Research Article

Hydrogen Bonds between Acidic Protons from Alkynes (C–H···O) and Amides (N–H···O) and Carbonyl Oxygen Atoms as Acceptor Partners

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Crystals of *tert*-butyl (2*S*)-2-(prop-2-yn-1-ylcarbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-NHCH₂CCH) have been obtained. The title compound crystallizes easily as sharp needles in orthorhombic system, space group $P 2_1 2_1 2_1$ with $a = 9.2890(2)$, $b = 9.7292(2)$, $c = 15.7918(4)$ Å, $V = 1427.18(6)$ Å³, and $Z = 4$. The main feature of the structure is the orientation of the carbamate and amide. Their dipoles add up and the molecule displays an electric dipole moment of 5.61 D from B3LYP/6-31G(d) calculations. The antiparallel H bonding of amides and the alignment of dipoles induce columnar stacking (the dipole moment along the columnar a axis is 4.46 D for each molecule). The other components across the other axes are, therefore weaker, (3.17 D and 1.23 D along the b and c axes, resp.). The resulting anisotropic columns pack side by side, in an antiparallel fashion mostly by (alkyne) CH···O=C (carbamate) interactions.

1. Introduction

The design of organic solid (crystal or supramolecular engineering) is still today challenging and of great importance [1, 2]. Understanding the details of weak intermolecular interactions plays definitely a major role in the rational design of ordered organic crystals. In our lab, we already achieved great molecular macroscopic order with specially designed peptides, macrocycles as precursors to organic nanotubes [3–5] or supramolecular walls [6]. Here, we present the crystal structure of the proline derivative **1** (Figure 1) which alkyne, amide, and carbamate functionalities are all involved in hydrogen bonding.

2. Materials and Methods

2.1. Synthesis. To Boc-L-proline N-hydroxysuccinimide ester (2.0 g, 6.4 mmol) in CH₂Cl₂ (40 mL) was added, at 0°C,

propargylamine (0.46 g, 8.4 mmol) and K₂CO₃ (1.43 g, 10.3 mmol). The reaction mixture was allowed to warm up to RT and was stirred for 72 h. Water (30 mL) was added and the organic phase was isolated. The remaining aqueous layer was extracted again with CH₂Cl₂ (2 × 30 mL). The combined organic layers were filtrated through a cotton plug and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel, eluted with Et₂O/Hexane (75:25), to yield the title product as a white solid (1.654 g, 78%).

Rf = 0.36 (Et₂O/Hexane 75:25); **T_{fus}** (108–111°C); **IR** (NaCl, ν cm⁻¹): 3242, 3055, 2982, 2288, 2117, 1688, 1536, 1402, 1324, 1258, 919, 885, and 718. **NMR¹H** (300 MHz, CDCl₃, δ ppm): 6.20 (br, 1H), 4.30–3.90 (m, 3H), 3.50–3.30 (m, 2H), 2.40–2.00 (m, 2H), 2.20 (brs, 1H), 2.00–1.80 (m, 2H), and 1.45 (s, 9H); **HRMS** (m/z): calcd for C₁₃H₂₀N₂O₃Na [MNa⁺]: 275.1366, found: 275.1367.

FIGURE 1: Structure of the proline derivative **1** (Boc-L-ProNHCH₂CCH).

2.2. X-Ray Crystallography. A dilute CDCl₃ solution of **1** (Figure 1) was left to stand in a small vial (partially screwed lid) at room temperature for several days. The alkyne **1** started crystallizing and the vial was kept until nearly complete evaporation of the solvent.

A colorless crystalline needle with approximate dimensions of $0.24 \times 0.25 \times 0.43 \text{ mm}^3$ was mounted on a Bruker AXS P4/SMART 1000 CCD diffractometer. The determination of unit cell parameters and data collections were performed with Cu-K α radiation ($\lambda = 1.54178 \text{ \AA}$). A total of 8432 frames were collected. The total exposure time was 4.68 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 25149 reflections to a maximum θ angle of 70.03° ($0.82 \text{ \AA}$ resolution), of which 2670 were independent (average redundancy: 9.419, completeness = 98.4%, $R_{\text{int}} = 1.90\%$, $R_{\text{sig}} = 0.96\%$) and 2655 (99.44%) were greater than $2\sigma(F^2)$. The final cell constants of $a = 9.2890(2) \text{ \AA}$, $b = 9.7292(2) \text{ \AA}$, $c = 15.7918(4) \text{ \AA}$, volume = $1427.18(6) \text{ \AA}^3$ and are based upon the refinement of the XYZ-centroids of 9807 reflections above $20 \sigma(I)$ with $5.596^\circ < 2\theta < 139.6^\circ$. Data were corrected for absorption effects using the multiscan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.900. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.7575 and 0.8531. The structure was solved and refined using the Bruker SHELXTL software package, using the space group $P 2_1 2_1 2_1$, with $Z = 4$ for the formula unit, $\text{C}_{13}\text{H}_{20}\text{N}_2\text{O}_3$. The final anisotropic full-matrix least-squares, refinement on F^2 with 166 variables converged at $R_1 = 2.46\%$, for the observed data and $wR_2 = 6.39\%$ for all data. The goodness of fit was 1.035. The largest peak in the final difference electron density synthesis was $0.196 \text{ e}^-/\text{\AA}^3$ and the largest hole was $-0.151 \text{ e}^-/\text{\AA}^3$ with an RMS deviation of $0.028 \text{ e}^-/\text{\AA}^3$. On the basis of the final model, the calculated density was 1.174 g/cm^3 and $F(000)$, 544 e^- . The crystal data, intensity collection conditions, and refinement parameters are presented in Table 1. All crystallographic data for this paper are deposited with the Cambridge Crystallographic Data Centre (CCDC-906056). The data can be obtained free of charge at <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (or from Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2

TABLE 1: Crystal data, intensity collection conditions, and refinement parameters for **1**.

CCDC No	906056
Empirical formula	$\text{C}_{13}\text{H}_{20}\text{N}_2\text{O}_3$
Formula weight	252.31
Temperature	100 K
Wavelength	$1.54178 \text{ \AA}$ Cu K α
Crystal system, space group	Orthorhombic, $P 2_1 2_1 2_1$
Unit cell dimensions	$a = 9.2890(2) \text{ \AA}$ $b = 9.7292(2) \text{ \AA}$ $c = 15.7918(4) \text{ \AA}$ $\alpha = \beta = \gamma = 90^\circ$
Volume	$1427.18(6) \text{ \AA}^3$
Z , calculated density	4, 1.174 Mg/m^3
Absorption coefficient μ	0.684 mm^{-1}
Absorption correction	Multiscan
Max. and min. transmission	0.85 and 0.77
Crystal size	$0.24 \times 0.25 \times 0.43 \text{ mm}$
$F(000)$	544
θ range for data collection	5.53 to 70.03°
Index ranges	$-11 \leq h \leq 11$, $-11 \leq k \leq 11$, $-19 \leq l \leq 19$
Reflections collected/unique	25149/2670 ($R_{\text{int}} = 0.0190$)
Refinement method	Full-matrix least squares on F^2
Completeness to theta = 25.00°	98.4%
Goodness of fit on F^2	1.035
Data/restraints/parameters	2670/0/166
Final R indices ($I > 2\sigma(I)$)	$R_1 = 0.0246$, $wR_2 = 0.0637$
R indices (all data)	$R_1 = 0.0247$, $wR_2 = 0.0639$
Largest diff. peak and hole	0.196 and $-0.151 \text{ e}^-/\text{\AA}^3$

1EZ, UK e-mail: deposit@ccdc.cam.ac.uk). See CIF file in Supplementary Material available online at <http://dx.doi.org/10.1155/2014/371629>.

3. Results and Discussion

The main feature of the crystal structure of the title compound Boc-L-Pro-NHCH₂CCH **1** is the columnar architecture and the orientation of the carbamate, amide, and alkyne groups (Figure 2). From B3LYP/6-31G(d) calculations, the electric dipole moment has a total theoretical value of 5.61 D , with a major contribution (4.46 D) along the a axis (which is nearly the orientation of both carbonyl groups). The other components across the other axes are, therefore, weaker (3.17 D and 1.23 D along the b and c axes, resp.). As expected, both nearly parallel carbonyls act as hydrogen bond acceptors toward the same NH group of a neighboring molecule. Between two consecutive molecules, the $\text{NH} \cdots \text{O}=\text{C}$ (amide) and $\text{NH} \cdots \text{O}=\text{C}$ (carbamate) distances are $2.218 \text{ \AA}$ and $3.141 \text{ \AA}$, respectively (corresponding to

FIGURE 2: View along b axis of the columnar polar stacking of **1**, which emphasizes the orientation of the amide, carbamate, and alkyne groups. Amide H bond interactions are represented with green dotted lines.

FIGURE 3: Plot of seven columns viewed along a axis, showing all the hydrogen bonds as dotted lines ($\text{NH} \cdots \text{O}=\text{C}$ (amide) inside column and (alkyne) $\text{CH} \cdots \text{O}=\text{C}$ (carbamate) between columns).

2.97 Å and 3.58 Å between N and O atoms). Therefore, the contribution of the carbamate carbonyl appears to be less important than that of the amide. This is also confirmed in the alignment of the corresponding carbonyls with the amide N–H groups. Thus, the $\text{C}=\text{O} \cdots \text{H}(\text{N})$ angles assume values of 141° and 79° for the amide and the carbamate, respectively. The latter being very distorted is accordingly much weaker than the former [7]. Finally, the linear terminal alkyne groups are disposed nearly perpendicularly to the polar column.

Columns are directly linked to one another by (alkyne) $\text{CH} \cdots \text{O}=\text{C}$ (carbamate) interactions (Figure 3) [8, 9]. Although the hydrogen bond character of the $\text{CH} \cdots \text{O}$ interaction has been a subject of controversy [10, 11], $\text{CH} \cdots \text{O}$ hydrogen bonds are now well accepted by the scientific community [12–15], especially hydrogen bonds formed by terminal acetylenes where the C–H groups can act as weak

hydrogen bond donors owing to their relatively high acidity [8].

The preference for linearity is the main structural feature distinguishing hydrogen bonds from van der Waals interactions [7]. In our case, the θ angle ($\text{CH} \cdots \text{O}$ angle) is near linearity with a value of 161.61° (Figure 4). This compares well with the known mean value for $\text{C}(\text{sp})\text{H} \cdots \text{O}$ angle of 152° [8, 13, 14]. Also, the distance D between the terminal alkyne C atom and the carbonyl O atom (3.100 Å) observed in the crystal of **1** is relatively short compared to the literature mean value (3.31 and 3.46 Å) obtained from crystallographic database studies [8, 12].

Finally, when we look along the c axis (Figure 5), the columns pile side by side through weak van der Waals noncovalent interactions. The closest distance between H atoms of the t -Bu group is 2.565 Å, which is slightly above the expected vdW radii.

FIGURE 4: Geometrical parameters of the $\text{CC-H}\cdots\text{O}=\text{C}$ hydrogen bond between columns (picture represents two molecules viewed along a axis).

FIGURE 5: Plot of 3 parallel polar columns viewed along c axis, showing the $\text{NH}\cdots\text{O}=\text{C}$ (amide) hydrogen bonds (as dotted lines) and the weak vdW $\text{H}\cdots\text{H}$ contact between $t\text{-Bu}$ (as yellow lines).

4. Conclusions

In conclusion, the crystal structure of the proline alkyne derivative **1** is dominated by three different interactions of different strengths: (1) hydrogen bonds between amides partners and mostly oriented parallel to the a axis, (2) hydrogen bonds between carbonyl oxygen atoms and slightly acidic alkyne hydrogen, whose orientation lies mainly in the bc plane, and (3) van der Waals interactions involving aliphatic residues.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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