The 3-[3α(2α-Hydroxy)pinane]-4,5-(pinan)-1,3-oxazolidine Synthesis, Structure and Properties

Magdalena Bialek,* Agata Trzesowska,† and Rafal Kruszynski†

Institute of Organic Chemistry, Technical University of Lodz, Zeromskiego 116, 90-924 Lodz, Poland
**E-mail: madziam2@o2.pl*
†Institute of General and Ecological Chemistry, Technical University of Lodz, Zeromskiego 116, 90-924 Lodz, Poland
Received August 4, 2006

The new pinane derivative containing unique multifused ring system was synthesized. The crystal, molecular and electronic structure of the title compound has been determined. Both pinane ring systems have the same conformation. The five-membered oxazolidine ring exists in twisted chair conformation. The structure is expanded through O-H···O hydrogen bond to semiinfinite hydrogen-bonded chain. The bond lengths and angles in the optimised structure are similar to the experimental ones. The CH_3 and CH_2 groups (except this of oxazolidine ring) are negatively charged whereas the CH groups are positively charged. The largest negative potential is on the oxygen atoms. The C-N natural bond orbitals are polarised towards the nitrogen atom (*ca.* 61% at N) whereas the C-O bond orbitals are polarised towards the oxygen atom (*ca.* 67% at O). It is consistent with the charges on the nitrogen and oxygen atom of oxazolidine ring and the direction of the dipole moment vector (3.08 Debye).

Key Words : Pinane, Natural bonding orbital, Oxazolidine, Crystal and molecular structure, Electronic structure

Introduction

Pinane and its countless derivatives have diverse applications in pharmaceutical, cosmetic and food industry. The pinane itself is wildly used as the raw material of the fine perfume and vitamin A, vitamin E, vitamin K, but the most important is using the pinane derivatives in asymmetric synthesis.[1] Pinane can be easily obtained from pinene, which is one of the most common and the most used natural sources of chirality. The commercially available 2α-hydroxypinan-3-one (99% enantiomeric purity) is frequently used as chiral auxiliary in the asymmetric alkylation of ketoimines and in synthesis of aminoacids and sphingosines.[2] 2α-hydroxypinan-3-one can be source of oximes which can be easily transferred to optically active amino alcohols[3] and in consequence to Shiff bases.[1] Mentioned amino alcohols are the raw compounds in asymmetric reduction of prochiral ketones.[4]

The chiral oxazolidine derivatives are also often used as chiral auxiliaries[5] or as promoters for enantioselective addition.[6] They replace commonly used homochiral ester enolates, because oxazolidine derivatives can provide more predictable diasteroselectivity and can be more easily regenerated. The use of chiral auxiliaries to transfer chirality, with predictable stereochemistry in newly formed stereocenters, is one of the most valuable tools in asymmetric synthesis. Unlike chiral catalysts, chiral auxiliaries are used in stoichiometric amounts to induce the stereoselective formation of stereogenic centers.[7] Combined systems containing two different chiral auxiliaries cause better stereoselectivity in asymmetric synthesis than compounds containing only groups of one type.[8] The title compound consolidates the benefits of oxazolidines and pinane, and it should act as very good chiral inductor for the stereoselective transformation in asymmetric iodolactamization[9] or asymmetric aldol reactions.[10] Additionaly, according to literature, it is first known ring system containing substitued at N atom oxazolidine ring fused with pinane.

Experimental

Synthesis. Enantiomeric derivatives were obtained from optically pure 2-hydroxypinan-3-one oxime according to Markowicz *et al.*[1] procedure. Optically pure oxime was obtained by crystallization of racemate from hexane (mp. = 121-122 °C). In the next step, the oxime was reduced by $LiAlH_4$ in diethyl ether giving 3α-(2α-hydroxy)pinanoamine. Then, from 3α-(2α-hydroxy)pinanoamine and 2-hydroxypinan-3-one the Schiff base was obtained in reversible reaction. To eliminate the hydrolysis, the Schiff base was azeotropically distilled over silica gel. Next Schiff base of 2α-hydroxypinan-3 and 3α(2α-hydroxy)pinanoamine was reduced by $LiAlH_4$ giving di[3α(2α-hydroxy)pinane)]amine. In the last step secondary amine was treated with 88% formic acid and 37% formaldehyde giving 3-[3α(2α-hydroxy)pinane]-4,5-(pinan)oxazolidine.

Synthesis of 2-hydroxypinan-3-one oxime (according to Burak and Chabudziński[3]): 150.0 g of 2α-hydroxypinan-3-one $[\alpha]_D^{20} = -28.42°$ (c = 0.5, $CHCl_3$), e.e. = 71% was dissolved in 500 mL of ethanol. Next 120 g of hydroxylamine hydrochloride dissolved in 150 mL of water and 120.0 g of sodium acetate was added. The mixture was shaken for a week and then ethanol was evaporated and 350 mL of water was added. The water layer was extracted by

chloroform, which was next dried by $MgSO_4$ and evaporated. Yield 138.7 g (85.5%), e.e. = 65%.

Optical purification 2-hydroxypinan-3-one oxime (according to Markowicz *et al.*[1] and Burak and Chabudziński[3]): A 100 g of oxime (e.e. = 65%) was eluted by boiling hexane (4 × 500 mL). The oxime solution was concentrated on vacuum rotary evaporator to 500 mL. The fractional crystallization gives 55.0 g of oxime ($[\alpha]_D^{20}$ = 19.2°, c = 3, $CHCl_3$). The obtained compound was crystallized from hexane-diethy ether mixture (2 : 1) giving 51.3 g of oxime $[\alpha]_D^{20}$ = 19.2° (c = 3, $CHCl_3$) mp. = 122 °C.

Synthesis of 3α-(2α-hydroxy)pinanoamine (according to Markowicz *et al.*[1]): To 30 g of $LiAlH_4$ dissolved in 500 mL diethyl ether 50 g of oxime dissolved in diethyl ether was dropped in. The mixture was boiled for 20 hours. The ether layer was decanted and evaporated. The resulting oil was distilled off and the residue was dissolved in 15 mL of 37% HCl. The solution was alkalized by 50% NaOH and extracted by diethyl ether. 25.11 g 2-hydroxypinan-3-on oxime was crystallized from hexane (20 mL) ($[\alpha]_D^{20}$ = −12.1° (c = 1, $CHCl_3$) (racemate is insoluble in hexane).

Synthesis of Schiff base of 2α-hydroxypinan-3 and 3α(2α-hydroxy)pinanoamine (according to Markowicz *et al.*[1]): 16.900 g (0. 1000 mol) of 3α-(2α-hydroxy)-pinanoamine, 16.800 g (0.1000 mol) of 2-hydroxypinan-3-one, 10 drops of $BF_3{\cdot}Et_2O$ and 3.0 g of silica gel was azeotropically distilled for 30 hours in 500 mL of toluene. During boiling the 3.0 g of silica gel and 10 drops of $BF_3{\cdot}Et_2O$ was added four times. The silica gel was filtered off and the toluene was evaporated, yield 91.1% (29.061 g, 0.0911 mol). The crude product was crystallized from hexane (100 mL). Yield 22.311 g $[\alpha]_D^{20}$ = −95.71° (c = 2, $CHCl_3$).

Synthesis of di[3α(2α-hydroxy)pinane)]amine (according to Markowicz *et al.*[1]): To 10.0 g of $LiAlH_4$ dissolved in 250 mL of diethyl ether heated at t = 35 °C was dropped 20.0 g of Schiff base dissolved in 250 mL diethyl ether. The mixture was heated for 1 hours (t = 35 °C). After cooling down 5 mL of water and 5 mL of methanol dissolved in 50 mL diethyl ether was added drop by drop. Next the water layer was washed by diethyl ether (5 × 50 mL). The ether extracts was washed by brine (3 × 50 mL) and dried over $MgSO_4$ and evaporated. Yield 19.88 g (98.8%), $[\alpha]_D^{20}$ = −35.61° (c = 2, $CHCl_3$).

Synthesis of 3-[3α(2α-hydroxy)pinane]-4,5-(pinan)-oxazolidine: 1 g of di[3α(2α-hydroxy)pinane)]amine was dissolved in 20 mL of toluene and cooled down to −20 °C. 20 mL of 88% formic acid was dropped and next 5 mL of 37% formaldehyde was slowly added. The mixture was heated for 60 hours under reflux (t = 80 °C) and then cooled down. Next 7 mL of 6 M HCl was added and the product was extracted by diethyl ether (3 × 10 mL). The ether extracts were washed twice by 5 mL of water and dried by $MgSO_4$. The water layer was alkalized by 50% NaOH and then extracted by diethyl ether again. Ether layer was washed twice by 5 mL of water, dried by $MgSO_4$ and evaporated. Yield 0.93 g (90.2%). The crystals suitable for X-ray determination were obtained by slow evaporation from diethyl ether.

Table 1. Crystal data and structure refinement for title comound

Empirical formula	$C_{21}H_{35}NO_2$
Formula weight	333.50 g/mol
Temperature	291.0(3) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	a = 7.3689(11) Å
	b = 11.0169(16) Å
	c = 23.985(3) Å
Volume	1947.1(5) Å^3
Z, Density (calculated)	4, 1.138 Mg/m^3
Absorption coefficient	0.071 mm^{-1}
F(000)	736
Crystal size	0.59 × 0.58 × 0.50 mm
θ range for data collection	3.15 to 25.14°
Index ranges	$-8 \le h \le 8$, $-13 \le k \le 13$, $-28 \le l \le 28$
Reflections collected	20632
Independent reflections	3471(R_{int} = 0.0762])
Completeness to 2theta=50	99.8%
Max. and min. transmission	0.964 and 0.954
Data / restraints / parameters	3471 / 0 / 224
Goodness-of-fit on F^2	1.064
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0369, wR2 = 0.0924
R indices (all data)	R1 = 0.0382, wR2 = 0.0936
Largest diff. peak and hole	0.118 and −0.214 e·Å^{-3}

Crystal structures determination and refinement. The X-ray intensity data were collected on a KM-4-CCD automatic diffractometer equipped with CCD detector, 22 seconds exposure time was used. The unit cell parameters were determined from least-squares refinement of the setting angles of 5461 strongest reflections. Details concerning crystal data and refinement are given in Table 1. Lorentz, polarization and numerical absorption corrections[11] were applied. The structure was solved by the direct methods and subsequently completed by the difference Fourier recycling. All the non-hydrogen atoms were refined anisotropically using full-matrix, least-squares technique. All hydrogen atoms were founded on difference Fourier synthesis and they were refined as "riding" on their parent atoms [d(C-H, CH) = 0.98 Å, d(C-H, CH_2) = 0.97 Å, d(C-H, CH_3) = 0.96 Å] and assigned isotropic temperature factors equal 1.2 times (CH, CH_2) or 1.5 times (CH_3) the value of equivalent temperature factor of the parent atom. The methyl group was allowed to rotate about their local threefold axis. The absolute configuration was determined on the basis of synthesis principles and was in agreement with value of Flack parameter.[12] SHELXS97,[13] SHELXL97[14] and SHELXTL[15] programs were used for all the calculations. Atomic scattering factors were those incorporated in the computer programs.

Computational details. Geometry optimisation and Natural Bond Orbital (NBO) analysis[16-18] were performed at the B3LYP/6-31++G(d,p) level of theory[19,20] using GAUSSIAN03^{TM}[21] program package.

Results and Discussion

A perspective view of the title compound showing absolute configuration, together with the atom-numbering scheme is depicted in Figure 1. Both pinane ring systems have almost the same conformation (Figure 2), the root mean square deviation of superimposed atoms is 0.061 Å (maximum deviation of 0.127 Å exists for C1 atom). The C(1)/(11)-C(2)/(12)-C(3)/(13)C(5)/(15)-C(6)/(16) atoms are close to planarity (maximum deviation of 0.072(1) and 0.018(1) Å exist respectively for C(1) and C(16) atoms). C(1) atom is slightly inclined inward gem-dimethyl group, and C(11) atom is slightly inclined outward gem-dimethyl group. The flapping atoms least squares planes C(2)-C(1)-C(6) and C(12)-C(11)-(16) are inclined at 11.7(1) and 2.5(1)° respectively to C(2)-C(3)-C(5)-C(6) and C(12)-C(13)-C(15)-C(16) least squares planes. The C(3)/(13)-C(4)/(14)-C(5)/(15) and C(3)/(13)-C(7)/(17)-C(5)/(15) least squares planes are inclined to C(1)/(11)-C(2)/(12)-C(3)/(13)-C(5)/(15)-C(6)/(16) least squares plane respectively at 69.85(8)-68.5(1)° and 76.17(6)-85.67(7)°. This conformation is similar to those found for other substitued pinanes like (dimethylphenylphosphinio)-monoisopinocampheylcyanoborate,[22] 3-(2-odo-1-methoxy-1-phenylethyl)-2,5,5,10,10-pentamethyl-4,6-dioxatricyclo[7.1.1.0^{2,7}]undecane,[23] (*η*6-*p*-cymene)-(isopinocampheyltris(pyrazolyl)borate)-ruthenium,[24] *cis*-3a,8,8-Trimethyl-3a,4,5,6,7,7a-hexahydro-4,6-methano-1,3,2-dioxathiolane 2-oxide[25] or 2-((2-hydroxypinylidene)-amino)-5,5,5-trifluoro-4-hydroxypentanenitrile.[26] The five-membered oxazolidine ring exists in twisted chair conformation[27] (C_S(C21/C11-C12) = 9.1(2)° and C_2(C11/O2-C21) = 7.2(2)°). For 1517 containing oxazolidine ring compounds included in CSD 5.27.1[28] only in one structure ring has similar conformation to title compound: the ring of 6-nitro-2,4-dipropionyl-8-oxa-2,4,6-triazabicyclo(3.3.0)octane.[29] In the structure can be found one medium strength hydrogen bond (O(1)-H(1O)···O(2#x−0.5, −y+1.5, −z+2), H···O distance 2.00 Å, O···O distance 2.8918(15) and O-H···O angle 161.5°) linking molecules to semiinfinite hydrogen-bonded chain along crystallographic a axis.

The bond lengths and angles in the optimised structure are similar to the experimental ones (Table 2). However, the geometry of C-N bond linking the rings is changed (Fig. 3). Apart from minor variation in the ring angles, the greatest difference is between the torsion angle around the C(1)-N(1) bond with −75.69° for crystal structure and −86.15° for optimised structure. The largest differences are found for the C-C bonds of both bicyclo[3.1.1]heptane ring systems. They are significantly elongated.

The calculated group charges calculated according to most popular schemes (Mulliken, Natural Population Analysis (NPA), Breneman, Merz-Kollman-Singh (MKS) charges) are listed in Table 3.[5] Generally, the CH_3 and CH_2 groups are negatively charged whereas the CH groups are positively charged. The methylene group of C(21) is exception. It has positive charge, which is probably caused by the larger electronegativity difference between carbon atom and neighbouring atoms and hence bigger polarisation of C(21)-O(2) and C(21)-N(1) bonds. The charges on the hydrogen atoms of the methylene group in the oxazolidine ring vary about 0.05.

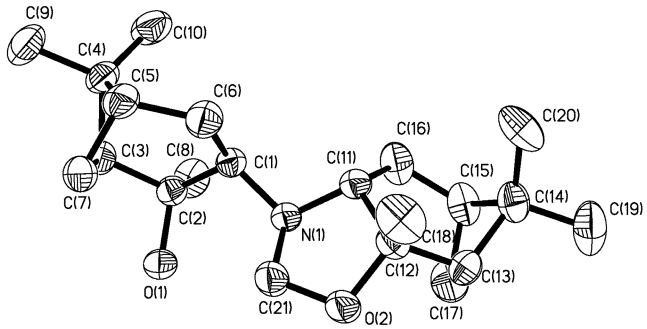

Figure 1. Molecular conformation of title compound showing displacement ellipsoids with 50% probability. Hydrogen atoms are omitted for clarity.

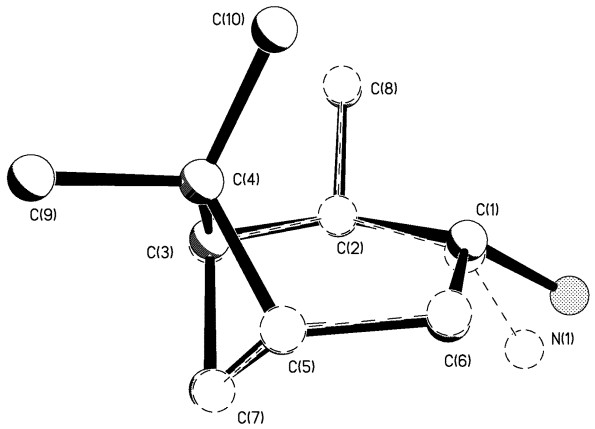

Figure 2. Superposition of pinane ring system (pinane indicated by C1 atom is depicted as solid lines and indicated by C11 atom is depicted as dashed lines).

The bond orders calculated using the re-calibrated bond order - bond length relationship of Gordy[30] are equal to 1.10 for C(21)-O(2) bond, 0.91 for O(2)-C(12) bond and 1.03 for C(21)-N(1) bond. The similar pattern of C-O bond orders was found in 3-(ptosyl)-1,3-oxazolidine and its derivatives.[31] The NLMO bond orders[32,33] are smaller (0.651, 0.643 and 0.756, respectively). The oxygen lone pair contributes a slight strengthening of the C(21)-O(2) bond (0.020) and

[5]However the calculation of effective atomic charges plays an important role in the application of quantum mechanical calculations to molecular systems, the unambiguous dividing up the overall molecular charge density in atomic contributions is still unresolved problem, and none of known procedures do not give fully reliable values of atomic charges. Thus a discussion of atomic charges should cover more than one algorithm of charge density division. Generally can be stated that less reliable values are given by Mulliken population analysis and more reliable results are provided by Breneman method (for detailed discussion on methodology and reliability of presented methods in model molecules see Martin, F.; Zipse, H. J. Computational Chem. **2005**, *26*, 97 and references therein).

Table 2. The selected experimental and optimised bond lengths (Å) and angles (°) for **1**

Bond length	Experimental	Optimised	Angle	Experimental	Optimised
N(1)–C(1)	1.471(2)	1.478	C(1)–N(1)–C(11)	111.28(10)	115.21
N(1)–C(11)	1.481(2)	1.484	C(1)–N(1)–C(21)	118.66(11)	119.99
N(1)–C(21)	1.464(2)	1.467	O(1)–C(2)–C(8)	107.93(12)	107.04
O(1)–C(2)	1.435(2)	1.437	C(1)–C(2)–O(1)	111.93(11)	110.58
O(2)–C(12)	1.450(2)	1.451	C(12)–O(2)–C(21)	107.70(11)	106.89
O(2)–C(21)	1.400(2)	1.410	C(3)–C(4)–C(5)	85.25(11)	86.31
C(1)–C(2)	1.566(2)	1.590	C(9)–C(4)–C(10)	107.19(14)	106.90
C(1)–C(6)	1.557(2)	1.575	C(11)–C(12)–C(13)	111.33(12)	111.58
C(2)–C(8)	1.527(2)	1.538	C(14)–C(15)–C(17)	88.83(13)	88.09
C(4)–C(9)	1.536(2)	1.541	C(19)–C(14)–C(20)	107.93(14)	107.33
C(4)–C(10)	1.524(2)	1.535	O(1)–C(2)–C(1)–N(1)	31.34(16)	25.47
C(5)–C(7)	1.535(2)	1.550	C(2)–C(1)–N(1)–C(21)	75.56(16)	86.15
C(11)–C(12)	1.544(2)	1.578	N(1)–C(11)–C(16)–C(15)	115.68(14)	110.55
C(12)–C(18)	1.524(2)	1.535	C(13)–C(17)–C(15)–C(14)	26.69(12)	27.18
C(14)–C(19)	1.528(2)	1.540	N(1)–C(1)–C(6)–C(5)	143.31(13)	137.38
C(14)–C(20)	1.519(3)	1.534	C(1)–C(2)–C(3)–C(7)	56.94(15)	53.84
C(15)–C(17)	1.524(3)	1.552	N(1)–C(21)–O(2)–C(12)	37.30(16)	41.46

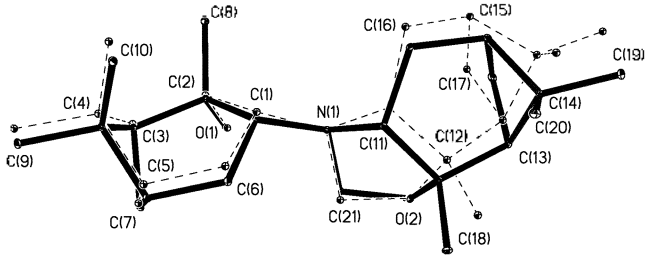

Figure 3. The experimental (solid lines) and optimised (dashed lines) molecular structure of title compound.

O(2)-C(12) bond (0.014), whereas the nitrogen lone pair contributes a slight strengthening of the C(21)-N(1) bond (0.016). The bond order can be also calculated by means of the bond-valence method (BVM),[34] according to which the bond valence (v_{ij}) is defined as a number of electron pairs forming the bond. For many years, this method was used only for inorganic compounds, occasionally for coordination compounds. Recently, Mohri[35] has suggested that BVM can be successfully used for organic compounds on condition that the mean bond length (1.42 Å for C-O bond and 1.47 Å for C-N bond) is treated as the bond-valence parameter value (R_{ij}). The bond orders calculated from the Brown-Altermatt equation ($v_{ij} = \exp[(R_{ij} - d_{ij})/0.37]$[36]) for bonds of bond lengths d_{ij} are equal to 0.92 v.u. for O(2)-C(12), 1.06 v.u for C(21)-O(2) and 1.02 v.u for C(21)-N(1) bond.

The depiction of negative molecular electrostatic potential surfaces (for value of −0.04 a.u.) and electron density surface (for value of 0.04 a.u.) (Fig. 4) indicates that the buildup of negative potential is the largest on the oxygen atoms. Such polarisation is consistent with the observed chemical reactivity of title compound *e.g.* forming of hydrogen bonds. The HOMO(92) orbital is localised primarily on the s C(1), p_x C(11), s C(21), and p_y, p_z nitrogen orbitals (Fig. 5). The s orbitals from C(1) and p_y, p_z orbitals from N(1)

Table 3. The group charges

The group	Mulliken charge	NPA charge	Breneman charge	MKS charge
N(1)	0.043	−0.585	−0.688	−0.321
O(1)	0.076	−0.278	−0.277	−0.290
O(2)	−0.207	−0.593	−0.630	−0.570
C(8)H3	−0.059	0.023	−0.143	−0.146
C(9)H3	−0.009	0.041	−0.091	−0.133
C(10)H3	−0.094	0.029	−0.101	−0.115
C(18)H3	0.179	0.033	−0.171	−0.165
C(19)H3	−0.036	0.043	−0.083	−0.123
C(20)H3	0.034	0.027	−0.103	−0.124
C(6)H2	0.100	0.007	−0.114	−0.191
C(7)H2	−0.036	0.033	−0.084	−0.139
C(16)H2	−0.065	0.021	−0.049	−0.132
C(17)H2	−0.104	0.033	−0.063	−0.146
C(21)H2	0.767	0.501	0.484	0.374
C(1)H	−1.400	0.177	0.505	0.262
C(3)H	0.437	0.007	0.096	0.189
C(5)H	0.521	−0.002	0.033	0.131
C(11)H	0.250	0.164	0.149	0.136
C(13)H	0.016	0.004	−0.053	0.006
C(15)H	0.476	0.002	0.030	0.109
C(2)	−0.168	0.245	0.301	0.326
C(4)	−0.180	−0.094	0.176	0.205
C(12)	−0.438	0.255	0.663	0.579
C(14)	−0.102	−0.092	0.217	0.175

have opposite signs, indicating that they combine to form an antibonding molecular orbital. The LUMO(93) orbital have more complicated character. It is formed from the s orbitals from carbon atoms: C(6), C(8), C(9), C(10), C(11), C(15), C(18), C(19) and C(20).

The bond features have been analysed in terms of the Natural Bond Orbital (NBO) scheme.[16-18] As expected, the

Table 4. Selected results of NBO analysis

Lone Pair Orbital n	Occupancy	Antibonding Orbital σ^*	Occupancy	Stabilisation energy (kcal/mol) $n \rightarrow \sigma^*$
N(1)	1.875	C(1)–C(6)	0.036	8.08
O(1)	1.952	C(1)–C(2)	0.056	6.13
O(2)	1.921	C(21)–H(21A)	0.046	6.94

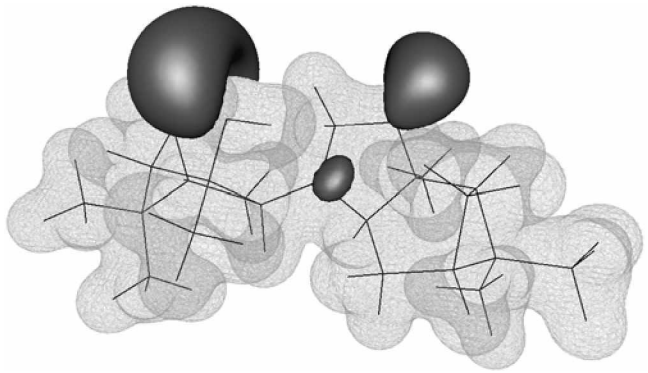

Figure 4. The negative molecular electrostatic potential surfaces (solid) and electron density surface (meshed) of title compound.

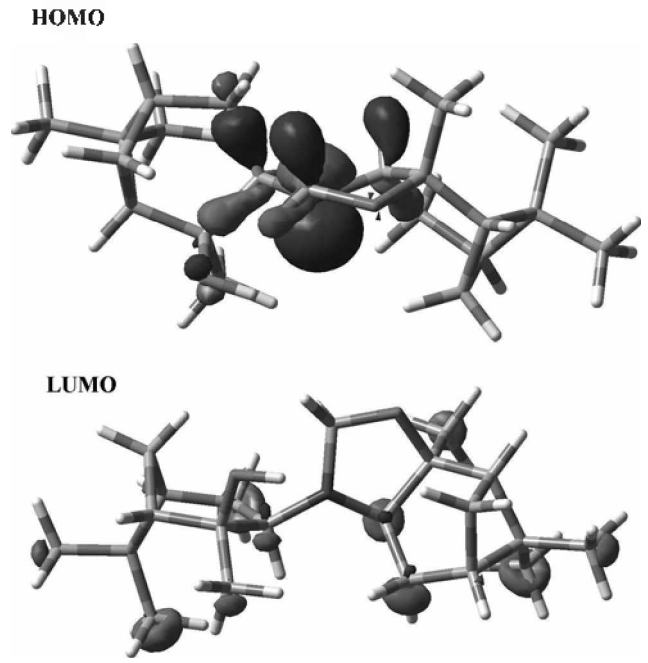

Figure 5. HOMO(92) and LUMO(93) orbitals for title compound.

C-N bond orbitals are polarised towards the nitrogen atom (*ca.* 61% at N) whereas the C-O bond orbitals are polarised towards the oxygen atom (*ca.* 67% at O). It is consistent with the charges on the nitrogen and oxygen atom of oxazolidine ring and the direction of the dipole moment vector (3.08 Debye). The occupancies of the lone pair ($n_{N(1)}$, $n_{O(1)}$, $n_{O(2)}$), antibonding bond orbitals ($\sigma^*_{C(1)\text{-}C(6)}$, $\sigma^*_{C(1)\text{-}C(2)}$, $\sigma^*_{C(21)\text{-}H(21A)}$ accordingly) and the stabilisation energy values indicate the (donor-acceptor) non-covalent interactions between py lone pairs on oxygen and nitrogen atoms and σ C-C, C-H bonds (Table 4).

Conclusion

The crystal, molecular and electronic structure of title compound has been established. Both pinane ring systems have resembling conformation and it is similar to those found for other substitued pinanes. The five-membered oxazolidine ring exist in twisted chair conformation. The structure is stabilised *via* O(1)-(1O)···O(2#x+0.5, −y+1.5, −z+2) medium strength hydrogen bond. In this way a semiinfinite hydrogen-bonded chain along crystallographic a axis is created. The bond lengths and angles in the optimised structure are similar to the experimental ones, however, the geometry of C-N bond linking the rings is changed. The methylene group of C(21) has positive charge, which is probably caused by the bigger electronegativity difference between carbon atom and neighbouring atoms and hence bigger polarisation of C(21)-O(2) and C(21)-N(1) bonds. The bond orders calculated using the re-calibrated bond order - bond length relationship of Gordy are equal to 1.10 for C(21)-O(2) bond, 0.91 for O(2)-C(12) bond and 1.03 for C(21)-N(1) bond. The largest negative potential is on the oxygen atoms. Such polarisation is consistent with the observed chemical reactivity of title compound *e.g.* forming of hydrogen bonds. The occupancies of the lone pair ($n_{N(1)}$, $n_{O(1)}$, $n_{O(2)}$), antibonding bond orbitals ($\sigma^*_{C(1)\text{-}C(6)}$, $\sigma^*_{C(1)\text{-}C(2)}$, $\sigma^*_{C(21)\text{-}H(21A)}$ accordingly) and the stabilisation energy values indicate the (donor-acceptor) non-covalent interactions between p_y lone pairs on oxygen and nitrogen atoms and σ^* C-C, C-H bonds.

Supplementary Data. Supplementary data for title compound are available from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK on request, quoting the deposition number: CCDC298863.

Acknowledgements. This work was financed by funds allocated by the Ministry of Education and Science to the Institute of General and Ecological Chemistry, Technical University of Łódź.

References

1. (a) Markowicz, S. W.; Pokrzeptowicz, K.; Karolak-Wojciechowska, J.; Czylkowski, R.; Omelaczuk, J.; Sobczak, A. *Tetrahedron: Asymm.* **2002**, *13*, 1981. (b) Markowicz, S. W.; Figlus, M.; Lejkowski, M.; Karolak-Wojciechowska, J.; Dzierzawska-Majewska, A.; Verpoort, F. *Tetrahedron: Asymm.* **2006**, *17*, 434.
2. Solladie-Cavallo, A.; Koessler, J. L. *J. Org. Chem.* **1994**, *59*, 3240.
3. Burak, A.; Chabudziński, Z. *Pol. J. Chem.* **1978**, *52*, 1721.
4. Masuil, M.; Shioiri, T. *Tetrahedron* **1995**, *51*, 8363.

5. O'Brien, P.; Warren, S. *Tetrahedron Letters* **1996**, *37*, 3051.
6. Wei-Min, D.; Hua, J. Z.; Xiao-Jiang, H. *Tetrahedron: Asymm.* **1996**, *7*, 1245.
7. Velázquez, F.; Olivo, H. F. *Curr. Org. Chem.* **2002**, *6*, 1.
8. (a) Iuliano, A.; Lecci, C.; Slavadori, P. *Tetrahedron: Asymm.* **2003**, *14*, 1345. (b) Lecci, C.; Iuliano, A. *Biomed. Chromatogr.* **2005**, *19*, 439. (c) Knölker, H. J.; Hermann, H. *Angew. Chem. Int. Ed. Eng.* **1996**, *35*, 341. (d) Karlsson, S. *Doctoral thesis*, Kungl Tekniska Högskolan, Stockholm, Sweeden, 2003.
9. Shen, M.; Li, C. *J. Org. Chem.* **2004**, *69*, 7906.
10. (a) Fernhdez, J. M. G.; Mellet, C. O.; Fuentes, J. *J. Org. Chem.* **1993**, *58*, 5192. (b) Ryu, I.; Murai, S.; Sonoda, N. *J. Org. Chem.* **1986**, *51*, 2391. (c) Bull, S. D.; Davies, S. G.; Nicholson, R. L.; Sanganee, H. J.; Smith, A. D. *Org. Biomol. Chem.* **2003**, *1*, 2886. (d) Agami, C.; Couty, F. *Europ J. Org. Chem.* **2004**, 677.
11. STOE & Cie. *X-RED*. Version 1.18; STOE & Cie GmbH: Darmstadt, Germany, 1999.
12. Flack, H. D. *Acta Cryst.* **1983**, *A39*, 876.
13. Sheldrick, G. M. *Acta Cryst.* **1990**, *A46*, 467.
14. Sheldrick, G. M. *SHELXL97*. Program for the Solution and Refinement of Crystal Structures; University of Göttingen: Germany, 1997.
15. Sheldrick, G. M. *SHELXTL*: release 4.1 for Siemens Crystallographic Research Systems, 1990.
16. Reed, A. E.; Curtis, L. A.; Weinhold, F. A. *Chem. Rev.* **1988**, *88*, 899.
17. Foster, J. P.; Weinhold, F. A. *J. Am. Chem. Soc.* **1980**, *102*, 7211.
18. Reed, A. E.; Weinhold, F. A. *J. Chem. Phys.* **1985**, *83*, 1736.
19. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.
20. Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1988**, *B37*, 785.
21. *Gaussian 03*, Revision A.1; Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, Jr., T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian, Inc.: Pittsburgh, PA, 2003.
22. Vedrenne, P.; Le Guen, V.; Toupet, L.; Le Gall, T.; Mioskowski, C. *J. Am. Chem. Soc.* **1999**, *121*, 1090.
23. Barluenga, J.; Alvarez-Perez, M.; Rodriguez, F.; Fananas, F. J.; Cuesta, J. A.; Garcia-Granda, S. *J. Org. Chem.* **2003**, *68*, 6583.
24. Bailey, P. J.; Pinho, P.; Parsons, S. *Inorg. Chem.* **2003**, *42*, 8872.
25. Hellier, D. G.; Motevalli, M. *Acta Cryst.* **1995**, *C51*, 116.
26. Matsukawa, Y.; Kumar, J. S. D.; Yoneyama, Y.; Katagiri, T.; Uneyama, K. *Tetrahedron Asymm.* **2000**, *11*, 4521.
27. Duax, L.; Norton, D. A. *Atlas of Steroid Structure*; IFI/Plenum: New York, 1975; vol. 1: pp 16-22.
28. Allen, F. H. *Acta Cryst.* **2002**, *B58*, 380.
29. Gilardi, R.; George, C.; Flippen-Anderson, J. L. *Acta Cryst.* **1992**, *C48*, 1528.
30. Kotelevskii, S. I.; Prezhdo, O. V. *Tetrahedron* **2001**, *57*, 5715.
31. Galvez-Ruiz, J. C.; Jaen-Gaspar, J. C.; Castellanos-Arzola, I. G.; Contreras, R.; Flores-Parra, A. *Heterocycles* **2004**, *63*, 2269.
32. Reed, A. E.; von Pagué Schleyer, P. *Inorg. Chem.* **1988**, *27*, 3969.
33. Reed, A. E.; von Pagué Schleyer, P. *J. Am. Chem. Soc.* **1990**, *112*, 1434.
34. Brown, I. D. *The Chemical Bond in Inorganic Chemistry. The Bond Valence Model*; Oxford University Press: New York, 2002.
35. Mohri, F. *Acta Cryst.* **2000**, *B56*, 626.
36. Brown, I. D.; Altermatt, D. *Acta Cryst.* **1985**, *B41*, 244.