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# Synthesis and crystal structure of *(R)*-(-)-*N*-dichloroacetyl-3-ethyl-1-oxa-4-aza-spiro-4.5-decane

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## Abstract

The title compound, *(R)*-(-)-*N*-dichloroacetyl-3-ethyl-1-oxa-4-aza-spiro-4.5-decane **3** was synthesized by a sequential procedure involving condensation of *(R)*-2-amino-butanol with cyclohexanone and acylation of the resultant intermediate spiro compound with dichloroacetyl chloride. The X-ray structure determination confirmed the structure and the product was further characterized by IR, $^1$H-NMR, and $^{13}$C-NMR spectroscopy, mass spectrometry, and elemental analysis.

**Keywords:** chiral compound; oxazolidine; single crystal X-ray diffraction.

## Introduction

Substituted oxazolidines are important heterocycles that show remarkable biological activities. Consequently, the synthesis of oxazolidine derivatives with many applications has been reported in the literature (Blazewska et al., 2003; Guirado et al., 2003). The discovery that some substituted oxazolidines containing a dichloroacetyl group act as a herbicide safener has drawn widespread attention in agricultural biochemistry (Sprague et al., 1999; Hatzios and Burgos, 2004; Nelson and Penner, 2006). Some examined substituted oxazolidines are chiral compounds and their biological activity is often related to their chirality (Kang et al., 2005; Sriharsha and Shashikanth, 2006). In the traditional way, the synthetic approach to *N*-dichloroacetyloxazolidine compounds involves a condensation reaction of a $\beta$-amino alcohol with an aldehyde or a ketone to form 1,3-oxazolidine followed by acylation with dichloroacetyl chloride in the presence of sodium hydroxide (Fu et al., 2009, 2010). Although *N*-dichloroacetyloxazolidine compounds have been synthesized successfully, none of the chiral *N*-dichloroacetyloxazolidine derivatives has been reported so far. In this paper, we report the synthesis and structure of *(R)*-(-)-*N*-dichloroacetyl-3-ethyl-1-oxa-4-aza-spiro-4.5-decane (**3**) by a sequential procedure involving condensation of *(R)*-2-amino-butanol **1** with cyclohexanone and acylation with dichloroacetyl chloride (Scheme 1).

## Results and discussion

The title compound **3** was synthesized from *(R)*-2-amino-butanol **1**, cyclohexanone, and dichloroacetyl chloride. In the synthesis of **3**, the intermediate product **2** (Scheme 1) was not isolated but subjected to acylation in the crude form. The target compound **3** was obtained in high yield and with high optical purity. The product was characterized by infrared (IR), $^1$H-NMR, and $^{13}$C-NMR spectroscopy, mass spectrometry, and elemental analysis.

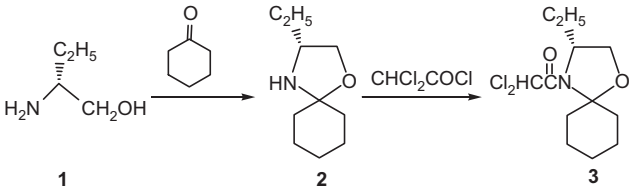
The structure of **3** was further studied by single crystal X-ray diffraction. The molecular structure and the packing view of the title compound are shown in Figures 1 and 2, respectively. The C2-O1 bond length of 1.2186(19) Å is indicative of a double bond C=O (1.21–1.23 Å). The p-$\pi$ conjunction between N1 and C2-O1 results in shorter bond length of C2-N1 [1.3404(18)] than the typical C-N bond length (1.472 Å). The X-ray structure analysis indicates that the title compound contains one chiral center at C5 with the *R* absolute configuration. This spiro compound consists of one cyclohexane ring and one oxazolidine ring. The dihedral angle between these two rings is 82.3°. The cyclohexane ring is in chair conformation.

## Experimental

All starting materials and solvents were commercially available and were used without further purification. The melting points were determined on Beijng Taike melting point apparatus (X-4) and are uncorrected. The IR spectrum was taken on a KJ-IN-27G IR spectrophotometer. The $^1$H-NMR and $^{13}$C-NMR spectra were recorded on a Bruker AVANVE 300 MHz spectrometer in $CDCl_3$ with TMS as the internal standard at 300 MHz and 75 MHz, respectively. The mass spectrometer was a SHIMADZU GC-MS-QP2010 instrument. The elemental analysis was performed on FLASH EA1112 elemental analyzer.

### *(R)*-(-)-*N*-dichloroacetyl-3-ethyl-1-oxa-4-aza-spiro-4.5-decane (3)

*(R)*-2-aminobutanol (0.067 mol) and cyclohexanone (0.067 mol) were mixed with toluene (20 ml), and the mixture was stirred at 33~34°C for 1 h, then cooled to 0°C, and treated with an




**Scheme 1** Route for the synthesis of the title compound.

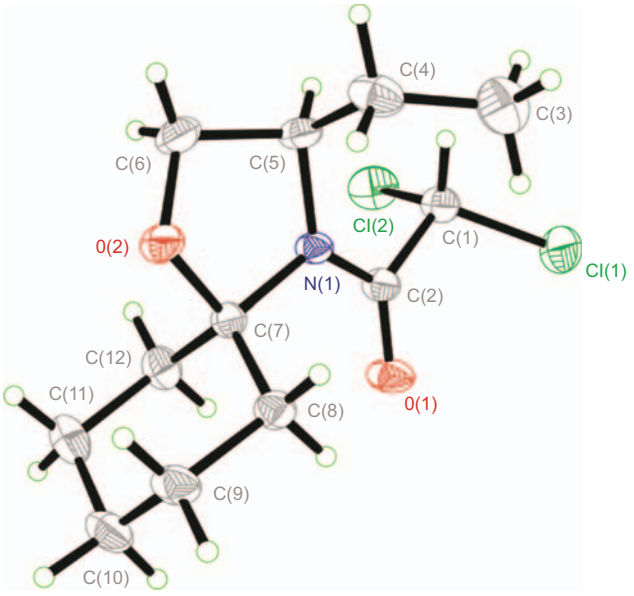



**Figure 1** Structure of the title compound, showing 50% probability ellipsoids.

aqueous solution of sodium hydroxide (33%, 10 ml). Then, dichloroacetyl chloride (7.3 ml, 0.076 mol) was added dropwise with stirring and cooling in an ice bath. Stirring was continued for an additional 3 h. The mixture was rinsed several times with water, and the organic solution was dried over anhydrous magnesium sulfate. After removal of the solvent by distillation under normal pressure, the residue was crystallized from a mixture of ethyl acetate and light petroleum until white crystals of **3** were obtained: yield 64%; mp 101–102°C; $[\alpha]_D^{20}$ (C=2, $CHCl_3$) -7.5°; IR (KBr): 1663(C=O), 1123(N-C-O), 1109 (-$CH_2$-O-C-), 802(C-Cl), 655(N-C=O) $cm^{-1}$; $^1$H-NMR: δ 6.07 (1H, s), 3.91 (2H, m), 3.78 (1H, m), 2.49 (2H, m), 1.56 (10H, m), 0.98 (3H, m); $^{13}$C-NMR($CDCl_3$, 75 MHz), δ: 160.3, 97.8, 66.3, 65.8, 59.2, 34.6, 28.4, 3.16, 24.5, 23.2, 23.0, 10.8; MS(EI) *m/z*: 279[M]$^+$. Analysis: Calculated for $C_{12}H_{19}Cl_2NO_2$: C, 51.60; H, 6.86; N, 5.02%; Found: C, 51.59; H, 6.90; N, 4.99%.

**Table 1** Crystal data of the title compound.

| | |
|---|---|
| CCDC deposit no. | 813604 |
| Molecular formula | $C_{12}H_{19}Cl_2NO_2$ |
| Molecular weight | 280.18 |
| Temperature | 298(2) K |
| Radiation λ | 0.71073 Å |
| Crystal system | Orthorhombic |
| Space group | P2(1)2(1)2(1) |
| *a*/Å | 6.4482(18) |
| *b*/Å | 10.899(3) |
| *c*/Å | 19.785(6) |
| V/Å$^3$ | 1390.5(7) |
| Z | 18 |
| Crystal size | 0.40×0.26×0.20 mm |
| Crystal color | Colorless |
| Absorption coefficient | 0.961 |
| Absorption correction $T_{min}$ and $T_{max}$ | 0.741 and 0.825 |
| F(000) | 702 |
| Reflections collected/unique | 12611/3364[R (int)=0.0211] |
| Range/indices (*h*,*k*,*l*) | -8,8; -14,14; -25,25 |
| θ limit (°) | 2.78–28.31 |
| No. of observed data | 3364 |
| No. of restraints | 0 |
| Goodness of fit on $F^2$ | 1.039 |
| $R^1$ $wR^2$ [I>2σ(I)] | 0.0319, 0.0736 |
| $R^1$ $wR^2$ (all data) | 0.0381, 0.0774 |

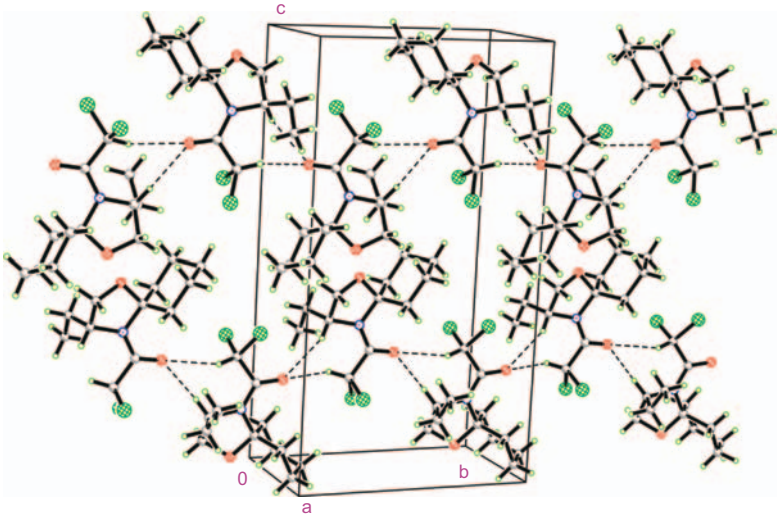



**Figure 2** Packing view of the title compound.

**Table 2** Selected bond lengths (Å) and angles (°) for the title compound.

| | | | |
|---|---|---|---|
| Cl(1)-C(1) | 1.7623(18) | C(7)-C(8) | 1.513(2) |
| Cl(2)-C(1) | 1.771(2) | C(7)-C(12) | 1.516(2) |
| O(2)-C(7) | 1.4289(18) | C(5)-C(6) | 1.517(2) |
| O(2)-C(6) | 1.430(2) | C(5)-C(4) | 1.522(3) |
| N(1)-C(2) | 1.3404(18) | C(4)-C(3) | 1.507(3) |
| N(1)-C(5) | 1.4822(19) | C(12)-C(11) | 1.529(2) |
| N(1)-C(7) | 1.4974(18) | C(8)-C(9) | 1.524(2) |
| O(1)-C(2) | 1.2186(19) | C(10)-C(9) | 1.509(3) |
| C(1)-C(2) | 1.538(2) | C(10)-C(11) | 1.516(3) |
| C(7)-O(2)-C(6) | 108.15(11) | O(1)-C(2)-N(1) | 124.45(14) |
| C(2)-N(1)-C(5) | 128.14(12) | O(1)-C(2)-C(1) | 119.70(14) |
| C(2)-N(1)-C(7) | 121.54(11) | N(1)-C(2)-C(1) | 115.79(12) |
| C(5)-N(1)-C(7) | 110.13(11) | N(1)-C(5)-C(6) | 99.20(13) |
| C(2)-C(1)-Cl(1) | 109.65(12) | N(1)-C(5)-C(4) | 113.45(14) |
| C(2)-C(1)-Cl(2) | 106.97(12) | C(6)-C(5)-C(4) | 111.83(14) |
| Cl(1)-C(1)-Cl(2) | 110.45(9) | C(3)-C(4)-C(5) | 116.78(15) |
| O(2)-C(7)-N(1) | 102.56(11) | C(7)-C(12)-C(11) | 111.10(14) |
| O(2)-C(7)-C(8) | 106.61(12) | C(7)-C(8)-C(9) | 110.27(14) |
| N(1)-C(7)-C(8) | 113.10(13) | C(9)-C(10)-C(11) | 111.30(15) |
| O(2)-C(7)-C(12) | 110.38(13) | C(10)-C(11)-C(12) | 111.68(15) |
| N(1)-C(7)-C(12) | 111.27(12) | C(10)-C(9)-C(8) | 111.23(14) |
| C(8)-C(7)-C(12) | 112.36(13) | O(2)-C(6)-C(5) | 103.69(13) |

Crystalographic data have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 813604. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK [fax: +44(1223)336033 or e-mail: deposit@ccdc.cam. ac.uk].

### X-ray data collection and structure refinement

The X-ray data were collected on a Bruker AXS II CCD area-detector diffractometer using graphite monochromated Mo *K*a radiation ($\lambda$=0.071073 nm) at 298(2) K. The structure was solved by direct methods using SHELXS-97, and refined by full matrix least squares on $F^2$, SHELXL-97. Minimum and maximum, final electron density was -0.234 and 0.136e$Å^{-3}$. Symmetry equivalent reflections were used to optimize crystal shape and size. All non-hydrogen atoms were refined anisotropically. The experimental data is reported in Tables 1 and 2.

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