Supporting Information

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Structural Simplification of Bioactive Natural Products with Multicomponent Synthesis. 2. Antiproliferative and Antitubulin Activities of Pyrano[3,2-c]pyridones and Pyrano[3,2-c]quinolones

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X-ray structure determination.

Details of the crystal data, data collection and structure refinement parameters for compound **15** are presented in Table 1. Single crystal X-ray diffraction experiment was carried out with a Bruker SMART APEX II diffractometer, with CCD area detector at 250K. Semiempirical method SADABS[1] was applied for absorption correction. The structure was solved by direct methods and refined by the full-matrix least-squares technique against F^2 with the anisotropic temperature parameters for all non-hydrogen atoms. Data reduction and further calculations were performed using Bruker SAINT+[2] and SHELXTL NT[3] program packages.

References

1. Sheldrick G.M. SADABS v.2.03, Bruker/Siemens Area Detector Absorption Correction Program, (2003) Bruker AXS, Madison, Wisconsin, USA.

2. SAINTP+ for NT. Data Reduction and Correction Program v. 6.2, (2001) Bruker AXS, Madison, Wisconsin, USA.

3. Sheldrick G.M. SHELXTL NT v. 6.12, Structure Determination Software Suite, (2001) Bruker AXS, Madison, Wisconsin, USA.

Table 1. Crystal data and structure refinement for **15**.

Identification code	paul6a	
Empirical formula	C19 H19 Cl2 N3 O3	
Formula weight	408.27	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 9.120(6) Å	α= 71.757(8)°.
	b = 10.251(6) Å	β= 74.660(9)°.
	c = 11.299(7) Å	γ = 80.836(9)°.
Volume	964.1(10) $Å^3$	
Z	2	
Density (calculated)	1.406 Mg/m^3	
Absorption coefficient	0.362 mm^{-1}	
F(000)	424	
Crystal size	0.30 x 0.30 x 0.20 mm^3	
Theta range for data collection	2.10 to 27.87°.	
Index ranges	-11<=h<=11, -13<=k<=13, -14<=l<=14	
Reflections collected	12392	
Independent reflections	4524 [R(int) = 0.0939]	
Completeness to theta = 27.87°	98.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9312 and 0.8993	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4524 / 0 / 247	
Goodness-of-fit on F^2	1.006	
Final R indices [I>2sigma(I)]	R1 = 0.0549, wR2 = 0.0932	
R indices (all data)	R1 = 0.1419, wR2 = 0.1139	
Largest diff. peak and hole	0.274 and -0.284 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **15**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	2268(1)	9248(1)	5098(1)	47(1)
Cl(2)	4201(1)	7207(1)	3555(1)	47(1)
O(1)	-1243(2)	10785(2)	1136(2)	32(1)
O(2)	-302(2)	14890(2)	1854(2)	27(1)
O(3)	-283(3)	17973(2)	2054(2)	50(1)
N(1)	-3184(3)	12034(2)	2189(2)	25(1)
N(2)	1890(3)	15852(2)	1299(2)	29(1)
N(3)	4754(3)	13630(2)	-251(2)	32(1)
C(1)	3251(3)	8719(3)	2785(3)	30(1)
C(2)	2413(3)	9611(3)	3471(3)	26(1)
C(3)	3357(3)	9044(3)	1490(3)	33(1)
C(4)	1672(3)	10831(3)	2839(3)	24(1)
C(5)	2609(3)	10256(3)	873(3)	29(1)
C(6)	1773(3)	11166(3)	1532(3)	22(1)
C(7)	1029(3)	12527(3)	842(3)	23(1)
C(8)	-621(3)	12784(3)	1472(3)	23(1)
C(9)	-1660(3)	11804(3)	1565(3)	23(1)
C(10)	-4216(3)	10994(3)	2352(3)	32(1)
C(11)	-3730(3)	13163(3)	2630(3)	26(1)
C(12)	-5385(3)	13324(3)	3246(3)	35(1)
C(13)	-2746(3)	14105(3)	2492(3)	25(1)
C(14)	-1189(3)	13880(3)	1920(3)	21(1)
C(15)	1225(3)	14786(3)	1280(3)	24(1)
C(16)	1880(3)	13730(3)	777(3)	22(1)
C(17)	3459(3)	13695(3)	209(3)	24(1)
C(18)	-1171(5)	17785(5)	3305(4)	79(2)
C(19)	-551(5)	16792(5)	4272(4)	89(2)

Table 3. Bond lengths [Å] and angles [°] for **15**.

Cl(1)-C(2)	1.730(3)
Cl(2)-C(1)	1.742(3)
O(1)-C(9)	1.251(3)
O(2)-C(15)	1.375(3)
O(2)-C(14)	1.385(3)
O(3)-C(18)	1.402(4)
O(3)-H(3A)	0.8999
N(1)-C(11)	1.372(4)
N(1)-C(9)	1.402(4)
N(1)-C(10)	1.471(4)
N(2)-C(15)	1.339(4)
N(2)-H(2A)	0.8600
N(2)-H(2B)	0.8601
N(3)-C(17)	1.158(3)
C(1)-C(3)	1.376(4)
C(1)-C(2)	1.388(4)
C(2)-C(4)	1.399(4)
C(3)-C(5)	1.390(4)
C(3)-H(3)	0.9500
C(4)-C(6)	1.389(4)
C(4)-H(4)	0.9500
C(5)-C(6)	1.383(4)
C(5)-H(5)	0.9500
C(6)-C(7)	1.521(4)
C(7)-C(8)	1.505(4)
C(7)-C(16)	1.531(4)
C(7)-H(7)	1.0000
C(8)-C(14)	1.348(4)
C(8)-C(9)	1.450(4)
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-C(13)	1.368(4)
C(11)-C(12)	1.492(4)

C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-C(14)	1.411(4)
C(13)-H(13)	0.9500
C(15)-C(16)	1.361(4)
C(16)-C(17)	1.413(4)
C(18)-C(19)	1.413(5)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800

C(15)-O(2)-C(14)	118.4(2)
C(18)-O(3)-H(3A)	110.3
C(11)-N(1)-C(9)	123.4(3)
C(11)-N(1)-C(10)	120.0(2)
C(9)-N(1)-C(10)	116.6(2)
C(15)-N(2)-H(2A)	122.6
C(15)-N(2)-H(2B)	118.8
H(2A)-N(2)-H(2B)	118.5
C(3)-C(1)-C(2)	119.9(3)
C(3)-C(1)-Cl(2)	119.9(2)
C(2)-C(1)-Cl(2)	120.2(3)
C(1)-C(2)-C(4)	119.7(3)
C(1)-C(2)-Cl(1)	121.3(2)
C(4)-C(2)-Cl(1)	119.0(2)
C(1)-C(3)-C(5)	119.9(3)
C(1)-C(3)-H(3)	120.0
C(5)-C(3)-H(3)	120.0
C(6)-C(4)-C(2)	120.7(3)
C(6)-C(4)-H(4)	119.6
C(2)-C(4)-H(4)	119.6
C(6)-C(5)-C(3)	121.4(3)
C(6)-C(5)-H(5)	119.3

C(3)-C(5)-H(5)	119.3
C(5)-C(6)-C(4)	118.4(3)
C(5)-C(6)-C(7)	121.2(3)
C(4)-C(6)-C(7)	120.4(2)
C(8)-C(7)-C(6)	113.2(2)
C(8)-C(7)-C(16)	108.1(2)
C(6)-C(7)-C(16)	110.4(2)
C(8)-C(7)-H(7)	108.4
C(6)-C(7)-H(7)	108.4
C(16)-C(7)-H(7)	108.4
C(14)-C(8)-C(9)	118.6(3)
C(14)-C(8)-C(7)	124.1(3)
C(9)-C(8)-C(7)	117.3(3)
O(1)-C(9)-N(1)	120.4(3)
O(1)-C(9)-C(8)	123.0(3)
N(1)-C(9)-C(8)	116.6(3)
N(1)-C(10)-H(10A)	109.5
N(1)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
N(1)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(13)-C(11)-N(1)	119.1(3)
C(13)-C(11)-C(12)	122.1(3)
N(1)-C(11)-C(12)	118.8(3)
C(11)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(11)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(11)-C(13)-C(14)	119.2(3)
C(11)-C(13)-H(13)	120.4
C(14)-C(13)-H(13)	120.4
C(8)-C(14)-O(2)	123.2(3)
C(8)-C(14)-C(13)	122.9(3)

O(2)-C(14)-C(13)	113.9(2)
N(2)-C(15)-C(16)	128.0(3)
N(2)-C(15)-O(2)	110.0(2)
C(16)-C(15)-O(2)	122.1(3)
C(15)-C(16)-C(17)	118.6(3)
C(15)-C(16)-C(7)	124.1(3)
C(17)-C(16)-C(7)	117.3(2)
N(3)-C(17)-C(16)	178.3(3)
O(3)-C(18)-C(19)	115.7(3)
O(3)-C(18)-H(18A)	108.4
C(19)-C(18)-H(18A)	108.4
O(3)-C(18)-H(18B)	108.4
C(19)-C(18)-H(18B)	108.4
H(18A)-C(18)-H(18B)	107.4
C(18)-C(19)-H(19A)	109.5
C(18)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(18)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for paul61. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl(1)	50(1)	49(1)	31(1)	-3(1)	-10(1)	15(1)
Cl(2)	45(1)	28(1)	63(1)	-10(1)	-21(1)	15(1)
O(1)	28(1)	26(1)	48(1)	-17(1)	-12(1)	0(1)
O(2)	16(1)	26(1)	38(1)	-12(1)	-2(1)	-1(1)
O(3)	58(2)	30(1)	48(2)	-9(1)	-1(1)	10(1)
N(1)	20(1)	25(1)	31(2)	-7(1)	-9(1)	-2(1)
N(2)	18(1)	28(2)	41(2)	-17(1)	-1(1)	0(1)
N(3)	21(2)	23(2)	47(2)	-13(1)	1(1)	2(1)
C(1)	20(2)	21(2)	47(2)	-7(2)	-10(1)	1(1)
C(2)	23(2)	25(2)	29(2)	-8(1)	-3(1)	-1(1)
C(3)	24(2)	30(2)	50(2)	-24(2)	-10(2)	6(1)
C(4)	20(2)	23(2)	25(2)	-8(1)	0(1)	2(1)
C(5)	28(2)	30(2)	29(2)	-12(1)	-7(1)	5(1)
C(6)	18(2)	17(2)	31(2)	-6(1)	-4(1)	-3(1)
C(7)	21(2)	22(2)	25(2)	-5(1)	-4(1)	-2(1)
C(8)	21(2)	21(2)	28(2)	-5(1)	-9(1)	-1(1)
C(9)	16(2)	23(2)	31(2)	-7(1)	-7(1)	1(1)
C(10)	19(2)	32(2)	45(2)	-13(2)	-5(1)	-5(1)
C(11)	20(2)	29(2)	30(2)	-10(1)	-6(1)	2(1)
C(12)	21(2)	34(2)	48(2)	-13(2)	-5(2)	-1(1)
C(13)	23(2)	22(2)	31(2)	-8(1)	-6(1)	2(1)
C(14)	20(2)	18(2)	25(2)	-3(1)	-7(1)	-2(1)
C(15)	20(2)	26(2)	25(2)	-4(1)	-4(1)	-2(1)
C(16)	17(2)	18(2)	29(2)	-5(1)	-6(1)	2(1)
C(17)	28(2)	16(2)	29(2)	-9(1)	-6(1)	1(1)
C(18)	52(3)	104(4)	60(3)	-27(3)	5(2)	33(3)
C(19)	63(3)	113(4)	55(3)	2(3)	0(2)	16(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **15**.

	x	y	z	U(eq)
H(3A)	-529	18810	1552	60
H(2A)	2833	15980	938	34
H(2B)	1342	16460	1643	34
H(3)	3939	8440	1017	39
H(4)	1092	11438	3310	29
H(5)	2675	10464	-18	35
H(7)	1091	12518	-52	28
H(10A)	-3630	10225	2052	47
H(10B)	-4990	11409	1854	47
H(10C)	-4717	10654	3260	47
H(12A)	-5644	12531	3998	52
H(12B)	-5994	13373	2634	52
H(12C)	-5605	14172	3510	52
H(13)	-3106	14901	2778	31
H(18A)	-2179	17516	3338	95
H(18B)	-1342	18680	3502	95
H(19A)	259	17177	4446	133
H(19B)	-128	15972	3986	133
H(19C)	-1355	16537	5054	133

Table 6. Torsion angles [°] for **15**.

C(3)-C(1)-C(2)-C(4)	0.5(4)
Cl(2)-C(1)-C(2)-C(4)	179.1(2)
C(3)-C(1)-C(2)-Cl(1)	-179.4(2)
Cl(2)-C(1)-C(2)-Cl(1)	-0.7(4)
C(2)-C(1)-C(3)-C(5)	-0.8(5)
Cl(2)-C(1)-C(3)-C(5)	-179.4(2)
C(1)-C(2)-C(4)-C(6)	-0.5(4)
Cl(1)-C(2)-C(4)-C(6)	179.4(2)
C(1)-C(3)-C(5)-C(6)	1.1(5)
C(3)-C(5)-C(6)-C(4)	-1.1(4)
C(3)-C(5)-C(6)-C(7)	176.6(3)
C(2)-C(4)-C(6)-C(5)	0.8(4)
C(2)-C(4)-C(6)-C(7)	-177.0(3)
C(5)-C(6)-C(7)-C(8)	130.9(3)
C(4)-C(6)-C(7)-C(8)	-51.4(4)
C(5)-C(6)-C(7)-C(16)	-107.8(3)
C(4)-C(6)-C(7)-C(16)	69.9(3)
C(6)-C(7)-C(8)-C(14)	120.8(3)
C(16)-C(7)-C(8)-C(14)	-1.8(4)
C(6)-C(7)-C(8)-C(9)	-61.0(3)
C(16)-C(7)-C(8)-C(9)	176.5(2)
C(11)-N(1)-C(9)-O(1)	-177.0(3)
C(10)-N(1)-C(9)-O(1)	2.6(4)
C(11)-N(1)-C(9)-C(8)	4.0(4)
C(10)-N(1)-C(9)-C(8)	-176.4(2)
C(14)-C(8)-C(9)-O(1)	177.5(3)
C(7)-C(8)-C(9)-O(1)	-0.8(4)
C(14)-C(8)-C(9)-N(1)	-3.5(4)
C(7)-C(8)-C(9)-N(1)	178.1(2)
C(9)-N(1)-C(11)-C(13)	-1.8(4)
C(10)-N(1)-C(11)-C(13)	178.7(3)
C(9)-N(1)-C(11)-C(12)	178.2(2)
C(10)-N(1)-C(11)-C(12)	-1.3(4)
N(1)-C(11)-C(13)-C(14)	-1.1(4)

C(12)-C(11)-C(13)-C(14)	178.9(3)
C(9)-C(8)-C(14)-O(2)	-178.7(2)
C(7)-C(8)-C(14)-O(2)	-0.5(4)
C(9)-C(8)-C(14)-C(13)	0.9(4)
C(7)-C(8)-C(14)-C(13)	179.2(2)
C(15)-O(2)-C(14)-C(8)	1.4(4)
C(15)-O(2)-C(14)-C(13)	-178.2(2)
C(11)-C(13)-C(14)-C(8)	1.5(4)
C(11)-C(13)-C(14)-O(2)	-178.9(2)
C(14)-O(2)-C(15)-N(2)	179.6(2)
C(14)-O(2)-C(15)-C(16)	0.2(4)
N(2)-C(15)-C(16)-C(17)	1.0(5)
O(2)-C(15)-C(16)-C(17)	-179.7(2)
N(2)-C(15)-C(16)-C(7)	177.9(3)
O(2)-C(15)-C(16)-C(7)	-2.8(4)
C(8)-C(7)-C(16)-C(15)	3.3(4)
C(6)-C(7)-C(16)-C(15)	-120.9(3)
C(8)-C(7)-C(16)-C(17)	-179.7(2)
C(6)-C(7)-C(16)-C(17)	56.0(3)

Symmetry transformations used to generate equivalent atoms: