Asian Journal of Chemistry; Vol. 24, No. 8 (2012), 3436-3438

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Synthesis and Crystal Structure of Benzofuran Derivative

YONG-ZHONG LU, GUANG-QI JIANG, XIAO-QIN and QIAN-JUN ZHANG*

College of Chemistry and Chemical Engineering, Guizhou University, Guiyang 550025, P.R. China

*Corresponding author: Tel: +86 851 8292313; E-mail: qianjunzhang@126.com

(*Received*: 6 July 2011; *Accepted*: 6 March 2012) AJC-11160

The single crystal of 5-nitro-3-*N*-(succinimidyl)-2-benzofuran acid ethyl ester (**3**) was obtained by recrystallization from petroleum ether-ethyl acetate (2:1 v/v) solution. Its structure was confirmed by EI-MS, ^{1}H NMR, ^{13}C NMR and single crystal X-ray diffraction analysis. It crystallized in the triclinic system, space group P-1 with unit cell parameters: a = 9.268(13) Å, b = 11.671(15) Å, c = 15.414(2) Å, α = 75.185 (5)º, β = 72.683 (5)º, γ = 71.301 (5)º. V = 1483.8 (3) Å^3, Z = 4, Mr = 332.27, Dc = 1.487 g/cm^3, μ = 0.120 mm^{-1}, F (000) = 688.0, R = 0.0414, wR = 0.1108 for 5148 reflections with I > 2σ (I). The crystal is stabilized by hydrogen bondings and C-H…π interactions and forming a 2D supramolecular layer structure.

Key Words: Benzofuran, Crystal structure, Synthesis.

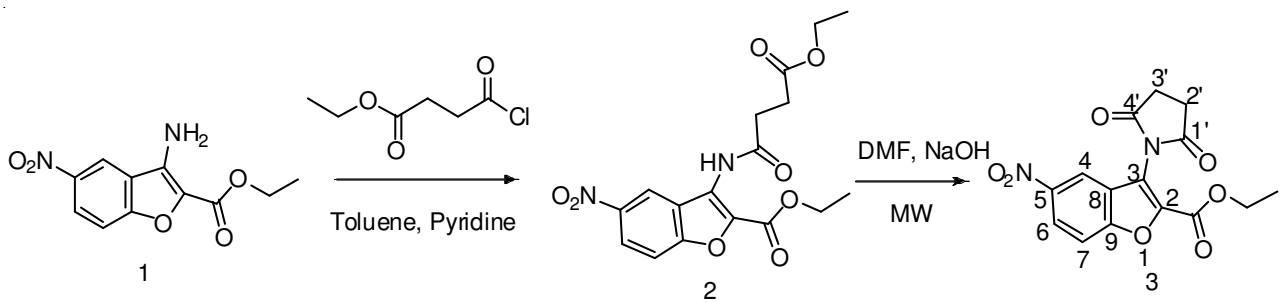
INTRODUCTION

Furan derivatives, especially the benzofuran derivatives was a class of compound with strong biological activities, such as anticancer[1], insecticidal[2], sterilization[3-5], antioxidant[6], anti-inflammatory activity[7], *etc*., so it attracted extensive attentions of chemists and biologists. Microwave technology has been proven as a powerful tool for speeding up reactions and the efficient preparation of new target molecules for drug discovery projects in industry and academia[8]. In this paper, we reported the synthesis of a new benzofuran derivative and presented its crystal structure.

EXPERIMENTAL

Compound **3** was synthesized following the procedure (**Scheme-I**). The raw materials 3-amino-5-nitro-2-benzofuran acid ethyl ester[9] and ethyl succinyl chloride[10] were prepared according to literature methods, respectively. Other reagents were AR grade and were used without further purification. The ^{1}H NMR spectrum was recorded on Bruker AV500 NMR spectrometer, $CDCl_3$ was used as the solvent, tetramethylsilane (TMS) was used as an internal standard.

Synthesis of 3-[(4-ethoxy-1,4-dioxobutyl)-aminol]-5-nitro-2-benzofuran acid ethyl ester (2): A solution of ethyl succinyl chloride (197 mg, 1.2 mmol) in toluene (5 mL) was added dropwise to a stirred solution of 3-amino-5-nitro-2-benzofuran acid ethyl ester (250 mg, 1 mmol) and pyridine (2 mL) in toluene (5 mL) at room temperature. The mixture was stirred for 1.5 h and then water (5 mL) was added. The resulting organic layer was separated using a separating funnel, washed with 10 % hydrochloric acid (2 mL) and 5 % sodium carbonate solution (2 mL), respectively. Then dried with magnesium sulfate and evaporated and the residue was crystallized from ethanol, yielding 79.7 % white crystals: m.p. 135-136 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 1.28 (t, 3H, *J* = 7.1 Hz, O-CH_2-CH_3), 1.47 (t, 3H, *J* = 7.1 Hz, O-CH_2-CH_3), 2.79-2.85



Scheme-I: Sythesis of compound **3**

(m, 4H, CH_2-CH_2), 4.18 (q, 2H, J = 7.2 Hz, O-CH_2-CH_3), 4.50 (q, 2H, J = 7.1 Hz, O-CH_2-CH_3), 7.57 (d, 1H, J = 9.1 Hz, Ar-H), 8.36 (dd, 1H, J = 2.3 Hz, 9.1 Hz, Ar-H), 9.39 (d, 1H, J = 2.3 Hz, Ar-H), 9.48 (s, 1H, N-H).

Synthesis of 5-nitro-3-*N*-(succinimidyl)-2-benzofuran acid ethyl ester (3): Compound 2 (365 mg, 1 mmol) and sodium hydroxide (44 mg, 1.1 mmol) were dissolved in DMF (5 mL). The reaction was conducted in a sealed microwave reaction vessel employing the following conditions: reaction time 4 min, microwave power 640 W. After cooling to room temperature, the mixture was neutralized by cautions addition of acetic acid. Water (3 mL) was then added dropwise and the organic layer was separated by means of a separating funnel, then evaporated, the residue was crystallized from Petroleum ether-ethyl acetate (2:1 v/v), yielding 72.6 % colourless crystals: m.p. 195-197 ºC; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 1.39 (t, 3H, J = 7.2 Hz, O-CH_2-CH_3), 3.05 (s, 4H, CH_2-CH_2), 4.41 (q, 2H, J = 7.3 Hz, O-CH_2-CH_3), 7.73 (d, 1H, J = 9.1 Hz, Ar-H), 8.42-8.45 (m, 2H, Ar-H); ^{13}C NMR ($CDCl_3$): δ (ppm) = 174.4 (C-1', C-4'), 157.5 (-COO-), 156.2 (C-9), 145.1 (C-5), 143.0 (C-3), 124.6 (C-8), 124.0 (C-2), 120.3 (C-6), 118.0 (C-4), 113.8 (C-7), 62.5 (O-CH_2-), 29.0 (C-2', C-3'), 14.2 (-CH_3); EI-MS: m/z (%) = 332 (100 %, M^+), 302 (14), 250 (58), 231 (60), 185 (17), 55 (71).

Crystal structure determination: The X-ray data were collected on a Bruker Apex-II CCD diffractometer using graphite monochromated MoK_α radiation (λ = 0.71073 Å) at 293 (2) K with crystal size 0.21 mm × 0.18 mm × 0.13 mm. A total of 5148 (R_{int} = 0.0249) independent reflections were collected by φ and ω scans technique in the range of 0.986 ≤ θ ≤ 25.00º from which 4122 [I >2σ (I)] reflection were corrected for Lorentz and polarization factors. The structure was solved by direct method using SHELXS-97[11] and refined using a full-matrix least-squares procedure on F^2 in SHELXS-97. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added theoretically and refined with riding model.

RESULTS AND DISCUSSION

X-ray crystal structure study shows there are two crystallographically independent molecules in the asymmetric unit, but no solvent molecules in the lattice. Fig. 1 shows the molecular structure of compound 3. It crystallizes in P-1 space group. The selected bond lengths and bond angles are given in Table-1. N-O distances range from 1.214 (2) to 1.219 (2) Å; C-N distances range from 1.389(2) to 1.463(2) Å; the C8-C7-N5-C15 torsion angel of 109.6(2)º and the C8-C7-N5-C31 torsion angel of -66.7(3)º. It is worth noting that the benzofuran ring (C1-C2-C3-C4-C5-O3-C8-C7-C6) and the pyrrolidine ring (N5-C31-C13- C14-C15) of compound 3 is obviously not coplanar, the dihedral angle between the two heterocyclic rings is *ca*. 59.42º.

Fig. 2 shows the packing diagram of the compound **3**. The crystal were stabilized by C-H…O intermolecular hydrogen bonds (as listed in Table-2) and C25-H25B…Cg (Cg: O3-C5-C6-C7-C8, Symmetry code: x, y, z) interactions with the C…Cg distance of 3.613(3) Å and C-H…Cg angle of 161º. These interactions were formed between adjacent molecules resulting in a 2D supramolecular layers.

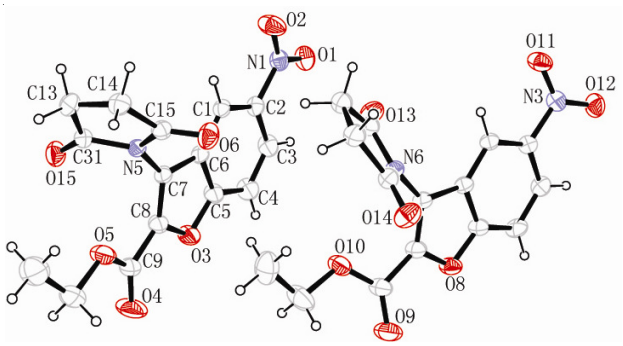


Fig. 1. Molecular structure of compound **3**

TABLE-1
SELECTED BOND DISTANCES (Å) AND ANGLES (º)

O1-N1	1.219(2)	O6-C15	1.205(2)	C5-O3-C8	106.26(13)
O2-N1	1.214(2)	N1-C2	1.463(2)	C15-N5-C31	113.20(14)
O3-C5	1.363(2)	N5-C7	1.404(2)	O6-C15-N5	123.60(16)
O3-C8	1.374(2)	N5-C15	1.389(2)	O4-C9-O5	124.9(2)
O3-C9	1.191(3)	C7-C8	1.348(2)	N5-C7-C8	126.89(16)
O5-C9	1.320(3)	C13-C14	1.515(3)	O1-N1-O2	122.50(17)

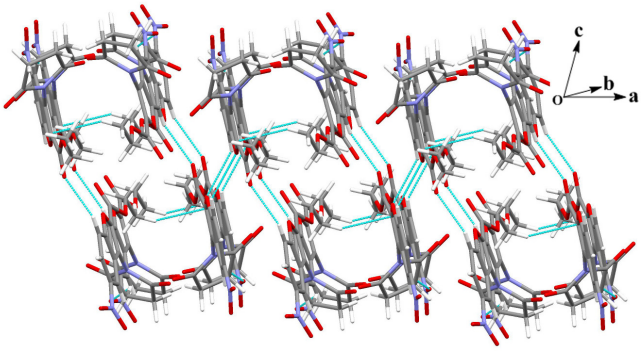


Fig. 2. Packing diagram of compound **3**

TABLE-2
HYDROGEN BOND AND C-H…π INTERACTIONS
DISTANCES (Å) AND ANGLES (°)

Type (D-H…A)	d (D-H)	d (H…A)	∠ (DHA)	d (D…A)	Symmetry code
C1-H1…O11	0.9300	2.4800	164.00	3.384(2)	1-x, 1-y, 1-z
C13-H13A…O1	0.9700	2.4600	145.00	3.299(2)	x, -1+y, z
C18-H18…O4	0.9300	2.3900	155.00	3.253(3)	2-x, 1-y, -z
C33-H33…O2	0.9300	2.4200	151.00	3.266(2)	1-x,1-y,1-z
C25-H25B…Cg	0.9600	2.6900	161.00	3.613(3)	x, y, z

Conclusion

A new benzofuran derivative has been synthesized and characterized by EI-MS, ^{1}H NMR, ^{13}C NMR and X-ray diffraction analysis. It crystallized in the triclinic system with P-1 space group. X-ray crystal structure study shows there are two crystallographically independent molecules in the asymmetric unit. The crystal packing were stabilized by C-H…O intermolecular hydrogen bondings and C-H…π interactions and these interactions resulting in a 2D supramolecular layer structure as illustrated in Fig. 2.

Supplementary material: Crystallographic data for the structure reported in this paper have been deposited with the Cambridge crystallographic data center as supplementary publication No. CCDC 831573.

ACKNOWLEDGEMENTS

The auothors gratefully acknowledged the financial support from the Foundation of Guizhou Province China (No. [2011]2067).

REFERENCES

1. J.D. Lambert, R.O. Meyers, B.N. Timmermann and R.T. Dorr, *Cancer Lett.*, **47**, 171 (2001).
2. G. Brader, H. Greger, M. Bacher, H. Kalchhauser and O. Hofer, *J. Nat. Prod.*, **61**, 1482 (1998).
3. J.T. Pechcek, F.E. Tisdell, H.D. Devries, *et al.*, WO Patent, 9847894 (1998).
4. S.S. Pelosi and C.N. Yu, US Patent, 4162257 (1979).
5. B.H. Lipshutz, *Chem. Rev.*, **86**, 795 (1986).
6. D.H. Silva, F.C. Pereira, M.V. Zanoni and M. Yoshida, *Phytochemistry*, **57**, 437 (2001).
7. M.L.C. Borsato, C.F.F. Grael and N.P. Lopes, *Phytochemistry*, **55**, 809 (2000).
8. F. Mavandadi and A. Pilotti, *Drug Discov. Today*, **11**, 165 (2006).
9. M.G. Liu, Y.G. Hu, G.P. Cheng, T. Xie and Z. Yang, *J. China Three Gorges Univ*. (*Nat. Sci.*), **2**, 174 (2007).
10. J.G. Wei, X.D. Ma, Y.T. Shen and J.C. Liu, *Appl. Chem. Ind.*, **5**, 20 (2002).
11. G.M. Sheldrick, SHELXL-97 Program for the Solution and Refinement of Crystal structures, University of Göttingen, Germany (1997).