

## Synthesis and cytotoxic activity of 3-[2-(1*H*-Indol-3-yl)-1,3-thiazol-4-yl]-1*H*-pyrrolo[3,2-*c*]pyridine hydrobromides, analogues of the marine alkaloid nortopsentin

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Dedicated to Professor Girolamo Cirrincione on the occasion of his retirement

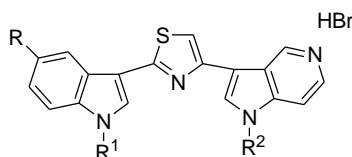
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### Abstract

A new series of thiazole nortopsentin analogues with a 5-azaindole moiety was conveniently synthesized in good to excellent yields by an Hantzsch reaction between thioamides and  $\alpha$ -bromoacetyl compounds. The cytotoxic activity of the new derivatives was tested against different human tumor cell lines of the NCI full panel. All tested compounds were active against all of the investigated cell lines showing GI<sub>50</sub> values from micro to submicromolar levels. Some of the new analogues exhibited good selectivities against different NCI sub-panels.



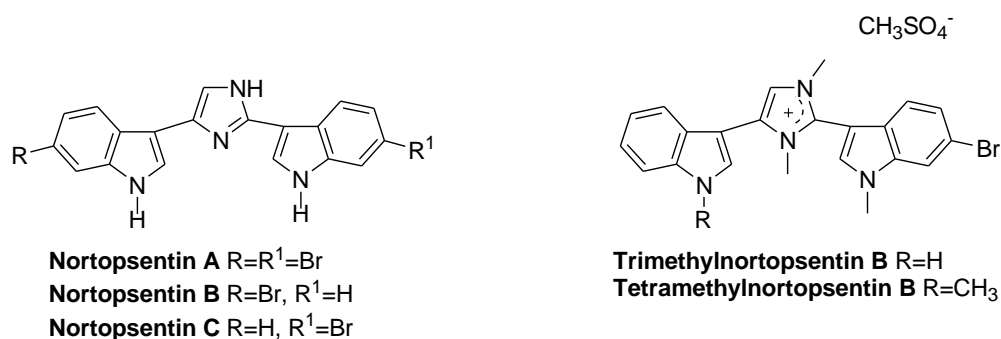
Indolyl-thiazolyl-5-azaindoles

GI<sub>50</sub> 0.18-26.3  $\mu$ M

**Keywords:** Marine bis-indolyl alkaloids, nortopsentin analogues, antitumor activity, 5-azaindole, thiazole

## Introduction

The marine environment covers approximately 70% of the earth's surface and represents a rich source of compounds with a wide range of biological activities.<sup>1</sup> For this reason several efforts have been made aiming to exploit the enormous potential of marine natural products, developing their total synthesis in laboratory or synthesizing derived molecules using their scaffolds as leads. Up to 2019, the clinical marine pharmaceutical pipeline consisted of 31 marine-derived compounds in active clinical trials and 9 approved marine-derived compounds.<sup>2</sup> Among the approved drugs, many compounds found application as anticancer drugs such as cytarabine used for the therapy of malignant acute myeloid, lymphocytic and myelogenous leukemia, trabectedin for tissue sarcoma, midostaurine for the acute myeloid leukemia, eribulin mesylate for breast cancer and liposarcoma.<sup>3</sup> Marine alkaloids constitute one of the most attractive class of natural products<sup>4</sup> and in particular bis-indolyl alkaloids, characterized by two indole units connected to a spacer through their 3 position, constitute a group of deep-sea sponge metabolites with very interesting pharmacological activities such as antiproliferative,<sup>5</sup> antiinflammatory,<sup>6</sup> antimicrobial,<sup>7</sup> and antiviral.<sup>8</sup> Nortopsentins A-C (Chart 1), isolated from the Halichondride sponge *Spongosorites ruetzleri* from deep water in the Bahamas, are the only family of bis-indolyl alkaloids bearing an imidazolidylbis[indole] skeleton. They exhibited *in vitro* cytotoxicity against P388 leukemia cells ( $IC_{50}$ , 4.5–20.7  $\mu$ M) and inhibited the growth of *Bacillus subtilis* and *Candida albicans*. Their methylated derivatives (Figure 1) showed a significant improvement in cytotoxicity against P388 cells compared to that of the parent compounds ( $IC_{50}$ , 0.8–2.1  $\mu$ M).<sup>9</sup> Furthermore, nortopsentin C inhibited neural nitric oxide synthase (bNOS) and calcineurin activities, suggesting its probable action against calmodulin, a common co-factor of these two enzymes.<sup>6</sup> More recently, the antiviral activity against tobacco mosaic virus (TMV) and anti-phytopathogenic-fungus property of nortopsentins A-C and their analogues were also reported.<sup>10</sup>

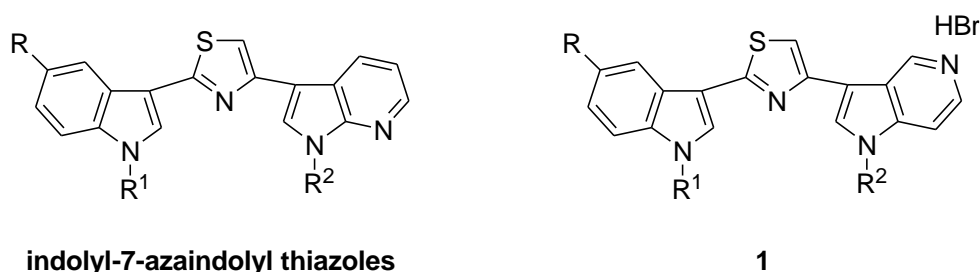


**Figure 1.** Structures of nortopsentins A-C and their methylated derivatives.

With the aim to search new bioactive nortopsentin analogues, the central imidazole ring of the marine alkaloid was replaced by different five-membered heterocycles and/or the indole moiety by other rings.<sup>11-17</sup> In this effort, our research group synthesized a large library of analogues in which the imidazole moiety of nortopsentins A-C was replaced by a thiazole core and one indole portion by an azaindole ring, leading to compounds that showed antiproliferative activity against a wide range of human tumor cell lines with  $GI_{50}$  values in the micro-submicromolar range. Among of them, the indolyl-7-azaindolyl thiazoles (Figure 2) resulted the most active derivatives, exhibiting antiproliferative activity in the micro-submicromolar range, CDK1 inhibition ( $IC_{50}$  0.64-0.89  $\mu$ M) and significant tumor volume inhibition in mouse xenograft models.<sup>18</sup>

A recent study demonstrated that the treatment of colorectal cancer stem cells (CR-CSCs) with indolyl-7-azaindolyl thiazoles induces reduction of CSCs viability, making them sensitive to conventional chemotherapy drugs, such as oxaliplatin and 5FU. Moreover, the combination therapy of these derivatives with CHK1 inhibitor Rabusertinib showed a synergistic effect, abrogating CR-CSCs proliferative and clonogenic potential.<sup>19</sup>

In addition to the frequently used 7-azaindoles, the 5-azaindole ring is a promising pharmacophore moiety found in different antitumor molecules, despite its uncommon presence in marine natural products.<sup>20,21</sup> Thus, continuing our studies on bioactive nitrogen heterocyclic systems<sup>22,23</sup> and to complete the structure-activity relationship (SAR) analysis of the nortopsentin azaindoles, herein we report a new series of indolyl-5-azaindolyl thiazoles of type **1** (Figure 2). We also describe the NCI's *in vitro* disease-oriented antitumor screen of the new synthesized analogues.

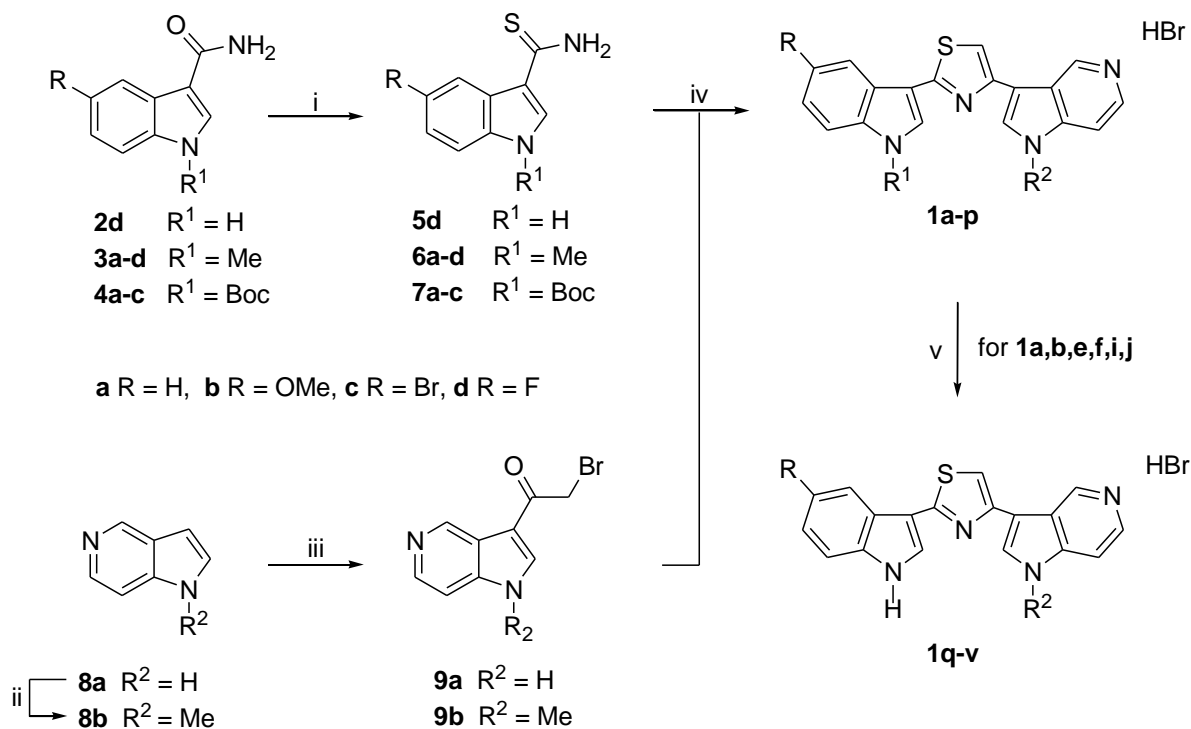


**Figure 2.** Azaindoles derivatives of thiazole nortopsentin analogues.

## Results and Discussion

The synthesis of new indolyl-5-azaindolyl thiazoles **1a-v** (Scheme 1) was conveniently carried out through a Hantzsch reaction between thioamides of type **5-7** and  $\alpha$ -bromoacetyl compounds **9a,b**. In detail, indole-3-carbothioamides **5d,6a-d,7a-c** (Scheme 1) were obtained from the corresponding carboxamides **2d, 3a-d** and **4a-c** using Lawesson's reagent under reflux in toluene or benzene as previously reported.<sup>18</sup> The 2-bromoethanones **9a,b** were efficiently synthesized (90-93%) by acylation of suitable 5-azaindoles **8a,b** with bromoacetyl bromide in the presence of aluminium chloride in anhydrous dichloromethane. The commercially available 5-azaindoles **8a** was converted into the corresponding *N*-methyl derivative **8b** by reaction with potassium *tert*-butoxide, tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1) as a catalyst and iodomethane in anhydrous toluene (Scheme 1).

The reaction between thioamides **5d,6a-d** and  $\alpha$ -bromoacetyl compounds **9a,b** in ethanol under reflux gave the desired 3-[2-(1*H*-indol-3-yl)-1,3-thiazol-4-yl]-1*H*-5-azaindoles **1c,d,g,h,k-p** as hydrobromide salts (58-84%) (Table 1). The reaction of thioamides **7a-c** with ethanones **9a,b** gave very unstable thiazoles **1a,b,e,f,i,j** that were used in the next step without purification. In particular, the subsequent deprotection of *N-tert*-butylcarboxylate derivatives **1a,b,e,f,i,j** using trifluoroacetic acid in dichloromethane under reflux afforded the corresponding thiazoles **1q-v** in good to excellent yields (62-93%) (Table 1).



**Scheme 1.** Synthesis of indolyl-5-azaindolyl thiazole hydrobromides **1a-v**. Reagents and conditions: (i) Lawesson's reagent, toluene or benzene, reflux, 0.5-24 h, 90-98%; (ii) *t*-BuOK, toluene, TDA-1, rt, 4 h; then MeI, rt, 16 h, 60%; (iii) AlCl<sub>3</sub>, DCM, BrCOCH<sub>2</sub>Br, reflux, 40 min (for derivative **9a**) or 15 min (for derivative **9b**), 90-93%; (iv) EtOH, reflux, 1 h, 58-84%; (v) TFA, DCM, reflux, 24 h, 62-93%.

**Table 1.** Substituted 3-[2-(1*H*-indol-3-yl)-1,3-thiazol-4-yl]-1*H*-5-azaindole hydrobromides **1a-v**

Compd.	R	R <sup>1</sup>	R <sup>2</sup>	Yield%	Compd.	R	R <sup>1</sup>	R <sup>2</sup>	Yield%
<b>1a</b>	H	Boc	H	ND <sup>a</sup>	<b>1l</b>	Br	Me	Me	66 <sup>b</sup>
<b>1b</b>	H	Boc	Me	ND <sup>a</sup>	<b>1m</b>	F	Me	H	56 <sup>b</sup>
<b>1c</b>	H	Me	H	84 <sup>b</sup>	<b>1n</b>	F	Me	Me	70 <sup>b</sup>
<b>1d</b>	H	Me	Me	52 <sup>b</sup>	<b>1o</b>	F	H	H	58 <sup>b</sup>
<b>1e</b>	OMe	Boc	H	ND <sup>a</sup>	<b>1p</b>	F	H	Me	67 <sup>b</sup>
<b>1f</b>	OMe	Boc	Me	ND <sup>a</sup>	<b>1q</b>	H	H	H	55 <sup>c</sup>
<b>1g</b>	OMe	Me	H	70 <sup>b</sup>	<b>1r</b>	H	H	Me	69 <sup>c</sup>
<b>1h</b>	OMe	Me	Me	53 <sup>b</sup>	<b>1s</b>	OMe	H	H	88 <sup>c</sup>
<b>1i</b>	Br	Boc	H	ND <sup>a</sup>	<b>1t</b>	OMe	H	Me	72 <sup>c</sup>
<b>1j</b>	Br	Boc	Me	ND <sup>a</sup>	<b>1u</b>	Br	H	H	62 <sup>c</sup>
<b>1k</b>	Br	Me	H	80 <sup>b</sup>	<b>1v</b>	Br	H	Me	93 <sup>c</sup>

<sup>a</sup>ND: not determined. The crude was used in the step v without further purification.

<sup>b</sup>Calculated over the step iv.

<sup>c</sup>Calculated over the two steps iv and v.

The isolated thiazoles **1c,d,g,h,k-v** were submitted to the National Cancer Institute (NCI; Bethesda, MD), and were prescreened according to the NCI protocol at a  $10^{-5}$  M dose (data not shown) on the full panel of approximately 55 human cancer cell lines derived from 9 human cancer cell types that have been grouped into disease subpanels including leukemia, non-small cell lung, colon, central nervous system, melanoma, ovarian, renal, prostate, and breast tumor cell lines. All tested thiazoles satisfied the criteria set by the NCI for activity in this assay and were selected for further screenings at five concentrations at 10-fold dilution ( $10^{-4}$ – $10^{-8}$  M) on the full panel. The growth inhibition activity of compounds was defined in terms of the  $GI_{50}$  value (which represents the molar concentration of the compound that inhibits 50% net cell growth).

The thiazoles **1c,d,g,h,k-v** were active against the total number of cell lines investigated, showing antitumor activity in the micromolar - submicromolar range ( $GI_{50}$  0.18–26.3  $\mu$ M) (Table2).

All derivatives were efficacious against the leukemia sub-panel (Table 2), with particularly selectivity towards K-562 cell line, eliciting  $GI_{50}$ s in the range 0.24–2.09  $\mu$ M. In addition, compounds **1l** and **1v** also exhibited good selectivity against CCRF-CEM cells of the same sub-panel, with  $GI_{50}$  values of 0.36  $\mu$ M and 0.42  $\mu$ M, respectively (Table 2).

Moreover, all compounds also proved to be active towards MDA-MB-468 and MCF7 cell lines of breast cancer sub-panel, for which thiazoles **1c** and **1d** were the most potent compounds, with  $GI_{50}$  values lower than or equal to 0.4  $\mu$ M (Table 2). Regarding MDA-MB-468 cell line, also thiazoles **1g** and **1q** exhibited good  $GI_{50}$  values (0.44  $\mu$ M and 0.23  $\mu$ M, respectively).

Likewise, towards HCT-116 cell line of the colon cancer sub-panel, the  $GI_{50}$ s were registered in the low micromolar range, with values of 0.93  $\mu$ M and 0.18  $\mu$ M for the most active compounds **1d** and **1l**, respectively.

**Table 2.** *In vitro* inhibition of cancer cell lines growth by thiazoles **1c,d,g,h,k-v**

Cell lines	$GI_{50}^{[a]}$															
	<b>1c</b>	<b>1d</b>	<b>1g</b>	<b>1h</b>	<b>1k</b>	<b>1l</b>	<b>1m</b>	<b>1n</b>	<b>1o</b>	<b>1p</b>	<b>1q</b>	<b>1r</b>	<b>1s</b>	<b>1t</b>	<b>1u</b>	<b>1v</b>
Leukemia																
CCRF-CEM	2.02	1.78	1.83	2.15	1.30	0.36	1.74	1.96	1.89	1.75	1.44	2.40	2.45	2.33	2.24	0.42
HL-60(TB)	2.03	1.94	1.68	1.96	1.71	1.48	1.76	1.93	2.07	2.19	2.02	2.17	1.51	1.90	2.09	2.11
K-562	1.76	2.09	0.72	1.90	0.24	0.24	0.46	1.70	0.37	1.48	2.05	1.85	1.72	1.78	0.98	0.35
RPMI-8226	2.00	1.76	1.83	1.84	1.58	1.57	1.77	1.98	1.77	1.86	1.25	2.14	2.08	2.02	2.48	2.13
Non-Small Cell Lung Cancer																
A549/ATCC	1.83	2.38	1.87	1.93	1.78	1.83	1.85	1.67	1.87	1.83	2.45	2.47	2.35	1.79	1.90	2.81
EKVX	1.64	1.56	1.76	1.77	1.54	1.86	1.72	1.87	1.66	1.62	1.78	1.92	1.99	1.92	1.73	2.50
HOP-62	1.48	1.67	1.81	1.90	1.61	1.90	1.73	1.92	1.53	1.54	1.71	1.79	2.08	1.92	1.65	3.17
HOP-92	1.51	1.35	1.64	1.96	1.77	1.52	1.65	1.64	1.38	1.49	1.44	1.52	1.79	1.90	1.72	2.98
NCI-H226	1.75	1.82	1.88	1.83	1.69	2.02	1.92	2.05	1.76	1.88	3.24	17.1	2.36	18.3	1.87	2.34
NCI-H23	1.65	1.64	1.81	1.81	1.65	1.93	1.72	1.94	1.58	1.62	1.85	1.77	1.76	2.12	1.64	2.73
NCI-H322M	1.67	1.63	1.69	1.78	1.82	1.77	1.65	1.81	1.52	1.79	2.05	2.53	1.85	1.87	1.75	3.64
NCI-H460	1.90	1.79	1.73	1.94	1.73	1.87	1.77	1.97	1.78	1.99	1.76	1.85	1.84	1.97	1.95	1.92
NCI-H522	1.73	2.00	1.65	1.77	1.84	1.76	1.67	1.77	1.68	1.79	1.92	2.02	1.81	1.74	1.79	2.05

Table 2. Continued

Cell lines	GI <sub>50</sub> <sup>[a]</sup>															
	1c	1d	1g	1h	1k	1l	1m	1n	1o	1p	1q	1r	1s	1t	1u	1v
Colon Cancer																
HCC-2998	1.22	1.26	1.85	1.89	1.76	1.90	1.64	1.86	1.92	1.95	1.87	2.01	1.87	1.88	1.98	2.10
HCT-116	1.61	0.93	1.69	1.90	1.21	0.18	1.63	1.66	1.61	1.22	1.71	1.73	1.77	1.77	1.66	1.56
HCT-15	1.37	1.51	1.25	1.54	1.35	1.75	1.33	1.68	1.33	1.67	1.56	1.79	1.95	1.88	1.65	1.38
HT29	1.82	1.98	1.20	1.43	1.59	1.60	1.44	1.47	1.35	1.69	2.07	2.01	2.23	1.53	1.71	1.57
KM12	1.11	1.00	1.73	1.84	1.71	1.97	1.63	1.79	1.67	1.83	2.02	1.65	1.76	1.87	1.91	2.33
SW-620	2.03	1.85	1.75	1.96	1.52	1.85	1.65	1.88	1.88	2.12	1.73	1.98	1.93	1.95	2.04	1.81
CNS Cancer																
SF-268	1.79	1.92	1.77	2.07	1.82	1.90	1.74	1.93	1.77	1.94	2.51	1.97	2.61	1.91	1.78	2.83
SF-295	1.77	1.63	1.69	1.66	1.69	1.81	1.64	1.71	1.68	1.74	1.58	1.81	1.70	12.3	1.71	1.77
SF-539	1.78	1.75	1.65	1.77	1.75	1.80	1.68	1.85	1.52	1.63	1.79	1.79	1.64	1.90	1.72	2.14
SNB-19	1.80	1.76	1.85	2.26	1.80	1.73	1.83	1.82	1.77	1.95	2.18	2.07	1.97	1.79	1.77	3.67
SNB-75	1.29	4.08	1.52	14.7	1.23	1.28	1.26	1.40	1.22	1.50	10.3	12.9	6.96	15.3	1.22	1.47
U251	1.90	1.86	1.87	1.85	1.69	1.78	1.80	1.80	1.69	1.87	1.93	1.95	1.91	1.91	1.77	1.99
Melanoma																
MALME-3M	1.68	2.01	1.74	2.02	1.80	1.95	1.57	1.97	1.82	1.93	1.65	1.94	2.00	2.11	2.14	2.23
M14	1.74	1.51	1.78	1.70	1.81	1.45	1.79	1.72	1.64	1.74	1.70	1.84	1.83	1.75	1.83	1.87
MDA-MB-435	1.79	1.77	1.59	1.59	1.70	1.76	1.64	1.67	1.81	1.85	1.75	1.87	1.68	1.71	1.66	1.78
SK-MEL-2	1.80	2.00	1.84	1.76	2.00	1.93	1.92	1.79	1.91	1.87	2.09	2.10	2.05	15.8	1.92	2.58
SK-MEL-28	1.71	1.77	1.63	1.71	1.78	1.85	1.63	1.79	1.90	1.86	1.84	1.80	1.94	1.79	1.73	1.70
SK-MEL-5	1.74	1.69	1.65	1.52	1.60	1.70	1.65	1.66	1.63	1.65	1.60	1.76	1.65	1.64	1.61	1.88
UACC-257	1.96	1.94	1.68	1.90	2.00	1.95	1.96	1.80	1.91	1.96	1.80	2.00	1.93	16.7	1.92	2.12
UACC-62	1.69	1.72	1.82	2.09	1.79	1.72	1.71	1.74	1.72	1.83	1.67	1.82	1.78	18.5	1.79	1.81
Ovarian Cancer																
IGROV1	1.37	1.61	1.91	1.92	1.63	1.76	1.86	1.96	1.41	1.59	1.33	1.73	1.93	1.93	1.69	2.27
OVCAR-3	1.69	2.16	1.88	1.99	1.90	1.89	1.94	1.95	1.80	1.83	1.98	1.96	2.18	1.85	1.91	2.08
OVCAR-4	1.24	1.46	1.89	2.10	1.82	1.68	1.82	1.70	1.61	1.60	2.96	2.30	2.94	2.14	1.70	2.35
OVCAR-5	1.76	1.77	1.64	1.81	1.81	1.78	1.68	1.68	1.93	1.91	2.59	2.62	2.37	2.00	1.79	2.22
OVCAR-8	1.91	2.68	1.99	2.01	1.93	1.90	2.11	2.02	1.91	1.95	1.97	2.03	2.37	2.19	2.13	1.92
NCI/ADR-RES	1.99	1.83	1.76	1.81	1.87	2.07	1.93	2.03	1.91	1.98	3.20	2.40	2.48	2.06	1.90	2.09
SK-OV-3	1.59	2.52	1.88	2.52	1.84	1.99	1.92	2.03	1.65	1.73	2.62	1.90	13.7	19.4	1.65	2.18
Renal Cancer																
786-0	1.93	1.95	1.70	1.60	1.78	1.41	1.69	1.51	1.98	1.85	1.89	1.90	1.84	1.54	1.81	1.63

Table 2. Continued

Cell lines	GI <sub>50</sub> <sup>[a]</sup>															
	1c	1d	1g	1h	1k	1l	1m	1n	1o	1p	1q	1r	1s	1t	1u	1v
A498	1.86	2.06	1.65	6.59	1.89	1.78	1.80	1.62	1.98	1.87	10.0	1.89	4.91	8.86	1.81	12.6
ACHN	1.60	1.80	1.77	1.73	1.72	1.97	1.74	1.84	1.61	1.74	1.72	1.93	1.66	1.82	1.77	2.01
CAKI-1	1.48	2.58	1.64	1.80	1.63	1.77	1.65	1.77	1.59	1.65	1.98	2.08	2.86	1.84	1.60	2.02
RXF 393	1.62	1.70	1.49	1.71	1.47	1.70	1.57	1.61	1.48	1.78	1.55	1.63	1.74	1.83	1.49	1.47
SN12C	1.76	1.66	1.69	1.85	1.56	1.53	1.68	1.70	1.52	1.72	1.67	1.74	1.83	1.64	1.79	1.75
TK-10	1.97	2.25	1.88	1.49	2.19	1.71	2.11	1.56	2.30	2.22	2.76	2.74	2.59	1.48	2.33	1.97
UO-31	1.38	1.47	1.58	1.58	1.57	1.63	1.57	1.64	1.33	1.42	1.21	1.64	1.75	1.80	1.47	1.89
Prostate Cancer																
PC-3	1.45	1.47	1.60	1.89	1.64	1.55	1.63	1.71	1.47	1.69	1.84	2.40	2.13	1.98	1.58	2.02
DU-145	1.74	2.13	1.75	1.78	1.82	1.74	1.71	1.74	1.69	1.80	3.36	2.24	2.73	1.70	1.68	2.25
Breast Cancer																
MCF7	0.30	0.32	1.47	1.70	1.33	1.78	1.23	1.93	1.48	1.27	1.43	1.22	1.66	1.81	1.53	1.77
MDA-MB- 231/ATCC	1.56	1.47	1.45	1.83	1.41	1.66	1.55	1.75	1.27	1.46	1.06	1.67	1.65	1.87	1.52	2.34
HS 578T	1.93	2.16	2.03	2.21	1.94	2.23	2.21	2.36	1.71	2.26	2.00	2.21	2.15	14.7	2.23	2.47
BT-549	9.00	1.68	1.81	1.80	1.93	1.61	1.80	1.71	1.65	1.63	8.82	1.78	8.96	1.79	1.86	26.3
MDA-MB- 468	0.40	0.27	0.44	1.62	1.38	1.79	1.40	1.86	1.51	1.45	0.23	nd	1.78	1.97	1.77	1.68

[a] The molar concentration that inhibits 50% net cell growth.

nd : not determined

## Conclusions

A new series of thiazole nortopsentin analogues of type **1**, in which the imidazole moiety of nortopsentins A-C was replaced by a thiazole core and one indole unit by a 5-azaindole ring, was efficiently synthesized in good to excellent yields. The new nortopsentin derivatives **1c,d,g,h,k-v** were active against the totality of the about 55 human tumor cell lines of NCI full panel, showing good antiproliferative activity in the micro-submicromolar range (GI<sub>50</sub> 0.18-26.3 μM). Thiazoles **1k**, **1l** and **1v** were particularly efficacious against leukemia sub-panel (GI<sub>50</sub> in the range 0.24-1.71 μM, 0.24-1.57 μM and 0.35-2.13 μM, respectively). Compound **1d** proved to be the most active against breast cancer sub-panel (GI<sub>50</sub> in the range 0.27-2.16 μM). Furthermore, analogues **1d** and **1l** showed a good selectivity against HCT-116 cell line of the colon cancer sub-panel (GI<sub>50</sub> of 0.93 μM and 0.18 μM, respectively). The encouraging biological results found for this new series confirmed the advantageous influence of the thiazole central core, in comparison with the other five-membered heterocycles, on the antiproliferative activity of this class of compounds. The reason of this

improved activity could be attributed to low lying C–S  $\sigma^*$  orbitals that, conferring small regions of low electron density on sulfur ( $\sigma$ -holes), may play an important role in the interaction with the biological target.<sup>24</sup>

## Experimental Section

**General.** All melting point were taken on a Büchi-Tottoly capillary apparatus and are uncorrected. IR spectra were determined in bromoform with a Shimadzu FT/IR 8400S spectrophotometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured at 200 and 50.0 MHz, respectively, in DMSO-*d*<sub>6</sub> solution, using a Bruker Avance II series 200 MHz spectrometer. Thiazoles **1c,d,g,h,k-v** were characterized only by <sup>1</sup>H NMR spectra, as due to their poor solubility <sup>13</sup>C NMR spectroscopy was not performed. Column chromatography was performed with Merk silica gel 230-400 mesh ASTM or with Büchi Sepacor chromatography module (prepacked cartridge system). Elemental analyses (C, H, N) were within  $\pm 0.4\%$  of theoretical values and were performed with a VARIO EL III elemental analyzer.

General procedures, analytical and spectroscopic data for intermediates **2d,3a-d,4a-c,5d,6a-d** and **7a-c** were previously reported.<sup>18</sup>

**Synthesis of 1-methyl-1H-pyrrolo[3,2-c]pyridine (8b).** To a suspension of 1H-pyrrolo[3,2-c]pyridine **8a** (0.50 g, 4.2 mmol) in toluene (30 mL), potassium *tert*-butoxide (0.64 g, 5.7 mmol) and tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1) (1-2 drops) were added at 0 °C. The reaction mixture was stirred at room temperature for 4 h, and then iodomethane (0.3 mL, 4.2 mmol) was added at 0 °C. TLC analysis (DCM/MeOH 9/1) revealed that methylation was completed after 16 h at room temperature. The solvent was evaporated under reduced pressure. The residue was treated with H<sub>2</sub>O (10 mL), extracted with EtOAc (3x10 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated, and purified by column chromatography using DCM/MeOH (98/2) as eluent to give the desired compound as yellow oil; yield: 60%; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.80 (s, 3H, CH<sub>3</sub>), 6.58 (dd, 1H, *J* 3.2, 0.9 Hz, H-3), 7.42 (d, 1H, *J* 3.2 Hz, H-2), 7.46 (d, 1H, *J* 5.9 Hz, H-7), 8.22 (d, 1H, *J* 5.9 Hz, H-6), 8.83 (s, 1H, H-4). <sup>13</sup>C NMR (50 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 32.4 (q), 99.9 (d), 105.2 (d), 124.9 (s), 130.8 (d), 139.5 (s), 140.0 (d), 143.0 (d). Anal. Calcd for C<sub>8</sub>H<sub>8</sub>N<sub>2</sub>: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.54; H, 5.87; N, 21.11.

**General synthesis of 2-bromo-1-(1H-pyrrolo[3,2-c]pyridin-3-yl)-ethanones (9a,b).** To a solution of the appropriate 5-azaindoles **8a,b** (4.2 mmol) in dry DCM (20 mL), anhydrous aluminum chloride (2.0 g, 14.8 mmol) was slowly added. The reaction mixture was heated under reflux and a solution of bromoacetyl bromide (0.37 mL, 4.2 mmol) in anhydrous DCM (2 mL) was added dropwise. The resulting solution was allowed to stir under reflux for 40 min (for derivative **9a**) or 15 min (for derivative **9b**). After cooling, water/ice were slowly added and the obtained precipitate was filtered off to give the pure desired compounds (**9a,b**).

**2-Bromo-1-(1H-pyrrolo[3,2-c]pyridin-3-yl)-ethanone (9a).** White solid; yield: 90%; mp 285 °C ; IR (cm<sup>-1</sup>) 3553, 1679; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 5.12 (s, 2H, CH<sub>2</sub>), 8.16 (d, 1H, *J* 6.6 Hz, H-7), 8.64 (d, 1H, *J* 6.6 Hz, H-6), 9.01 (s, 1H, H-2), 9.50 (s, 1H, H-4), 13.74 (bs, 1H, NH). <sup>13</sup>C NMR (50 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 46.8 (t), 110.8 (d), 115.0 (s), 121.7 (s), 133.5 (d), 136.5 (d), 140.2 (d), 143.3 (s), 186.5 (s). Anal. Calcd for C<sub>9</sub>H<sub>7</sub>BrN<sub>2</sub>O: C, 45.22; H, 2.95; N, 11.72. Found: C, 45.36; H, 2.87; N, 11.57.

**2-Bromo-1-(1-methyl-1H-pyrrolo[3,2-c]pyridin-3-yl)-ethanone (9b).** White solid; yield: 93%; mp 120-121 °C; IR (cm<sup>-1</sup>) 1659; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 4.08 (s, 3H, CH<sub>3</sub>), 5.06 (s, 2H, CH<sub>2</sub>), 8.34 (d, 1H, *J* 6.7 Hz, H-7), 8.74 (d, 1H, *J* 6.7 Hz, H-6), 9.07 (s, 1H, H-2), 9.48 (s, 1H, H-4). <sup>13</sup>C NMR (50 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 34.3 (q), 46.6 (t), 109.6 (d), 114.1 (s), 121.7 (s), 133.5 (d), 136.3 (d), 143.6 (d), 143.7 (s), 186.1 (s). Anal. Calcd for C<sub>10</sub>H<sub>9</sub>BrN<sub>2</sub>O: C, 47.46; H, 3.58; N, 11.07. Found: C, 47.35; H, 3.74; N, 11.25.

**General procedure for the synthesis of thiazoles (1a-p).** A suspension of the proper thioamides **5d,6a-d,7a-c** (2.5 mmol) and  $\alpha$ -bromoacetyl derivatives **9a,b** (2.5 mmol) in ethanol (10 mL) was heated under reflux for 1 h. After cooling, the precipitate obtained, was filtered off and dried. Thiazoles **1c,d,g,h,k-p** were recrystallized from ethanol to give the pure compounds as hydrobromide salts. Thiazoles **1a,b,e,f,i,j** were very unstable and were immediately used for the next step without purification and characterization.

**3-[2-(1-Methyl-1H-indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1c).** Yellow solid; yield: 84%, mp 273-274°C; IR (cm<sup>-1</sup>) 3416, 3170; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.92 (s, 3H, CH<sub>3</sub>), 7.30-7.37 (m, 2H, Ar), 7.57-7.62 (m, 1H, Ar), 8.03-8.11 (m, 2H, Ar), 8.28-8.34 (m, 2H, Ar), 8.49-8.69 (m, 2H, Ar), 9.78 (s, 1H, H-4'), 13.25 (bs, 1H, NH), 15.22 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>15</sub>BrN<sub>4</sub>S: C, 55.48; H, 3.68; N, 13.62. Found: C, 55.36; H, 3.78; N, 13.53.

**1-Methyl-3-[2-(1-methyl-1H-indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1d).** Yellow solid; yield: 52%, mp 251-252°C; IR (cm<sup>-1</sup>) 3381; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.91 (s, 3H, CH<sub>3</sub>), 4.08 (s, 3H, CH<sub>3</sub>), 7.30-7.38 (m, 2H, Ar), 7.57-7.62 (m, 1H, Ar), 8.01 (s, 1H, Ar), 8.21-8.35 (m, 3H, Ar), 8.57-8.61 (m, 2H, Ar) 9.76 (s, 1H, H-4'), 15.30 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>20</sub>H<sub>17</sub>BrN<sub>4</sub>S: C, 56.48; H, 4.03; N, 13.17. Found: C, 56.62; H, 3.87; N, 13.39.

**3-[2-(5-Methoxy-1-methyl-1H-indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1g).** Yellow solid; yield: 70%, mp 264-265°C; IR (cm<sup>-1</sup>) 3422, 3164; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.89 (s, 6H, CH<sub>3</sub>, OCH<sub>3</sub>), 6.96 (dd, 1H, *J* 8.9, 2.5 Hz, H-6), 7.50 (d, 1H, *J* 8.9 Hz, H-7), 7.77 (d, 1H, *J* 2.5 Hz, H-4), 8.00 (s, 1H, Ar), 8.07 (d, 1H, *J* 6.6 Hz, H-7'), 8.20 (m, 1H, Ar), 8.52-8.56 (m, 2H, Ar), 9.76 (s, 1H, Ar), 13.20 (bs, 1H, NH), 15.15 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>20</sub>H<sub>17</sub>BrN<sub>4</sub>OS: C, 54.43; H, 3.88; N, 12.69. Found: C, 54.69; H, 3.77; N, 12.46.

**3-[2-(5-Methoxy-1-methyl-1H-indol-3-yl)-1,3-thiazol-4-yl]-1-methyl-1H-pyrrolo[3,2-c]pyridine hydrobromide (1h).** Yellow solid; yield: 53%, mp 277-278°C; IR (cm<sup>-1</sup>) 3377; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.88 (s, 3H, CH<sub>3</sub>), 3.89 (s, 3H, CH<sub>3</sub>), 4.08 (s, 3H, OCH<sub>3</sub>), 6.96 (dd, 1H, *J* 8.9, 2.5 Hz, H-6), 7.50 (d, 1H, *J* 8.9 Hz, H-7), 7.76 (d, 1H, *J* 2.5 Hz, H-4), 7.96 (s, 1H, Ar), 8.18 (s, 1H, Ar), 8.23 (d, 1H, *J* 6.8 Hz, H-7'), 8.52 (s, 1H, Ar), 8.58 (d, 1H, *J* 6.8 Hz, H-6'), 9.73 (s, 1H, H-4'), 15.12 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>21</sub>H<sub>19</sub>BrN<sub>4</sub>OS: C, 55.39; H, 4.21; N, 12.30. Found: C, 55.23; H, 4.38; N, 12.46.

**3-[2-(5-Bromo-1-methyl-1H-indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1k).** Yellow solid; yield: 80%, mp 309-310°C; IR (cm<sup>-1</sup>) 3610, 3496; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.92 (s, 3H, CH<sub>3</sub>), 7.45 (dd, 1H, *J* 8.7, 1.9 Hz, H-6), 7.61 (d, 1H, *J* 8.7 Hz, H-7), 8.06 (s, 1H, Ar), 8.08 (d, 1H, *J* 7.4 Hz, H-7'), 8.34 (s, 1H, Ar), 8.40 (d, 1H, *J* 1.9 Hz, H-4), 8.45-8.53 (m, 2H, Ar), 9.72 (s, 1H, H-4'), 13.17 (bs, 1H, NH), 15.13 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>14</sub>Br<sub>2</sub>N<sub>4</sub>S: C, 46.55; H, 2.88; N, 11.43. Found: C, 46.27; H, 2.71; N, 11.70.

**3-[2-(5-Bromo-1-methyl-1H-indol-3-yl)-1,3-thiazol-4-yl]-1-methyl-1H-pyrrolo[3,2-c]pyridine hydrobromide (1l).** Yellow solid; yield: 66%, mp 321-322°C; IR (cm<sup>-1</sup>) 3490; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.92 (s, 3H, CH<sub>3</sub>), 4.10 (s, 3H, CH<sub>3</sub>), 7.46 (dd, 1H, *J* 8.7, 1.9 Hz, H-6), 7.61 (d, 1H, *J* 8.7 Hz, H-7), 8.04 (s, 1H, Ar), 8.25 (d, 1H, *J* 6.8 Hz, H-7'), 8.33 (s, 1H, Ar), 8.40 (d, 1H, *J* 1.9 Hz, H-4), 8.54 (s, 1H, Ar), 8.60 (d, 1H, *J* 6.8 Hz, H-6'), 9.69 (s, 1H, H-4'), 15.16 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>20</sub>H<sub>16</sub>Br<sub>2</sub>N<sub>4</sub>S: C, 47.64; H, 3.20; N, 11.11. Found: C, 47.39; H, 3.11; N, 11.24.

**3-[2-(5-Fluoro-1-methyl-1H-indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1m).** Yellow solid; yield: 56%, mp 309°C; IR (cm<sup>-1</sup>) 3604, 3428; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.92 (s, 3H, CH<sub>3</sub>), 7.19 (td, 1H, *J* 9.2, 7.9, 2.6 Hz, H-6), 7.63 (dd, 1H, *J* 7.9, 4.5 Hz, H-7), 7.99 (dd, 1H, *J* 9.2, 2.6 Hz, H-4), 8.04 (s, 1H, Ar), 8.07 (d, 1H, *J* 6.6 Hz, H-7'), 8.34 (s, 1H, Ar), 8.51 (d, 1H, *J* 6.6 Hz, H-6'), 8.58 (d, 1H, *J* 2.6 Hz, H-2'), 9.73 (s, 1H, H-4'), 13.21 (bs, 1H, NH), 15.15 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>14</sub>BrFN<sub>4</sub>S: C, 53.16; H, 3.29; N, 13.05. Found: C, 53.37; H, 3.16; N, 12.92.

**3-[2-(5-Fluoro-1-methyl-1H-indol-3-yl)-1,3-thiazol-4-yl]-1-methyl-1H-pyrrolo[3,2-c]pyridine hydrobromide (1n).** Yellow solid; yield: 70%, mp 305°C; IR (cm<sup>-1</sup>) 3604; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 3.92 (s, 3H, CH<sub>3</sub>), 4.10 (s, 3H, CH<sub>3</sub>), 7.20 (td, 1H, *J* 9.3, 7.9, 2.7 Hz, H-6), 7.64 (dd, 1H, *J* 7.9, 4.5 Hz, H-7), 8.02 (s, 1H, Ar), 8.06 (d, 1H, *J* 9.3, 2.7 Hz, H-4), 8.25 (d, 1H, *J* 6.8 Hz, H-7'), 8.34 (s, 1H, Ar), 8.59 (s, 1H, Ar), 8.60 (d, 1H, *J* 6.8 Hz, H-6'), 9.71 (s, 1H, H-4'), 15.05 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>20</sub>H<sub>16</sub>BrFN<sub>4</sub>S: C, 54.18; H, 3.64; N, 12.64. Found: C, 53.90; H, 3.56; N, 12.72.

**3-[2-(5-Fluoro-1H-indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1o).** Yellow solid; yield: 58%, mp 254°C; IR (cm<sup>-1</sup>) 3610, 3559, 3399; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 7.12 (td, 1H, *J* 9.2, 7.9, 2.6 Hz, H-6), 7.55 (dd, 1H, *J* 7.9, 4.6 Hz, H-7), 7.98 (dd, 1H, *J* 9.2, 2.6 Hz, H-4), 8.05 (s, 1H, Ar), 8.07 (d, 1H, *J* 6.3 Hz, H-7'), 8.33 (d, 1H, *J* 2.9 Hz, H-2), 8.51 (d, 1H, *J* 6.3 Hz, H-6'), 8.59 (d, 1H, *J* 2.4 Hz, H-2'), 9.76 (s, 1H, H-4'), 12.06 (d, 1H, *J* 2.9 Hz, NH), 13.21 (d, 1H, *J* 2.4 Hz, NH), 15.13 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>18</sub>H<sub>12</sub>BrFN<sub>4</sub>S: C, 52.06; H, 2.91; N, 13.49. Found: C, 51.88; H, 2.67; N, 13.70.

**3-[2-(5-Fluoro-1H-indol-3-yl)-1,3-thiazol-4-yl]-1-methyl-1H-pyrrolo[3,2-c]pyridine hydrobromide (1p).** Yellow solid; yield: 67%, mp 263°C; IR (cm<sup>-1</sup>) 3616, 3387; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 4.09 (s, 3H, CH<sub>3</sub>), 7.12 (td, 1H, *J* 9.2, 7.9, 2.6 Hz, H-6), 7.55 (dd, 1H, *J* 7.9, 4.6 Hz, H-7), 8.00 (dd, 1H, *J* 9.2, 2.6 Hz, H-4), 8.03 (s, 1H, Ar), 8.23 (d, 1H, *J* 6.8 Hz, H-7'), 8.31 (d, 1H, *J* 2.9 Hz, H-2), 8.58 (s, 1H, Ar), 8.60 (d, 1H, *J* 6.8 Hz, H-6'), 9.73 (s, 1H, H-4'), 12.03 (d, 1H, *J* 2.9 Hz, NH), 15.11 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>14</sub>BrFN<sub>4</sub>S: C, 53.16; H, 3.29; N, 13.05. Found: C, 53.31; H, 3.11; N, 13.17.

**General procedure for the synthesis of thiazoles (1q-v).** To a suspension of appropriate thiazole **1a,b,e,f,i,j** (0.38 mmol) in dichloromethane (10 mL), trifluoacetic acid (0.5 mL) was added. The reaction was heated at reflux for 24 h. The solvent was dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated under reduced pressure and the residue recrystallized with ethanol to afford the desired thiazoles **1q-v**.

**3-[2-(1H-Indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1q).** Yellow solid; yield: 55%, mp 380-381°C; IR (cm<sup>-1</sup>) 3393, 3113, 3228. <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 7.25-7.31 (m, 2H, Ar), 7.52-7.57 (m, 1H, Ar), 8.02 (s, 1H, Ar), 8.07 (d, 1H, *J* 6.6 Hz, H-7'), 8.25-8.32 (m, 2H, Ar), 8.52 (d, 1H, *J* 6.6 Hz, H-6'), 8.58 (d, 1H, *J* 2.4 Hz, H-2'), 9.80 (s, 1H, H-4'), 11.88 (d, 1H, *J* 2.4 Hz, NH), 13.06 (bs, 1H, NH), 14.82 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>18</sub>H<sub>13</sub>BrN<sub>4</sub>S: C, 54.42; H, 3.30; N, 14.10. Found: C, 54.21; H, 3.18; N, 14.32.

**3-[2-(1H-Indol-3-yl)-1,3-thiazol-4-yl]-1-methyl-1H-pyrrolo[3,2-c]pyridine hydrobromide (1r).** Yellow solid; yield: 69%, mp 194°C; IR (cm<sup>-1</sup>) 3610, 3553; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 4.09 (s, 3H, CH<sub>3</sub>), 7.25-7.29 (m, 2H, Ar), 7.52-7.58 (m, 1H, Ar), 7.99 (s, 1H, Ar), 8.21-8.33 (m, 3H, Ar), 8.57-8.62 (m, 2H, Ar), 9.78 (s, 1H, H-4'), 11.91 (bs, 1H, NH), 15.03 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>15</sub>BrN<sub>4</sub>S: C, 55.48; H, 3.68; N, 13.62. Found: C, 55.63; H, 3.77; N, 13.85.

**3-[2-(5-Methoxy-1H-indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1s).** Yellow solid; yield: 88%, mp 147°C; IR (cm<sup>-1</sup>) 3359, 3216, 3125; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 3.87 (s, 3H, OCH<sub>3</sub>), 6.91 (dd, 1H, *J* 8.8, 2.5 Hz, H-6), 7.43 (d, 1H, *J* 8.8 Hz, H-7), 7.76 (d, 1H, *J* 2.5 Hz, H-4), 7.99 (s, 1H, Ar), 8.07 (d, 1H, *J* 6.6 Hz, H-7'), 8.19 (d, 1H, *J* 2.9 Hz, H-2), 8.51 (d, 1H, *J* 6.6 Hz, H-6'), 8.56 (d, 1H, *J* 2.4 Hz, H-2'), 9.76 (s, 1H, H-4'), 11.76 (bs, 1H, NH), 13.08 (bs, 1H, NH), 14.88 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>15</sub>BrN<sub>4</sub>OS: C, 53.40; H, 3.54; N, 13.11. Found: C, 53.65; H, 3.80; N, 13.38.

**3-[2-(5-Methoxy-1H-indol-3-yl)-1,3-thiazol-4-yl]-1-methyl-1H-pyrrolo[3,2-c]pyridine hydrobromide (1t).** Yellow solid; yield: 72%, mp 241°C; IR (cm<sup>-1</sup>) 3422, 3199; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 3.87 (s, 3H, CH<sub>3</sub>), 4.08 (s, 3H, OCH<sub>3</sub>), 6.91 (dd, 1H, *J* 8.8, 2.5 Hz, H-6), 7.43 (d, 1H, *J* 8.8 Hz, H-7), 7.75 (d, 1H, *J* 2.5 Hz, H-4), 7.95 (s, 1H, Ar), 8.18 (d, 1H, *J* 2.8 Hz, H-2), 8.23 (d, 1H, *J* 6.8 Hz, H-7'), 8.53 (s, 1H, Ar), 8.59 (d, 1H, *J* 6.8 Hz, H-6'), 9.77 (s, 1H, H-4'), 13.06 (bs, 1H, NH), 15.07 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>20</sub>H<sub>17</sub>BrN<sub>4</sub>OS: C, 54.43; H, 3.88; N, 12.69. Found: C, 54.28; H, 3.69; N, 12.51.

**3-[2-(5-Bromo-1H-indol-3-yl)-1,3-thiazol-4-yl]-1H-pyrrolo[3,2-c]pyridine hydrobromide (1u).** Yellow solid; yield: 62%, mp 198°C; IR (cm<sup>-1</sup>) 3684, 3604, 3559; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 7.37-7.54 (m, 2H, Ar), 8.04-8.10 (m, 2H, Ar), 8.32-8.39 (m, 2H, Ar), 8.50-8.55 (m, 2H, Ar), 9.75 (s, 1H, H-4'), 12.10 (bs, 1H, NH), 13.07 (bs, 1H, NH), 14.92 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>18</sub>H<sub>12</sub>Br<sub>2</sub>N<sub>4</sub>S: C, 45.40; H, 2.54; N, 11.77. Found: C, 45.21; H, 2.47; N, 12.06.

**3-[2-(5-Bromo-1H-indol-3-yl)-1,3-thiazol-4-yl]-1-methyl-1H-pyrrolo[3,2-c]pyridine hydrobromide (1v).** Yellow solid; yield: 93%, mp 241°C; IR (cm<sup>-1</sup>) 3678, 3604; <sup>1</sup>H NMR (200 MHz, DMSO-*d*<sub>6</sub>) δ: 4.08 (s, 3H, CH<sub>3</sub>), 7.38 (dd, 1H, *J* 8.6, 1.9 Hz, H-6), 7.51 (d, 1H, *J* 8.6 Hz, H-7), 8.00 (s, 1H, Ar), 8.22 (d, 1H, *J* 6.8 Hz, H-7'), 8.30 (d, 1H, *J* 2.9 Hz, H-2), 8.36 (d, 1H, *J* 1.9 Hz, H-4), 8.51 (s, 1H, Ar), 8.59 (d, 1H, *J* 6.8 Hz, H-6'), 9.71 (s, 1H, H-4'), 12.11 (d, 1H, *J* 2.9 Hz, NH), 15.22 (bs, 1H, NH<sup>+</sup>). Anal. Calcd for C<sub>19</sub>H<sub>14</sub>Br<sub>2</sub>N<sub>4</sub>S: C, 46.55; H, 2.88; N, 11.43. Found: C, 46.76; H, 2.72; N, 11.24.

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## Supplementary Material

Copies of <sup>1</sup>H NMR spectra of thiazoles **1c,d,g,h,k-v** are available.

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