



Synthesis and Structural Characterization of N-(2-Carboxyphenyl)-exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboximide

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The compound N-(2-carboxyphenyl)-exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboximide (C₁₅H₁₁NO₅, M_r = 285.25) was synthesized and characterized by elemental analysis, ¹H NMR spectra, IR spectra and single crystal X-ray diffraction. The crystal belongs to monoclinic, space group P2₁/n, with a = 8.4994(8), b = 14.6499(15), c = 10.2880(10) Å, β = 101.5890(10)°, V = 1254.9(2) Å³, Z = 4, D_c = 1.510 g/cm³, λ = 0.71073 Å, (MoK_α) = 0.115 mm⁻¹, F₍₀₀₀₎ = 592. The final refinement gave R = 0.0374, wR(F²) = 0.0856 for 2,201 observed reflections with I > 2σ(I). The structure of the compound comprises a racemic mixture of chiral molecules containing four stereogenic centres. X-Ray diffraction analysis reveals that the cyclohexane ring tends towards a boat conformation, the tetrahydrofuran ring and the dihydrofuran ring adopt envelope conformations. The dihedral angle between the pyrrolidine-2,5-dione plane and the aromatic ring is 65.0 (1)°. The crystal structure is stabilized by O-H...O and C-H...O hydrogen bonds.

Key Words: N-(2-Carboxyphenyl)-exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboximide, Synthesis.

INTRODUCTION

The imide moiety is an integral structural part of various important bioactive molecules such as fumaramidmycin, granulatimide, isogranulatimide and rebeccamycin. These molecules are reported to exhibit antitumor, antiinflammatory and antimicrobial activities¹⁻³. 7-Oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride has been widely employed in clinical practice, as it is less toxic and much easier to be synthesized^{4,5}. Its derivatives are also pharmacologically active⁶. Furthermore, 7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboximide and its N-substituent compounds have recently become an intense research topic in heterocyclic chemistry because of their antitumor, antiviral, analgesic, sedative and fungicidal activities⁷. In the previous work, N-phenyl-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboximide was synthesized and its structure was characterized⁸.

In this paper, the title compound N-(2-carboxyphenyl)-exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboximide was synthesized and its molecular structure was investigated by elemental analysis, ¹H NMR spectra, IR spectra and X-ray crystallographic techniques.

EXPERIMENTAL

Infrared absorption spectra were obtained from a Nicolet NEXUS 670 FT-IR spectrometer in KBr discs and were

reported in cm⁻¹ units. ¹H NMR spectra were determined on a Bruker DRX-400 NMR spectrometer with TMS as internal standard in DMSO-*d*₆. Carbon, nitrogen and hydrogen analyses were performed on an elemental analysensysteme GmbH Vario EL analyzer. Furan, maleic anhydride and *o*-aminobenzoic acid were purchased from Weifang Runze (China). All other chemicals used in this work were of analytical grade.

The synthesis of exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride was followed from literature^{8,9}.

A mixture of exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride (0.332 g, 2 mmol) and *o*-aminobenzoic acid (0.274 g, 2 mmol) in methanol (5 mL) was stirred for 5 h at room temperature and then refluxed for 1 h. After cooling the precipitate was filtered and dried, the title compound was obtained. Yield: 82 %. m.p. 158.3-158.9 °C. The crude product of 20 mg was dissolved in methanol of 10 mL. The solution was filtered to remove impurities and then the filtrate was left for crystallization at room temperature. The single crystal suitable for X-ray determination was obtained by evaporation from the methanol solution after 5 days.

Anal. calcd. (%) for C₁₅H₁₁NO₅: C 63.15, H 3.86, N 4.91. Found (%): C 63.06, H 4.97, N 5.01. Selected IR (KBr) data (cm⁻¹): 3075 (A r-H), 1775, 1683 (C=O), 1600 (C=C), 1197 (C-O-C), 718 (=C-H). ¹H NMR (DMSO-*d*₆, ppm) δ: 8.05 (d, 1H, ArH), 7.78 (d, 1H, ArH), 7.58 (dd, 1H, ArH), 7.14 (dd,

1H, ArH), 5.87 (s, 2H, C₁₃H, C₁₄H), 4.73 (s, 2H, C₁₂H, C₁₅H), 3.10 (s, 2H, C₁₀H, C₁₁H).

Data collection and structure determination: A single crystal X-ray data of title compound was collected on a Bruker SMART diffractometer with a graphite monochromatized MoK α radiation ($\lambda = 0.71073$ Å). The structure was solved by SHELXS-97 and refined with SHELXL-97¹⁰. The positions of the H atoms bonded to C atoms were calculated (C-H distance 0.96 Å) and refined using a riding model. The H atom displacement parameters were restricted to be 1.2U_{eq} of the parent atom. The details of the X-ray data collection, experimental conditions and structure solution and structure refinements are given in Table-1. Some selected bond distances and angles are listed in Table-2. The molecular structures with the atom-numbering scheme are shown in Fig. 1. CIF file containing complete information on the studied structure was deposited with CCDC, deposition number 775724 and is freely available upon request from the following web site: www.ccdc.cam.ac.uk/data_request/cif.

TABLE-1
CRYSTAL AND EXPERIMENTAL
DATA FOR THE TITLE COMPOUND

Compound	C ₁₅ H ₁₁ NO ₅
Colour/shape	Light yellow/block
Formula weight	285.25
CCDC deposit no.	775724
Crystal system	Monoclinic
Space group	P2 ₁ /n
Unit cell dimensions	a = 8.4994(8) Å b = 14.6499(15) Å c = 10.2880(10) Å $\beta = 101.5890(10)^\circ$
Volume	1254.9(2) Å ³
Z	4
Density (calculated)	1.510 g cm ⁻³
Absorption coefficient	0.115 mm ⁻¹
F ₍₀₀₀₎	592
Crystal size (mm)	0.50 × 0.49 × 0.47
θ range for data collection	2.45–25.01°
Index ranges	−9 ≤ h ≤ 10; −17 ≤ k ≤ 16; −12 ≤ l ≤ 6
Reflections collected	6,115
Independent reflections	2,201
Reflections observed (I > 2σ(I))	1,644
Refinement method	Full-matrix least-squares on F ²
Data/parameters	2201/190
Goodness-of-fit on F ²	1.063
R indices [I > 2σ(I)]	R ₁ = 0.0374; wR ₂ = 0.0856
R indices (all data)	R ₁ = 0.0570; wR ₂ = 0.1020
Largest diff. peak and hole	0.249 and −0.183 e Å ⁻³

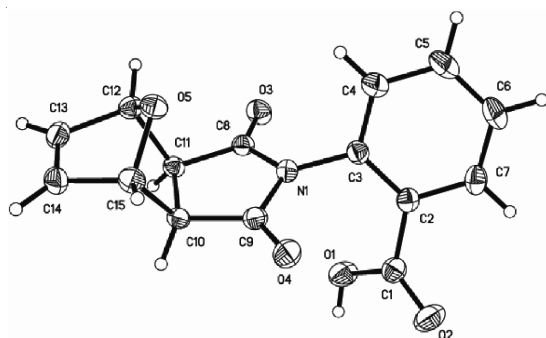


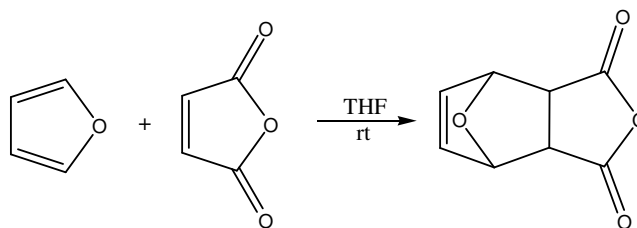
Fig. 1. Molecular structure of the title compound

TABLE-2
SELECTED BOND LENGTHS (Å) AND BOND ANGLES (°)

Bond	Length (Å)	Bond	Angle (°)
N(1)–C(8)	1.382(2)	C(8)–N(1)–C(9)	112.46(16)
N(1)–C(9)	1.403(3)	C(8)–N(1)–C(3)	124.16(16)
N(1)–C(3)	1.439(2)	C(9)–N(1)–C(3)	123.34(16)
O(1)–C(1)	1.316(2)	C(12)–O(5)–C(15)	96.03(14)
O(2)–C(1)	1.204(2)	O(2)–C(1)–O(1)	123.4(2)
O(3)–C(8)	1.215(2)	O(2)–C(1)–C(2)	122.87(19)
O(4)–C(9)	1.203(2)	O(1)–C(1)–C(2)	113.66(17)
O(5)–C(12)	1.433(2)	C(4)–C(3)–N(1)	118.06(18)
O(5)–C(15)	1.441(2)	C(2)–C(3)–N(1)	121.08(17)
C(8)–C(11)	1.495(3)	O(3)–C(8)–N(1)	124.52(18)
C(9)–C(10)	1.503(3)	O(3)–C(8)–C(11)	126.73(18)
C(10)–C(11)	1.539(3)	N(1)–C(8)–C(11)	108.75(16)
C(10)–C(15)	1.560(3)	O(4)–C(9)–N(1)	123.57(18)
C(11)–C(12)	1.573(3)	O(4)–C(9)–C(10)	127.99(18)
C(12)–C(13)	1.505(3)	N(1)–C(9)–C(10)	108.43(16)
C(13)–C(14)	1.316(3)	O(5)–C(12)–C(13)	102.33(16)
C(14)–C(15)	1.508(3)	O(5)–C(12)–C(11)	101.21(14)

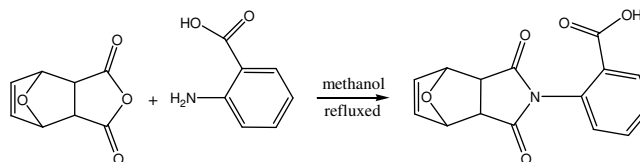
RESULTS AND DISCUSSION

Furan reacts in a Diels-Alder reaction with maleic anhydride in tetrahydrofuran at room temperature to give exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride as shown in **Scheme-I**.



Scheme-I: Synthesis of exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride

The condensation reaction between exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride and *o*-aminobenzoic acid proceeded smoothly in methanol at room temperature for 5 h and refluxed temperature for 1 h, respectively, leading to the title compound in high yield (**Scheme-II**). The elemental analysis, IR spectra and ¹H NMR data clearly indicated that the condensation reaction between exo-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboxylic anhydride and *o*-aminobenzoic acid in a ratio of 1:1.



Scheme-II: Synthesis of the title compound

The structure of the title compound, C₁₅H₁₁NO₅, comprises a racemic mixture of chiral molecules containing four stereogenic centres. As seen from Fig. 1, the cyclohexane ring tends towards a boat conformation and the tetrahydrofuran ring and the dihydrofuran ring adopt envelope conformations. The dihedral angle between the pyrrolidine-2,5-dione plane

and the aromatic ring is 65.0 (1)°. As seen from Table-2, the bond lengths and bond angles are as expected. And they are comparable to those in the similar compounds^{10,11}. In 7-oxabicyclo(2,2,1)hept-5-ene-2,3-dicarboximide group, the C-C bonds lengths [1.495(3)1.573(3) Å], except C13-C14 double bond length [1.316(3) Å], are longer than the normal single bond length. The degree of lengthening of the C-C bonds in the title compound is in good agreement with that of corresponding C-C bonds in N-phenyl-7-oxa-bicyclo[2,2,1]hept-5-ene-2,3-dicarboximide⁸, N-methyl-7-oxabicyclo(2,2,1)hept-5-ene-2,3-exo-dicarboximide¹¹ and exo-4-[(4-bromophenyl)amino]-10-oxa-4-azatricyclo(5,2,1,0^{2,6})dec-8-ene-3,5-dine¹². The crystal structure is stabilized by O-H...O and C-H...O intermolecular hydrogen bonds (Fig. 2 and Table-3). The existence of the benzene ring is great helpful to forming a strong π - π stacking interactions¹³.

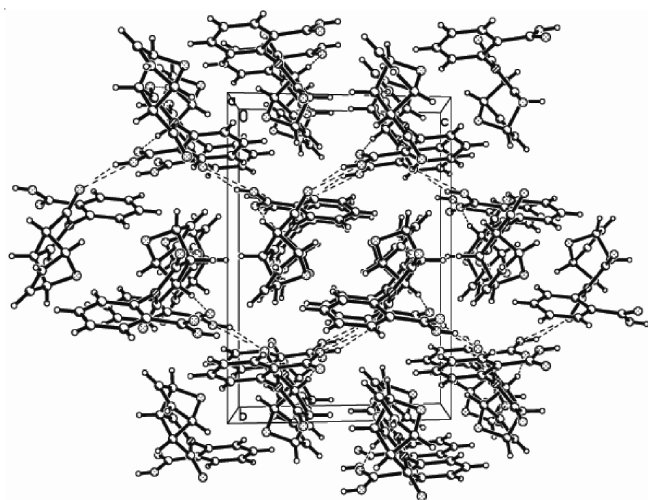


Fig. 2. Crystal packing of the title compound

TABLE-3
HYDROGEN BOND SCHEMES (Å, °)

D-H...A	D-H	H...A	D-A	D-H...A
O1-H1...O3 ⁱ	0.82	1.985	2.744	154
C11-H11...O2 ⁱⁱ	0.98	2.568	3.444	149
C13-H13...O4 ⁱⁱ	0.93	2.564	3.488	173

Symmetry codes: (i) $-1/2 + x, 1/2 - y, -1/2 + z$, (ii) $1 + x, y, z$.

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