)	0.1909 (2)	0.0221 (3)
H8	0.4042	0.4368	0.1399	0.027*
C9	0.50675 (13)	0.55602 (14)	0.2860 (2)	0.0226 (4)
H9	0.5663	0.5091	0.2981	0.027*
C10	0.51596 (12)	0.66705 (14)	0.3629 (2)	0.0206 (3)
O10	0.60716 (8)	0.71525 (10)	0.46465 (16)	0.0246 (3)
C101	0.69796 (12)	0.64907 (15)	0.4723 (2)	0.0246 (4)
H10A	0.6929	0.5732	0.5302	0.037*
H10B	0.7582	0.6911	0.5473	0.037*
H10C	0.7051	0.6375	0.3446	0.037*
C11	0.42913 (12)	0.73624 (14)	0.3421 (2)	0.0197 (3)
H11	0.4351	0.8124	0.3944	0.024*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0162 (7)	0.0173 (6)	0.0240 (7)	0.0003 (5)	0.0061 (5)	0.0001 (5)
N2	0.0218 (7)	0.0164 (7)	0.0273 (7)	0.0013 (5)	0.0068 (5)	0.0013 (5)
N3	0.0193 (7)	0.0210 (7)	0.0282 (7)	0.0032 (6)	0.0050 (5)	−0.0004 (5)
C4	0.0180 (8)	0.0217 (8)	0.0231 (8)	−0.0002 (6)	0.0044 (6)	−0.0023 (6)
C41	0.0208 (8)	0.0227 (8)	0.0333 (9)	−0.0003 (7)	0.0063 (7)	−0.0023 (7)
F41	0.0208 (5)	0.0346 (6)	0.0561 (7)	−0.0003 (4)	0.0124 (5)	0.0076 (5)
F42	0.0264 (6)	0.0381 (7)	0.0607 (8)	0.0041 (5)	0.0132 (5)	−0.0195 (5)
C5	0.0176 (8)	0.0214 (8)	0.0249 (8)	−0.0017 (6)	0.0058 (6)	−0.0004 (6)
C6	0.0185 (8)	0.0185 (8)	0.0224 (7)	0.0024 (6)	0.0080 (6)	0.0013 (6)
C7	0.0184 (8)	0.0201 (8)	0.0218 (7)	−0.0011 (6)	0.0057 (6)	0.0004 (6)
O7	0.0193 (6)	0.0192 (6)	0.0334 (6)	−0.0002 (5)	0.0031 (5)	−0.0056 (5)
C71	0.0284 (9)	0.0190 (8)	0.0295 (8)	−0.0025 (7)	0.0059 (7)	−0.0037 (6)
C8	0.0223 (8)	0.0183 (8)	0.0265 (8)	−0.0001 (6)	0.0076 (6)	−0.0013 (6)
C9	0.0208 (8)	0.0206 (8)	0.0275 (8)	0.0028 (6)	0.0082 (6)	0.0002 (6)
C10	0.0169 (8)	0.0210 (8)	0.0240 (8)	−0.0023 (6)	0.0054 (6)	0.0008 (6)
O10	0.0162 (6)	0.0223 (6)	0.0340 (6)	0.0004 (5)	0.0042 (5)	−0.0040 (5)
C101	0.0171 (8)	0.0246 (8)	0.0320 (9)	0.0028 (6)	0.0063 (6)	0.0020 (7)
C11	0.0200 (8)	0.0176 (8)	0.0229 (8)	0.0001 (6)	0.0080 (6)	−0.0001 (6)

Geometric parameters (Å, º)

N1—C5	1.354 (2)	O7—C71	1.4266 (19)
N1—N2	1.3633 (18)	C71—H71A	0.9800
N1—C6	1.4284 (19)	C71—H71B	0.9800
N2—N3	1.3111 (19)	C71—H71C	0.9800
N3—C4	1.360 (2)	C8—C9	1.395 (2)
C4—C5	1.361 (2)	C8—H8	0.9500
C4—C41	1.488 (2)	C9—C10	1.387 (2)
C41—F42	1.3614 (19)	C9—H9	0.9500
C41—F41	1.3677 (19)	C10—O10	1.3752 (18)
C41—H41	1.0000	C10—C11	1.388 (2)
C5—H5	1.0095	O10—C101	1.4274 (19)
C6—C11	1.380 (2)	C101—H10A	0.9800
C6—C7	1.400 (2)	C101—H10B	0.9800
C7—O7	1.3637 (19)	C101—H10C	0.9800
C7—C8	1.385 (2)	C11—H11	0.9500
C5—N1—N2	110.52 (13)	O7—C71—H71B	109.5
C5—N1—C6	129.69 (13)	H71A—C71—H71B	109.5
N2—N1—C6	119.71 (12)	O7—C71—H71C	109.5
N3—N2—N1	106.99 (12)	H71A—C71—H71C	109.5
N2—N3—C4	108.67 (13)	H71B—C71—H71C	109.5
N3—C4—C5	109.43 (14)	C7—C8—C9	120.67 (15)
N3—C4—C41	121.09 (14)	C7—C8—H8	119.7
C5—C4—C41	129.48 (15)	C9—C8—H8	119.7

F42—C41—F41	106.56 (13)	C10—C9—C8	120.03 (15)
F42—C41—C4	110.47 (13)	C10—C9—H9	120.0
F41—C41—C4	108.72 (13)	C8—C9—H9	120.0
F42—C41—H41	110.3	O10—C10—C9	124.31 (14)
F41—C41—H41	110.3	O10—C10—C11	115.76 (14)
C4—C41—H41	110.3	C9—C10—C11	119.92 (15)
N1—C5—C4	104.39 (14)	C10—O10—C101	116.05 (12)
N1—C5—H5	118.6	O10—C101—H10A	109.5
C4—C5—H5	137.0	O10—C101—H10B	109.5
C11—C6—C7	121.39 (14)	H10A—C101—H10B	109.5
C11—C6—N1	119.55 (14)	O10—C101—H10C	109.5
C7—C6—N1	119.03 (14)	H10A—C101—H10C	109.5
O7—C7—C8	125.29 (14)	H10B—C101—H10C	109.5
O7—C7—C6	116.37 (13)	C6—C11—C10	119.61 (14)
C8—C7—C6	118.34 (14)	C6—C11—H11	120.2
C7—O7—C71	116.94 (12)	C10—C11—H11	120.2
O7—C71—H71A	109.5		

C5—N1—N2—N3	0.16 (16)	C11—C6—C7—O7	178.38 (13)
C6—N1—N2—N3	177.20 (12)	N1—C6—C7—O7	−3.5 (2)
N1—N2—N3—C4	0.33 (16)	C11—C6—C7—C8	−1.8 (2)
N2—N3—C4—C5	−0.70 (18)	N1—C6—C7—C8	176.34 (13)
N2—N3—C4—C41	179.89 (13)	C8—C7—O7—C71	4.7 (2)
N3—C4—C41—F42	−58.4 (2)	C6—C7—O7—C71	−175.52 (13)
C5—C4—C41—F42	122.30 (18)	O7—C7—C8—C9	−179.53 (14)
N3—C4—C41—F41	−175.02 (13)	C6—C7—C8—C9	0.7 (2)
C5—C4—C41—F41	5.7 (2)	C7—C8—C9—C10	0.8 (2)
N2—N1—C5—C4	−0.56 (17)	C8—C9—C10—O10	177.57 (14)
C6—N1—C5—C4	−177.23 (14)	C8—C9—C10—C11	−1.2 (2)
N3—C4—C5—N1	0.76 (17)	C9—C10—O10—C101	6.7 (2)
C41—C4—C5—N1	−179.90 (15)	C11—C10—O10—C101	−174.54 (13)
C5—N1—C6—C11	−138.24 (17)	C7—C6—C11—C10	1.5 (2)
N2—N1—C6—C11	45.36 (19)	N1—C6—C11—C10	−176.70 (13)
C5—N1—C6—C7	43.6 (2)	O10—C10—C11—C6	−178.78 (13)
N2—N1—C6—C7	−132.84 (15)	C9—C10—C11—C6	0.1 (2)