

Synthesis and X-ray diffraction data of 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline

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The compound 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline (**2**) (chemical formula $C_{23}H_{22}N_2$) was synthesized through the free-solvent oxidation reaction mediated by elemental sulfur from the corresponding 2-ethyl-6-(pyridin-4-yl)-5,6,6a,11b-tetrahydro-7H-indeno[2,1-c]quinoline (**1**), an adduct easily obtained, using the Lewis acid-promoted [4 + 2] cycloaddition reaction. Preliminary molecular characterization was performed by Fourier transform-infrared and gas chromatography-mass spectrometry. The X-ray powder diffraction (XRPD) pattern for the title compound was analyzed and found to be crystallized in monoclinic system, space group $P2_1/n$ ($N^\circ 14$) with refined unit-cell parameters $a = 20.795$ (8) Å, $b = 7.484$ (2) Å, $c = 10.787$ (2) Å and $\beta = 93.96^\circ$ (2). The volume of the unit cell is $V = 1674.8$ (6) Å³. © 2013 International Centre for Diffraction Data. [doi:10.1017/S0885715613000730]

Key words: indeno[2, 1-c]quinolines, antitumoral activity, X-ray powder diffraction

I. INTRODUCTION

Quinoline derivatives are important natural and synthetic compounds with remarkable and diverse pharmacological properties (Kouznetsov *et al.*, 2005). Within the quinoline family, tetracyclic and pseudo-planar compounds with antitumoral activity as topoisomerases (topo) inhibitors are the more biological relevant examples (Gelderblom and Sparreboom, 2006).

Since the discovery of camptothecin, a natural topoisomerase (topo I) inhibitor (Priel *et al.*, 1991; Pommier, 2006), a constant search for new compounds with the ability to inhibit the topoisomerases I/II enzymes has been undertaken (Li *et al.*, 2006). The most relevant indenoquinoline compound because of its potent cytotoxicity against different leukemia lines (Ohyama *et al.*, 1999; Twelves *et al.*, 1999) is the 6-[[2(dimethylamino)ethyl]amino]-3-hydroxy-7H-indeno[2,1-c]quinolin-7-one, known as TAS-103. The exhibited anticancer activity is because of its ability to function as a dual inhibitor of both topo I/II, and it has been investigated in clinical studies (Ewesuedo *et al.*, 2001; Ishida and Asao, 2002).

In our preliminary studies of TAS-103 analogs, we have reported a work where the diastereoselective synthesis of corresponding 6-pyridinyl-(tetrahydro)indeno[2,1-c]quinolines based on the Lewis acid-catalyzed imino Diels–Alder reaction (Kouznetsov *et al.*, 2009) was described and their biological activity was studied. It was found that these compounds were active against MCF-7, H-460, and SF-268 cancer cell

lines making them potential anti-cancer agents (Kouznetsov *et al.*, 2006). However, the information about the crystallographic study by X-ray diffraction of this type of derivatives has been little explored.

In this regard, our ongoing research program focused on the chemistry of the anti-tumoral bioactive (tetrahydro) indeno[2,1-c]quinoline derivatives and its X-ray crystallographic study. Here, we discuss a simple methodology for preparation of compound 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline (**2**) through the free-solvent oxidation reaction mediated by elemental sulfur from the corresponding 2-ethyl-6-(pyridin-4-yl)-5,6,6a,11b-tetrahydro-7H-indeno[2,1-c]quinoline (**1**) (Kouznetsov *et al.*, 2006) and report the results of the molecular characterization (FT-IR, GC-MS) and X-ray powder diffraction (XRPD) data.

II. EXPERIMENTAL

A. Synthesis

As shown in Figure 1, the compound $C_{23}H_{22}N_2$ was synthesized according to the following experimental procedure: A homogenate mixture of 2-ethyl-6-(pyridin-4-yl)-5,6,6a,11b-tetrahydro-7H-indeno[2,1-c]quinoline (**1**) (0.5 mmol) and elemental sulfur (1.5 mmol) was melted at 210–215 °C for 10 min. After completion of the reaction indicated by the complete liberation of H_2S (g), the reaction mixture was directly purified by column chromatography using alumina and eluted with petroleum ether-ethyl acetate to obtain 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline (**2**) as white pale-yellow crystals with 82% yield. The purified compound was recrystallized by slow evaporation in methanol solution. The

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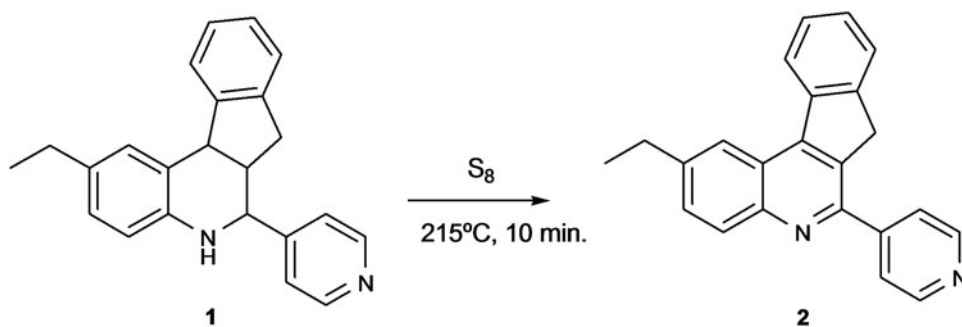


Figure 1. Synthesis of 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline (2).

TABLE I. X-ray powder diffraction data of 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline (2).

$2\theta_{\text{obs}} (^{\circ})^a$	$d_{\text{obs}} (\text{\AA})$	$(I/I_0)_{\text{obs}}$	h	k	l	$2\theta_{\text{calc}} (^{\circ})$	$d_{\text{calc}} (\text{\AA})$	$\Delta 2\theta (^{\circ})$
8.501	10.3930	100	2	0	0	8.518	10.3727	0.017
8.955	9.8671	15	-1	0	1	8.985	9.8346	0.030
9.485	9.3169	8	1	0	1	9.509	9.2935	0.024
12.536	7.0554	8	1	1	0	12.564	7.0400	0.028
14.720	6.0131	22	-3	0	1	14.729	6.0096	0.009
14.850	5.9608	5	-1	1	1	14.863	5.9557	0.013
15.161	5.8392	32	1	1	1	15.188	5.8290	0.027
15.687	5.6446	42	3	0	1	15.692	5.6428	0.005
16.430	5.3909	38	0	0	2	16.462	5.3806	0.032
			-2	1	1	16.462	5.3804	
17.033	5.2014	19	2	1	1	17.047	5.1972	0.014
			4	0	0	17.083	5.1864	
17.421	5.0864	1	-3	1	0	17.447	5.0790	0.026
18.008	4.9219	3	-2	0	2	18.025	4.9173	0.017
18.920	4.6867	1	-3	1	1	18.923	4.6859	0.003
19.683	4.5067	1	3	1	1	19.688	4.5056	0.005
20.319	4.3671	29	0	1	2	20.311	4.3688	-0.008
20.504	4.3281	52	-1	1	2	20.522	4.3242	0.018
20.977	4.2315	22	1	1	2	20.998	4.2274	0.021
21.595	4.1118	4	-2	1	2	21.607	4.1096	0.012
22.966	3.8694	12	-4	0	2	22.961	3.8702	-0.005
23.440	3.7922	4	-3	1	2	23.449	3.7908	0.009
			5	0	1	23.488	3.7845	
23.758	3.7421	4	0	2	0	23.758	3.7421	0.000
24.145	3.6830	10	1	2	0	24.148	3.6826	0.003
24.540	3.6246	2	-5	1	0	24.512	3.6288	-0.028
25.284	3.5196	36	2	2	0	25.281	3.5200	-0.003
25.642	3.4713	21	1	2	1	25.643	3.4712	0.001
26.437	3.3687	5	-2	2	1	26.434	3.3690	-0.003
26.839	3.3191	3	2	2	1	26.810	3.3226	-0.029
27.079	3.2903	10	-3	2	0	27.072	3.2911	-0.007
27.613	3.2278	11	-1	1	3	27.621	3.2269	0.008
28.076	3.1756	1	-3	2	1	28.068	3.1766	-0.008
29.049	3.0714	4	0	2	2	29.042	3.0721	-0.007
			2	1	3	29.408	3.0347	
29.427	3.0328	5	4	2	0	29.409	3.0346	-0.018
			-6	0	2	29.708	3.0048	
29.726	3.0030	4	-3	1	3	29.729	3.0028	0.003
31.221	2.8625	2	3	1	3	31.224	2.8623	0.003
			-4	1	3	31.648	2.8249	
31.672	2.8228	2	6	0	2	31.688	2.8214	0.016
32.068	2.7888	1	-6	1	2	32.073	2.7885	0.005
33.264	2.6913	2	0	0	4	33.276	2.6903	0.012
			-4	2	2	33.277	2.6902	
33.817	2.6485	3	-2	0	4	33.810	2.6491	-0.007
34.033	2.6322		-5	1	3	34.037	2.6319	0.004
			7	1	1	34.075	2.6290	
34.664	2.5857	2	-1	2	3	34.667	2.5855	0.003

Continued

TABLE I. Continued

$2\theta_{\text{obs}} (^{\circ})^a$	$d_{\text{obs}} (\text{\AA})$	$(I/I_0)_{\text{obs}}$	h	k	l	$2\theta_{\text{calc}} (^{\circ})$	$d_{\text{calc}} (\text{\AA})$	$\Delta 2\theta (^{\circ})$
35.020	2.5602	2	2	0	4	35.002	2.5615	-0.018
35.979	2.4941	1	-2	1	4	{ 35.933	2.4972	
36.543	2.4569	10	1	1	4	{ 35.987	2.4936	0.008
			-4	0	4	36.517	2.4586	-0.026
			0	3	1	{ 36.959	2.4303	
36.995	2.4280	3	-3	1	4	{ 36.979	2.4290	-0.016
			-7	0	3	{ 37.992	2.3665	
38.058	2.3625	2	-4	2	3	{ 38.026	2.3644	-0.032
38.495	2.3367	1	-4	1	4	38.510	2.3358	0.015
39.368	2.2869	1	-8	1	2	{ 39.366	2.2870	-0.002
			-9	0	1	{ 39.374	2.2865	
39.989	2.2528	2	6	2	2	39.989	2.2528	0.000
41.276	2.1855	1	-1	2	4	{ 41.282	2.1852	0.006
			0	2	4	{ 41.298	2.1844	
			1	0	5	{ 42.492	2.1257	
42.530	2.1239	2	-6	2	3	{ 42.524	2.1242	-0.006
43.096	2.0973	3	-4	3	2	{ 43.106	2.0968	0.010
			-3	0	5	{ 43.112	2.0966	
43.656	2.0717	3	-1	1	5	43.652	2.0719	-0.004
			6	0	4	{ 44.018	2.0555	
			-2	1	5	{ 44.033	2.0548	
			-4	2	4	{ 44.033	2.0548	
44.063	2.0535	3	4	3	2	{ 44.084	2.0526	0.021
44.888	2.0177	5	-3	1	5	{ 44.860	2.0189	-0.028
			3	0	5	{ 44.930	2.016	
			-7	2	3	{ 45.304	2.0001	
45.321	1.9994	1	10	1	0	{ 45.326	1.9992	0.005
45.818	1.9788	2	-5	2	4	45.809	1.9792	-0.009
46.172	1.9645	1	8	1	3	{ 46.174	1.9644	0.002
			5	3	2	{ 46.208	1.9630	
			9	2	0	46.219	1.9626	
			8	2	2	{ 46.684	1.9441	
46.700	1.9435	1	3	3	3	{ 46.713	1.9430	0.013
			10	1	1	46.727	1.9424	
			7	2	3	{ 47.742	1.9035	
47.793	1.9016	1	-5	1	5	{ 47.773	1.9023	-0.020

^aCuK α_1 with $\lambda = 1.5406 \text{ \AA}$.

melting point (uncorrected) was between 162 and 164 °C and the density was 1.268 g cm^{-3} , which was measured by the flotation method in an aqueous solution of potassium iodine.

Its structural characterization was carried out by Fourier transform-infrared spectroscopy (FT-IR) and mass spectrometry with electron impact (MS-EI). Analysis of FT-IR revealed the following characteristic absorption bands (ν , cm^{-1}) 2968 (C-H); 1591 (C=C); 1541 (C=C) and 1375 (C-H), while MS-EI analysis showed the characteristic molecular peak $m/z = 326$ (M^{+*}).

B. Powder data collection

A small portion of the compound $\text{C}_{23}\text{H}_{22}\text{N}_2$ was gently ground in an agate mortar and sieved to a grain size of less than $38 \mu\text{m}$. The specimen was mounted on a polymethyl methacrylate (PMMA) specimen holder. The XRPD pattern was recorded with a D8 Advance Bruker diffractometer operating in DaVinci geometry equipped with a Cu-target X-ray tube (40 kV and 30 mA) using a nickel filter and a 1-dimensional LynxEye detector. A receiving slit (RS) of 0.6 mm and primary and secondary soler slits (SS) of 2.5° were used. The scan range was $2\text{--}70^{\circ} 2\theta$ with a step size of

$0.015 26^{\circ}$ and a count time of 2 s per step. XRPD data were collected at room temperature (25°C).

PowderX program (Dong, 1999) was used to remove the background (Sonneveld and Visser, 1975), smoothing (Savitzky and Golay, 1964), to eliminate the CuK α_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 X-ray powder diffraction data for the compound (**2**) are given in the Table I. All reflections were indexed

TABLE II. Parameters obtained by X-ray powder diffraction for the compound 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline (**2**).

a ($\text{\AA}$)	20.795 (8)
b ($\text{\AA}$)	7.484 (2)
c ($\text{\AA}$)	10.787 (2)
β ($^{\circ}$)	93.96 (2)
V ($\text{\AA}^3$)	1674.8 (6)
Z	4
M_{20}	17.9
F_{30}	40.0 (0.0136, 55)
D_m (g cm^{-3})	1.268

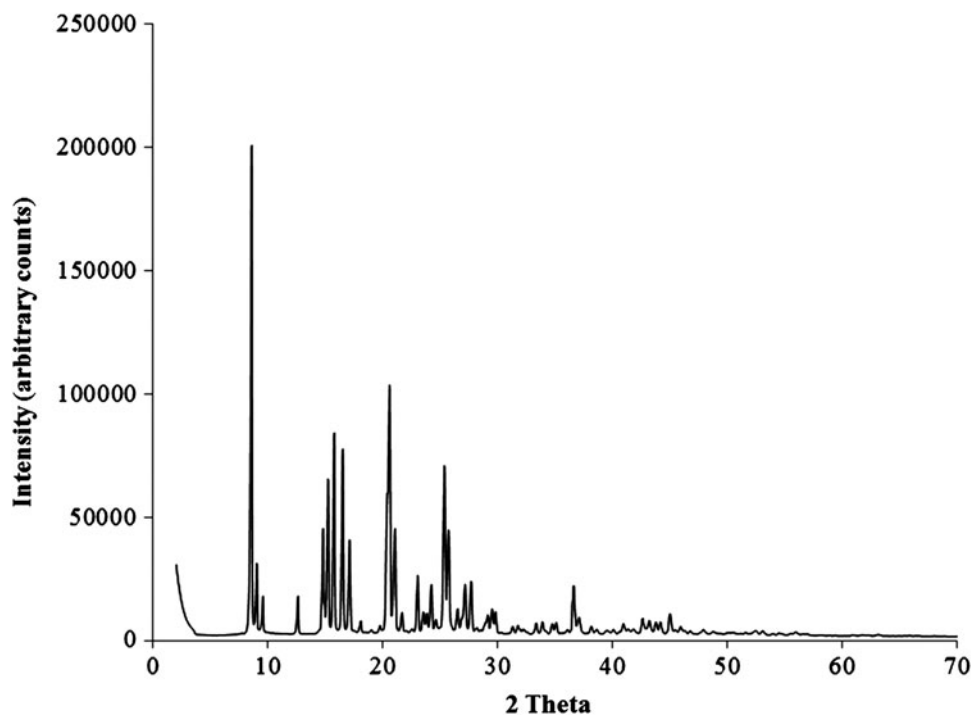


Figure 2. Powder X-ray diffraction pattern of 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline (**2**).

successfully using the DICVOL06 program (Boultif and Louër, 2004) on a monoclinic system unit cell and the peak positions, each with an absolute error of 0.03° (2θ), were used in the calculations. The CHEKCELL program (Laugier and Bochu, 2002) was used to estimate the space group, $P2_1/n$ (No. 14), which was compatible with the systematic absences and with the crystal density. The unit-cell parameters of the compound (**2**) were refined with the program NBS*AIDS83 software (Miguell *et al.*, 1981). Its crystal data, X-ray density, and figures of merit M_{20} (de Wolff, 1968) and F_{20} (Smith and Snyder, 1979) are compiled in Table II. The X-ray powder pattern of the compound 2-ethyl-6-(pyridin-4-yl)-7H-indeno[2,1-c]quinoline (**2**) is shown in Figure 2.

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