# Evidence for the *exo*-Anomeric Stereoelectronic Effect in Cyclic Orthoester Aminals from X-Ray Structural Data. Crystal Structures of Three 2-Amino-1,3-oxazolidin-4-one Derivatives

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The crystal structures of three 2-amino-1,3-oxazolidin-4-one derivatives are reported. 5,5-Dimethyl-2-dimethylamino-3-phenyloxazolidin-4-one crystallizes in the space group $P2_1/c$ with $a = 15.540(3)$, $b = 7.016(2)$, $c = 12.491(4)$ Å, $\beta = 105.6(2)°$; 1 342 reflections with $I \geqslant 2.5 \, \sigma(I)$ were used in the refinement. 4-Benzyl-2,2-dimethyl-1-oxa-4,6-diazaspiro[4,5]decan-3-one crystallizes in the space group $P2_1/c$ with $a = 15.188(6)$, $b = 12.074(2)$, $c = 8.468(1)$ Å, $\beta = 100.03(2)°$; 2 068 reflections with $I \geqslant 3\sigma(I)$ were used in the refinement. 4-Benzyl-2,2-dimethyl-1-oxa-4,6-diazaspiro[4,6]undecan-3-one crystallizes in the space group $P2_1/c$ with $a = 9.460(5)$, $b = 20.192(6)$, $c = 9.012(3)$ Å, $\beta = 110.66(4)°$; 1 873 reflections with $I \geqslant 3\sigma(I)$ were used in the refinement. The analysis of bond distances of the three structures has shown that *exo*-cyclic C–N bonds (*exo* with respect to the oxazolidinone ring) are significantly shorter than the standard $C(sp^3)$–$N(sp^3)$ distance by 0.050 Å on average. This could be the main factor determining the stability of the three cyclic orthoester aminals, the stabilization being attributable to an *exo*-anomeric effect involving the interaction between the nitrogen $sp^3$-like lone pair, in an antiperiplanar orientation, and the $\sigma^*$ orbital of the *endo* C–O bond.

5,5-Dimethyl-2-dimethylamino-3-phenyloxazolidin-4-one (1) is obtained upon base promoted cyclocondensation of *N*-phenyl-2-bromo-2-methylpropanamide onto the carbonyl group of



(1)

(2)



(3)
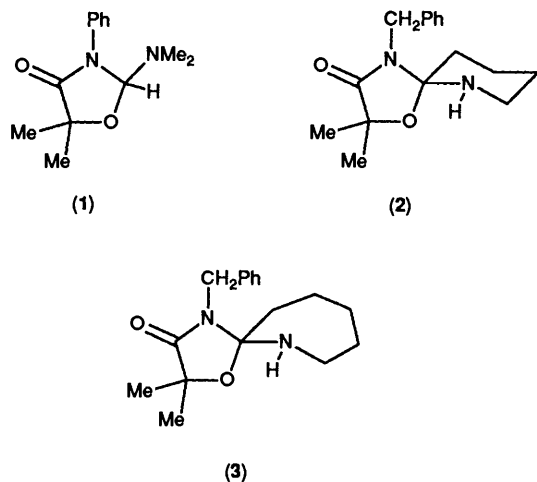
the dipolar aprotic solvent *N,N*-dimethylformamide (DMF).[1] Analogous monocyclic aminals were also obtained from 2-bromoamides and DMF or other amide partners.[2,3] Accordingly, base promoted cyclocondensation of 2-bromoisobutyramides with common-ring lactams afforded the spiranic 4-benzyl-2,2-dimethyl-1-oxa-4,6-diazaspiro[4,5]decan-3-one (2) (from piperidin-2-one) and 4-benzyl-2,2-dimethyl-1-oxa-4,6-diazaspiro[4,6]undecan-3-one (3) (from perhydroazepin-2-one) as crystals.[4] The more strained spiro derivative from pyrrolidin-2-one was obtained in lower yield as an oil[4] and could not be submitted to X-ray analysis.

These cyclic orthoester aminals carry the endocyclic nitrogen

as part of an amido group. While non-cyclic orthoester aminals are known to be barely stable and liable to decompose to orthoamides and amide acetals (which may be further hydrolized by environmental water[5]), the cyclic orthoester aminals studied here display a remarkable stability. On the basis of their X-ray determined structural data the stability is largely attributable to an *exo*-anomeric effect.[6]

## Results and Discussion

Crystal data, experimental details and solution and refinement of the structures are reported in Table 1 and final co-ordinates in Tables 2–4. Bond distances and angles and a selection of torsion angles are given in Tables 5–8, and ORTEP[7] views of the molecules are shown in Figures 1–3.† The oxazolidinone rings in the three compounds are not perfectly planar and their conformations can be described by means of puckering[8] and asymmetry[9,10] parameters given in Table 8. The different conformations found in the solid state are indicative of the flexibility of the five-membered rings. The crystal packing of compound (1) is characterized by a C–H $\cdots$ O intermolecular short contact which, following the considerations of Taylor and Kennard,[11] may be considered to be a weak hydrogen bond. This hydrogen atom is bonded to the C(5) carbon atom which, in turn, is linked to three more electronegative atoms [N(1), N(2), and O(2)]; its consequent acidic character makes it an ideal candidate for involvement in hydrogen bond formation. Parameters for the C–H $\cdots$ O interaction are: C(5)–H(5), 1.00(2); C(5) $\cdots$ O(1) $(x, \frac{1}{2} - y, \frac{1}{2} + z)$, 3.480(3); H(5) $\cdots$ O(1),

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† Tables of thermal parameters and hydrogen atom co-ordinates have been deposited at the Cambridge Crystallographic Data Centre. For details, see 'Instructions for Authors (1990),' *J. Chem. Soc., Perkin Trans. 2*, in the January issue.

**Table 1.** Crystal data, solution and refinement.[a]

| Compound | (1) | (2) | (3) |
|---|---|---|---|
| Formula | $C_{13}H_{18}N_2O_2$ | $C_{16}H_{22}N_2O_2$ | $C_{17}H_{24}N_2O_2$ |
| $M$ | 234.30 | 274.36 | 288.39 |
| Space group | $P2_1/c$ | $P2_1/c$ | $P2_1/c$ |
| Cell parameters | | | |
| $a$/Å | 15.540(3) | 15.188(6) | 9.460(5) |
| $b$/Å | 7.016(2) | 12.074(2) | 20.192(6) |
| $c$/Å | 12.491(4) | 8.468(1) | 9.012(3) |
| $\beta$/° | 105.6(2) | 100.03(2) | 110.66(4) |
| $V$/Å$^3$ | 1 312(1) | 1 529.1(7) | 1 611(1) |
| $Z$ | 4 | 4 | 4 |
| $D_{calc}$/Mg m$^{-3}$ | 1.19 | 1.19 | 1.19 |
| $F(000)$ | 504 | 592 | 624 |
| $\mu$(Mo-K$_\alpha$)/cm$^{-1}$ | 0.8 | 0.7 | 0.7 |
| Crystal size/mm$^3$ | 0.31 × 0.19 × 0.52 | 0.36 × 0.40 × 0.52 | 0.26 × 0.29 × 0.55 |
| No. of independent reflections | 2 845 | 3 334 | 3 720 |
| Observed [$I \geqslant n\sigma(I)$] | 1 342 ($n$ = 2.5) | 2 068 ($n$ = 3) | 1 843 ($n$ = 3) |
| *Refinement* | | | |
| Hydrogen atoms | isotropic | isotropic | isotropic |
| Non-hydrogen atoms | anisotropic | anisotropic | anisotropic |
| $R_1$, $R_2$ | 0.041, 0.045 | 0.040, 0.052 | 0.037, 0.045 |
| Max. shift/error | 0.06 | 0.03 | 0.07 |
| Largest $\Delta F$ peak | 0.131 | 0.115 | 0.106 |
| $S$ | 1.4 | 1.6 | 1.4 |
| No. of variables | 226 | 269 | 286 |

[a] Data collection instrument: Enraf–Nonius CAD-4; $T$ 295 K; radiation Mo-K$_\alpha$ ($\lambda$ = 0.710 69) graphite monochromated; $\omega/2\ \theta$ scan; 25 centring reflections in the 10–14° $\theta$ range; 3 monitored reflections every 2 h; $\theta_{min} - \theta_{max}$ = 2–27°; solution by MULTAN82;[24] full-matrix refinement; $R_1 = \Sigma|\Delta F_0|/\Sigma|F_0|$, $R_2 = [\Sigma w(\Delta F_0)^2/\Sigma w(F_0)^2]^{\frac{1}{2}}$; weights $w = 4F_0^2/[\sigma^2(F_0) + p(F_0^2)^2]$, $p$ = 0.04, 0.05, 0.04 for compounds (1), (2), and (3) respectively. All calculations performed by the CAD4 SDP[25] and PARST[26] systems of programs; scattering factors from ref. 23.

**Table 2.** Positional (× 10$^4$) parameters with esds in parentheses for compound (1).

| Atom | $x$ | $y$ | $z$ |
|---|---|---|---|
| O(1) | −2 793(1) | 2 071(3) | −1 338(1) |
| O(2) | −3 728(1) | 4 970(2) | 313(1) |
| N(1) | −2 405(1) | 3 571(3) | 369(1) |
| N(2) | −2 392(1) | 6 417(3) | 1 394(1) |
| C(1) | −2 971(1) | 2 990(3) | −601(2) |
| C(2) | −3 899(1) | 3 654(3) | −591(2) |
| C(3) | −4 419(2) | 1 945(4) | −345(2) |
| C(4) | −4 396(2) | 4 644(4) | −1 646(2) |
| C(5) | −2 850(1) | 4 688(3) | 1 039(2) |
| C(6) | −2 293(2) | 7 656(4) | 505(2) |
| C(7) | −2 739(2) | 7 417(4) | 2 205(2) |
| C(8) | −1 495(1) | 2 970(3) | 783(2) |
| C(9) | −942(1) | 2 985(4) | 90(2) |
| C(10) | −72(2) | 2 338(4) | 496(2) |
| C(11) | 238(2) | 1 707(4) | 1 562(2) |
| C(12) | −313(2) | 1 722(4) | 2 249(2) |
| C(13) | −1 184(1) | 2 364(3) | 1 863(2) |

**Table 3.** Positional (× 10$^4$) parameters with esds in parentheses for compound (2).

| Atom | $x$ | $y$ | $z$ |
|---|---|---|---|
| O(1) | 2 611.6(8) | −1 727.9(9) | −3 453(1) |
| O(2) | 3 686.0(7) | −253.7(9) | −91(1) |
| N(1) | 2 289.2(8) | −633(1) | −1 414(1) |
| N(2) | 2 526.4(9) | −681(1) | 1 401(1) |
| C(1) | 2 839(1) | −1 166(1) | −2 244(2) |
| C(2) | 3 788(1) | −923(1) | −1 447(2) |
| C(3) | 4 278(1) | −1 986(2) | −870(2) |
| C(4) | 4 272(1) | −261(2) | −2 542(2) |
| C(5) | 2 764(1) | −123(1) | 52(2) |
| C(6) | 2 568(1) | 1 107(1) | 151(2) |
| C(7) | 3 024(1) | 1 600(1) | 1 732(2) |
| C(8) | 2 758(1) | 959(2) | 3 104(2) |
| C(9) | 2 980(1) | −254(2) | 2 964(2) |
| C(10) | 1 323(1) | −722(1) | −1 776(2) |
| C(11) | 843(1) | 247(1) | −2 663(2) |
| C(12) | 1 206(1) | 854(1) | −3 766(2) |
| C(13) | 725(1) | 1 692(2) | −4 634(2) |
| C(14) | −126(1) | 1 927(2) | −4 410(2) |
| C(15) | −497(1) | 1 335(2) | −3 318(3) |
| C(16) | −17(1) | 501(2) | −2 247(2) |

2.49(1) Å; and C(5)–H(5)··· O(1), 169(1)°. The two spiro-heterocycles form crystals in which the molecules are linked in chains by means of rather long N–H··· O hydrogen bonds between the N–H group of the piperidine or azepine rings and the O(1) amidic oxygen of the oxazolidinone ring.

The hydrogen bond parameters are: N(2)–H(N2), 0.87(1); N(2)··· O(1) ($x$, $-\frac{1}{2} - y$, $\frac{1}{2} + z$), 3.133(2); H(N2)··· O(1), 2.28(1) Å; and N(2)–H(N2)··· O(1), 164(1)° for compound (2) and N(2)–H(N2), 0.82(2); N(2)··· O(1) ($x$, $\frac{1}{2} - y$, $\frac{1}{2}$ + $z$), 3.126(2); H(N2)··· O(1), 2.36(2) Å; and N(2)–H(N2)··· O(1), 156(2)° for compound (3).

Table 9 reports the relevant bond distances for the four 2-amino-1,3-oxazolidin-4-one derivatives of known molecular

structure, *i.e.* compounds (1)–(3) obtained from a 2-bromo-isobutyramide and a related self cyclocondensation product of a 2-bromopropanamide.[12] The standard bond distances for the molecular fragment of interest are reported for comparison.[13] The geometries of the four structures are quite similar. In particular, distances C(1)–N(1), C(5)–N(1) and C(1)–O(1) [on average 1.348(5), 1.457(7), and 1.219(7) Å] fit fairly well those reported for the amide group in $\alpha$-lactams and also the two ring C–O distances C(5)–O(2) and C(2)–O(2) [on average 1.440(7) and 1.429(3) Å] correspond to the accepted value of 1.426 Å in

**Table 4.** Positional ($\times 10^4$) parameters with esds in parentheses for compound (3).

| Atom | x | y | z |
|---|---|---|---|
| O(1) | 5 443(1) | 2 132.2(7) | 225(1) |
| O(2) | 5 593(1) | 838.9(6) | 2 848(1) |
| N(1) | 4 033(1) | 1 669.9(7) | 1 571(1) |
| N(2) | 4 192(1) | 1 445.3(7) | 4 159(2) |
| C(1) | 5 246(2) | 1 721(1) | 1 133(2) |
| C(2) | 6 331(2) | 1 178(1) | 1 940(2) |
| C(3) | 6 560(2) | 705(1) | 751(2) |
| C(4) | 7 816(2) | 1 454(1) | 3 027(3) |
| C(5) | 4 176(2) | 1 142(1) | 2 734(2) |
| C(6) | 3 004(2) | 593(1) | 2 184(2) |
| C(7) | 1 592(2) | 636(1) | 2 608(2) |
| C(8) | 1 831(2) | 398(1) | 4 280(2) |
| C(9) | 2 783(2) | 850(1) | 5 589(2) |
| C(10) | 4 305(2) | 1 022(1) | 5 504(2) |
| C(11) | 2 806(2) | 2 151(1) | 1 108(2) |
| C(12) | 1 368(2) | 1 904(1) | −113(2) |
| C(13) | 1 375(2) | 1 515(1) | −1 359(2) |
| C(14) | 57(2) | 1 287(1) | −2 472(2) |
| C(15) | −1 300(2) | 1 455(1) | −2 368(3) |
| C(16) | −1 341(2) | 1 853(1) | −1 159(3) |
| C(17) | −15(2) | 2 077(1) | −21(2) |

**Table 5.** Bond distances/Å, bond angles/° and a selection of torsion angles/°, with esds in parentheses, for compound (1).

Bond distances

| O(1)–C(1) | 1.215(3) | C(1)–C(2) | 1.519(2) |
|---|---|---|---|
| O(2)–C(2) | 1.427(3) | C(2)–C(3) | 1.523(4) |
| O(2)–C(5) | 1.434(3) | C(2)–C(4) | 1.506(4) |
| N(1)–C(1) | 1.354(4) | C(8)–C(9) | 1.374(4) |
| N(1)–C(5) | 1.450(3) | C(8)–C(13) | 1.372(4) |
| N(1)–C(8) | 1.432(3) | C(9)–C(10) | 1.386(4) |
| N(2)–C(5) | 1.416(3) | C(10)–C(11) | 1.362(4) |
| N(2)–C(6) | 1.451(3) | C(11)–C(12) | 1.366(5) |
| N(2)–C(7) | 1.450(4) | C(12)–C(13) | 1.384(4) |

Bond angles

| C(2)–O(2)–C(5) | 110.8(2) | C(1)–C(2)–C(4) | 113.5(3) |
|---|---|---|---|
| C(1)–N(1)–C(5) | 112.5(3) | C(3)–C(2)–C(4) | 111.4(3) |
| C(1)–N(1)–C(8) | 125.1(2) | O(2)–C(5)–N(1) | 103.3(2) |
| C(5)–N(1)–C(8) | 121.9(2) | O(2)–C(5)–N(2) | 113.1(2) |
| C(5)–N(2)–C(6) | 114.9(2) | N(1)–C(5)–N(2) | 111.5(3) |
| C(5)–N(2)–C(7) | 112.5(3) | N(1)–C(8)–C(9) | 119.6(3) |
| C(6)–N(2)–C(7) | 112.4(2) | N(1)–C(8)–C(13) | 119.9(4) |
| O(1)–C(1)–N(1) | 127.7(4) | C(9)–C(8)–C(13) | 120.5(4) |
| O(1)–C(1)–C(2) | 125.4(3) | C(8)–C(9)–C(10) | 118.7(3) |
| N(1)–C(1)–C(2) | 106.9(2) | C(9)–C(10)–C(11) | 121.2(4) |
| O(2)–C(2)–C(1) | 103.3(3) | C(10)–C(11)–C(12) | 119.7(4) |
| O(2)–C(2)–C(3) | 110.2(2) | C(11)–C(12)–C(13) | 120.2(3) |
| O(2)–C(2)–C(4) | 109.7(2) | C(8)–C(13)–C(12) | 119.7(3) |
| C(1)–C(2)–C(3) | 108.5(2) | | |

Torsion angles

| O(2)–C(5)–N(2)–C(6) | −57.1(4) | H(5)–C(5)–N(2)–C(6) | −176(1) |
|---|---|---|---|
| O(2)–C(5)–N(2)–C(7) | 73.3(4) | H(5)–C(5)–N(2)–C(7) | −46(1) |
| O(2)–C(5)–N(1)–C(8) | 179.8(3) | C(2)–O(2)–C(5)–N(2) | 137.5(3) |
| N(1)–C(5)–N(2)–C(6) | 58.8(4) | C(2)–O(2)–C(5)–N(1) | 16.9(4) |
| N(1)–C(5)–N(2)–C(7) | −170.9(3) | C(2)–O(2)–C(5)–H(5) | −106(1) |

**Table 6.** Bond distances/Å, bond angles/° and a selection of torsion angles/°, with esds in parentheses, for compound (2).

Bond distances

| O(1)–C(1) | 1.227(2) | C(5)–C(6) | 1.520(2) |
|---|---|---|---|
| O(2)–C(2) | 1.434(2) | C(6)–C(7) | 1.518(2) |
| O(2)–C(5) | 1.434(2) | C(7)–C(8) | 1.508(3) |
| N(1)–C(1) | 1.345(2) | C(8)–C(9) | 1.512(3) |
| N(1)–C(5) | 1.459(2) | C(10)–C(11) | 1.508(2) |
| N(1)–C(10) | 1.450(2) | C(11)–C(12) | 1.376(2) |
| N(2)–C(5) | 1.426(2) | C(11)–C(16) | 1.384(2) |
| N(2)–C(9) | 1.475(2) | C(12)–C(13) | 1.382(2) |
| C(1)–C(2) | 1.510(2) | C(13)–C(14) | 1.368(2) |
| C(2)–C(3) | 1.521(2) | C(14)–C(15) | 1.366(3) |
| C(2)–C(4) | 1.509(3) | C(15)–C(16) | 1.379(3) |

Bond angles

| C(2)–O(2)–C(5) | 111.9(1) | O(2)–C(5)–C(6) | 108.4(1) |
|---|---|---|---|
| C(1)–N(1)–C(5) | 112.7(5) | N(1)–C(5)–N(2) | 109.0(1) |
| C(1)–N(1)–C(10) | 123.5(1) | N(1)–C(5)–C(6) | 112.7(1) |
| C(5)–N(1)–C(10) | 122.9(1) | N(2)–C(5)–C(6) | 109.8(1) |
| C(5)–N(2)–C(9) | 114.2(1) | C(5)–C(6)–C(7) | 111.6(1) |
| O(1)–C(1)–N(1) | 126.2(2) | C(6)–C(7)–C(8) | 109.6(1) |
| O(1)–C(1)–C(2) | 126.1(2) | C(7)–C(8)–C(9) | 110.1(1) |
| N(1)–C(1)–C(2) | 107.7(1) | N(2)–C(9)–C(8) | 109.5(1) |
| O(2)–C(2)–C(1) | 103.9(1) | N(1)–C(10)–C(11) | 115.6(1) |
| O(2)–C(2)–C(3) | 109.5(1) | C(10)–C(11)–C(12) | 122.4(2) |
| O(2)–C(2)–C(4) | 109.0(1) | C(10)–C(11)–C(16) | 119.4(1) |
| C(1)–C(2)–C(3) | 110.8(1) | C(11)–C(12)–C(13) | 120.9(2) |
| C(1)–C(2)–C(4) | 111.0(1) | C(12)–C(13)–C(14) | 120.2(2) |
| C(3)–C(2)–C(4) | 112.4(1) | C(13)–C(14)–C(15) | 119.8(2) |
| O(2)–C(5)–N(1) | 103.1(1) | C(14)–C(15)–C(16) | 120.2(2) |
| O(2)–C(5)–N(2) | 113.8(1) | C(11)–C(16)–C(15) | 120.9(2) |

Torsion angles

| O(2)–C(5)–N(2)–H(N2) | −62(1) |
|---|---|
| O(2)–C(5)–N(2)–C(9) | 64.4(2) |
| O(2)–C(5)–N(1)–C(10) | 178.3(1) |
| N(1)–C(5)–N(2)–H(N2) | 53(1) |
| N(1)–C(5)–N(2)–C(9) | 178.8(1) |
| C(6)–C(5)–N(2)–H(N2) | 177(1) |
| C(6)–C(5)–N(2)–C(9) | −57.3(2) |
| C(2)–O(2)–C(5)–N(2) | 110.9(1) |
| C(2)–O(2)–C(5)–N(1) | −7.0(2) |
| C(2)–O(2)–C(5)–C(6) | −126.7(1) |

the ultimate reason for the stability of the orthoester aminal fragment incorporated into the oxazolidinone ring. This stabilization has to be attributed to an *exo*-anomeric interaction involving the *exo* C(5)–N(2) and *endo* C(5)–O(2) bonds, where *exo* and *endo* are referred to the oxazolidinone ring.

'Anomeric' ('*endo*-anomeric') or '*exo*-anomeric' stereoelectronic effects have been invoked[6,14,15] to describe the preference shown by the electronegative substituents to adopt the axial rather than the expected equatorial position at the anomeric C-1 carbon atom of a pyranose ring or, respectively, to explain the preferred conformation adopted by the OR group linked to the anomeric centre. While the existence of these stereoelectronic effects is well documented by X-ray and neutron diffraction data for the acetal $R_2C(OR)_2$ group present in carbohydrates and related compounds,[16–19] only a few structural results are available for anomeric effects in the case of acetal functions with one or two nitrogen atoms (the only structural example concerns the application of stereoelectronic effects to an understanding of the oxidative transformations of purines[20]). However, some theoretical and spectroscopic studies on this class of compounds have been reported. *ab initio* Calculations[21] for aminodihydroxymethane [$CH(OH)_2NH_2$] showed that stereoelectronic effects cause a shortening of the C–N bond when the nitrogen lone pair is antiperiplanar to a

dialkyl ethers. The only relevant change in bond distance concerns the exocyclic C(5)–N(2) bonds, the observed mean value of 1.425(9) Å being significantly shorter than the accepted value for the $C(sp^3)$–$N(sp^3)$ bond of 1.469(14) Å obtained as an average of 1 201 independent observations.[13] This implies a non-irrelevant strengthening of the C–N bond itself and could be

**Table 7.** Bond distances/Å, bond angles/° and a selection of torsion angles/°, with esds in parentheses, for compound (3).

Bond distances

| | | | |
|---|---|---|---|
| O(1)–C(1) | 1.225(2) | C(6)–C(7) | 1.516(3) |
| O(2)–C(2) | 1.425(2) | C(7)–C(8) | 1.521(3) |
| O(2)–C(5) | 1.444(2) | C(8)–C(9) | 1.512(2) |
| N(1)–C(1) | 1.343(2) | C(9)–C(10) | 1.509(3) |
| N(1)–C(5) | 1.467(2) | C(11)–C(12) | 1.501(2) |
| N(1)–C(11) | 1.457(2) | C(12)–C(13) | 1.373(3) |
| N(2)–C(5) | 1.418(3) | C(12)–C(17) | 1.384(3) |
| N(2)–C(10) | 1.456(3) | C(13)–C(14) | 1.375(2) |
| C(1)–C(2) | 1.503(2) | C(14)–C(15) | 1.363(3) |
| C(2)–C(3) | 1.507(3) | C(15)–C(16) | 1.365(4) |
| C(2)–C(4) | 1.507(2) | C(16)–C(17) | 1.386(2) |
| C(5)–C(6) | 1.523(2) | | |

Bond angles

| | | | |
|---|---|---|---|
| C(2)–O(2)–C(5) | 112.7(1) | N(1)–C(5)–N(2) | 107.6(1) |
| C(1)–N(1)–C(5) | 113.2(2) | N(1)–C(5)–C(6) | 115.1(2) |
| C(1)–N(1)–C(11) | 122.8(2) | N(2)–C(5)–C(6) | 112.5(2) |
| C(5)–N(1)–C(11) | 123.5(2) | C(5)–C(6)–C(7) | 118.8(2) |
| C(5)–N(2)–C(10) | 118.4(2) | C(6)–C(7)–C(8) | 113.3(2) |
| O(1)–C(1)–N(1) | 126.6(2) | C(7)–C(8)–C(9) | 115.0(2) |
| O(1)–C(1)–C(2) | 125.4(2) | C(8)–C(9)–C(10) | 114.6(2) |
| N(1)–C(1)–C(2) | 108.0(2) | N(2)–C(10)–C(9) | 112.7(2) |
| O(2)–C(2)–C(1) | 103.9(2) | N(1)–C(11)–C(12) | 114.4(2) |
| O(2)–C(2)–C(3) | 109.0(2) | C(11)–C(12)–C(13) | 121.7(2) |
| O(2)–C(2)–C(4) | 109.7(2) | C(11)–C(12)–C(17) | 120.3(2) |
| C(1)–C(2)–C(3) | 111.3(2) | C(13)–C(12)–C(17) | 118.1(2) |
| C(1)–C(2)–C(4) | 111.5(2) | C(12)–C(13)–C(14) | 121.6(2) |
| C(3)–C(2)–C(4) | 111.2(2) | C(13)–C(14)–C(15) | 120.0(2) |
| O(2)–C(5)–N(1) | 102.0(2) | C(14)–C(15)–C(16) | 119.6(2) |
| O(2)–C(5)–N(2) | 113.9(2) | C(15)–C(16)–C(17) | 120.6(2) |
| O(2)–C(5)–C(6) | 105.4(2) | C(12)–C(17)–C(16) | 120.1(2) |

Torsion angles

| | |
|---|---|
| O(2)–C(5)–N(2)–H(N2) | 68(1) |
| O(2)–C(5)–N(2)–C(10) | −68.5(2) |
| O(2)–C(5)–N(1)–C(11) | −176.4(2) |
| N(1)–C(5)–N(2)–H(N2) | −44(1) |
| N(1)–C(5)–N(2)–C(10) | 179.2(2) |
| C(6)–C(5)–N(2)–H(N2) | −172(1) |
| C(6)–C(5)–N(2)–C(10) | 51.4(2) |
| C(2)–O(2)–C(5)–N(2) | −111.2(1) |
| C(2)–O(2)–C(5)–N(1) | 4.4(2) |
| C(2)–O(2)–C(5)–C(6) | 124.9(2) |
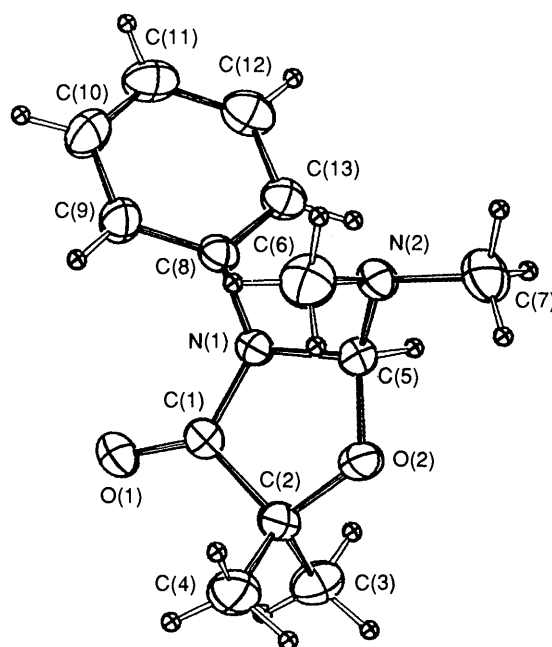


**Figure 1.** An ORTEP view of compound (1) showing the thermal ellipsoids at 40% probability.

C–O polar bond. More recently, the anomeric stabilization of 2-methylaminotetrahydropyrans has been studied by $^1$H and $^{13}$C NMR spectroscopy and a strong preference for rotamers in which the *exo*-cyclic heteroatom lone pair is antiperiplanar with respect to the *endo*-cyclic C–O bond has been demonstrated.[22] In general, several anomeric effects could take place in the three structures under examination, and these could produce opposite influences on the structural parameters. Nevertheless, the configurational and conformational characteristics of the present compounds indicate that only the *exo*-anomeric $n$-$\sigma^*$ interaction involving the overlap between the free electron pair at the N(2) atom and the antibonding $\sigma^*$ orbital of the neighbouring C–O bond is actually activated. From the Newman projections in Figure 4 and from the values of the torsion angles in Tables 5–7 it is evident that the two substituents in the N(2) atoms [C(6) and C(7) in (1), H(N2)

**Table 8.** Puckering and asymmetry parameters for the oxazolidinone rings, calculated using the atoms in the sequence N(1), C(1), C(2), O(2), C(5).

| Compound | Puckering parameters | | Asymmetry parameters | | Conformation |
|---|---|---|---|---|---|
| | $q_2$/Å | $\varphi_2$/° | $\Delta C_2$/Å | $\Delta C_s$/Å | |
| (1) | 0.170(3) | 97(1) | N(1): 0.014(1) | O(2): 0.025(2) | $^3T_4/E_4$ |
| (2) | 0.075(1) | −21(1) | C(2): 0.002 8(5) | C(5): 0.015 8(7) | $^1T_5$ |
| (3) | 0.043(3) | 147(2) | C(2): 0.006 5(6) | C(5): 0.002 1(1) | $E_5$ |

**Table 9.** Selected distances/Å and angles/° in 2-amino-1,3-oxazolidin-4-one derivatives and their comparison with tabulated values.

| Compound | C(5)–O(2) | C(5)–N(2) | C(5)–N(1) | C(1)–N(1) | C(1)–O(1) | C(2)–O(2) | Ref. |
|---|---|---|---|---|---|---|---|
| (1) | 1.434(3) | 1.416(3) | 1.450(3) | 1.354(4) | 1.215(3) | 1.427(3) | This work |
| (2) | 1.434(2) | 1.426(2) | 1.459(2) | 1.345(2) | 1.227(2) | 1.434(2) | This work |
| (3) | 1.444(2) | 1.418(3) | 1.467(2) | 1.343(2) | 1.225(2) | 1.425(2) | This work |
| | 1.45(1) | 1.44(1) | 1.45(1) | 1.35(1) | 1.21(1) | 1.43(1) | 12 |
| Average | 1.440(7) | 1.425(9) | 1.457(7) | 1.348(5) | 1.219(7) | 1.429(3) | |
| Standard values | 1.426$^a$ | 1.469$^b$ | 1.462$^c$ | 1.347$^c$ | 1.225$^c$ | 1.426$^a$ | 13 |

$^a$ In dialkyl ethers. $^b$ C(sp$^3$)–N(sp$^3$) single bond. $^c$ In α-lactams.
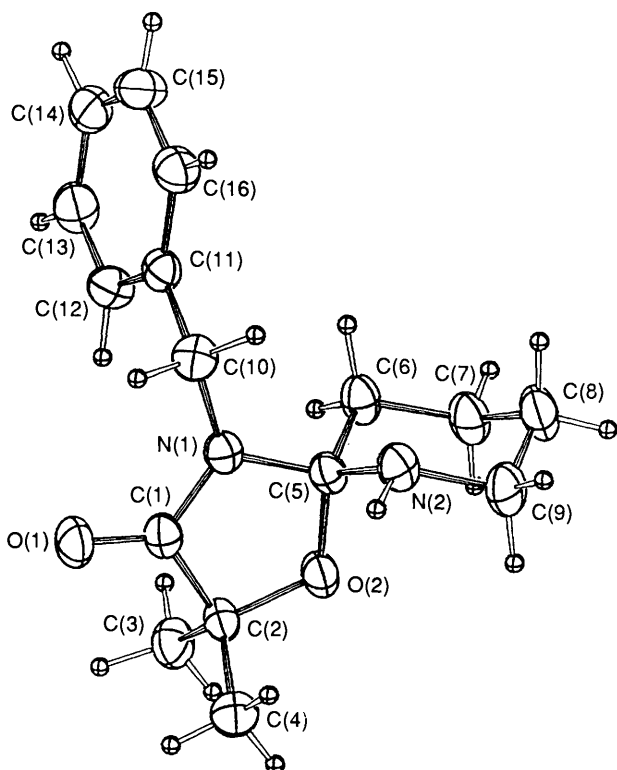
**Figure 2.** An ORTEP view of compound (2) showing the thermal ellipsoids at 40% probability.
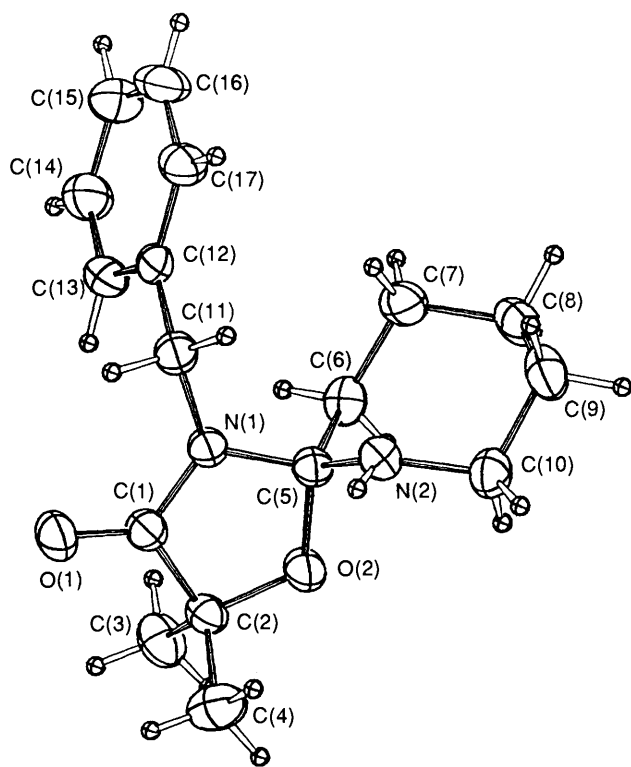


**Figure 3.** An ORTEP view of compound (3) showing the thermal ellipsoids at 40% probability.

and C(9) in (2), H(N2) and C(10) in (3)] are situated both in a synclinal (or *gauche*) conformation with respect to the C(5)–O(2) bond.

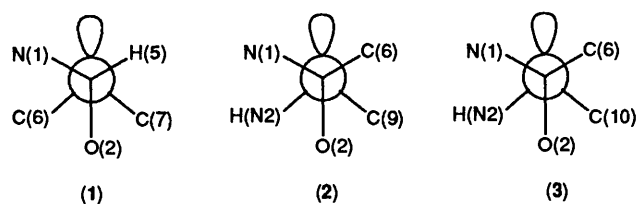The consequence is the arrangement of the sp³-like lone pair



**Figure 4.** The Newman projections along the C(5)–N(2) bonds showing the antiperiplanar arrangements of the N(2) non-bonded electron pairs with respect to the C(5)–O(2) bonds.
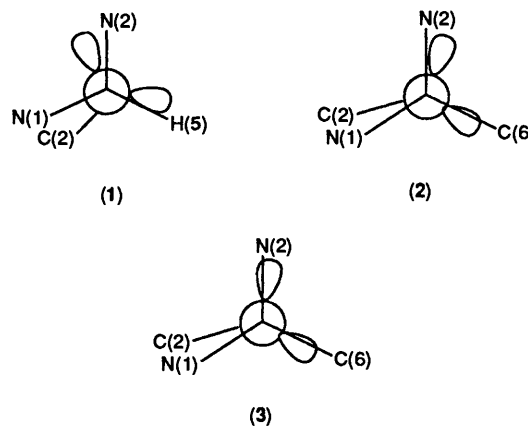


**Figure 5.** The Newman projections along the C(5)–O(2) bonds showing the eclipsed positions of the O(5) non-bonded electron pairs.

of nitrogen N(2) in an antiperiplanar orientation with respect to the C(5)–O(2) bond. This is the orbital having the most favourable alignment with which to produce the *exo*-cyclic stabilization—the '*exo*-anomeric effect'—as revealed by a significant shortening of the C(5)–N(2) bond distances (on average 1.420 Å) when compared with the C(5)–N(1) ring bond distances (on average 1.459 Å). On the other hand, no other competitive anomeric effects can be present because the lone pair of the N(1) atom is implicated in the amidic conjugation and the lone pairs of the endocyclic oxygen [O(2)] are oriented in a way which is not antiperiplanar to N(1) or N(2) (Figure 5). This is in agreement with the observations of Cossé-Barbi and Dubois,[15] i.e. five-membered rings usually escape the *endo*-anomeric effect.

## References

1 F. Maran, E. Vianello, G. Cavicchioni, and F. D'Angeli, *J. Chem. Soc., Chem. Commun.*, 1985, 660, and references therein.
2 F. Maran, E. Vianello, F. D'Angeli, G. Cavicchioni, and G. Vecchiati, *J. Chem. Soc., Perkin Trans. 2*, 1987, 33.
3 F. D'Angeli, G. Cavicchioni, G. Catelani, P. Marchetti, and F. Maran, *Gazz. Chim. Ital.*, 1989, 119, 471.
4 P. Scrimin, G. Cavicchioni, F. D'Angeli, A. Goldblum, and F. Maran, *J. Chem. Soc., Perkin Trans. 1*, 1988, 43.
5 R. H. De Wolfe, 'Carboxylic Ortho Acid Derivatives,' Academic Press, New York, 1970, p. 441.
6 P. Deslongchamps, 'Stereoelectronic Effects in Organic Chemistry,' Pergamon Press, Oxford, 1983.
7 C. K. Johnson, 'ORTEP,' Report ORNL-5138, Oak Ridge National Laboratory, Tennessee, USA, 1976.
8 D. Cremer and J. A. Pople, *J. Am. Chem. Soc.*, 1975, 97, 1354.

9 W. L. Duax, C. M. Weeks, and D. C. Rohrer, 'Topics in Stereochemistry,' eds. E. L. Eliel and N. Allinger, J. Wiley, New York, 1976, vol. 9, p. 271.

10 M. Nardelli, *Acta Crystallogr., Sect. C*, 1983, **39**, 1141.

11 R. Taylor and O. Kennard, *J. Am. Chem. Soc.*, 1982, **104**, 5063.

12 G. Zanotti, F. Filira, A. Del Pra, G. Cavicchioni, A. C. Veronese, and F. D'Angeli, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2249.

13 F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1987, S1.

14 C. Romers, C. Altona, H. R. Buys, and E. Havinga, 'Topics in Stereochemistry,' eds. E. L. Eliel and N. L. Allinger, J. Wiley, New York, 1969, vol. 4, p. 39.

15 R. U. Lemieux and S. Koto, *Tetrahedron*, 1974, **30**, 1933.

16 C. A. Jeffrey, J. A. Pople, and L. Radom, *Carbohydr. Res.*, 1972, **25**, 117.

17 A. J. Kirby, 'The Anomeric Effect and Related Stereoelectronic Effect at Oxygen,' Springer, Berlin, 1983.

18 A. J. Briggs, R. Glenn, P. G. Jones, A. J. Kirby, and P. Ramaswamy, *J. Am. Chem. Soc.*, 1984, **106**, 6200.

19 A. Cossé-Barbi and J. E. Dubois, *J. Am. Chem. Soc.*, 1987, **109**, 1503.

20 M. Poje and I. Vickovič, *Acta Crystallogr., Sect. C*, 1987, **43**, 539, 542, 545, 547.

21 J. M. Lehn and G. J. Wipff, *J. Am. Chem. Soc.*, 1974, **96**, 4048.

22 H. Booth, J. M. Dixon, K. H. Kedhair, and S. A. Readshaw, *Tetrahedron*, 1990, **46**, 1625.

23 D. T. Cromer and J. T. Waber, 'International Tables for X-Ray Crystallography,' Kynoch Press, Birmingham, UK, 1974, vol. 4.

24 P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. Declerq, and M. M. Woolfson, 'MULTAN82. A System of Computer Programs for the Automatic solution of Crystal Structures from X-Ray Diffraction Data,' Universities of York and Louvain, 1982.

25 B. A. Frenz, 'Structure Determination Package,' College Station, Texas and Enraf-Nonius, Delft, 1978.

26 M. Nardelli, *Comput. Chem.*, 1983, **7**, 95.