Synthesis and X-ray diffraction data of (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate, $C_{14}H_{13}ClN_4O_3S$

Fausto M. Güiza,[1] Arnold R. Romero Bohórquez,[1] J. A. Henao,[2] and H. A. Camargo [3,a)]
[1]*Grupo de Investigación en Compuestos Orgánicos de Interés Medicinal (CODEIM), Escuela de Química, Facultad de Ciencias, Universidad Industrial de Santander, A.A. 678, Carrera 27, Calle 9 Ciudadela Universitaria, Bucaramanga, Colombia*
[2]*Grupo de Investigación en Química Estructural (GIQUE), Escuela de Química, Facultad de Ciencias, Universidad Industrial de Santander, A.A. 678, Carrera 27, Calle 9 Ciudadela Universitaria, Bucaramanga, Colombia*
[3]*Grupo de Investigación en Nuevos Materiales y Energías Alternativas (GINMEA), Universidad Santo Tomás, Facultad de Química Ambiental, Campus Universitario Floridablanca, Santander, Colombia*

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The new compound (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate was synthesized by the 1,3-dipolar cycloaddition reaction between (4*R*)-methyl-3-propionyl-thiazolidin-4-carboxylate (**1**) and 4-chlorophenylazide using the click chemistry approach. Molecular characterization was carried out by infrared spectroscopy and mass spectrometry. The X-ray powder diffraction study determined that the title compound crystallized in an orthorhombic system with unit-cell parameters $a = 20.876$ (2) Å, $b = 12.111$ (1) Å, and $c = 6.288$ (9) Å. The volume of the unit cell is $V = 1589.7$ (2) Å^3. All measured diffraction maxima were indexed and are consistent with the $P222_1$ space group (No. 17). No detectable impurities were observed. © *2019 International Centre for Diffraction Data*. [doi:10.1017/S088571561900085X]

Key words: thiazolidines, antineoplastic activity, X-ray powder diffraction

I. INTRODUCTION

Thiazolidines are a family of heterocyclic compounds with meaningful biological activity shown in the different biological tests that have been carried out (Eftekhari-Sis and Zirak, 2015). The antineoplastic activity of the thiazolidine compounds has been widely studied. The 2-arylthiazolidine-4-carboxylamide derivatives (ATCAAs) developed have presented the most striking IC_{50} values (Li *et al.*, 2007). These compounds contain within their structure the residual fragment of the aldehyde used in the synthesis, and according to the aldehyde used (Gududuru *et al.*, 2005), a chiral center within the thiazolidine ring can be generated or not. This chiral center generates conformational isomers that at the time of the biological tests must be separated, which in some cases cannot be carried out by traditional methods. The use of formaldehyde in the synthesis of thiazolidine generates the ring without this new chiral center, which leads to a single compound.

Another heterocycle of great interest in medicinal chemistry is 1,2,3-triazole. This five-member heterocyclic nucleus has three nitrogen atoms within an aromatic electronic cloud, which gives this ring special properties that lead to a wide range of biological activities. There are many drugs that contain the 1,2,3-triazole ring within its structure. Rufinamide (Bonacorso *et al.*, 2013), cefatrizine (He *et al.*, 2014), and vorozole (Wouters *et al.*, 1994) are some examples. The antitumor activity of vorozole led to the creation of many triazole derivatives, in which it was sought to enhance this activity. In this search, molecular hybridization (Esra Önen *et al.*, 2008) has turned out to be a very powerful tool for the synthesis of biologically active compounds.

In order to obtain new heterocycle compounds with promising antitumoral activity, we have focused our efforts on the synthesis and characterization of new hybrids thiazolidine/1,2,3-triazole compounds. In this sense, in the present work, the simple synthesis of the compound (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate (**3**) through the 1,3-dipolar cycloaddition reaction, based on the click chemistry approach, is shown. Furthermore, the results of molecular characterization (FTIR and GC-MS) and X-ray powder diffraction (XRPD) data are reported.

II. EXPERIMENTAL

A. Synthesis

The synthetic scheme to synthetize the title compound (**3**) is as follows (Figure 1): first, 0.192 g (0.955 mmol) of

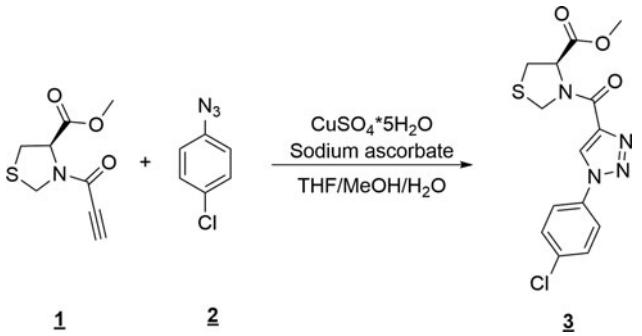

Figure 1. Synthesis of (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate.

a)Author to whom correspondence should be addressed. Electronic mail: hernando.camargo@ustabuca.edu.co

TABLE I. XRPD data of (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate.

$2\theta_{obs}$ (°)	d_{obs} (Å)	$(I/I_0)_{obs}$	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
8.493	10.4028	53	2	0	0	8.464	10.4383	−0.029
11.185	7.9044	7	2	1	0	11.182	7.9068	−0.003
14.633	6.0487	26	0	2	0	14.616	6.0555	−0.017
14.712	6.0164	2	1	0	1	14.702	6.0205	−0.010
15.238	5.8099	64	1	2	0	15.222	5.8158	−0.016
15.881	5.5760	6	0	1	1	15.869	5.5804	−0.012
16.457	5.3821	28	2	0	1	16.445	5.3860	−0.012
16.934	5.2316	33	2	2	0	16.913	5.2379	−0.021
18.029	4.9163	25	2	1	1	18.010	4.9213	−0.019
18.504	4.7911	6	4	1	0	18.497	4.7930	−0.007
19.016	4.6632	6	3	0	1	19.007	4.6653	−0.009
19.431	4.5646	35	3	2	0	19.416	4.5681	−0.015
20.406	4.3486	7	3	1	1	20.383	4.3535	−0.023
20.802	4.2667	14	1	2	1	20.789	4.2695	−0.013
21.274	4.1731	36	5	0	0	21.263	4.1753	−0.011
21.983	4.0401	1	0	3	0	22.000	4.0370	0.017
22.129	4.0138	36	4	0	1	22.117	4.0159	−0.012
22.404	3.9651	7	1	3	0	22.413	3.9636	0.009
22.470	3.9536	2	4	2	0	22.471	3.9534	0.001
23.330	3.8098	100	4	1	1	23.318	3.8118	−0.012
23.617	3.7641	1	2	3	0	23.610	3.7652	−0.007
24.068	3.6946	3	3	2	1	24.061	3.6957	−0.007
25.466	3.4949	1	3	3	0	25.488	3.4919	0.022
25.597	3.4773	84	5	0	1	25.590	3.4783	−0.007
25.915	3.4353	2	5	2	0	25.899	3.4374	−0.016
26.220	3.3961	7	0	3	1	26.212	3.3971	−0.008
26.585	3.3503	11	1	3	1	26.563	3.3530	−0.022
27.600	3.2293	9	2	3	1	27.591	3.2303	−0.009
27.925	3.1925	7	4	3	0	27.918	3.1932	−0.007
28.351	3.1455	1	0	0	2	28.366	3.1438	0.015
28.704	3.1076	5	1	0	2	28.693	3.1088	−0.011
29.231	3.0527	1	3	3	1	29.231	3.0528	0.000
29.312	3.0445	8	6	0	1	29.313	3.0444	0.001
29.603	3.0152	17	5	2	1	29.594	3.0161	−0.009
29.791	2.9966	13	1	4	0	29.793	2.9964	0.002
30.251	2.9521	1	6	1	1	30.246	2.9525	−0.005
30.572	2.9218	4	2	1	2	30.577	2.9214	0.005
30.789	2.9017	6	5	3	0	30.783	2.9023	−0.006
30.861	2.8951	1	7	1	0	30.853	2.8958	−0.008
31.390	2.8475	3	4	3	1	31.395	2.8471	0.005
32.198	2.7779	2	3	4	0	32.216	2.7763	0.018
32.799	2.7283	1	0	4	1	32.804	2.7279	0.005
32.897	2.7204	2	6	2	1	32.903	2.7200	0.006
33.217	2.6950	2	7	0	1	33.221	2.6946	0.004
33.466	2.6755	4	7	2	0	33.466	2.6755	0.000
33.955	2.6380	1	2	4	1	33.938	2.6393	−0.017
33.993	2.6352	1	5	3	1	33.994	2.6351	0.001
34.056	2.6305	9	7	1	1	34.058	2.6303	0.002
34.322	2.6107	2	8	0	0	34.337	2.6096	0.015
34.588	2.5912	1	3	2	2	34.608	2.5898	0.020
35.155	2.5507	4	8	1	0	35.150	2.5510	−0.005
35.317	2.5394	1	3	4	1	35.311	2.5398	−0.006
35.732	2.5108	1	5	0	2	35.722	2.5115	−0.010
36.171	2.4813	1	0	3	2	36.185	2.4804	0.014
36.959	2.4302	2	6	3	1	36.952	2.4307	−0.007
37.205	2.4147	2	2	3	2	37.229	2.4132	0.024
37.491	2.3970	2	8	2	0	37.498	2.3965	0.007
38.038	2.3637	4	8	1	1	38.036	2.3639	−0.002
38.574	2.3321	1	6	0	2	38.565	2.3327	−0.009
38.801	2.3190	4	9	0	0	38.790	2.3196	−0.011
39.322	2.2895	1	6	1	2	39.302	2.2906	−0.020
39.853	2.2602	1	0	5	1	39.851	2.2603	−0.002
40.225	2.2401	3	4	3	2	40.222	2.2403	−0.003
41.044	2.1973	1	4	5	0	41.048	2.1971	0.004
41.445	2.1770	1	6	2	2	41.449	2.1767	0.004
42.001	2.1494	1	3	5	1	41.995	2.1497	−0.006

Continued

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TABLE I. Continued

$2\theta_{obs}$ (°)	d_{obs} (Å)	$(I/I_0)_{obs}$	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
42.169	2.1412	1	9	1	1	42.155	2.1419	−0.014
42.374	2.1314	4	5	3	2	42.350	2.1325	−0.024
43.695	2.0699	2	8	3	1	43.706	2.0695	0.011
44.821	2.0205	3	6	3	2	44.839	2.0197	0.018
45.762	1.9811	4	10	0	1	45.758	1.9813	−0.004
46.612	1.9470	1	2	2	3	46.639	1.9459	0.027
47.490	1.9130	3	1	6	1	47.469	1.9138	−0.021
49.140	1.8526	1	3	6	1	49.140	1.8525	0.000
49.356	1.8449	4	9	1	2	49.362	1.8448	0.006
50.574	1.8033	1	4	6	1	50.569	1.8035	−0.005
51.415	1.7758	1	6	1	3	51.411	1.7759	−0.004
52.528	1.7408	2	11	2	1	52.544	1.7403	0.016
53.162	1.7215	1	10	1	2	53.162	1.7215	0.000
54.785	1.6743	1	8	4	2	54.815	1.6734	0.030
56.911	1.6167	1	12	2	1	56.940	1.6159	0.029
59.390	1.5550	4	9	0	3	59.384	1.5551	−0.006
59.806	1.5451	5	3	5	3	59.797	1.5453	−0.009
61.426	1.5082	1	10	4	2	61.433	1.5081	0.007
62.080	1.4939	1	11	5	0	62.079	1.4939	−0.001
64.782	1.4379	1	8	4	3	64.778	1.4380	−0.004
65.664	1.4208	3	13	1	2	65.690	1.4202	0.026
67.361	1.3890	1	10	3	3	67.373	1.3888	0.012

thiazolidine (**1**) was dissolved in a methanol/water mixture, then 0.269 g (0.764 mmol) of sodium ascorbate and 0.011 g (0.047 mmol) of copper sulfate ($CuSO_4 \cdot 5H_2O$) were added. Once homogenized and under vigorous stirring, 0.220 g (1432 mmol) of 4-chlorophenylazide (**2**) performed was added. Finally, the reaction mixture was left at room temperature for 11 h. After the reaction, the mixture was diluted in water (30 ml) and extracted with ethyl acetate (3 × 40 ml). The organic phase was separated and dried over anhydrous Na_2SO_4, concentrated in vacuo, and the resulting product was purified by column chromatography using silica gel and a petroleum ether:ethyl acetate mixture to obtain the compound (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate (**3**) as a white powder in a yield of 80%. The melting temperature (uncorrected) was between 145 and 147°C and the density was 1.507 g cm^{-3}, which was taken by the flotation method in an aqueous solution of potassium iodine. The measured density is in accordance with the calculated density (1.550 g cm^{-3}).

The structural characterization was carried out using Fourier transform-infrared spectroscopy (FTIR) and mass spectrometry with electron impact (MS-EI). Analysis of FTIR revealed the following characteristic absorption bands (υ, cm^{-1}) 2968 (C–H); 1591 (C=C); 1541 (C=C), and 1375 (C–H), while that MS-EI analysis showed the characteristic molecular peak $m/z = 326$ ($M^{+\cdot}$), which agrees with the molecular weight calculated with the formula of the title compound.

TABLE II. Parameters obtained by XRPD for the compound (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate.

a (Å)	20.876 (2)
b (Å)	12.111 (1)
c (Å)	6.288 (9)
V (Å^3)	1589.7 (2)
Z	4
M_{20}	19.4
F_{30}	52.7 (0.0129, 44)
D_m (g cm^{-3})	1.507
D_{cal} (g cm^{-3})	1.550

B. Powder data collection

A small portion of the title compound $C_{14}H_{13}ClN_4O_3S$ was gently ground in an agate mortar and sieved to a grain size less than 38 μm. The specimen was mounted on a polymethyl methacrylate (PMMA) holder. The XRPD pattern was recorded with a D8 ADVANCE BRUKER diffractometer operating in DaVinci geometry equipped with an X-ray tube (Cu$K\alpha$ radiation: $\lambda = 1.5418$ Å, 40 kV, and 30 mA) using a nickel filter and a one-dimensional LynxEye detector. A receiving slit (RS) of 0.6 mm and the primary and secondary soller slits (SS) of 2.5° were used. The scan range was 2°–70° in 2θ with a step size of 0.01526° and a counting time of 2 s $step^{-1}$. XRPD data were collected at room temperature (298 K).

PowderX program (Dong, 1999) was used to remove the background (Sonneveld and Visser, 1975) and smoothing (Saviztky and Golay, 1964) as well as to eliminate the $K\alpha_2$ component (Rachinger, 1948), and the second derivative method was used to determine the position and intensities of the diffraction peaks.

III. RESULTS AND DISCUSSION

The XRPD data for the compound (**3**) are given in Table I. All reflections were indexed successfully using the DICVOL14 program (Boultif and Loüer, 2004) on an orthorhombic system unit cell. A maximum absolute error of 0.03° 2θ was the $\Delta 2\theta$ limit for indexing a given observed diffraction line. The CHEKCELL program (Laugier and Bochu, 2002) suggests $P222_1$ (No. 17) as the possible space group, which is consistent with the systematic absences and with the crystal density. The unit-cell parameters of compound (**3**) were refined with the program NBS*AIDS83 (Mighell

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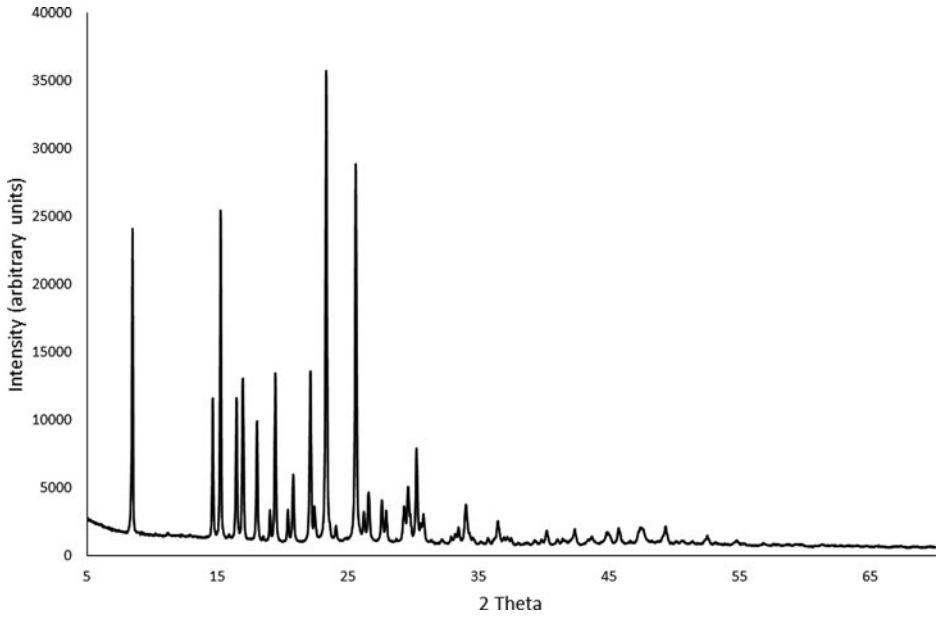

Figure 2. XRPD of (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate.

et al., 1981). The crystal data, density, and figures of merit M_{20} (de Wolff, 1968) and F_{20} (Smith and Snyder, 1979) are compiled in Table II. The XRPD pattern of (4*R*)-methyl-3-(1-(4-chlorophenyl)-1*H*-1,2,3-triazole-4-carbonyl)thiazolidin-4-carboxylate (**3**) is shown in Figure 2.

DEPOSITED DATA

CIF and/or RAW data files were deposited with ICDD. You may request this data from ICDD at info@icdd.com.

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