NEW DIFFRACTION DATA

Synthesis and X-ray diffraction data of 2-morpholino-2-(3,4,5-trimethoxyphenyl)acetonitrile, (C₁₅H₂₀N₂O₄)

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The α-aminonitrile, 2-morpholino-2-(3,4,5-trimethoxyphenyl)acetonitrile ($C_{15}H_{20}N_2O_4$), was prepared through a silica sulfuric acid-catalyzed Strecker reaction between 3,4,5-trimethoxybenzaldehyde, morpholine, and two different cyanide sources. Molecular characterization was performed by Fourier transform infrared spectroscopy, gas chromatography–mass spectrometry, (^{1}H, ^{13}C – mono and bidimensional) nuclear magnetic resonance; crystallographic characterization was completed by X-ray powder diffraction of polycrystalline samples. The title compounds crystallized in a monoclinic system and unit-cell parameters are reported [$a = 13.904(2)$, $b = 5.1696(6)$, $c = 21.628(3)$ Å, $\beta = 104.31(1)°$, unit-cell volume $V = 1506.3(3)$ Å^3, $Z = 4$]. All measured lines were indexed with the $P2_1/a$ (No. 14) space group. © 2016 International Centre for Diffraction Data.
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Key words: α-Aminonitriles, girgensohnine alkaloid, X-ray powder diffraction data

I. INTRODUCTION

Strecker reaction, studied using different Lewis acids (Royer *et al.*, 2005; Surya *et al.*, 2007) or bases (Takahashi *et al.*, 2005) as catalysts, and NaCN, KCN, trimethylsilylcyanide, acetone cyanohydrin as cyanide sources, provides an important tool for construction of small and functionalized nitrogen-containing molecules as the α-aminonitriles. The α-aminonitriles are key intermediates for synthesis of natural and un-natural aminoacids and compounds of great interest that show remarkable biological activities (Chaturvedi *et al.*, 2012) such as anticancer, antifungal, antibiotic, etc. The alkaloid girgensohnine, racemic piperidinic α-aminonitrile, is a cyanogenic metabolite extracted with a yield of no more than 0.05% from *Girgensohnia oppositiflora* (Amaranthaceae), shrub that grows in the Russia and Iran deserts. There are not many studies related to the synthesis of compounds structurally related to this alkaloid (Vargas Méndez and Kouznetsov, 2013).

In searching for safer and environmentally friendly protocol to preparing the 2-morpholino-2-(3,4,5-trimethoxyphenyl) acetonitrile, the Strecker reaction was performed using acetone cyanohydrin as a cyanide source and silica sulfuric acid (SSA) as catalyst, in MeCN at room temperature for over 20 h (Figure 1). Structural elucidation was made using spectroscopic techniques [Fourier transform infrared spectroscopy (FTIR), gas chromatography–mass spectrometry (GC–MS), proton nuclear magnetic resonance (^{1}H NMR), and carbon-13 nuclear magnetic resonance (^{13}C NMR)] allowing the identification of the main spectral features (the CN function, hydrogen linked with nitrile group, aromatic, and N-heterocyclic protons)
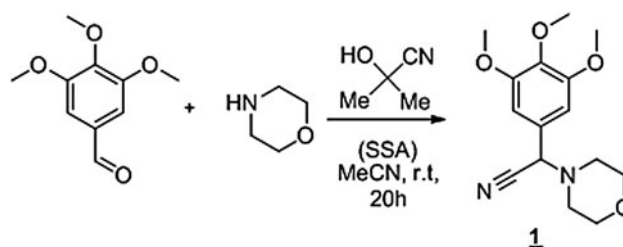

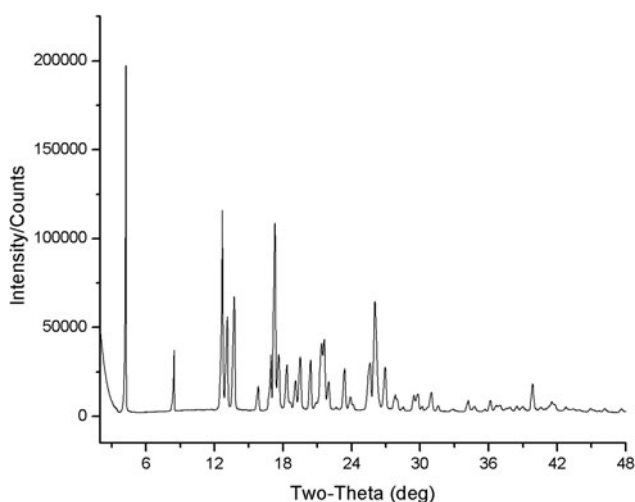Figure 1. Preparation of 2-morpholino-2-(3,4,5-trimethoxyphenyl) acetonitrile (**1**).

Figure 2. X-ray powder diffraction pattern of 2-morpholino-2-(3,4,5-trimethoxyphenyl)acetonitrile (**1**).

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TABLE I. X-ray powder diffraction data of 2-morpholino-2-(3,4,5-trimethoxyphenyl)acetonitrile (**1**).

$2\theta_{obs}$ (°)	d_{obs} (Å)	$(I/I_0)_{obs}$	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
4.204	21.0014	100	0	0	1	4.213	20.9565	0.009
8.427	10.4841	19	0	0	2	8.432	10.4782	0.005
12.659	6.9871	2	0	0	3	12.662	6.9855	0.003
12.767	6.9282	48	−2	0	1	12.761	6.9315	−0.006
13.136	6.7344	23	2	0	0	13.133	6.7359	−0.003
13.744	6.4379	25	−2	0	2	13.748	6.4360	0.004
14.754	5.9993	<1	2	0	1	14.764	5.9955	0.010
15.848	5.5876	5	−2	0	3	15.846	5.5881	−0.002
16.905	5.2405	13	0	0	4	16.910	5.2391	0.005
17.299	5.1220	53	2	0	2	17.307	5.1196	0.008
17.661	5.0179	13	0	1	1	17.656	5.0192	−0.005
18.367	4.8265	11	1	1	0	18.367	4.8265	0.000
18.498	4.7926	1	−1	1	1	18.480	4.7972	−0.018
18.684	4.7454	1	−2	0	4	18.695	4.7426	0.011
19.137	4.6340	7	0	1	2	19.128	4.6361	−0.009
19.546	4.5380	14	−1	1	2	19.541	4.5392	−0.005
20.439	4.3417	11	2	0	3	20.437	4.3420	−0.002
20.927	4.2415	2	1	1	2	20.918	4.2433	−0.009
21.182	4.1910	5	0	0	5	21.181	4.1913	−0.001
21.368	4.1550	4	0	1	3	21.365	4.1555	−0.003
21.658	4.1000	12	2	1	0	21.652	4.1011	−0.006
22.036	4.0305	6	−2	1	2	22.036	4.0304	0.000
22.697	3.9146	<1	2	1	1	22.694	3.9152	−0.003
23.298	3.8150	5	1	1	3	23.292	3.8159	−0.006
23.429	3.7939	11	−2	1	3	23.423	3.7948	−0.006
23.937	3.7145	3	2	0	4	23.938	3.7143	0.001
24.170	3.6793	1	0	1	4	24.166	3.6798	−0.004
25.474	3.4938	3	−2	1	4	25.467	3.4948	−0.007
25.641	3.4714	7	−2	0	6	25.643	3.4712	0.002
25.807	3.4495	1	−3	1	1	25.805	3.4497	−0.002
26.056	3.4171	17	−3	1	2	26.050	3.4178	−0.006
26.18	3.4012	9	1	1	4	26.168	3.4027	−0.012
26.332	3.3819	<1	−4	0	3	26.362	3.3780	0.030
26.448	3.3673	<1	4	0	0	26.443	3.3680	−0.005
26.789	3.3252	2	2	1	3	26.792	3.3249	0.003
26.880	3.3142	2	−1	1	5	26.888	3.3132	0.008
26.991	3.3008	7	−3	1	3	26.984	3.3016	−0.007
27.385	3.2542	<1	0	1	5	27.372	3.2557	−0.013
27.659	3.2226	1	2	0	5	27.686	3.2195	0.027
27.704	3.2174	3	−4	0	4	27.699	3.2180	−0.005
27.828	3.2034	2	4	0	1	27.827	3.2035	−0.001
28.035	3.1802	3	−2	1	5	28.034	3.1803	−0.001
28.556	3.1233	1	−3	1	4	28.544	3.1247	−0.012
29.457	3.0298	4	−2	0	7	29.479	3.0276	0.022
29.576	3.0179	2	2	1	4	29.590	3.0165	0.014
29.761	2.9996	2	4	0	2	29.779	2.9977	0.018
29.828	2.9930	2	0	0	7	29.820	2.9938	−0.008
30.210	2.9560	2	−1	1	6	30.203	2.9567	−0.007
30.637	2.9158	<1	−3	1	5	30.642	2.9153	0.005
30.889	2.8925	5	0	1	6	30.872	2.8941	−0.017
31.013	2.8813	4	−2	1	6	31.007	2.8818	−0.006
31.047	2.8782	3	−4	1	2	31.041	2.8787	−0.006
31.617	2.8276	1	−4	1	3	31.614	2.8278	−0.003
31.686	2.8216	1	4	1	0	31.682	2.8219	−0.004
32.727	2.7342	1	2	1	5	32.743	2.7328	0.016
32.755	2.7319	1	−4	1	4	32.754	2.7320	−0.001
32.941	2.7169	1	1	1	6	32.933	2.7175	−0.008
33.443	2.6773	<1	−2	0	8	33.471	2.6751	0.028
34.207	2.6192	2	0	0	8	34.202	2.6196	−0.005
34.571	2.5924	1	4	1	2	34.559	2.5933	−0.012
34.651	2.5866	1	0	2	0	34.676	2.5848	0.025
34.802	2.5758	1	−4	0	7	34.798	2.5761	−0.004
34.961	2.5644	<1	0	2	1	34.947	2.5654	−0.014
35.403	2.5334	<1	−1	2	1	35.391	2.5342	−0.012
35.670	2.5150	1	2	0	7	35.675	2.5147	0.005
35.774	2.5080	1	1	2	1	35.750	2.5096	−0.024

Continued

TABLE I. Continued

$2\theta_{obs}$ (°)	d_{obs} (Å)	$(I/I_0)_{obs}$	h	k	l	$2\theta_{calc}$ (°)	d_{calc} (Å)	$\Delta 2\theta$ (°)
35.965	2.4951	2	−1	2	2	35.983	2.4939	0.018
36.132	2.4839	3	−3	1	7	36.100	2.4861	−0.032
36.186	2.4804	2	2	1	6	36.175	2.4811	−0.011
36.540	2.4571	1	−4	1	6	36.526	2.4580	−0.014
36.692	2.4473	2	4	1	3	36.706	2.4464	0.014
36.801	2.4403	2	1	2	2	36.786	2.4413	−0.015
36.889	2.4347	2	−5	1	1	36.887	2.4348	−0.002
36.962	2.4300	2	−5	1	3	36.967	2.4297	0.005
37.074	2.4230	2	−1	2	3	37.083	2.4224	0.009
37.220	2.4138	1	2	2	0	37.229	2.4132	0.009
37.585	2.3912	1	−2	0	9	37.591	2.3908	0.006
37.640	2.3878	1	5	1	0	37.615	2.3893	−0.025
37.908	2.3715	2	−4	0	8	37.912	2.3713	0.004
38.510	2.3358	1	0	1	8	38.496	2.3367	−0.014
38.632	2.3288	1	0	0	9	38.636	2.3285	0.004
38.970	2.3093	3	−6	0	3	38.950	2.3105	−0.020
39.045	2.3051	<1	−5	1	5	39.055	2.3045	0.010
39.243	2.2939	<1	4	1	4	39.242	2.2940	−0.001
39.654	2.2711	1	−2	2	4	39.680	2.2696	0.026
39.868	2.2594	3	2	0	8	39.857	2.2600	−0.011
40.132	2.2451	<1	6	0	0	40.128	2.2453	−0.004
40.250	2.2388	<1	3	2	0	40.223	2.2402	−0.027
40.599	2.2203	2	−6	0	5	40.588	2.2209	−0.011
40.689	2.2156	1	−3	2	3	40.719	2.2141	0.030
41.029	2.1981	1	3	2	1	41.010	2.1990	−0.019
41.305	2.1840	<1	−4	0	9	41.294	2.1846	−0.011
41.459	2.1763	<1	6	0	1	41.459	2.1763	0.000
41.487	2.1749	<1	−1	1	9	41.506	2.1739	0.019
41.566	2.1709	2	4	0	6	41.564	2.1710	−0.002
41.848	2.1569	2	−2	0	10	41.824	2.1581	−0.024
42.541	2.1234	<1	0	1	9	42.547	2.1231	0.006
42.788	2.1117	<1	−3	1	9	42.778	2.1122	−0.010
42.859	2.1084	<1	−6	1	3	42.837	2.1094	−0.022
43.134	2.0955	<1	0	0	10	43.132	2.0956	−0.002
43.211	2.0920	<1	6	0	2	43.210	2.0921	−0.001
43.425	2.0822	1	−6	1	4	43.377	2.0844	−0.048
43.501	2.0787	<1	0	2	6	43.523	2.0777	0.022
43.655	2.0717	1	−4	2	2	43.649	2.0720	−0.006
45.000	2.0129	<1	−4	1	9	45.015	2.0123	0.015
45.031	2.0116	<1	4	2	1	45.029	2.0117	−0.002
45.915	1.9749	1	3	2	4	45.944	1.9737	0.029
46.175	1.9644	<1	−2	0	11	46.163	1.9649	−0.012
47.650	1.9069	2	3	1	8	47.629	1.9077	−0.021

TABLE II. Parameters obtained by X-ray powder diffraction for 2-morpholino-2-(3,4,5-trimethoxyphenyl)acetonitrile (**1**).

Information	**1**
Crystal system	Monoclinic
Space group	$P2_1/a$ (14)
a (Å)	13.904 (2)
b (Å)	5.1696 (6)
c (Å)	21.628 (3)
β (°)	104.31 (1)
V (Å^3)	1506.3 (3)
Z	4
M_{20}	54.1
F_{30}	151.4 (0.0051.39)
D_m	1.29 g cm^{-3}

of these compounds. The X-ray powder diffraction (XRPD) data are reported. Crystallographic information by X-ray diffraction about this type of derivative has been little explored.

II. EXPERIMENTAL

A. Synthesis

The analog of girgensohnine alkaloid was prepared via one-pot reaction mode. An equimolar mixture of 3,4,5-trimethoxybenzaldehyde (1 mmol) and morpholine (1.1 mmol) was stirred. The acetone cyanohydrin (1.5 mmol) and the catalyst SSA (1:1 by weight) were then added in acetonitrile (15 ml) at room temperature (20 h, 30 min). The progress of the reaction was monitored by thin layer chromatography (TLC) (ether:ethyl acetate, 10:1). Then, the reaction mixture was filtered and evaporated of the solvent, the residue was purified by column chromatography on alumina (100–200 mesh) eluting with petroleum ether: ethyl acetate (15:1) to furnish title compound as white solid.

2-morpholino-2-(3,4,5-trimethoxyphenyl)acetonitrile (**1**). Yield: 77%, mp: 137–139 °C. IR (KBr): 2224 v ($_{C\equiv N}$), 1248 v ($_{N-C}$) cm^{-1}. ^{1}H NMR (DMSO-d6, 400 MHz) δ (ppm): 6.74 (2H, s, 2,6-H$_{Ar}$), 4.74 (1H, s, 10-H), 3.87 (6H, s, 3,5-OCH$_3$),

3.83 (3H, s, 4-OCH$_3$), 3.79–3.66 (4H, m, 3,5-H$_{Morph}$), 2.68–2.43 (4H, m, 2,6-H$_{Morph}$). ^{13}C NMR (100 MHz) δ (ppm): 153.7 (3,5-C$_{Ar}$), 138.5 (4-C$_{Ar}$), 128.2 (1-C$_{Ar}$), 115.5 (-CN), 105.1 (+, 2,6-C$_{Ar}$), 66.9 (−, 3,5-C$_{Morph}$), 62.8 (+, 10-C), 61.2 (+, 4-OCH$_3$), 56.5 (+, 3–5-OCH$_3$), 50.3 (−, 2,6-C$_{Morph}$). GC–MS (70 eV): t$_R$ = 21.3 min, m/z = (292, M$^+$), 207 (52), 206 (100), 176 (14), 86 (20), 66 (14). Anal.Calcd. (analytically calculated) for C$_{15}$H$_{20}$N$_2$O$_4$: C, 61.63; H, 6.90; N, 9.58; Found: C, 61.47; H, 6.63; N, 9.45.

B. Powder data collection

The title compound was ground and sieved to a grain size less than 38 μm. Powder diffraction pattern was recorded at room temperature (298 K) on a BRUKER D8 ADVANCE diffractometer working in the Bragg-Brentano geometry using Cu$K\alpha$ radiation (λ = 1.541 84 Å), operating at 40 kV and 40 mA. The pattern was recorded in steps of 0.0156° (2θ), from 5° to 50° at 0.8 s step^{-1}. The diffractometer was equipped with the primary and secondary Soller slits of 2.5°, divergence slit of 0.6 mm, Ni filter of 0.02 mm, and a LynxEye detector.

III. RESULTS AND DISCUSSION

The experimental XRPD pattern of the title compound (Figure 1, compound **1**) is depicted in Figure 2 and the XRPD data are given in Table I. Powder X program (Dong, 1999) was used to remove the background (Sonneveld and Visser, 1975), smooth the profile (Saviztky and Golay, 1964), to eliminate the $K\alpha_2$ component (Rachinger, 1948), and the second derivative method was used to determine the peak observed positions and intensities. The indexing of the pattern was performed with the program DICVOL06 (Boultif and Loüer, 2004) with an absolute error of 0.03° (2θ). The title compound crystallized in a monoclinic system with space group $P2_1/a$ (No. 14) estimated by the CHEKCELL program (Laugier and Bochu, 2002), which was compatible with the systematic absences. The calculated density for Z = 4 is in accordance with the measured value, D_m = 1.29 g cm^{-3}. The analysis of the entire pattern (111 diffraction maxima) with NBS*AIDS83 (Mighell *et al.*, 1981) resulted in a unit cell with parameters: a = 13.904(2), b = 5.1696(6), c = 21.628(3) Å, β = 104.31(1)°, and V = 1506.3 (3) Å^3. The set of reflections observed are consistent with space group $P2_1/a$ (No. 14). The de Wolf (de Wolff, 1968) and Smith–Snyder (Smith and Snyder, 1979) figures of merit were M_{20} = 54.1 and F_{30} = 151.4(0.0051, 39), respectively. The parameters of the unit cell are compiled in Table II.

SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit http://dx.doi.org/10.1017/S0885715616000075

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