Acta Crystallographica Section C
**Crystal Structure Communications**
ISSN 0108-2701

# The *endo* and *exo* isomers of 1-(4-isopropyl-3,5-dioxa-8-aza-bicyclo[5.1.0]octan-8-yl)pyrrolidine-2,5-dione

**Anil Kumar Tripathi, Clemens Bruhn, Susanne Flock and Herbert Frauenrath***

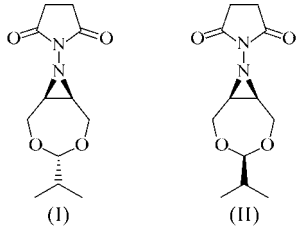
Institute for Chemistry, University of Kassel, Heinrich-Plett-Straße 40, 34132 Kassel, Germany
Correspondence e-mail: frauenrath@uni-kassel.de

Received 12 October 2005
Accepted 27 October 2005
Online 19 November 2005

The crystal structures of the title compounds, $C_{12}H_{18}N_2O_4$, have been determined in order to establish the relative configurations. In both structures, the isopropyl substituent strongly prefers the quasi-equatorial position. Therefore, the *exo* isomer adopts a dioxepanoaziridine pattern of a chair–chair (CC) conformation and the *endo* isomer a boat–chair (BC) conformation.

## Comment

Fused aziridines, *e.g.* *N*-arenesulfonyl-protected 1,3-dioxepanoaziridines, are of interest as potent antihypoglycaemic agents (Dumić *et al.*, 1993, 1995; Oresić *et al.*, 2001; Filić *et al.*, 1996). Such compounds have been prepared from *trans*-acetylaminochlorodioxepanes by ring-closure dehydrohalogenation and subsequent *N*-protection with arenesulfonyl chlorides. Direct aziridination of 4,7-dihydro-1,3-dioxepines using sulfonyl azides as the nitrogen source failed (Dumić *et al.*, 1993). The crystal structures of these compounds have been thoroughly studied in order to develop quantitative structure–property and structure–activity relationship models.



(I) (II)

Recently, we have developed a new aziridination procedure using *N*-aminosuccinimide as the nitrogen source and iodosylbenzene diacetate as the oxidizing agent, which directly leads to N-amino-protected fused dioxepanoaziridines (Flock *et al.*, 2005). Thus, a diastereomeric mixture of the title compounds, (I) and (II) (Figs. 1 and 2), was obtained from 2-isopropyl-4,7-dihydro-1,3-dioxepin, *N*-aminosuccinimide and iodosylbenzene diacetate. The relative configurations of these compounds are of interest with respect to their reactivity and stability.

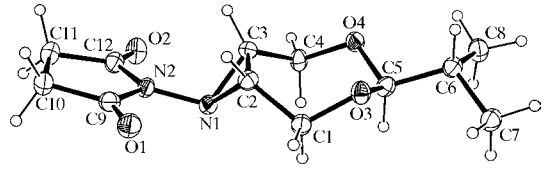



**Figure 1**
The *exo* isomer, (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small circles of arbitrary radii.

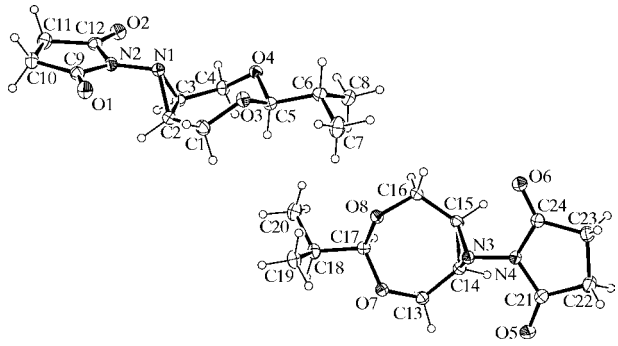



**Figure 2**
The asymmetric unit of the *endo* isomer, (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small circles of arbitrary radii.

Separation of the diastereomeric mixture by column chromatography afforded (I) and (II) as colourless solids. However, determination of the relative configurations using nuclear Overhauser experiments failed because of the flexibility of the dioxepinane moiety in solution. After recrystallization from diethyl ether–acetone and evaporation from acetone, respectively, (I) and (II) crystallized as well formed plate-like colourless crystals.

The *exo* isomer, (I), crystallizes in the non-centrosymmetric space group $P2_1$ with $Z' = 1$, but the absolute configuration could not be determined. The *endo* isomer, (II), crystallizes in space group $P2_1/c$ with $Z' = 2$. The difference between the two independent molecules in (II) lies in the conformation of the isopropyl substituent around the C5—C6 and C17—C18 bonds (Fig. 2). Neither isomer shows any strong intermolecular interactions.

In both isomers, the isopropyl substituent at the acetalic unit was found in a quasi-equatorial position. Analysis of the *endo* isomer, (II), reveals that the dioxepanoaziridine moiety adopts a boat–chair (BC) conformation, while for the *exo* isomer, (I), the preferred conformation in the solid state is the chair–chair (CC) conformation. The substituent on the aziridine N atom occupies, in both cases, the *anti* position with respect to the dioxepane ring, which supports previous results found for 8-sulfonyl-protected bicyclooctane derivatives (Dumić *et al.*, 1995).

 DOI: 10.1107/S0108270105035134  

## Experimental

Under a nitrogen atmosphere, small portions of iodosyl benzene diacetate (3.865 g, 12 mmol) were added at room temperature to a solution of 2-isopropyl-4,7-dihydro-1,3-dioxepine (2.560 g, 18 mmol) and *N*-aminosuccinimide (1.141 g, 10 mmol) in dry acetonitrile (30 ml) over a period of 2.5 h. After stirring for a further 15 h, the reaction mixture was evaporated under reduced pressure. The oily residue was purified by column chromatography (silica gel, cyclohexane 100 → ethyl acetate–cyclohexane 80:20) to give the separated isomers, (I) and (II), as colourless solids (total yield 1.602 g, 6.3 mmol, 63%). Single crystals of isomer (I) (*exo*) for X-ray diffraction studies were obtained by slow evaporation from acetone (m.p. 413–415 K). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.90 [*d*, 6H, *J* = 6.84 Hz, CH(C*H*$_3$)$_2$], 1.84 [*m*, 1H, C*H*(CH$_3$)$_2$], 2.63 [*s*, 4H, CO–(CH$_2$)$_2$–CO], 2.82 (*m*, 2H, CH–N), 3.84 (*m*, 2H, O–CH$_2$), 4.12 (*d*, 1H, *J* = 6.84 Hz, O–CH*R*–O), 4.56 (*m*, 2H, O–CH$_2$); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 172.45 (2C, CO), 112.42 (1C, O–CH*R*–O), 66.64 (2C, O–CH$_2$), 47.46 (2C, CH–N), 31.56 [1C, *C*H(CH$_3$)$_2$], 26.46 [2C, CO–(*C*H$_2$)$_2$–CO], 17.74 [2C, CH(*C*H$_3$)$_2$]. Single crystals of isomer (II) (*endo*) for X-ray diffraction studies were obtained by recrystallization from diethyl ether–acetone (10:1 *v*/*v*) at 253 K (m.p. 415–417 K). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.88 [*d*, 6H, *J* = 6.88 Hz, CH(C*H*$_3$)$_2$], 1.83 [*m*, 1H, C*H*(CH$_3$)$_2$], 2.62 [*s*, 4H, CO–(CH$_2$)$_2$–CO], 2.71 (*m*, 2H, CH–N), 3.94 (*d*, 1H, *J* = 6.83 Hz, O–CH*R*–O), 3.98 (*m*, 2H, O–CH$_2$), 4.62 (*m*, 2H, O–CH$_2$); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 172.70 (2C, CO), 111.28 (1C, O–CH*R*–O), 65.36 (2C, O–*C*H$_2$), 48.15 (2C, CH–N), 32.23 [1C, *C*H(CH$_3$)$_2$], 26.60 [2C, CO–(*C*H$_2$)$_2$–CO], 17.72 [2C, CH(*C*H$_3$)$_2$]. APCI–MS, mixture of isomers: *m*/*z* (%) = 255 (100) [*M* + H]$^+$; 287 (21) [*M* + H + MeOH]$^+$.

### Isomer (I)

*Crystal data*

| | |
|---|---|
| $C_{12}H_{18}N_2O_4$ | $D_x$ = 1.363 Mg m$^{-3}$ |
| $M_r$ = 254.28 | Mo $K\alpha$ radiation |
| Monoclinic, $P2_1$ | Cell parameters from 7302 reflections |
| $a$ = 6.1449 (11) Å | $\theta$ = 1.6–26.0° |
| $b$ = 7.8343 (10) Å | $\mu$ = 0.10 mm$^{-1}$ |
| $c$ = 13.080 (3) Å | $T$ = 153 (2) K |
| $\beta$ = 100.250 (15)° | Plate, colourless |
| $V$ = 619.6 (2) Å$^3$ | 0.47 × 0.41 × 0.05 mm |
| $Z$ = 2 | |

*Data collection*

| | |
|---|---|
| Stoe IPDS-2 diffractometer | 998 reflections with $I > 2\sigma(I)$ |
| Rotation scans | $R_{int}$ = 0.057 |
| Absorption correction: integration (*X-RED32*; Stoe & Cie, 2004) | $\theta_{max}$ = 25.5° |
| $T_{min}$ = 0.954, $T_{max}$ = 0.995 | $h = -7 \rightarrow 7$ |
| 8393 measured reflections | $k = -9 \rightarrow 9$ |
| 1244 independent reflections | $l = -15 \rightarrow 15$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | H-atom parameters constrained |
| $R[F^2 > 2\sigma(F^2)]$ = 0.036 | $w = 1/[\sigma^2(F_o^2) + (0.044P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $wR(F^2)$ = 0.076 | $(\Delta/\sigma)_{max}$ = 0.004 |
| $S$ = 1.02 | $\Delta\rho_{max}$ = 0.14 e Å$^{-3}$ |
| 1244 reflections | $\Delta\rho_{min}$ = −0.21 e Å$^{-3}$ |
| 165 parameters | |

### Isomer (II)

*Crystal data*

| | |
|---|---|
| $C_{12}H_{18}N_2O_4$ | $D_x$ = 1.330 Mg m$^{-3}$ |
| $M_r$ = 254.28 | Mo $K\alpha$ radiation |
| Monoclinic, $P2_1/c$ | Cell parameters from 10318 reflections |
| $a$ = 24.470 (3) Å | $\theta$ = 1.7–25.6° |
| $b$ = 8.8444 (8) Å | $\mu$ = 0.10 mm$^{-1}$ |
| $c$ = 11.8252 (14) Å | $T$ = 153 (2) K |
| $\beta$ = 97.119 (9)° | Plate, colourless |
| $V$ = 2539.6 (5) Å$^3$ | 0.66 × 0.65 × 0.25 mm |
| $Z$ = 8 | |

*Data collection*

| | |
|---|---|
| Stoe IPDS-2 diffractometer | 2623 reflections with $I > 2\sigma(I)$ |
| Rotation scans | $R_{int}$ = 0.033 |
| Absorption correction: integration (*X-RED32*; Stoe & Cie, 2004) | $\theta_{max}$ = 25.0° |
| $T_{min}$ = 0.914, $T_{max}$ = 0.972 | $h = -29 \rightarrow 29$ |
| 18062 measured reflections | $k = -10 \rightarrow 10$ |
| 4465 independent reflections | $l = -13 \rightarrow 14$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | $w = 1/[\sigma^2(F_o^2) + (0.0484P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $R[F^2 > 2\sigma(F^2)]$ = 0.031 | $(\Delta/\sigma)_{max} < 0.001$ |
| $wR(F^2)$ = 0.084 | $\Delta\rho_{max}$ = 0.21 e Å$^{-3}$ |
| $S$ = 0.90 | $\Delta\rho_{min}$ = −0.15 e Å$^{-3}$ |
| 4465 reflections | Extinction correction: *SHELXL97* (Sheldrick, 1997) |
| 330 parameters | Extinction coefficient: 0.0028 (4) |
| H-atom parameters constrained | |

H atoms were treated as riding, with C—H distances in the range 0.98–1.00 Å and $U_{iso}$(H) = 1.2$U_{eq}$(C). The Friedel-equivalent reflections were merged.

For both compounds, data collection: *X-AREA* (Stoe & Cie, 2004); cell refinement: *X-AREA*; data reduction: *X-RED32* (Stoe & Cie, 2004); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *PLATON* (Spek, 2003).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD1417). Services for accessing these data are described at the back of the journal.

## References

Dumić, M., Filić, D., Vinković, M. & Jamnicky, B. (1993). *Tetrahedron Lett.* **34**, 3639–3642.
Dumić, M., Vinković, M., Filić, D., Jamnicky, B., Eškinja, M. & Kamenar, B. J. (1995). *Med. Chem.* **38**, 3034–3042.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Filić, D., Vinković, M., Jamnicky, B. & Dumić, M. (1996). *Croat. Chem. Acta*, **69**, 631–641.
Flock, S., Frauenrath, H. & Tripathi, A. (2005). In preparation.
Oresić, M., Filić, D., Prugovečki, B., Vinković, M. & Dumić, M. (2001). *Croat. Chem. Acta*, **74**, 667–682.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Stoe & Cie (2004). *X-AREA* (Version 1.211) and *X-RED32* (Version 1.06). Stoe & Cie, Darmstadt, Germany.