Synthesis and X-ray diffraction data of 1-*N*-(3-pyridylmethyl) aminonaphthalene hydrochloride

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The title compound 1-*N*-(3-pyridylmethyl)aminonaphthalene hydrochloride ($C_{16}H_{15}N_2Cl$) was obtained by a reaction of α-naphthylamine (**1**) and *N*-pyridincarboxaldehyde (**2**) in anhydrous ethanol in the first step. The formed imine (**3**) was reduced with sodium borohydride in anhydrous methanol to give the product 1-*N*-(3-pyridylmethyl)aminonaphthalene (**4**). Finally, the hydrochloride was prepared by addition of a hydrochloric acid–ethyl acetate solution (ratio 1:3) with constant stirring and maintaining the temperature between 0 and 5 °C, obtaining a yellow polycrystalline solid corresponding to the respective derivative (**5**). The X-ray powder diffraction pattern for the new compound (**5**) was obtained. The compound (**5**) crystallizes in a monoclinic system with the space group $P2_1/m$ (No. 11) and refined unit-cell parameters: $a = 16.257$ (8) Å, $b = 9.236$ (7) Å, $c = 13.221$ (6) Å, $\beta = 94.87°$ (5), $Z = 6$, and $V = 1978$ (1) Å^3. © *2014 International Centre for Diffraction Data* [doi:10.1017/S0885715614000049].

Key words: derivatization, X-ray powder diffraction, 1-naphthalene ammonium salt

I. INTRODUCTION

The solubility of drugs is a major problem for the pharmaceutical industry because it is a determining factor in their pharmacokinetics, causing differences in the dissolution rate at the sites where their pharmacological action should be exerted. Derivatization of bioactive compounds through their corresponding salt formation is considered to be the most effective and used method to increase the solubility of both acidic and basic pharmaceutical products (Serajuddin, 2007) In pharmacology, amines are compounds of high commercial interest because a large number of these have diverse biological activities, including antifungal, antiviral, and antimycotic activities. Secondary amines with naphthalenic rings are of great importance in pharmaceutical chemistry for searching compounds with biological activity (Vargas *et al.*, 2003; Kouznetsov *et al.*, 2008). Allylamines based on naphthalene rings, such as terbinafine and naftifine, are good options in the treatment of the diseases caused by fungus (Schäfer-Korting *et al.*, 2008). Many drugs and biologically important amines are typically used as salts, which are less susceptible to decomposition by oxidation and other reactions, because they are soluble in water and are easily transformed into solutions for use in the form of syrups or injectable solutions (Graham and Fryhte, 2011). In previous studies, we reported the results of crystallographic studies of related amine compounds (Camargo *et al.*, 2010, 2011). In this study, we report the synthesis and crystallographic characterization of a new compound 1-*N*-(3-pyridylmethyl) aminonaphthalene hydrochloride.

II. EXPERIMENTAL

A. Synthesis

The new compound 1-*N*-(3-pyridylmethyl)aminonaphthalene (**4**) was prepared by first synthesizing an intermediary imine obtained by reaction of α-naphthylamine (**1**) and 3-pyridincarboxaldehyde (**2**) in anhydrous ethanol to obtain the intermediary imine (**3**) the reduction of which with $NaBH_4$ in anhydrous methanol yields amine (**4**). This compound was purified with a chromatographic column. Finally, the hydrochloride salt of the organic compound (**4**) was prepared by addition of hydrochloric acid–ethyl acetate solution in the ratio of 1:3 with constant stirring and maintaining the temperature between 0 and 5 °C for 20 min, obtaining the respective derivative, 1-*N*-(3-pyridylmethyl)aminonaphthalene hydrochloride (**5**)

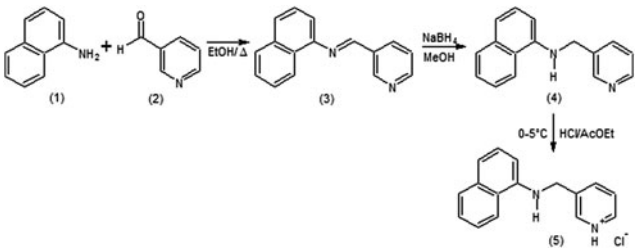

Figure 1. Synthesis of 1-*N*-(3-pyridylmethyl)aminonaphthalene hydrochloride.

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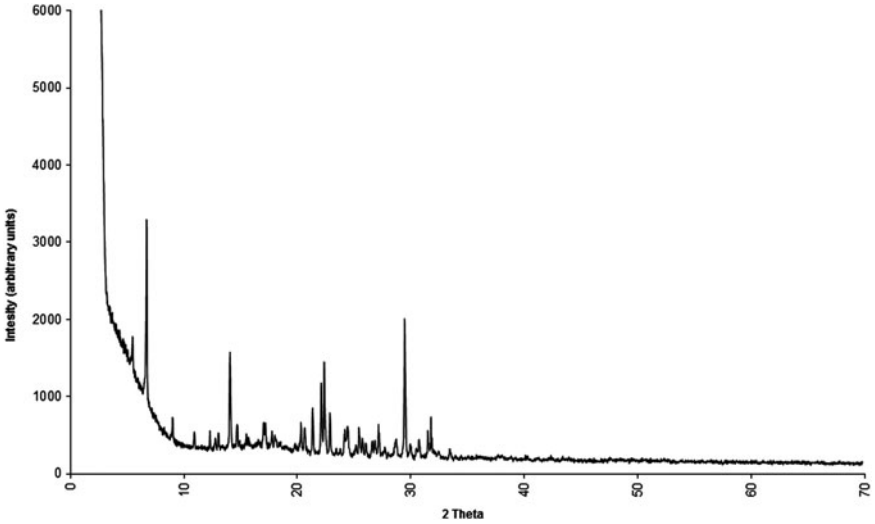

Figure 2. Powder X-ray diffraction pattern of 1-*N*-(3-pyridylmethyl)aminonaphthalene hydrochloride.

TABLE I. X-ray powder diffraction data of 1-*N*-(3-pyridylmethyl)aminonaphthalene hydrochloride. Cu$K\ \alpha_1$ radiation ($\lambda = 1.5406$ Å).

$2\theta_{obs}$ (°)	d_{obs} (Å)	I_{obs}	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
5.497	16.0640	19	1	0	0	5.451	16.1987	−0.046
6.743	13.0982	97	0	0	1	6.705	13.1732	−0.038
8.286	10.6622	4	−1	0	1	8.278	10.6731	−0.008
9.022	9.7940	13	1	0	1	8.998	9.8205	−0.024
10.938	8.0823	9	2	0	0	10.915	8.0993	−0.023
12.318	7.1797	11	−2	0	1	12.323	7.1766	0.005
14.081	6.2845	58	−1	0	2	14.067	6.2905	−0.014
14.942	5.9243	5	1	0	2	14.931	5.9285	−0.011
17.046	5.1975	17	−1	1	2	17.040	5.1993	−0.006
17.200	5.1513	16	−3	0	1	17.198	5.1519	−0.002
17.783	4.9837	12	1	1	2	17.763	4.9892	−0.020
19.048	4.6555	2	−3	1	0	19.023	4.6615	−0.025
20.340	4.3626	18	−3	0	2	20.347	4.3611	0.007
			0	2	1	20.361	4.3582	
20.652	4.2974	15	3	1	1	20.656	4.2966	0.004
21.368	4.1550	30	1	0	3	21.393	4.1501	0.025
22.130	4.0136	46	3	0	2	22.138	4.0122	0.008
			2	2	0	22.139	4.0119	
			−2	0	3	22.177	4.0052	
22.392	3.9672	63	−4	0	1	22.396	3.9666	0.004
			0	1	3	22.401	3.9657	
22.889	3.8822	28	−2	2	1	22.880	3.8836	−0.009
			2	2	1	23.430	3.7937	
23.461	3.7888	5	1	1	3	23.482	3.7856	0.021
			4	0	1	23.505	3.7818	
24.187	3.6767	15	−2	1	3	24.201	3.6746	0.014
			−4	1	1	24.403	3.6447	
24.437	3.6397	19	1	2	2	24.412	3.6433	−0.025
25.451	3.4969	20	4	1	1	25.429	3.4998	−0.022
25.767	3.4547	11	2	1	3	25.738	3.4586	−0.029
26.610	3.3472	9	3	2	1	26.621	3.3458	0.011
			−4	1	2	26.630	3.3447	
26.851	3.3177	10	−3	1	3	26.832	3.3199	−0.019
			−1	0	4	27.148	3.2821	
27.186	3.2775	20	3	0	3	27.220	3.2735	0.034
27.508	3.2399	2	5	0	0	27.510	3.2397	0.002
27.733	3.2141	6	−5	0	1	27.771	3.2098	0.038
28.746	3.1031	10	0	1	4	28.757	3.1020	0.011
			−5	1	1	29.436	3.0319	
29.479	3.0276	100	3	2	2	29.467	3.0288	−0.012
			−2	2	3	29.497	3.0258	
			−1	3	0	29.508	3.0247	

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Table I. Continued

$2\theta_{obs}$ (°)	d_{obs} (Å)	I_{obs}	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
29.976	2.9785	10	−2	1	4	29.988	2.9774	0.012
30.743	2.9060	13	2	2	3	30.789	2.9017	0.046
31.053	2.8776	2	−2	3	0	31.050	2.8779	−0.003
			−5	1	2	31.229	2.8619	
31.270	2.8582	1	4	0	3	31.266	2.8585	−0.004
31.544	2.8340	18	−4	2	2	31.549	2.8335	0.005
31.814	2.8105	24	5	0	2	31.773	2.8141	−0.041
33.105	2.7038	1	6	0	0	33.156	2.6998	0.051

The entire synthesis process is shown in Figure 1, and the title compound was obtained by first reacting 2.00 g of (**1**) (14 mmol) with 1.79 g of (**2**) (17 mmol; 1.60 ml) in ethanol (40 ml) and backflowing for 8 h to yield the pure product (**3**) as yellow oil (2.77 g, 11.92 mmol; 85%), $C_{16}H_{12}N_2$ (MW 232.3 g mol^{-1}). IR: 1624, 1569, 1420, and 774 cm^{-1}. This was followed by reaction of 2.77 g of (**3**) (11.92 mmol) with 1.35 g of $NaBH_4$ (35.77 mmol) in anhydrous methanol (40 ml), removal of the solvent, and concentration to yield the pure amine (**4**) as a shine white solid (2.51 g, 10.72 mmol; 90%): m.p. 74–76 °C. $C_{16}H_{14}N_2$ (MW 234.3 g mol^{-1}). IR: 3378, 1583, 1533, 1408, and 768 cm^{-1}. GC–MS (70 eV): t_R = 26.63 min, m/z M^+ 234(100), 115(60), 142(55), 233(17). ^{1}H-NMR (400 MHz, $CDCl_3$, Me_4Si) δ 8.65 (d, J = 1.6 Hz, 1H), 8.50 (dd, J = 4.8, 1.6 Hz, 1H), 7.75 (ddd, J = 20.0, 12.5, 5.5 Hz, 3H), 7.45–7.36 (m, 2H), 7.28–7.20 (m, 3H), 6.52 (dd, J = 7.0, 1.5 Hz, 1H), 4.68 (s, 1H), and 4.48 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$, Me_4Si) δ 149.38, 148.94, 142.69, 135.37, 134.63, 134.31, 128.83, 126.52, 125.96, 125.05, 123.71, 123.47, 119.83, 118.28, 105.07, and 46.09. Finally, 0.41 g of (**4**) (1.75 mmol) was dissolved in ethyl acetate (30 ml) followed by slow addition of the HCl acidified solution to yield (**5**) as a yellow polycrystalline solid (0.40 g, 1.48 mmol; 84%): m.p. 136–139 °C. $C_{16}H_{15}N_2Cl$ (MW 271.77 g mol^{-1}).

B. Powder data collection

A small portion of the title compound was gently ground in an agate mortar and sieved to a grain size less than 37 μm (greater than 400 mesh). The specimen was mounted on a zero-background specimen holder (Buhrke *et al.*, 1998). The X-ray powder diffraction (XRPD) pattern was recorded with a D8 FOCUS BRUKER diffractometer operating in Brag-Brentano geometry equipped with a Cu target X-ray tube (40 kV and 40 mA), a nickel filter and a one-dimensional LynxEye detector. A fixed antiscatter slit of 8.0 mm, a receiving slit of 1.0 mm, a soller slit of 2.5°, and a detector slit of 3.0 mm were used.

The scan range was 3–70° 2θ with a step size of 0.02° and a count time of 2 s per step. Powder data were collected at room temperature (298 K).

PowderX analytical software (Dong, 1999) was used to remove the background (Sonnerveld and Visser, 1975), to smoothen the experimental XRD pattern (Saviztky and Golay, 1964), and finally to eliminate the Cu$K\alpha_2$ component (Rachinger, 1948). The second derivative method was used to determine the position and intensity of the Cu$K\alpha_1$ diffraction peak of each reflection.

TABLE II. Parameters obtained by X-ray powder diffraction for 1-*N*-(3-pyridylmethyl)aminonaphthalene hydrochloride (**5**).

Parameter	Compound (5)
a (Å)	16.257 (8)
b (Å)	9.236 (7)
c (Å)	13.221 (6)
β (°)	94.87 (5)
V (Å^3)	1978 (1)
Z	6
M_{20}	11.6
F_{30}	18.6 (0.0172, 94)

III. RESULTS AND DISCUSSION

The X-ray powder pattern and the XRPD data for the title compound (**5**) are given in Figure 2 and Table I, respectively. All reflections were indexed successfully using the DICVOL06 program (Boultif and Loüer, 2006) on a monoclinic unit cell and the peak positions, each with an absolute error of 0.03° in 2θ, were used in the calculations. The space group, $P2_1/m$ (No. 11), estimated by the program CHEKCELL (Laugier and Bochu, 2002) was compatible with the systematic absences. The unit-cell parameters of the compound (**5**) were refined with the program NBS*AIDS83 software (Miguell *et al.*, 1981). Its crystal data and figures of merit M_{20} (Wolff, 1968) and F_{30} (Smith and Snyder, 1979) are compiled in Table II.

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Boultif, A. and Loüer, D. (**2006**). "Indexing of powder diffraction patterns of low symmetry lattices by successive dichotomy method," J. Appl. Crystallogr. **37**, 724–731.

Buhrke, V., Jenkins, R., and Smith, D. (**1998**). *Preparation of Specimens for X-ray Fluorescence and X-ray Diffraction Analysis* (Wiley, New York), pp. 141–142.

Camargo, H. A., Henao, J. A., Amado, D. F., and Kouznetsov, V. V. (**2010**). "Synthesis and X-ray diffraction data of 1-N-4-pyridylmethylamino naphthalene," Powder Diffr. **25**(1), 72–74.

Camargo, H. A., Habran, N. M., Henao, J. A., Amado, D. F., and Kouznetsov, V. V. (**2011**). "Synthesis and X-ray diffraction data of 1-[*N*-(methyl)-(3,5-dimethylphenylamino)]methylnaphthalene," Powder Diffr. **26**(1), 74–77.

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de Wolff, P. M. (**1968**). "A simplified criterion for the reliability of a powder pattern indexing," *J. Appl. Crystallogr.* **1**, 108–113.
Dong, C. (**1999**). "PowderX: Windows-95-based program for powder X-ray diffraction data processing," J. Appl. Crystallogr. **32**, 838.
Graham, T. W. and Fryhte, G. B. (**2011**). *The Chemistry of Biologically Important Amines* (Wiley, México), Vol. **10**, pp. 922–924.
Kouznetsov, V. V., Vargas, L. Y., Sortino, M., Vásquez, Y., Gupta, M. D., Freile, M., Enriz, R. D., and Zacchino, S. A. (**2008**). "Antifungal and cytotoxic activities of some *N*-substituted aniline derivates bearing a hetaryl fragment," Bioorg. Med. Chem. **16**, 794–809.
Laugier, J. and Bochu, B. (**2002**). *CHEKCELL*. "LMGP-Suite Suite of Programs for the interpretation of X-ray. Experiments", ENSP/ Laboratoire des Matériaux et du Génie Physique, BP 46. 38042 Saint Martin d'Hères, France. http://www.inpg.fr/LMGP and http://www.ccp14.ac.uk/tutorial/lmgp/.
Miguell, A. D., Hubbard, C. R., and Stalick, J. K. (**1981**). *NBS* AIDS80: A FORTRAN Program for Crystallographic Data Evaluation* (Technical Note 1141). Washington, DC: National Bureau of Standards.
Rachinger, W. A. (**1948**). "A correction for the α_1 α_2 doublet in the measurement of widths of X-ray diffraction lines," J. Sci. Instrum. **25**, 254.
Saviztky, A. and Golay, M. J. (**1964**) "Smoothing and differentiation of data by simplified least squares procedures," Anal. Chem. **36**, 1627–1639.
Schäfer-Korting, M. Schoellmann, C., and Korting, H. C. (**2008**). "Fungicidal activity plus reservoir effect allows short treatment courses with Terbinafine in Tinea Pedis," Skin Pharmacol. Physiol. **21**, 203–210.
Serajuddin, A. (**2007**). "Salt formation to improve drug solubility," Adv. Drug Deliv. Rev. **59**, 603–616.
Smith, G. S. and Snyder, R. L. (**1979**). "*FN:* A criterion for rating powder diffraction patterns and evaluating the reliability of powder-pattern indexing," J. Appl. Crystallogr. **12**, 60–65.
Sonneveld, E. J. and Visser, J. W. (**1975**). "Automatic collection of powder diffraction data from photographs," J. Appl. Crystallogr. **8**, 1–7.
Vargas, L. Y., Castelli, M. V., Kouznetsov, V. V., Urbina, J. M., López, S. N., Sortino, M., Enriz, R. D., Ribas, J. C., and Zacchino, S. A. (**2003**). "*In vitro* antifungal activity of new series of homoallylamines and related compounds with inhibitory properties of the synthesis of fungal cell wall polymers," *Bioorg. Med. Chem.* **11**, 1531–1550.