ORGANIC COMPOUNDS

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(*R*)-Spiro[(2*R*)-*N*-acetyl-2-phenyl-1,3-thiazolidine-4,3′-(3a′*R*,6a′*S*)-5′,6a′-dimethyl-3a′,-6a′-dihydro-3*H*-furo[2,3-*b*]furan-2-one]†

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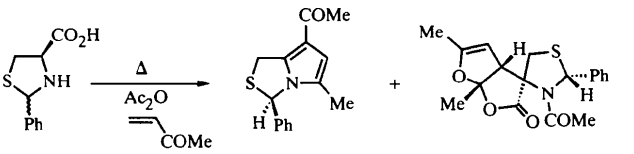
Abstract

In the title compound, $C_{18}H_{19}NO_4S$, the two furan rings are fused *cis*. The dihydrofuran ring is practically planar and the saturated furan-2-one ring is only slightly puckered. The thiazolidine ring has a twisted conformation about the C4—S1 bond. The environment around the spiro atom is nearly tetrahedral.

Comment

1,3-Dipolar cycloaddition reactions of oxazolium-5-oxides (münchnones) have proved to be a useful method in the synthesis of pyrroles (Padwa, 1991). The method can also be used as a route to heterocycles in which another ring system is annulated to pyrrole. We have recently described the use of *N*-acetyl-2-phenyl-(2*R*,4*R*)-thiazolidine-4-carboxylic acids to generate 5*H*,7*H*-thiazolo[3,4-*c*]oxazolium-1-oxides with internal dipolarophiles (Pinho e Melo *et al.*, 1999). The intramolecular 1,3-dipolar cycloaddition of these mesoionic species led to the synthesis of new 3,4-dihydro-1*H*-pyrrolo[1,2-*c*]thiazole derivatives, compounds with potential pharmacological importance (Durée *et al.*, 1989). We have decided to extend our study to the intermolecular 1,3-dipolar cycloaddition of 5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-oxides. 2-Phenylthiazolidine-4-carboxylic acid, (1), was heated in acetic anhydride and methyl vinyl ketone was used as the dipolarophile (scheme). Two products were obtained – the expected methyl (*R*)-7-acetyl-3-phenyl-5-methyl-1*H*,3*H*-pyrrolo-[1,2-*c*]thiazole-7-carboxylate, (2), in 25% yield and the title compound, (3), in 7% yield. The structure of (3) was established by X-ray crystallography.



(1) (2) 25% (3) 7%

The two furan rings are fused *cis*, the dihedral angle between the least-squares planes of these rings is 58.56 (9)°. The dihydrofuran ring is practically planar – the r.m.s. deviation of the atoms from the least-squares plane is 0.024 Å and the absolute maximum deviation from the plane is 0.032 (1) Å for atom C6a′. This is expected owing to the presence of the double bond between atoms C4′ and C5′. Accordingly, the methyl C15 atom is practically in the plane of the ring. The saturated furan-2-one ring is only slightly puckered [Cremer & Pople (1975) puckering parameters: q_2 = 0.080 (2) Å, φ_2 = 17.2 (17)°], the puckering corresponding to a small twist around the O1—C2′ bond. The twofold asymmetry parameter ΔC_2(O1—C2′) is 0.6 (2)°. The absolute configuration, as determined by a Flack analysis, assigns the *R*,*R*,*R*,*S* chirality to the four atoms C2, C3a′, C5 and C6a′, respectively, which is the expected configuration from the synthesis route.

The two Csp^3—O bonds in the furan ring system, C6a′—O6′ and C6a′—O1, have practically identical values which are slightly shorter than the tabulated Csp^3—O2 bonds in ring systems (Allen *et al.*, 1987). Comparing the lengths of the two Csp^2—O bonds, C5′—O6′ and C2′—O1, with the tabulated value in furan (1.368 Å), there is a lengthening of the C5′—O6′ bond [1.395 (4) Å] and a shortening of the C2′—O1 bond [1.351 (3) Å].

The thiazolidine ring has a twisted conformation about the C4—S1 bond. Its twofold asymmetry parameter (Duax *et al.*, 1976) ΔC_2(S1—C4) is 4.37 (19)°. The puckering parameters (Cremer & Pople, 1975) q_2 and φ_2 are 0.529 (9) Å and 343.8 (3)°, respectively. The phase angle φ_2 of the pure twisted conformation is 342°. S1 and C4 are on opposite sides of the plane passing through C2, N1 and C5 at −0.492 (8) and 0.404 (7) Å, respectively. The values of the S—C bond lengths are in good agreement with tabulated values (Allen *et al.*, 1987) and the C—S—C bond angle is close to the values observed in other thiazolidine compounds. The exocyclic angles around the N1 atom show some asymmetry. However, the sum of the valence angles around N1 is 359.9 (3)°, indicating no significant pyramidalization of this atom. The environment of the spiro C5

† Alternative name: (3a*R*,6a*S*,2′*R*)-3′-acetyl-3a,6a-dihydro-5,6a-dimethyl-2′-phenyl-(*R*)-spiro[furo[2,3-*b*]furan-3,4′-[1′,3′]thiazolidin]-2(3*H*)-one.

atom is nearly tetrahedral, with bond angles in the range 103.4 (2)–111.8 (2)°.

The phenyl ring has an axial position with respect to the thiazolidine ring with torsion angles −106.2 (3) (C5—N1—C2—C6) and 89.2 (2)° (C4—S1—C2—C6). The dihedral angle between the least-squares planes of the phenyl and thiazolidine rings is 79.86 (10)°. Inspection of the displacement ellipsoids of the phenyl ring show a large anisotropy of the C8, C9 and C10 atoms and a somewhat large dispersion of the ring C—C bond lengths [1.359 (5)–1.399 (5) Å]. This suggests that a minor disorder of the ring, of either static or dynamic nature, may be present, which is not unexpected due to the probable low potential barrier for rotation around the single C2—C6 bond.

The geometry of the acetyl group is normal. It is almost coplanar with the thiazolidine group, the angle between the least-squares plane of the N1–acetyl group and that defined by N1, C2 and C5 is only 4.7 (4)°. The short carboxyl C12=O2 bond agrees with the observation that the O2 atom is not involved in strong hydrogen bonding (see below).

Cohesion of the structure is mainly due to van der Waals interactions. Inspection of close contact distances shows that C2···O6(x, $y-1$, z) [3.505 (5) Å], has a geometry that may correspond to a weak intermolecular C—H···O interaction. In addition the C7···N1 and C14···O2 distances [2.888 (5) and 3.183 (5) Å] also qualify as possible intramolecular hydrogen bonds. Inspection of C—H···π_{arene} interactions reveals that the interaction C4—H4A···Cg(y, x, $-z$) (3.621 Å; where Cg is the ring centroid of the phenyl ring) may also be relevant in the crystal packing.

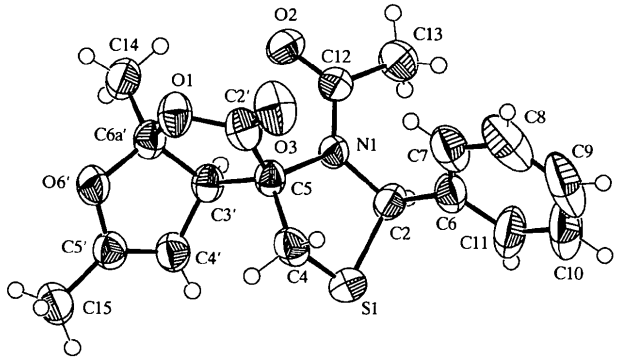


Fig. 1. *ORTEP*II (Johnson, 1976) plot of the title compound. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as filled circles of an arbitrary radius.

Experimental

2-Phenylthiazolidine-4-carboxylic acid, (1) (0.52 g, 2.5 mmol), methyl vinyl ketone (1 ml, 12.5 mmol) and Ac_2O (10 ml) were heated at 368–373 K for 12 h. The reaction was cooled to room temperature and then diluted with CH_2Cl_2 (25 ml). The organic phase was washed with a saturated aqueous solution of $NaHCO_3$, then with water, dried with Na_2SO_4, and evaporated off. The products were isolated by flash chromatography [hexane–ethyl acetate (3:1), hexane–ethyl acetate (1:1) and then ethyl acetate]. Methyl (*R*)-7-acetyl-3-phenyl-5-methyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazole-7-carboxylate, (2), was obtained in 25% yield and the title compound, (3), in 7% yield. Compound (3): m.p. 475–478 K (from hexane–ethyl acetate); IR (KBr): 3020, 2940, 1788 and 1655 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$/DMSO-d_6) δ (p.p.m.): 1.87 (6H, *m*), 1.90 (3H, *s*), 3.09 (1H, *d*, J = 12 Hz), 3.37 (1H, *d*, J = 12 Hz), 3.47 (1H, *s*), 4.93 (1H, *m*), 5.99 (1H, *s*), 7.30–7.35 (1H, *m*, ArH), 7.40–7.47 (2H, *m*, ArH) and 7.63–7.66 (2H, *m*, ArH); MS (*m/z*): 345 (M^+, 23%), 302 (25), 179 (48) and 148 (53); analysis calculated for $C_{18}H_{19}NO_4S$: C 62.59, H 5.54, N 4.06, S 9.28%; found C 62.62, H 5.57, N 4.02, S 9.30%.

Crystal data

$C_{18}H_{19}NO_4S$
M_r = 345.40
Tetragonal
$P4_32_12$
a = 8.321 (8) Å
c = 48.92 (2) Å
V = 3387 (5) Å^3
Z = 8
D_x = 1.355 Mg m^{-3}
D_m not measured
Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 25 reflections
θ = 12.10–25.94°
μ = 1.887 mm^{-1}
T = 293 (2) K
Prismatic
0.46 × 0.42 × 0.27 mm
Light yellow

Data collection

Enraf–Nonius CAD-4 diffractometer
Profile data from ω–2θ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.487, T_{max} = 0.601
4537 measured reflections
1912 independent reflections (plus 936 Friedel-related reflections)
2536 reflections with $I > 2\sigma(I)$
R_{int} = 0.068
θ_{max} = 67.81°
$h = 0 \rightarrow 9$
$k = 0 \rightarrow 10$
$l = 0 \rightarrow 57$
3 standard reflections
frequency: 180 min
intensity decay: 5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.121
S = 1.048
2848 reflections
215 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0613P)^2 + 1.0005P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.202 e Å^{-3}
$\Delta\rho_{min}$ = −0.203 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997*a*)
Extinction coefficient: 0.0030 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.01 (3)

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

S1—C4	1.795 (4)	O6′—C5′	1.395 (4)
S1—C2	1.817 (3)	O6′—C6a′	1.432 (3)
O1—C2′	1.351 (3)	C3a′—C4′	1.491 (4)
O1—C6a′	1.434 (4)	C4′—C5′	1.327 (4)

C4—S1—C2	88.8 (1)	N1—C5—C4	104.3 (2)
C12—N1—C5	119.1 (2)	C2′—C5—C3a′	103.4 (2)
C12—N1—C2	124.4 (2)	O1—C2′—C5	111.4 (2)
C5—N1—C2	116.4 (2)	C4′—C3a′—C6a′	101.8 (2)
C2′—O1—C6a′	111.6 (2)	C5′—C4′—C3a′	110.2 (3)
C5′—O6′—C6a′	107.5 (2)	C4′—C5′—O6′	112.9 (3)
N1—C2—S1	103.8 (2)	O6′—C6a′—C3a′	107.3 (2)

The H atoms were placed at calculated positions and refined as riding using the *SHELXL*97 (Sheldrick, 1997*a*) defaults. Examination of the structure with *PLATON* (Spek, 1995) showed that there are no solvent-accessible voids in the crystal lattice. All calculations were performed on a Pentium 150 MHz PC running LINUX.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *SDP-Plus* (Frenz, 1985). Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*b*). Program(s) used to refine structure: *SHELXL*97. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1275). Services for accessing these data are described at the back of the journal.

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N,N′-Diphenylguanidinium dihydrogen phosphate

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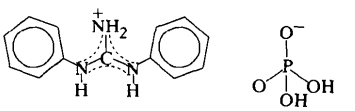
Abstract

The two phenyl rings of the title compound, $C_{13}H_{14}N_3^+ \cdot H_2PO_4^-$, are oriented *anti* with respect to the unsubstituted N atom of the cation, which has approximate C_2 symmetry. Bond lengths and angles within the guanidinium moiety are close to those expected for a central Csp^2 atom. The anions form infinite $(H_2PO_4^-)_n$ chains running along the *c* axis. The amino groups of the cation interact with these chains *via* hydrogen bonds.

Comment

The structure determination of the title compound, (I), was undertaken as part of a current research project to study the structure and physical properties (optical and dielectric) of a series of diphenylguanidine (dpg) compounds. Much of the current interest in guanidine compounds and derivatives is due to their biological activity, in particular their neuroleptic and antipsychotic properties. This is the case for *N,N′*-di-*ortho*-tolylguanidine and its congeners, which are selective ligands for the haloperidol-sensitive σ receptor (Weber *et al.*, 1986; Largent *et al.*, 1987). It is also well known that certain *N,N′*-diarylguanidines are potent ligands for the *N*-methyl-D-aspartate/PCP receptor [PCP is phencyclidine or *N*-(1-phenylcyclohexyl)piperidine] and these compounds have shown neuroprotective properties against glutamate-induced neuronal cell death (Olney *et al.*, 1989). Our interest in guanidine compounds is motivated by their potential applications in non-linear optics (Zyss *et al.*, 1993).



(I)

Several studies have shown that dpg is a very flexible molecule, due to the low potential barrier for rotation of the phenyl rings, and a number of different molecular conformations (*syn–syn*, *syn–anti* and *anti–anti*) have