

Two 5-oxa-2,6-diazaspiro[3.4]octan-1-one derivatives from the [3+2] cycloaddition of methylenelactams with nitrones

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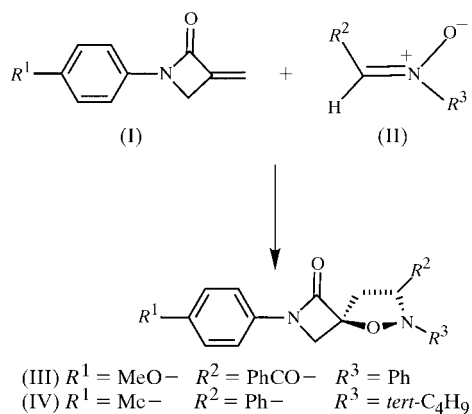
Received 17 November 1999

Accepted 10 January 2000

The two title 5-oxa-2,6-diazaspiro[3.4]octan-1-one adducts, 7-benzoyl-2-(4-methoxyphenyl)-6-phenyl-5-oxa-2,6-diazaspiro[3.4]octan-1-one, C₂₅H₂₂N₂O₄, (III), and 6-*tert*-butyl-2-(4-methylphenyl)-7-phenyl-5-oxa-2,6-diazaspiro[3.4]octan-1-one, C₂₂H₂₆N₂O₂, (IV), were obtained from a stereospecific [3+2] 1,3-cycloaddition of 3-methylene azetidins as dipolarophiles with nitrones. The lactam ring is conjugated with the *p*-methoxyphenyl or *p*-methylphenyl moiety. The envelope conformations of the isoxazolidine rings in (III) and (IV) are different, leading the substituents to be pseudo-axial in (III) and pseudo-equatorial in (IV).

Comment

Spirocompounds which incorporate highly strained methylenelactam moieties were unknown compounds at the beginning of our work. In a preliminary communication (Rigolet *et al.*, 1998), it was shown that 1,3-dipolar cycloaddition of nitrones



and 3-methylene isoindolones proceeded with low stereoselectivity. Nevertheless, complete stereospecificity was possible when 3-methylene azetidins, (I), were reacted

as dipolarophiles. The present X-ray study was undertaken to elucidate the geometry of the title bicyclic adducts, (III) and (IV). The structures are depicted with the atom-labelling schemes in Fig. 1 and Fig. 2, respectively.

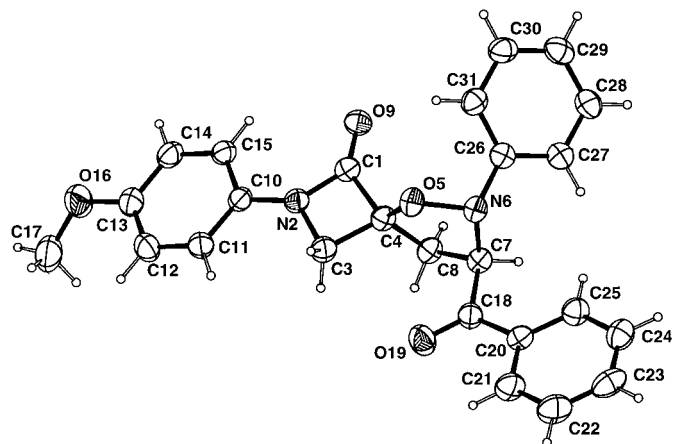


Figure 1

Perspective view of the molecule of (III) showing 30% probability displacement ellipsoids. H atoms are drawn as spheres of arbitrary radii.

In both (III) and (IV), the lactam ring (2-azetidone) is planar [maximum deviation 0.027 (2) Å for (III) and 0.045 (3) Å for (IV)] and is conjugated with the *p*-methoxyphenyl or *p*-methylphenyl substituent at N2. The dihedral angle between the two best mean planes (phenyl/azetidone) is 16.7 (2)° in (III) and 12.2 (4)° in (IV). The folding occurs at atom N2 which appears slightly tetrahedral, being 0.101 (2) Å and 0.054 (5) Å out of the plane of atoms C3, C1 and C10 in (III) and (IV), respectively.

The conformations of the two molecules differ essentially by the conformations of the isoxazolidine rings. These five-membered rings adopt a different envelope conformation, where C7 is displaced by -0.542 (3) Å in (III) and 0.580 (8) Å in (IV) out of the best mean plane passing through atoms O5, C4, C8 and N6, the sign of the displacement being correlated with the positive distance of O9 from the mean plane. The substituents at N6 and C7 are pseudo-axial in (III) and pseudo-equatorial in (IV). The possible transition state of the cycloaddition process may be clearly depicted from this structure.

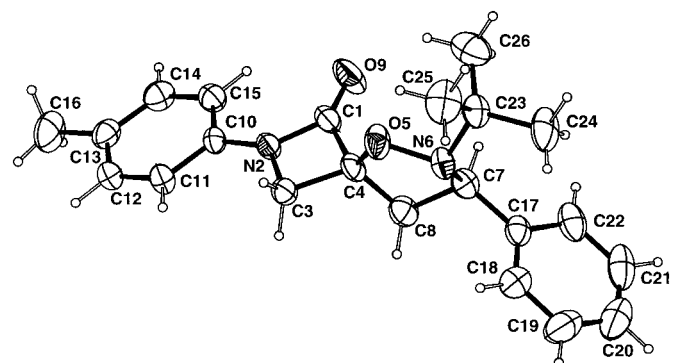


Figure 2

Perspective view of the molecule of (IV) showing 30% probability displacement ellipsoids. H atoms are drawn as spheres of arbitrary radii.

Experimental

Compounds (III) and (IV) were obtained from dipolar cycloadditions of (I) and (II) in toluene at 353 K. Crystals were isolated by recrystallization from ethanol solutions.

Compound (III)

Crystal data

C₂₅H₂₂N₂O₄
M_r = 414.45
 Monoclinic, *P*2₁/*n*
a = 9.368 (5) Å
b = 19.776 (7) Å
c = 11.484 (8) Å
 β = 101.92 (4)°
V = 2082 (2) Å³
Z = 4

D_x = 1.322 Mg m⁻³
 Cu *K*α radiation
 Cell parameters from 25 reflections
 θ = 9.6–18.2°
 μ = 0.735 mm⁻¹
T = 293 (2) K
 Prism, colourless
 0.36 × 0.20 × 0.13 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
 $\theta/2\theta$ scans
 6167 measured reflections
 3711 independent reflections
 2276 reflections with *I* > 2σ(*I*)
R_{int} = 0.043

θ_{\max} = 66.95°
h = -11 → 10
k = -20 → 23
l = 0 → 13
 3 standard reflections
 frequency: 120 min
 intensity decay: 2%

Refinement

Refinement on *F*²
R [*F*² > 2σ(*F*²)] = 0.050
wR (*F*²) = 0.120
S = 1.078
 3711 reflections
 282 parameters
 H atoms constrained

$w = 1/[\sigma^2(F_o^2) + (0.0724P)^2 + 0.164P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = -0.013$
 $\Delta\rho_{\max} = 0.21 \text{ e \AA}^{-3}$
 $\Delta\rho_{\min} = -0.19 \text{ e \AA}^{-3}$
 Extinction correction: *SHELXL93* (Sheldrick, 1993)
 Extinction coefficient: 0.0026 (4)

Table 1

Selected geometric parameters (Å, °) for (III).

C1–O9	1.212 (3)	C4–O5	1.438 (3)
C1–N2	1.361 (3)	O5–N6	1.452 (2)
C1–C4	1.548 (3)	N6–C7	1.474 (3)
N2–C10	1.408 (3)	C7–C8	1.520 (3)
N2–C3	1.475 (3)	C4–C8	1.527 (3)
C3–C4	1.532 (3)		
N2–C1–C4	90.9 (2)	N2–C3–C4	87.4 (2)
C1–N2–C3	95.5 (2)	C1–C4–C3	86.0 (2)
O9–C1–N2–C10	15.1 (4)	O5–C4–C8–C7	11.2 (2)
N2–C3–C4–O5	120.4 (2)	C3–N2–C10–C11	5.8 (4)
N2–C3–C4–C8	-115.1 (2)	C1–N2–C10–C15	-10.5 (4)
C8–C4–O5–N6	13.5 (2)	C12–C13–O16–C17	-22.1 (5)
C4–O5–N6–C26	91.6 (2)	C8–C7–C18–O19	-12.7 (3)
C4–O5–N6–C7	-33.3 (2)	O19–C18–C20–C21	0.9 (4)
O5–N6–C7–C8	39.5 (2)	O5–N6–C26–C27	-165.0 (2)
N6–C7–C8–C4	-31.3 (2)		

Compound (IV)

Crystal data

C₂₂H₂₆N₂O₂
M_r = 350.45
 Triclinic, *P*1̄
a = 6.272 (2) Å
b = 10.687 (3) Å
c = 15.327 (4) Å
 α = 103.39 (2)°
 β = 87.79 (3)°
 γ = 95.62 (2)°
V = 994.5 (5) Å³
Z = 2
D_x = 1.170 Mg m⁻³
 Cu *K*α radiation
 Cell parameters from 25 reflections
 θ = 9.2–19.1°
 μ = 0.593 mm⁻¹
T = 293 (2) K
 Prism, colourless
 0.20 × 0.20 × 0.06 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
 $\theta/2\theta$ scans
 7202 measured reflections
 3554 independent reflections
 1374 reflections with *I* > 2σ(*I*)
R_{int} = 0.096

θ_{\max} = 67.14°
h = -7 → 7
k = -12 → 12
l = -18 → 18
 3 standard reflections
 frequency: 120 min
 intensity decay: 6%

Refinement

Refinement on *F*²
R [*F*² > 2σ(*F*²)] = 0.083
wR (*F*²) = 0.218
S = 1.167
 3548 reflections
 236 parameters
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.1516P)^2]$ where
 $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.005$
 $\Delta\rho_{\max} = 0.23 \text{ e \AA}^{-3}$
 $\Delta\rho_{\min} = -0.27 \text{ e \AA}^{-3}$
 Extinction correction: *SHELXL93* (Sheldrick, 1993)
 Extinction coefficient: 0.0005 (9)

Table 2

Selected geometric parameters (Å, °) for (IV).

C1–O9	1.207 (6)	C4–O5	1.418 (5)
C1–N2	1.370 (6)	C4–C8	1.500 (7)
C1–C4	1.527 (7)	O5–N6	1.465 (5)
N2–C10	1.388 (6)	N6–C7	1.485 (6)
N2–C3	1.473 (6)	C7–C8	1.528 (6)
C3–C4	1.537 (6)		
N2–C1–C4	92.1 (4)	N2–C3–C4	87.9 (4)
C1–N2–C3	94.0 (4)	C1–C4–C3	85.5 (4)
O9–C1–N2–C10	8.9 (11)	O5–N6–C7–C8	-34.9 (5)
N2–C3–C4–O5	121.0 (5)	N6–C7–C8–C4	37.7 (5)
N2–C3–C4–C8	-112.0 (5)	C3–N2–C10–C11	4.9 (8)
C8–C4–O5–N6	5.0 (5)	C1–N2–C10–C15	-3.3 (9)
C4–O5–N6–C23	146.3 (4)	C8–C7–C17–C18	-65.7 (7)
C4–O5–N6–C7	19.6 (5)	O5–N6–C23–C24	-178.1 (4)

The coordinates of the methyl H atoms on C17 in (III) were refined isotropically. All other H atoms were treated as riding.

For both compounds, data collection: *CAD-4 Software* (Enraf–Nonius, 1987); cell refinement: *CAD-4 Software*; data reduction: *NONIUS* (Riche, 1989); program(s) used to solve structure: *SHELXS86* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993); molecular graphics: *R3M* (Riche, 1983) and *ORTEP* (Johnson, 1965).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GS1071). Services for accessing these data are described at the back of the journal.

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