

Article

# Synthesis and Crystal Structures of Two New Oxaspirocyclic Compounds

Jinhe Jiang and Wulan Zeng \*

MicroScale Science Institute, Department of Chemistry, Chemical Engineering and Environmental Engineering, Weifang University, Weifang 261061, China; jiangjinhe2006@163.com

\* Correspondence: wulanzeng@163.com; Tel.: +86-536-8785802

Academic Editor: Helmut Cölfen

Received: 3 August 2016; Accepted: 6 October 2016; Published: 18 October 2016

**Abstract:** Two new oxaspirocyclic compounds, 8-(4-(dimethylamino)benzylidene)-6,10-dioxaspiro[4.5]decane-7,9-dione (**1**) and 8-(4-hydroxybenzylidene)-6,10-dioxaspiro[4.5]decane-7,9-dione (**2**) have been synthesized and their structures determined by single crystal X-ray crystallography. Compound **1**,  $C_{17}H_{19}NO_4$ , belongs to the monoclinic system, space group P21/c with  $a = 6.2554(13)$  Å,  $b = 14.605(3)$  Å,  $c = 16.265(3)$  Å,  $\beta = 95.97(3)^\circ$ ,  $V = 1477.9(5)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.354$  g/cm<sup>3</sup>,  $F(000) = 640$ ,  $\mu(\text{MoK}\alpha) = 0.097$  mm<sup>-1</sup>, the final  $R = 0.0570$  and  $wR = 0.1667$ . Compound **2**,  $C_{15}H_{14}O_5$ , is also of the monoclinic system, space group P21/c with  $a = 10.739(2)$  Å,  $b = 18.348(4)$  Å,  $c = 6.7799(14)$  Å,  $\beta = 104.20(3)^\circ$ ,  $V = 1295.1(5)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.407$  g/cm<sup>3</sup>,  $F(000) = 608$ ,  $\mu(\text{MoK}\alpha) = 0.106$  mm<sup>-1</sup>, the final  $R = 0.0568$  and  $wR = 0.1739$ . Some C–H $\cdots$ O intra- and intermolecular hydrogen bonds and  $\pi\cdots\pi$  stacking interactions are both observed in the two lattice structures. The difference between them is that one type of C–H $\cdots\pi$  supramolecular interaction (**1**) and one type of O–H $\cdots$ O intermolecular hydrogen bond (**2**) are observed.

**Keywords:** synthesis; crystal structure; 6,10-dioxaspiro[4.5]decane-7,9-dione

## 1. Introduction

In recent years, many efforts have been devoted to the preparation and characterization of spiro compounds due to diverse industrial and biomedical applications in medicine [1–3], catalysis [4], 18F-radiolabeling [5] and optical material [6–8]. The asymmetric characteristic of the molecules, owing to the chiral spiro carbon, is one of the important criteria of the biological activities. Also, it has been found that the selectivities and activities of spiro compounds will be stronger by inducing an oxygen atom. The presence of oxaspirocyclic compounds in various natural products has also emerged, increasing interest due to their important biological activities, such as antimicrobial [9,10], antitumor [11], antiproliferative [12], antiviral [13], antiplasmodial [14] and antihistamic [15] activity etc. Based on these reasons, our group began to synthesize various oxaspirocyclic compounds and study their chemical properties [16–19]. In addition, to the best of our knowledge, oxaspirocyclic compounds derived from 6,10-dioxaspiro[4.5]decane-7,9-dione are very rare. In this paper, we describe the synthesis of two new oxaspirocyclic compounds: 8-(4-(dimethylamino)benzylidene)-6,10-dioxaspiro[4.5]decane-7,9-dione **1** and 8-(4-hydroxybenzylidene)-6,10-dioxaspiro[4.5]decane-7,9-dione **2**. Their structures are also characterized by elemental analysis, IR, NMR and single-crystal X-ray diffraction.

## 2. Results and Discussion

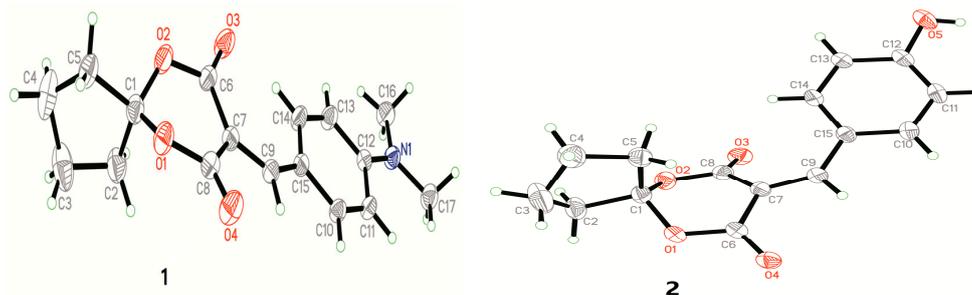
### 2.1. Crystal Structures

Selected bond lengths and angles of the two compounds are listed in Table 1. The molecular structures of **1** and **2** are shown in Figure 1. The packing arrangements in the unit cell of **1** and **2** are illustrated in Figure 2, respectively.

**Table 1.** Selected bond lengths (Å) and bond angles (°) of the two compounds.

Compound 1		Compound 2	
O(1)–C(8)	1.367(3)	O(2)–C(8)	1.353(3)
O(1)–C(1)	1.422(3)	O(2)–C(1)	1.423(3)
C(9)–C(7)	1.373(3)	C(7)–C(9)	1.356(3)
C(15)–C(9)	1.428(3)	C(9)–C(10)	1.447(3)
O(3)–C(6)	1.201(3)	O(4)–C(6)	1.214(3)
O(4)–C(8)	1.202(3)	O(3)–C(8)	1.202(3)
O(2)–C(6)	1.360(3)	O(1)–C(6)	1.339(2)
O(2)–C(1)	1.415(3)	O(1)–C(1)	1.454(3)
C(12)–N(1)	1.362(3)	O(5)–C(12)	1.355(3)
N(1)–C(16)	1.446(3)	C(10)–C(15)	1.399(3)
N(1)–C(17)	1.448(3)	C(7)–C(6)	1.475(3)
C(7)–C(9)–C(15)	137.76(2)	C(7)–C(9)–C(15)	129.67(2)
C(2)–C(1)–C(5)	106.3(2)	C(2)–C(1)–C(5)	106.3(2)
O(2)–C(1)–O(1)	109.63(2)	O(2)–C(1)–O(1)	108.55(2)
C(6)–C(7)–C(8)	117.6(2)	C(6)–C(7)–C(8)	115.54(2)
C(10)–C(15)–C(14)	115.4(2)	C(10)–C(15)–C(14)	117.61(2)
C(10)–C(15)–C(9)	116.42(2)	C(10)–C(15)–C(9)	119.42(19)

The two compounds both consist of a phenyl ring and 6,10-dioxaspiro[4.5]decane-7,9-dione group which connects a five-membered cyclopentane ring with the other O-containing six-membered ring by a C spiro atom (Figure 1). The selected bond lengths and bond angles of compound **1** are similar to those of **2** correspondingly.



**Figure 1.** The molecular structures of **1** and **2** with the atomic numbering scheme.

As can be seen from the Table 1, the C(7)–C(9)–C(15) bond angle of 137.76(2)° (**1**), 129.67(2)° (**2**) is likewise in agreement with those reported earlier (136.78(18)°, 136.5(2)°) [18]. The C9–C7 bond length of 1.373(3) Å (**1**), 1.356(3) Å (**2**) is indicative of the considerable double-bond character, while the C9–C15 bond length of 1.428(3) Å (**1**), 1.447(3) Å (**2**) is the typical C–C single bond. The 1,3-dioxane rings of the two compounds are both in a distorted envelope conformation with atom C(1), common to the cyclopentane ring forming the flap. It is noteworthy that the cyclopentane rings of the two compounds exhibit a different configuration. The cyclopentane ring of **1** is in half-chair configuration with puckering parameters [20] for  $q_2 = 0.335(4)$  Å,  $\varphi_2 = 96.3(6)^\circ$ ; while the cyclopentane ring in **2** exhibits an envelope configuration with puckering parameters for  $q_2 = 0.298$  Å,  $\varphi_2 = 55.14^\circ$ .

In **1**, all atoms in the 4-dimethylamino benzylidene group are fairly planar (Plane equation:  $2.469x + 4.909y + 13.165z = 10.899$ ), with the maximum deviation from the mean plane of  $0.069(3)$  Å. The four atoms—O2, O3, C6 and C7—form a plane (Plane equation:  $2.047x + 2.929y + 14.384z = 10.021$ ), with the largest deviation of  $0.014(3)$  Å. The dihedral angle between the two planes is  $9.53^\circ$ . In **2**, all atoms in the 4-hydroxybenzylidene group are also quite planar, (Plane equation:  $-2.6309x - 0.2671y + 6.7792z = 1.0129$ ), and the largest deviation from the least squares plane is  $0.035(3)$  Å. The four atoms—O4, O1 C6 and C7—form a plane (Plane equation:  $-5.2019x + 2.6946y + 6.4742z = 0.4529$ ), with no deviation. The dihedral angle between the two planes is  $17.71^\circ$ .

The two compounds have a similar structure. There are  $\pi \cdots \pi$  stacking interactions and some C–H $\cdots$ O intra- and intermolecular hydrogen bonds in the two lattice structures. In addition, one type of C–H $\cdots$  $\pi$  supramolecular interaction in **1** is also present. One classical intermolecular hydrogen bond of O–H $\cdots$ O is also observed in **2** (Tables 2 and 3). All above hydrogen bonds and intermolecular interactions play a significant role in stabilizing the crystal structures (Figure 3).

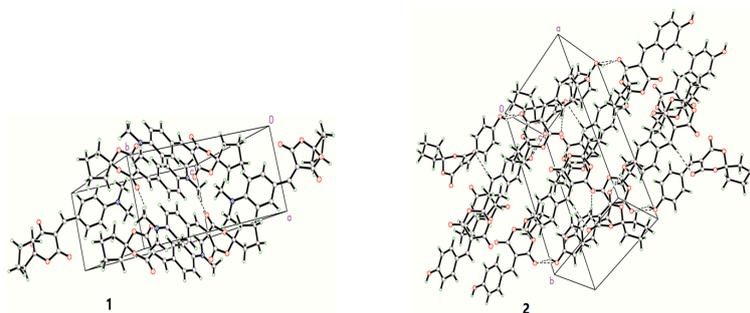


Figure 2. The packing arrangement in a unit cell of **1** and **2**.

Table 2. Intra- and intermolecular hydrogen bonds and C–H $\cdots$  $\pi$  supramolecular interactions in **1** and **2**.

D–H $\cdots$ A	Symmetry	D–H(Å)	H $\cdots$ A(Å)	D $\cdots$ A(Å)	$\angle$ D–H $\cdots$ A ( $^\circ$ )
C(9)–H(9A) $\cdots$ O(4) ( <b>1</b> )	intra	0.93(2)	2.357(3)	2.795(3)	108.5(2)
C(14)–H(14A) $\cdots$ O(3) ( <b>1</b> )	intra	0.93(2)	2.116(2)	2.900(3)	141.1(3)
C(17)–H(17A) $\cdots$ O(4) ( <b>1</b> )	$1 - x, 1 - y, 1 - z$	0.96(3)	2.558(2)	3.466(3)	157.7(19)
C(9)–H(9A) $\cdots$ O(4) ( <b>2</b> )	intra	0.93(2)	2.489(2)	2.846(2)	102.9(2)
C(14)–H(14A) $\cdots$ O(3) ( <b>2</b> )	intra	0.93(2)	2.535(3)	3.008(2)	111.8(2)
C(9)–H(9A) $\cdots$ O(3) ( <b>2</b> )	$x, 1/2 - y, -1/2 + z$	0.93(2)	2.539(2)	3.458(3)	169.8(19)
O(5)–H(5A) $\cdots$ O(4) ( <b>2</b> )	$1 + x, 1/2 - y, 1/2 + z$	0.82(2)	1.976(2)	2.707(2)	148.0(3)
C(3)–H(3B) $\cdots$ Cg(3) ( <b>1</b> )	$1/2 - x, 1/2 + y, 3/2 - z$	0.97(3)	3.127(2)	3.832(2)	130.8(2)

Cg(3) ring denotes the phenyl ring of compound **1**: C(10)–C(15).

Table 3. Aromatic-aromatic interactions of **1** and **2**.

Ring	Symmetry	Dihedral Angles ( $^\circ$ )	Distance Between Ring Centroids (Å)	Perpendicular Distance of Cg(I) on Ring J(Å)	Perpendicular Distance of Cg(J) on Ring I(Å)
Cg(3) $\cdots$ Cg(3) <sup>a</sup> ( <b>1</b> )	$-x, 1 - y, 1 - z$	0.02(2)	5.112(3)	3.691(2)	3.691(2)
Cg(3) $\cdots$ Cg(3) <sup>b</sup> ( <b>2</b> )	$x, 1/2 - y, -1/2 + z$	1.89(2)	4.048(2)	3.353(2)	3.426(3)
Cg(3) $\cdots$ Cg(3) <sup>b</sup> ( <b>2</b> )	$x, 1/2 - y, 1/2 + z$	1.89(2)	4.048(2)	3.426(3)	3.353(2)

<sup>a</sup> Cg(3) ring denotes the phenyl ring of compound **1**: C(10)–C(15); <sup>b</sup> Cg(3) ring denotes the phenyl ring of compound **2**: C(10)–C(15).

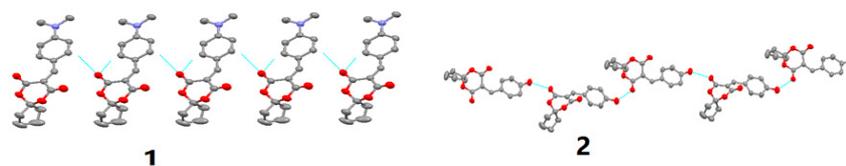


Figure 3. Hydrogen bonds and intermolecular interactions of **1** and **2**.

## 2.2. IR Spectra

The IR spectra of the two compounds show a little difference. The broad absorptions at  $3265\text{ cm}^{-1}$  for **2** are assigned to the O–H stretching vibration of PhOH. The strong bands at  $1705\text{ cm}^{-1}$  **1** and  $1745\text{ cm}^{-1}$  **2**, respectively, are due to the C=O stretching vibration of the 1,3-dioxane ring. The broad absorptions at  $1167\text{ cm}^{-1}$ ,  $1126\text{ cm}^{-1}$  for **1** and at  $1204\text{ cm}^{-1}$ ,  $1163\text{ cm}^{-1}$  for **2** are assigned to the C–O stretching vibration of the 1,3-dioxane ring. Meanwhile, a similar band at  $1609\text{ cm}^{-1}$  and  $1688\text{ cm}^{-1}$  was observed in the IR spectra of **1** and **2**, respectively, indicating C=C stretching vibration of  $\text{N}(\text{CH}_3)_2\text{-ph-C=C}$  in **1** and  $\text{HO-ph-C=C}$  in **2**. The IR spectra of the two compounds are in agreement with the structural data.

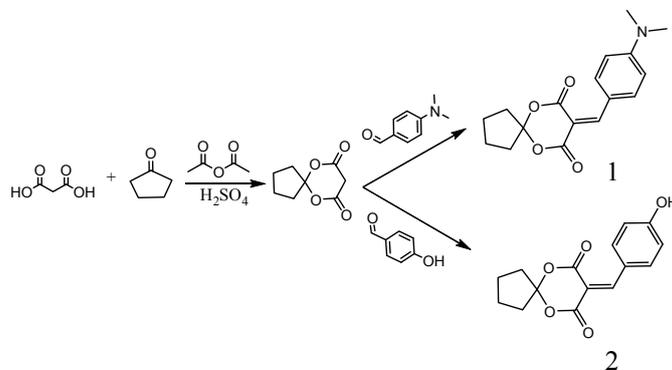
## 3. Experimental Section

### 3.1. Materials and Methods

All the reagents and solvents from commercial sources were used without further purification. The IR spectra were recorded as KBr pellets with a Nicolet FT-IR 510P Spectrometer (Nicolet Instrument Inc., Madison, WI, USA). The analyses of C, H, and N were made on an Elementar Vario EL III elemental analyzer (Elementar, Hanau, Germany).  $^1\text{H}$  NMR spectra were recorded on a Bruker Avance-400 spectrometer (Bruker, Elisabethhof, The Netherlands) with  $\text{CH}_3\text{COCH}_3$  as the solvent. Melting points were measured by using a melting point apparatus made in Shanghai Instrument Limited Company. The X-ray single-crystal data collection for the compounds **1** and **2** were performed on a Bruker Smart-1000 CCD diffractometer.

### 3.2. Preparation of Two Oxaspirocyclic Compounds

The synthetic route is shown in Scheme 1.



**Scheme 1.** Synthesis of two new oxaspirocyclic compounds.

The mixture of malonic acid (6.24 g, 0.06 mol) and acetic anhydride (9 mL) in strong sulfuric acid (0.25 mL) was stirred with a water bath at 303K. After dissolving, cyclopentanone (5.04 g, 0.06 mol) was added dropwise into the solution for 2 h. The reaction was allowed to proceed for 3 h. Then the mixture was cooled, washed with water and filtered. The intermediate compound, 6,10-dioxaspiro[4.5]decane-7,9-dione, was obtained. 4-(dimethylamino)benzaldehyde (1.49 g, 0.01 mol) was added to the ethanol solution (20 mL) containing 6,10-dioxaspiro[4.5]decane-7,9-dione (1.70 g, 0.01 mol). Then the mixture was stirred and refluxed for 3 h. After cooling to room temperature, the precipitate was filtered off and dried. Yield 36%, m.p.:  $162.6\sim 163.1\text{ }^\circ\text{C}$ . Anal. Calcd. for  $\text{C}_{17}\text{H}_{19}\text{NO}_4$ : C, 67.76; H, 6.36; N, 4.65. Found: C, 67.68; H, 6.28; N, 4.78.  $^1\text{H}$  NMR (ppm): 8.20 (d, 2H, Ar–H), 8.17 (s, 1H, =CH–), 6.80 (d, 2H, Ar–H), 3.2 (s, 6H, N– $(\text{CH}_3)_2$ ), 2.15 (m, 4H, cyclopentane–H), 1.84 (s, 4H, cyclopentane–H). The red single crystals of **1** were obtained by evaporation of a solution in petroleum ether and ethyl acetate (2:1 = v/v) after a few days.

The synthesis procedure of **2** was similar to that of **1**, except that 4-(dimethylamino)benzaldehyde was replaced by 4-hydroxybenzaldehyde (1.22 g, 0.01 mol). Yield 36%, m.p.: 164.66~165.2 °C. Anal. Calcd. for C<sub>15</sub>H<sub>14</sub>O<sub>5</sub>: C, 65.69; H, 5.15; Found: C, 65.53; H, 5.08. <sup>1</sup>H NMR (ppm): 9.66 (s, 1H, –OH), 8.15 (s, 1H, =CH–) 8.22–8.24 (m, 2H, Ar–H), 6.99–7.0 (d, 2H, Ar–H), 2.19 (s, 4H, cyclopentane–H), 1.86 (s, 4H, cyclopentane–H). The yellow crystals suitable for X-ray diffraction analysis were obtained by slow evaporation of a solution in petroleum ether and ethyl acetate (1:1 = v/v).

### 3.3. Crystallography

The structures of two compounds were solved by direct methods and refined by full-matrix least-squares techniques on  $F^2$  using SHELXS-97 and SHELXL-97 programs [21]. The non-hydrogen atoms were refined anisotropically. All hydrogen atoms were positioned with idealized geometry and were refined isotropic with an Uiso(H) = 1.2Ueq(C) of the corresponding parent atom using a riding model. The contributions of hydrogen atoms were included in the structure-factor calculations. The atomic scattering factors and anomalous dispersion corrections were taken from International Table for X-ray Crystallography [22]. The final cycle of refinement gave  $R = 0.0570$  and  $wR = 0.1667$  ( $R = 0.0568$  and  $wR = 0.1739$  for **2**) with  $w = 1/(\sigma^2(F_o^2) + (0.0995 P)^2 + 0.4137 P)$  ( $w = 1/(\sigma^2(F_o^2) + (0.0937 P)^2 + 0.5137 P)$  for **2**), where  $P = (F_o^2 + 2F_c^2)/3$ . Crystallographic data are summarized in Table 4. CCDC-1486129 (**2**) and CCDC-1486130 (**1**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk.

**Table 4.** Crystal and experimental data for **1** and **2**.

Compounds	1	2
CCDC No.	1486130	1486129
Empirical formula	C <sub>17</sub> H <sub>19</sub> NO <sub>4</sub>	C <sub>15</sub> H <sub>14</sub> O <sub>5</sub>
Color/shape	red/block	yellow/block
Formula weight	301.33	274.26
Crystal system	Monoclinic	Monoclinic
Space group	P21/n	P21/c
Unit cell dimensions	a = 6.2554(13) Å, α = 90° b = 14.605(3) Å, β = 95.97(3)° c = 16.265(3) Å, γ = 90°	a = 10.739(2) Å, α = 90° b = 18.348(4) Å, β = 104.20(3)° c = 6.7799(14) Å, γ = 90°
Volume/Å <sup>3</sup>	1477.9(5)	1295.1(5)
Z	4	4
D <sub>x</sub> /g cm <sup>−3</sup>	1.354	1.407
μ/mm <sup>−1</sup>	0.097	0.106
F(000)	640	608
Crystal size/mm <sup>3</sup>	0.25 × 0.18 × 0.12	0.18 × 0.12 × 0.10
θ <sub>min</sub> /θ <sub>max</sub> /°	3.06/27.48	3.29/27.48
Limiting indices	−7 ≤ h ≤ 8, −18 ≤ k ≤ 18, −21 ≤ l ≤ 21	−13 ≤ h ≤ 13, −23 ≤ k ≤ 23, −8 ≤ l ≤ 7
Reflections collected	14232	11961
Independent reflections	3370 [R(int) = 0.0330]	2964 [R(int) = 0.0360]
Reflections observed(I>2σ(I))	2184	2286
Refinement method	Full-matrix least-squares on $F^2$	Full-matrix least-squares on $F^2$
Data/restraints/parameters	3370/0/199	2964/0/181
Goodness-of-fit on $F^2$	1.146	1.112
R <sub>1</sub> /wR <sub>2</sub> (I>2σ(I))	0.0570/0.1667	0.0568/0.1739
R <sub>1</sub> /wR <sub>2</sub> (all data)	0.0866/0.2009	0.0711/0.1869
Δρ <sub>max</sub> /Δρ <sub>min</sub> /e Å <sup>−3</sup>	0.389/−0.318	0.763/−0.380

#### 4. Conclusions

Two new oxaspirocyclic spiro compounds, 8-(4-(dimethylamino)benzylidene)-6,10-dioxaspiro[4.5]decane-7,9-dione (**1**) and 8-(4-hydroxybenzylidene)-6,10-dioxaspiro[4.5]decane-7,9-dione (**2**), have been synthesized and characterized by elemental analysis, IR and single-crystal X-ray diffraction. Some C–H···O intra- and intermolecular hydrogen bonds and  $\pi\cdots\pi$  stacking interactions are both observed in the two lattice structures. The difference between them is that one type of C–H··· $\pi$  supramolecular interaction (**1**) and one type of O–H···O intermolecular hydrogen bond (**2**) are observed.

**Supplementary Materials:** The following are available online at <http://www.mdpi.com/2073-4352/6/10/134/s1>. cif 1: the cif file of compound 1; cif 2: the cif file of compound 2.

**Acknowledgments:** This project was supported by the National Natural Science Foundation of China (No. 51541205), the Project of Shandong Province Higher Educational Science and Technology Program (No. J11LC62) and the Development Plan of Science and Technology of Weifang.

**Author Contributions:** Jinhe Jiang synthesized compound **1** and compound **2**. Wulan Zeng conceived and designed the experiments and wrote the paper.

**Conflicts of Interest:** The authors confirm that this article content has no conflict of interest.

#### References

1. Lippa, B.; Pan, G.; Corbett, M.; Li, C.; Kauffman, G.S.; Pandit, J.; Robinson, S.; Wei, L.; Kozina, E.; Marr, E.S.; et al. Synthesis and structure based optimization of novel Akt inhibitors. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3359–3363. [[CrossRef](#)] [[PubMed](#)]
2. Djigoue, G.B.; Ngatcha, B.T.; Roy, J.; Poirier, D. Synthesis of 5 $\alpha$ -androstane-17-spiro- $\delta$ -lactones with a 3-keto, 3-hydroxy, 3-spirocarbamate or 3-spiromorpholinone as inhibitors of 17  $\beta$ -hydroxysteroid dehydrogenases. *Molecules* **2013**, *18*, 914–933. [[CrossRef](#)] [[PubMed](#)]
3. Anikina, L.V.; Vikharev, Y.B.; Rozhkova, Y.S.; Shklyayev, Y.V. Synthesis and biological activity of 3-spiro[adamantane-2,3'-isoquinolines]. *Pharm. Chem. J.* **2013**, *46*, 707–710. [[CrossRef](#)]
4. Cirah, D.E.; Dayan, O.; Özdemir, N.; Hacıoglu, N. A new phosphazene derivative, spiro-N<sub>3</sub>P<sub>3</sub> [(O<sub>2</sub>C<sub>12</sub>H<sub>8</sub>)<sub>2</sub> (OC<sub>6</sub>H<sub>6</sub>N-3)<sub>2</sub>] and its Ru(II) complex: Syntheses, crystal structure, catalytic activity and antimicrobial activity studies. *Polyhedron* **2015**, *88*, 170–175.
5. Rotstein, B.H.; Stephenson, N.A.; Vasdev, N.; Liang, S.H. Spirocyclic hypervalent iodine(III)-mediated radiofluorination of non-activated and hindered aromatics. *Nat. Commun.* **2014**, *5*, 4365. [[CrossRef](#)] [[PubMed](#)]
6. Li, H.; Pang, M.L.; Wu, B.P.; Meng, J.B. Synthesis, crystal structure and photochromism of a novel spiro [indoline–naphthaline] oxazine derivative. *J. Mol. Struct.* **2015**, *1087*, 73–79. [[CrossRef](#)]
7. Saragi, T.P.I.; Spehr, T.; Siebert, A.; Fuhrmann-Lieker, T.; Salbeck, J. Spiro compounds for organic optoelectronics. *Chem. Rev.* **2007**, *107*, 1011–1065. [[CrossRef](#)] [[PubMed](#)]
8. Pudzich, R.; Fuhrmann-Lieker, T.; Salbeck, J. Spiro compounds for organic electroluminescence and related applications. *Adv. Polym. Sci.* **2006**, *199*, 83–142.
9. Liu, R.D.; Kong, D.L.; Wu, M.S.; Li, G.Z. Synthesis, structure and antimicrobial activity of 2-phenyl-4H-spiro[benzo[e][1,4,2]oxazaphosphinine-3,3'-indolin]-2'-one 2-oxide. *Chin. J. Struct. Chem.* **2014**, *33*, 204–208.
10. DanDia, A.; Singh, R.; Saini, D. Ionic liquid-mediated three-component synthesis of fluorinated spiro-thiazine derivatives and their antimycobacterial and DNA cleavage activities. *J. Chem. Sci.* **2013**, *125*, 1045–1053. [[CrossRef](#)]
11. El-Desoky, S.I.; Badria, F.A.; Abozeid, M.A.; Abdel-Rahman, A.H. Synthesis and antitumor studies of novel benzopyrano-1,2,3-selenadiazole and spiro[benzopyrano]-1,3,4-thiadiazoline derivatives. *Med. Chem. Res.* **2013**, *22*, 2105–2114. [[CrossRef](#)]
12. Yu, B.; Shi, X.J.; Qi, P.P.; Yu, D.Q.; Liu, H.M. Design, synthesis and biological evaluation of novel steroidal spiro-oxindoles as potent antiproliferative agents. *J. Steroid Biochem. Mol. Biol.* **2014**, *14*, 121–134. [[CrossRef](#)] [[PubMed](#)]
13. Van Hes, R.; Smit, A.; Kralt, T.; Peters, A. Synthesis and antiviral activities of adamantane spiro compounds. *J. Med. Chem.* **1972**, *15*, 132–136. [[CrossRef](#)]

14. Sundaram, R.; Ganesan, R.; Murugesan, G. In vitro antiplasmodial activity of spiro benzofuran compound from mangrove plant of southern india. *Asian Pac. J. Trop. Med.* **2012**, *5*, 358–361. [[CrossRef](#)]
15. Arya, K.; Rawat, D.H.; Dandia, A.; Sasai, H. Bronsted acidic ionic liquids: Green, efficient and reusable catalyst for synthesis of fluorinated spiro [indole-thiazinones/hiazolidinones] as antihistamic agents. *J. Fluorine Chem.* **2012**, *137*, 117–122. [[CrossRef](#)]
16. Zeng, W.L.; Li, Y.F.; Liu, Y.; Jian, F.F. Crystal structure of 1,5-dioxaspiro[5.5]undecane-2,4-dione, C<sub>9</sub>H<sub>12</sub>O<sub>4</sub>. *Z. Kristallogr. NCS* **2010**, *5*, 498–500. [[CrossRef](#)]
17. Zeng, W.L.; Li, Y.F.; Guo, H.M. Syntheses and Crystal Structures of 1,5-dioxaspiro[5.5]undecane-2,4-dione Derivatives. *J. Chem. Crystallogr.* **2013**, *43*, 223–227. [[CrossRef](#)]
18. Zeng, W.L.; Cai, X.; Guo, H.M. Synthesis, experimental and theoretical characterization of 3-(4-(dimethylamino) benzylidene)-1,5-dioxaspiro [5.5]undecane-2,4-dione. *Chin. J. Struct. Chem.* **2013**, *32*, 1603–1610.
19. Zeng, W.L.; Jiang, J.H. Synthesis and Crystal Structures of Two Novel O, N-Containing Spiro Compounds. *Crystals* **2016**, *6*, 69. [[CrossRef](#)]
20. Cremer, D.J.; Pople, A. A general definition of ring puckering coordinates. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358. [[CrossRef](#)]
21. Sheldrick, G.M. A short history of SHELX. *Acta Cryst.* **2008**, *A64*, 112–122. [[CrossRef](#)] [[PubMed](#)]
22. SMART and SAINT. *Area Detector Control and Integration Software*; Siemens Analytical X-Ray Systems Inc.: Madison, WI, USA, 1996.



© 2016 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) license (<http://creativecommons.org/licenses/by/4.0/>).