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Synthesis and Structure of *bis*(2,5-Dioxopyrrolidin-1-yl)adipate

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bis(2,5-Dioxopyrrolidin-1-yl)adipate was prepared from adipate. Its structure was determined by single crystal X-ray diffraction analysis. The crystals are monoclinic space group $P2_1/c$ with a = 5.2972(3), b = 7.5196(5), c = 19.2660(13) Å, α = 90.00, β = 99.776(6), γ = 90.00°, V = 756.28(8) Å^3, Z = 2, F(000) = 356.0, D_c = 1.494 g/cm^3, μ = 1.070 mm^{-1}, the final R = 0.0511 and wR = 0.1135. A total of 2484 reflections were collected, of which 1342 were independent (R_{int} = 0.0255).

Keywords: Adipate derivative, Synthesis, Crystal structure.

INTRODUCTION

Adipate derivative and N-hydroxy succinimide derivatives are important structural elements in the preparation of polypeptide or antisense oligonucleotides (ODNs) which have a diverse range of clinical applications in the treatmentof a variety of diseases such as viral infection[1], tumor[2], vessel restenosis[3], fulminant septic shock[4], asthma and allergies[5]. In our earlier paper, we have reported the application of N-hydroxy succinimide derivative on the synthesis of antisense oligonucleotides[6]. To improve the function of compounds with new and attractive characteristics, structural modifications of linker have been extensively investigated. As a periodical result, we report a novel linker derivative for the preparation of modified nanogold.

EXPERIMENTAL

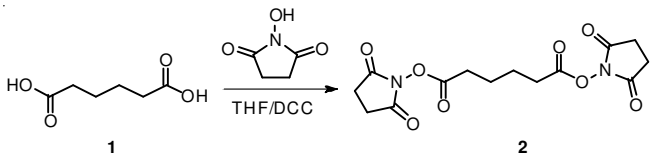
Determination of crystal structure: The crystal of title compound with dimensions of 0.26 mm × 0.24 mm × 0.20 mm was mounted on Xcalibur Eos Gemini diffractometer with a graphite-monochromated CuK_α radiation (λ = 1.54184 Å) by using a phi and scan modes at 291.15(2) K in the range of $9.32° \leq 2\theta \leq 133.96°$. The crystal belongs to monoclinic system with space group $P2_1/c$ and crystal parameters of a = 5.2972(3), b = 7.5196(5), c = 19.2660(13) Å, α = 90.00, β = 99.776(6), γ = 90.00°, V = 756.28(8) Å^3, Z = 2, F(000) = 356.0, D_c = 1.494 g/cm^3. The absorption coefficient μ = 1.070 mm^{-1}. The final R_1 = 0.0404 (> 2σ(I)) and wR_2 = 0.1028. A total of 2484 reflections were collected, of which 1342 were independent (R_{int} = 0.0255). The structure was solved by direct methods with SHELXS-97[4] and refined by the full-matrix least squares method on F_2 data using SHELXL-97[5]. The empirical absorption corrections were applied to all intensity data. H atom of N-H was initially located in a difference Fourier map and were refined with the restraint Uiso(H) = 1.2 Ueq(N). Other H atoms were positioned geometrically and refined using a riding model, with d(C-H) = 0.93-0.97 Å and Uiso(H) = 1.2 Ueq(C) or 1.5 Ueq(C-methyl).

Synthesis of title compound: As shown in **Scheme-I**, to a solution of N-hydroxy succinimide (0.05 mol) in tetrahydrofuran (80 mL) was added a solution of dicyclohexylcarbodiimide (DCC) (0.175 mol) in tetrahydrofuran (20 mL). The mixture was heated to 55 °C under stirring and kept for 1 h. Then compound **1** was added to the mixture stirring for another 2 h at room temperature. After the compound **1** disappeared by TLC detection, the mixture was filtered and the filtrate was evaporated under diminished pressure. The residue was dissolved with ethyl acetate (50 mL) and washed with saturated sodium chloride, water, orderly. Then the organic phase was dried over anhydrous $MgSO_4$ for 8 h. Evaporation of the dry solution gave **2** as a white ceraceous solid (76 % yield). HRMS: Calcd for $C_{14}H_{16}O_8N_2$ 340.0907; found 341.0990 $[M + H]^+$.

RESULTS AND DISCUSSION

Slow evaporation of title compound in MeOH and EtOAc (1:1) afforded colourless crystals suitable for X-ray analysis.

Structure of the title compound: The structure of title compound **2** has been confirmed by single crystal X-ray diffraction analysis. Crystallographic and refinement parameters



Scheme-I: Route for the synthesis of compound **2**

are given in Table-1. The selected bond lengths and bond angles are listed in Tables 2-4, respectively. The structure was solved by direct methods. Anisotropic displacement parameters were applied to all nonhydrogen atoms in full-matrix least-square refinements based on F^2. The hydrogen atoms were set in calculated positions with a common fixed isotropic thermal parameter.

The molecular structure and the packing view of the title compound are shown in Figs. 1 and 2, respectively.

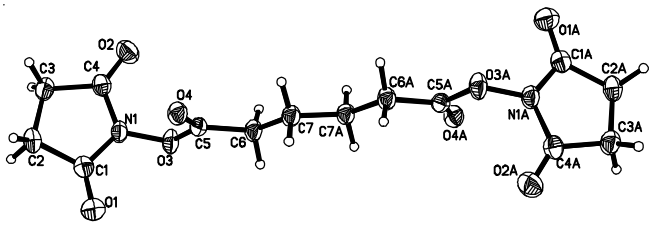


Fig. 1. Molecular structure of the title compound

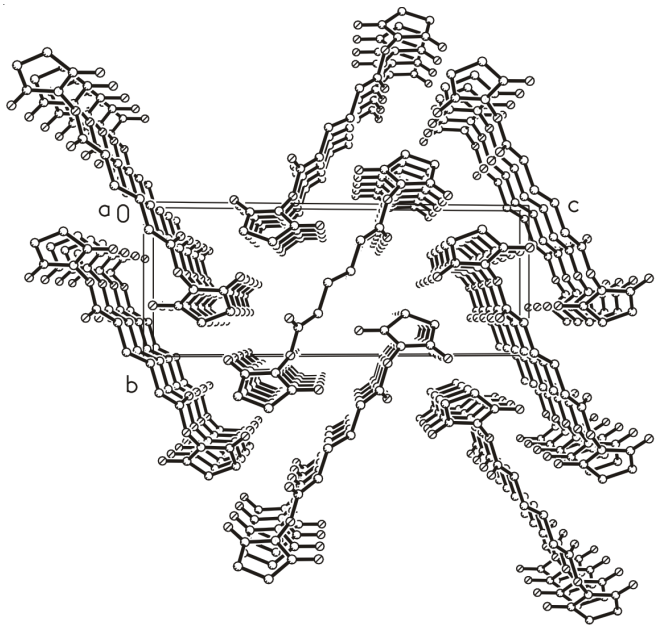


Fig. 2. Crystal packing for the title compound

TABLE-1
CRYSTAL DATA AND STRUCTRE REFINEMENT OF TITLE COMPOUND

Items	Values
Empirical formula	$C_{14}H_{16}N_2O_8$
Formula weight	340.29
Crystal system	Monoclinic
Unit cell dimensions	
a/Å	5.2972(3)
b/Å	7.5196(5)
c/Å	19.2660(13)
Unit cell angles (°)	
α/°	90.00
β/°	99.776(6)
γ/°	90.00
Volume/Å^3	756.28(8)
Z	2
Temperature (K)	291.15
Space group	$P2_1/c$
Calculated density (g/cm^3)	1.494
μ(mm^{-1})	1.070
F(000)	365.0
Crystal size (mm^3)	0.26 × 0.24 × 0.20
2θ Range for data collection (°)	9.32 to 133.96
Reflections collected	2484
Independent reflections	1342[R_{int} = 0.0255]
Final R indexes [I ≥ 2σ(I)]	R_1 = 0.0404, wR_2 = 0.1135

TABLE-2
SELECTED BOND LENGTHS [Å] OF TITLE COMPOUND

Bonds lengths	X-Ray crystal	Bonds lengths	X-Ray crystal
O1-C1	1.200(3)	N1-C1	1.375(3)
O2-C4	1.191(3)	N1-C4	1.390(3)
O3-N1	1.387(2)	C7-C7'[1]	1.524(3)
O3-C5	1.411(2)	O4-C5	1.182(2)

[1]1-X, -Y, -Z

The title compound crystallizes in the monoclinic space group $P2_1/c$. The unit cell contains two molecules of title compound. As can be seen in Fig. 1, the molecular structure consists of two five-member ring (N1, C1, C2, C3, C4 and N1A, C1A, C2A, C3A, C4A) which are fairly planar with plane equation -3.4768 (0.0044) × -5.6710 (0.0054) y + 1.7512 (0.0199) z = 0.4919 (0.0084). The distance of the two planes is 4.460 Å and the centre distance of the five-members rings is 12.983 Å. There is no any classic intermolecular or intramolecular hydrogen bonds in the structure cell[7,8], which maybe the primary reason that the compound possesses a lower melt point (56 °C).

TABLE-3
SELECTED BOND ANGLES [°] AND TORSIONAL ANGLES [°] OF TITLE COMPOUND

Bonds angles	X-ray crystal	Bonds angles	X-ray crystal
N1-O3-C5	112.52(14)	O2--C4-N1	124.08(19)
O3-N1-C4	120.25(16)	O2-C4-C3	130.5(2)
C1-N1-O3	122.89(17)	N1-C4-C3	105.37(17)
C1-N1-C4	116.85(17)	O3-C5-C6	107.80(15)
O1-C1-N1	125.1(2)	O4-C5-O3	121.64(16)
O1-C1- C2	129.71(19)	O4-C5- C6	130.56(19)
N1-C1-C2	105.24(18)	C5-C6-C7	113.29(16)
C1-C2-C3	106.41(16)	C6-C7-C7[1]	111.8(2)

[1]1-X, -Y, -Z

TABLE-4
SELECTED BOND TORSIONAL ANGLES [°] OF TITLE COMPOUND

Bonds angles	X-ray crystal	Bonds angles	X-ray crystal
O1-C1-C2-C3	-178.1(2)	O3-N1-C1-C2	-179.05(17)
O3-N1-C1-O1	1.3(3)	O3-N1-C4-O2	-3.3(3)
O3-N1-C4-C3	175.45(17)	O3-C5-C6-C7	-178.92(17)
O4-C5-C6-C7	1.5(3)	N1-O3-C5-O4	10.1(3)
N1-O3-C5-C6	-169.59(16)	N1-C1-C2-C3	2.3(2)
C1-N1-C4-O2	175.4(2)	C1-N1-C4-C3	-5.8(2)
C1-C2-C3-C4	-5.5(2)	C2-C3-C4-O2	-174.7(2)
C2-C3-C4-N1	6.6(2)	C4-N1-C1-O1	-177.4(2)
C4-N1-C1-C2	2.2(2)	C5-O3-N1-C1	-93.8(2)
C5-O3-N1-C4	84.8(2)	C5-C6-C7-C7[1]	-173.1(2)

Supplementary material: CCDC 1009056 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge CrystallographicData Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; email: deposit@ ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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