Synthesis and X-ray diffraction data of 6,8-dimethyl-*cis*-2-vinyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol and 8-chloro-9-methyl-*cis*-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol

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The 6,8-dimethyl-*cis*-2-vinyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2a) (Chemical formula $C_{14}H_{19}NO$) and 8-chloro-9-methyl-*cis*-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2b) (Chemical formula $C_{14}H_{18}ClNO$) were prepared *via* the reductive cleavage of the bridged N-O bond of the corresponding 1,4-epoxytetrahydro-1-benzazepines. The X-ray powder diffraction patterns for the new compounds were obtained. The compound 2a was found to crystallize in an orthorhombic system with space group $Pmn2_1$ (No. 31), refined unit-cell parameters $a = 19.422(6)$ Å, $b = 6.512(3)$ Å, $c = 9.757(4)$ Å and $V = 1234.0(5)$ Å^3. The compound 2b was found to crystallize in a monoclinic system with space group $P2_1/m$ (No. 11), refined unit-cell parameters $a = 17.570(4)$ Å, $b = 8.952(3)$ Å, $c = 14.985(4)$ Å, $\beta = 101.66(2)°$, and $V = 2308.3(9)$ Å^3. © *2011 International Centre for Diffraction Data*. [DOI: 10.1154/1.3656975]

Key words: tetrahydro-1-benzazepine, X-ray powder diffraction data, antiparasitic agents

I. INTRODUCTION

Tetrahydro-1-benzazepine derivatives exhibit a broad spectrum of diverse and important pharmacological properties. For example, different tetrahydro-1-benzazepines have been reported as potent arginine vasopressin antagonists for both V_{1A} and V_2 receptors (Matthews *et al*., 2003; Shimada *et al*., 2000), and some other derivatives have been reported as potent inhibitors of cyclin dependent kinases (Schultz *et al*., 1999). Other tetrahydro-1-benzazepine derivatives such as paullones exhibited potent activity against parasites of *Leishmania mexicana* (Knockaert *et al*., 2002) and *Trypanosoma cruzi* (Zuccotto *et al*., 2001), the etiologic agents of the leishmaniasis and Chagas disease, respectively. This broad spectrum of biological activity awakened the interest of the synthetic chemists in this heterocyclic system. In this context, we have developed an efficient synthetic method to obtain new *cis*-2-aryl-4-hydroxytetrahydro-1-benzazepines starting from *ortho*-allyl-*N*-benzylanilines (Gómez *et al*., 2006). Compounds of this type showed promising activity against *T. cruzi* and *Leishmania chagasi* parasites (Palma *et al*., 2009, Gómez-Ayala *et al*., 2006, 2010). Additionally, we have also described the stereoselective synthesis of *cis*-4-hydroxy-2-alkenyltetrahydro-1-benzazepines (Acosta *et al*, 2010). In this work, we report the X-ray powder diffraction (XRPD) data of 6,8-dimethyl-*cis*-2-vinyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2a) and 8-chloro-9-methyl-*cis*-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2b).

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II. EXPERIMENTAL

A. Synthesis

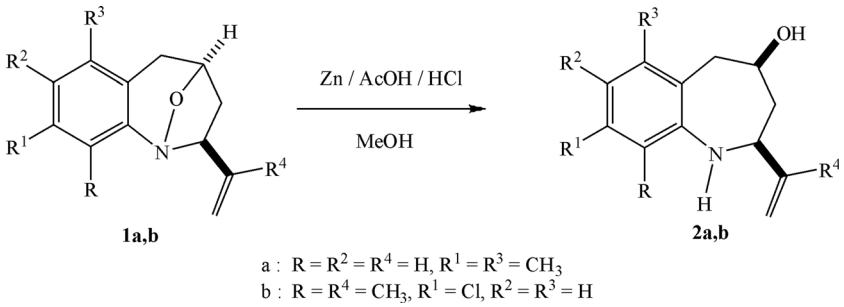
As shown in Figure 1, the synthesis of the compounds 2a and 2b involves the treatment of a methanolic cooled ice bath solution of the 1,4-epoxy-cycloadducts 1a and 1b with a seven-fold molar excess of glacial acetic acid, ten-fold molar excess of zinc powder, and seven-fold molar excess of hydrochloric acid (37% HCl). The organic crudes were purified by column chromatography on silica gel using heptane/ethyl acetate (compositions ranged from 10:1 to 1:1 v/v) as eluent to give 2a and 2b in 94% and 90% yields, respectively.

B. Powder data collection

A small portion of the title compounds were gently ground in an agate mortar and sieved to a grain size less than 38 μm. The specimens were mounted on a zero-background specimen holder (Buhrke *et al*., 1998). The XRPD patterns were recorded with a D8 FOCUS BRUKER diffractometer operating in Bragg-Brentano geometry equipped with an X-ray tube (Cu $K\alpha$ radiation: $\lambda = 1.5406$ Å, 40 kV and 40 mA) using a nickel filter and a one-dimensional LynxEye detector. A fixed antiscatter slit of 8 mm, receiving slit of 1 mm, soller slits of 2.5°, and a detector slit of 3 mm were used.

The scan range was from 2° to 70° 2θ with a step size of 0.02° 2θ and a count time of 0.4 s/step. XRPD data were collected at room temperature (298 K).

PowderX program (Dong, 1999) was used to remove the background (Sonneveld and Visser, 1975), smoothing (Saviztky and Golay, 1964), to eliminate the $K\alpha_2$ component



a : $R = R^2 = R^4 = H$, $R^1 = R^3 = CH_3$
b : $R = R^4 = CH_3$, $R^1 = Cl$, $R^2 = R^3 = H$

Figure 1. Synthesis of the *cis*-2-alkenyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ols **2a,b**.

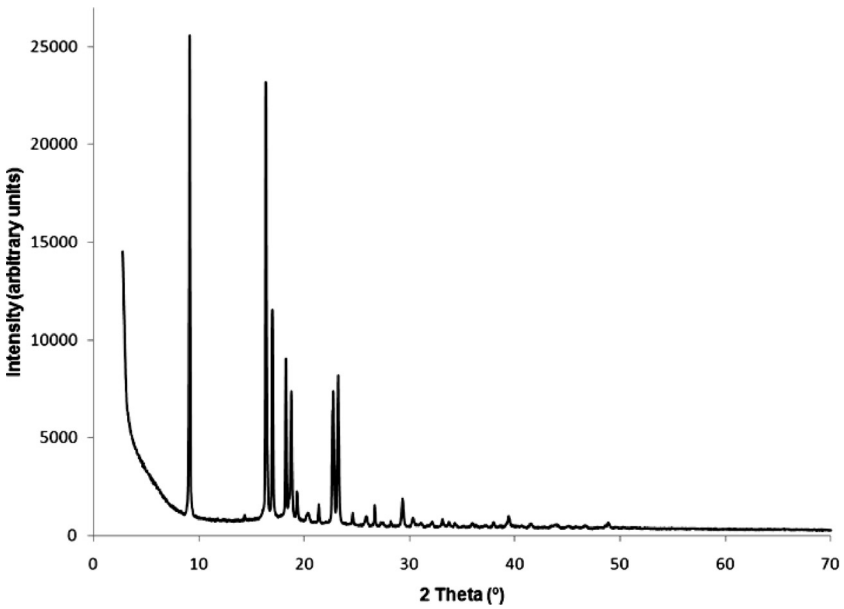


Figure 2. X-ray powder diffraction pattern of 6,8-dimethyl-*cis*-2-vinyl-2,3,4,5-tetrahydro-1*H*-benzo[-*b*]azepin-4-ol (**2a**).

(Rachinger, 1948) and the second derivative method was used to determine the peak positions and intensities of the diffraction peaks.

III. RESULTS AND DISCUSSION

The X-ray powder diffraction (XRPD) patterns of the compounds 2a and 2b are shown in Figures 2 and 3, respectively. XRPD data for the compounds are given in Tables I and II. The XRPD patterns were successfully indexed using the DICVOL06 program (Boultif and Louër, 2006) with an absolute error of 0.03° 2θ. Compounds 2a and 2b were found to be orthorhombic and monoclinic, respectively. The space groups, $Pmn2_1$ (No. 31) for 2a and $P2_1/m$ (No. 11) for 2b, were estimated by the CHEKCELL program (Laugier and Bochu, 2002), which were compatible with the

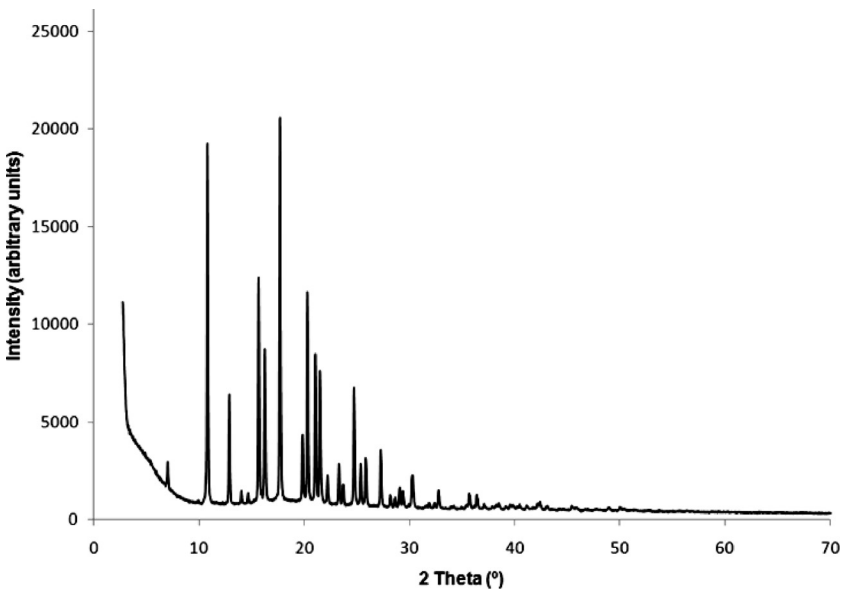


Figure 3. X-ray powder diffraction pattern of 8-chloro-9-methyl-*cis*-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2b).

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TABLE I. X-ray powder diffraction data of 6,8-dimethyl-*cis*-2-vinyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2a).

$2\theta_{obs}$ (°)	d_{obs} (Å)	$(I/I_0)_{obs}$	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
9.121	9.6881	100	2	0	0	9.099	9.7112	−0.022
14.362	6.1622	4	1	1	0	14.334	6.1742	−0.028
			0	1	1	16.352	5.4164	
16.381	5.4068	92	2	1	0	16.376	5.4086	−0.005
			3	0	1	16.419	5.3946	
16.993	5.2134	45	1	1	1	16.981	5.2173	−0.013
18.258	4.8552	35	4	0	0	18.256	4.8556	−0.002
18.770	4.7238	29	2	1	1	18.744	4.7304	−0.026
19.315	4.5917	9	3	1	0	19.317	4.5912	0.002
20.339	4.3627	4	2	0	2	20.356	4.3593	0.016
21.375	4.1536	6	3	1	1	21.372	4.1543	−0.003
22.740	3.9072	29	0	1	2	22.757	3.9043	0.017
23.225	3.8268	32	1	1	2	23.219	3.8278	−0.006
			2	1	2	24.554	3.6225	
24.594	3.6168	5	4	1	1	24.603	3.6155	0.009
25.874	3.4407	4	4	0	2	25.868	3.4415	−0.006
			3	1	2	26.640	3.3434	
26.685	3.3379	6	5	1	0	26.700	3.3360	0.015
27.397	3.2528	3	0	2	0	27.369	3.2560	−0.028
28.251	3.1564	3	5	1	1	28.249	3.1566	−0.002
29.333	3.0424	7	4	1	2	29.330	3.0427	−0.003
30.317	2.9458	4	2	2	1	30.344	2.9433	0.026
31.074	2.8757	3	1	1	3	31.055	2.8775	−0.019
			3	2	1	32.083	2.7876	
32.103	2.7859	3	2	1	3	32.088	2.7872	−0.015
33.139	2.7011	3	4	2	0	33.099	2.7043	−0.040
			6	0	2	33.187	2.6973	
33.724	2.6556	3	3	1	3	33.746	2.6539	0.022
34.348	2.6088	3	2	2	2	34.349	2.6087	0.001
			4	2	1	34.385	2.6060	
35.127	2.5527	2	7	1	0	35.128	2.5526	0.001
			3	2	2	35.915	2.4984	
35.944	2.4965	3	4	1	3	35.954	2.4958	0.010
			5	2	0	35.961	2.4953	
			5	0	3	35.986	2.4937	
36.349	2.4696	2	7	1	1	36.351	2.4695	0.002
37.118	2.4202	2	5	2	1	37.160	2.4175	0.042
37.967	2.3680	3	2	0	4	38.005	2.3657	0.037
			4	2	2	38.014	2.3652	
38.630	2.3289	2	5	1	3	38.632	2.3288	0.002
39.402	2.2850	4	1	2	3	39.401	2.2850	−0.001
			0	1	4	39.416	2.2842	
			2	1	4	40.538	2.2235	
40.582	2.2212	2	5	2	2	40.575	2.2216	−0.007
41.503	2.1740	3	8	0	2	41.514	2.1735	0.010
			7	2	1	43.826	2.0641	
43.873	2.0619	2	8	1	2	43.878	2.0617	0.005
			4	3	0	45.749	1.9817	
45.794	1.9798	2	5	2	3	45.796	1.9798	0.002
46.716	1.9429	2	2	3	2	46.710	1.9431	−0.006
			1	2	4	46.728	1.9424	
			10	0	0	46.732	1.9422	
			4	3	1	46.738	1.9420	
			1	0	5	46.748	1.9416	
48.841	1.8632	3	8	1	3	48.816	1.8641	−0.025

TABLE II. X-ray powder diffraction data of 8-chloro-9-methyl-*cis*-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2b).

$2\theta_{obs}$ (°)	d_{obs} (Å)	$(I/I_0)_{obs}$	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
7.054	12.5214	13	−1	0	1	7.076	12.4816	0.022
10.820	8.1702	83	−2	0	1	10.808	8.1788	−0.012
12.919	6.8471	30	2	0	1	12.926	6.8431	0.007
14.035	6.3050	7	1	0	2	14.034	6.3054	−0.001
14.664	6.0360	6	−2	1	1	14.657	6.0389	−0.007
			0	1	2	15.601	5.6756	
15.659	5.6546	59	−1	1	2	15.645	5.6597	−0.014
16.282	5.4396	42	2	1	1	16.289	5.4371	0.007
17.679	5.0128	100	3	0	1	17.689	5.0099	0.010
			0	2	0	19.814	4.4771	
19.837	4.4721	22	1	0	3	19.830	4.4735	−0.007
			−4	0	1	20.287	4.3738	
20.296	4.3719	58	3	1	1	20.295	4.3721	−0.001
21.065	4.2141	43	−1	2	1	21.064	4.2142	−0.001
21.477	4.1341	39	3	0	2	21.489	4.1318	0.012
22.201	4.0009	11	1	1	3	22.196	4.0019	−0.005
			0	2	2	23.255	3.8219	
23.293	3.8158	15	−1	2	2	23.285	3.8171	−0.008
23.685	3.7535	9	3	1	2	23.697	3.7517	0.012
			2	2	1	23.730	3.7465	
			−1	0	4	23.733	3.7461	
24.743	3.5953	36	2	1	3	24.746	3.5950	0.003
			4	1	1	24.775	3.5908	
25.346	3.5112	15	−5	0	1	25.338	3.5122	−0.008
25.862	3.4423	16	5	0	0	25.868	3.4415	0.006
27.259	3.2689	19	−5	1	1	27.253	3.2697	−0.006
28.179	3.1643	6	1	2	3	28.176	3.1645	−0.003
28.583	3.1205	6	−4	0	4	28.583	3.1204	0.000
29.380	3.0376	8	3	2	2	29.392	3.0364	0.012
29.772	2.9985	4	−1	0	5	29.802	2.9955	0.030
			−5	1	3	30.240	2.9531	
30.253	2.9519	12	2	2	3	30.257	2.9515	0.004
			4	2	1	30.281	2.9492	
			4	0	3	30.290	2.9483	
			−5	0	4	31.826	2.8095	
31.877	2.8051	4	−2	3	1	31.891	2.8039	0.014
			1	0	5	31.925	2.8010	
32.354	2.7648	4	0	3	2	32.355	2.7648	0.001
			−5	2	1	32.372	2.7634	
			−1	3	2	32.377	2.7629	
			1	2	4	32.751	2.7322	
32.759	2.7316	8	6	1	0	32.763	2.7313	0.004
			−5	2	0	32.796	2.7286	
34.184	2.6209	3	2	0	5	34.186	2.6207	0.002
			−2	3	3	35.652	2.5163	
35.665	2.5154	7	2	1	5	35.668	2.5152	0.003
36.413	2.4654	7	−4	3	1	36.413	2.4654	0.000
			4	2	3	36.460	2.4624	
37.090	2.4220	4	3	0	5	37.092	2.4219	0.002
			−6	2	2	37.129	2.4195	
			3	3	2	37.129	2.4195	
37.843	2.3755	4	2	3	3	37.836	2.3759	−0.007
			4	3	1	37.856	2.3747	
			1	2	5	37.858	2.3746	

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TABLE II. (*Continued.*)

$2\theta_{obs}$ (°)	d_{obs} (Å)	$(I/I_0)_{obs}$	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
38.190	2.3547	4	1	0	6	38.165	2.3561	−0.025
			−4	0	6	38.452	2.3392	
38.474	2.3380	4	3	1	5	38.476	2.3379	0.002
39.135	2.3000	3	−4	3	3	39.115	2.3011	−0.020
39.541	2.2773	4	1	1	6	39.518	2.2786	−0.023
			−5	3	1	39.593	2.2744	
			−4	1	6	39.796	2.2633	
39.830	2.2614	5	2	2	5	39.824	2.2617	−0.006
40.516	2.2247	4	−6	1	5	40.520	2.2245	0.004
			4	0	5	40.526	2.2242	
41.136	2.1926	4	−8	0	1	41.132	2.1928	−0.004
42.167	2.1413	4	0	4	2	42.171	2.1412	0.004
			−1	4	2	42.188	2.1403	
42.381	2.1310	5	3	2	5	42.399	2.1302	0.018
			−8	1	1	42.405	2.1299	
43.003	2.1016	4	3	0	6	42.999	2.1018	−0.004
			3	1	6	44.229	2.0462	
			−3	4	2	44.236	2.0459	
44.239	2.0457	3	−5	3	4	44.238	2.0458	−0.001
			−8	0	4	44.262	2.0447	
			3	4	1	44.283	2.0438	
			−8	1	4	45.464	1.9934	
45.489	1.9924	3	−4	4	1	45.480	1.9927	−0.009
			4	2	5	45.500	1.9919	

TABLE III. Crystal-structure data for 6,8-dimethyl-*cis*-2-vinyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2a) and 8-chloro-9-methyl-*cis*-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-4-ol (2b).

Crystal System	2a Orthorhombic	2b Monoclinic
a (Å)	19.422(6)	17.570(4)
b (Å)	6.512(3)	8.952(3)
c (Å)	9.757(4)	14.985(4)
β(°)	–	101.66(2)
V (Å^3)	1234.0(5)	2308.3(9)
Z	4	8
M_{20}	21.3	15.3
F_{30}	31.8 (0.0141, 67)	21.0 (0.0074, 193)
D_m	1.125 g/cm^3	1.436 g/cm^3

systematic absences and with the crystal densities (1.125 g/cm^3 for 2a and 1.436 g/cm^3 for 2b) in each case. The unit-cell parameters for both compounds were refined with the NBS*AIDS83 program (Miguell *et al.*, 1981). Their crystal data, X-ray densities as well as figures of merit M_{20} (de Wolff, 1968) and F_{20} (Smith and Snyder, 1979) are compiled in Table III.

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