Synthetic 2-Aroylindole Derivatives as a New Class of Potent Tubulin-Inhibitory, Antimitotic Agents[||]

Siavosh Mahboobi,*[,†] Herwig Pongratz,[†] Harald Hufsky,[†] Jörg Hockemeyer,[†] Markus Frieser,[†] Alexei Lyssenko,[†] Dietrich H. Paper,[†] Jutta Bürgermeister,[†] Frank-D. Böhmer,[‡] Heinz-Herbert Fiebig,[§] Angelika M. Burger,[§] Silke Baasner,[#] and Thomas Beckers*[,#]

Faculty of Chemistry and Pharmacy, Institute of Pharmacy, University of Regensburg, D-93040 Regensburg, Germany, Research Unit Molecular Cell Biology, Medical Faculty, Friedrich Schiller University, D-07747 Jena, Germany, Oncotest GmbH, Am Flughafen 12-14, D-79108 Freiburg, Germany, ASTA Medica AG, Department of Cancer Research, D-60314 Frankfurt/Main, Germany

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A new class of simple synthetic antimitotic compounds based on 2-aroylindoles was discovered. (5-Methoxy-1*H*-2-indolyl)-phenylmethanone (**1**) as well as analogous 3-fluorophenyl- (**36**) and 3-methoxyphenyl (**3**) derivatives displayed high cytotoxicity of $IC_{50} = 20$ to 75 nM against the human HeLa/KB cervical, SK-OV-3 ovarian, and U373 astrocytoma carcinoma cell lines. The inhibition of proliferation correlated with the arrest in the G2/M phase of the cell cycle. In in vitro assays with tubulin isolated from bovine brain, in general antiproliferative activity correlated with inhibition of tubulin polymerization. Thus, the antimitotic activity of 2-aroylindoles is explained by interference with the mitotic spindle apparatus and destabilization of microtubules. In contrast to colchicine, vincristine, nocodazole, or taxol, **1** did not significantly affect the GTPase activity of β-tubulin. Interestingly, selected compounds inhibited angiogenesis in the chorioallantoic membrane (CAM) assay. In xenograft experiments, **1** was highly active after oral administration at 200 mg/kg against the human amelanocytic melanoma MEXF 989 in athymic nude mice. We conclude, that 2-aroylindoles constitute an interesting new class of antitubulin agents with the potential to be clinically developed for cancer treatment.

Introduction

The discovery of various compounds from natural sources as being cytotoxic by interfering with the mitotic spindle apparatus has attracted much attention within the last two decades, and microtubles have become an attractive pharmacological target for anticancer drug discovery.[1−4] Microtubules are hollow tubes consisting of heterodimers of α- and β-tubulin that polymerize parallel to a cylindrical axis, playing important roles in processes such as cell shape, intracellular transport, and mitosis.[5] In cell mitosis, microtubules are forming the mitotic spindle, a bipolar, self-organizing machine that uses energy from nucleotide hydrolysis to segregate sister chromatids accurately into daughter cells.[6] The rapid switch between growing and shortening states of microtubules, a process known as dynamic instability and driven by β-tubulin dependent GTP hydrolysis, is essential for movement of chromosomes.[7] Proteins such as the microtubule associated proteins (MAPs) bind to and modify microtubule properties.[5,8] In the absence of MAPs, $\alpha\beta$-tubulin heterodimers polymerize only by treatment with high concentrations of glycerol or organic acids.[9]

Interfering with the dynamic instability of microtubules, spindle poisons arrest dividing cells in G2/M phase of the cell cycle, causing mitotic catastrophy and finally apoptotic cell death. The well-known natural tubulin binding molecules affecting microtubule dynamics are colchicine, the vinca alkaloids vinblastine and vincristine, rhizoxin, maytansine, combretastatin A4, epothilone, and taxanes.[10] They bind to distinct sites within β-tubulin and, by destabilization or stabilization of microtubules, lead to mitotic catastrophy.[11] Taxol (INN: paclitaxel) and the semisynthetic analogue Taxotere (INN: docetaxel) are stabilizing tubulin inhibitors used routinely for treatment of advanced cancer patients. New studies now convincingly show that tubulin inhibitors might also target proliferating endothelial cells and thereby affect tumor vascularization.[12] Most solid tumors can only grow beyond a critical size by inducing the formation of new blood vessels, a process called tumor neovascularization.[13,14] Antiangiogenic compounds, however, might also be used for the treatment of several nonmalignant diseases, like macular degeneration, arthritis, or psoriasis.[15]

As said, by antagonizing tumor cell proliferation and neovascularization, tubulin inhibitors are potent anticancer drugs. Nevertheless, clinically available compounds such as paclitaxel or vincristine are facing severe disadvantages, namely, (i) high toxicity, (ii)

[||] Abbreviations: MAP − microtubule associated protein, XTT-sodium 3′-[1-(phenylaminocarbonyl)-3,4-tetrazolium]-bis-(4-methoxy-6-nitro)-benzene sulfonic acid hydrate, DMSO − dimethyl sulfoxide, FACS − fluorescence activated cell sorting, CAM − chorioallantoic membrane, GTP − guanosine trisphosphate, PBS − phosphate buffered saline, PI − propidium iodide, EDTA − ethylendiamine-*N*,*N*,*N*′,*N*′-tetraacetic acid.

* Correspondence to S. Mahboobi, Institute of Pharmacy, University of Regensburg, D-93040 Regensburg, Germany (Fax: +49-941-9431737, e-mail: siavosh.mahboobi@chemie.uni-regensburg.de) and to T. Beckers, ASTA Medica AG, Department of Cancer Research, D-60314 Frankfurt/Main, Germany (e-mail: T.Beckers@vff.uni-frankfurt.de).

[†] University of Regensburg.

[‡] Friedrich Schiller University.

[§] Oncotest GmbH.

[#] ASTA Medica AG.

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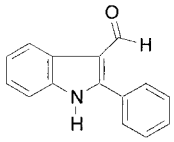
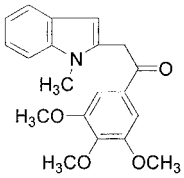
Chart 1. Indole Derivatives as Inhibitors of Tubulin Polymerization

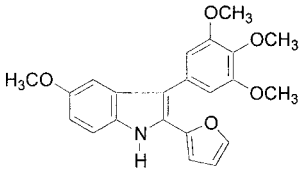
3-Formyl-2-phenylindole



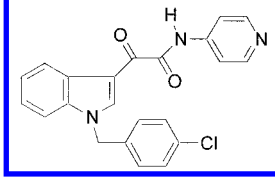
Heterocombretastatines, e. g.



Diarylindoles, e. g.



D-24851 / N-(Pyridin-4-yl)-(1-(4-chlorbenzyl)-indol-3-yl)-glyoxylamid



marginal oral bioavailability and poor solubility, (iii) complex synthesis or isolation procedures, and finally (iv) development of drug resistance in patients. Therefore, synthetic low molecular weight compounds with oral bioavailability and high therapeutic index for first and second line therapy are urgently needed.

By screening for new antimitotic drugs, we identified 2-aroylindoles representing a novel class of simple compounds with high cytotoxicity. In this paper, we describe that more than 150 compounds were synthesized and tested in different biological assays, identifying derivatives with a potency comparable to paclitaxel. 2-Aroylindoles are antimitotic in a cell cycle specific manner by binding to β-tubulin and destabilization of microtubules. Together with 3-formyl-2-phenylindoles,[16] heterocombretastatins or diarylindoles,[17,18] and *N*-(pyridin-4-yl)-(1-(4-chlorbenzyl)-indol-3-yl)-glyoxylamid,[19] they constitute a class of tubulin inhibitors with the indole moiety as a core structure (Chart 1). In the present paper, structure−activity-relationship (SAR) as well as biological properties of selected 2-aroylindoles are presented.

Results and Discussion

Synthesis of 2-Aroylindole Derivatives and SAR for Antimitotic Activity in Human Cancer Cells. Substituted 2-aroylindole derivatives **IV** were easily prepared as shown in the general reaction sequence in Scheme 1[20,21] by coupling the lithiated indole species **I** and the acid chloride **III** in THF at −78 °C. Alkali hydrolysis of the resulting *N*-phenylsulfonyl-protected ketone **IVb** yielded **IV** in good yields. In some cases, however, if the acid chloride **III** was not easily available, the ketone **IVb** was prepared from the aldehyde **II** followed by oxidation of the resulting carbinol **IVa** using PDC/PTFA in CH_2Cl_2. According to Scheme 1, we prepared (5-methoxy-1*H*-2-indolyl)-phenylmethanone **1** and phenyl-substituted derivatives **2**−**22**, **24**, **26**, and **28**−**40**. When various N-protected ketones **IVb** with electron-withdrawing substituents (e.g., F, Cl, NO_2) in the phenylring ortho to the carbonyl-group (**22a**, **35a**, **38a**, **39a**) were used as starting material for hydrolysis by NaOH in ethanol at 75 °C, 3-ethoxy substituted indole-derivatives **IV** were isolated in small amounts additionally to the desired product (not shown in Scheme 1 and Table 1). The amino-compounds **23**, **25**, and **27** were synthesized by catalytic reduction of the corresponding nitro-compounds **22**, **24**, and **26** with palladium on charcoal (Pd/C) in methanol at room temperature. Removing the benzyl-group from compound **15** by heating with Pd/C and ammonium formate in methanol/THF 1/1 afforded the alcohol **16**, which was reacted with butanoic acid chloride to yield the ester-derivative **17**.

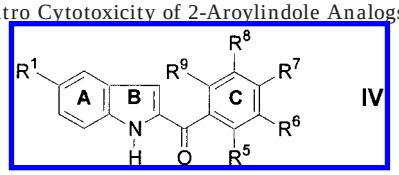
To evaluate the role of the indole substitution pattern in **IV**, we synthesized various derivatives of the indole building block (**41**−**59**), i.e., instead of lithiated 5-methoxyindole (**Ia**), various other indoles [5-methylindole (**Ib**), 5-benzyloxyindole (**Ic**), 4-methoxyindole (**Id**), 3-methylindol (**Ie**), and metalated unsubstituted indole (**If**)] were used for coupling with some of the acid chlorides **III** or aldehydes **II** according to the general reaction procedure described in Scheme 1. Furthermore, replacing the indole structure in Scheme 1 with lithiated aza-indoles **Ig** and **Ih,** yielded compounds **60**−**63** and **64**−**67**, respectively.

Additionally, we substituted the phenylring in **1** by other cyclic systems. Thus, compounds **68**−**76** of type **V** (Scheme 2) were prepared by the same methodology as described in Scheme 1, employing **Ia** and various cyclic aldehydes and acid chlorides instead of benzaldehydes **II** and benzoyl chlorides **III**, respectively.

Finally, starting from **1**, some N-alkylated species **77**−**81** of type **VI** were prepared in good yields by reaction with NaH and alkylhalides in DMF at room temperature (Scheme 3).

The parent compound 2-benzoylindole **1** and all the substituted derivatives **2**−**67** as well as the precursor compounds **1a**−**15a**, **18a**−**22a**, **24a**, **26a**, **28a**−**76a**, and, if prepared, the carbinols of type **IVb** were assayed in a screening for cytotoxicity against the human cervical epitheloid carcinoma HeLa/KB and the human ovarian adenocarcinoma SK-OV-3 cell line. As shown in Table 1, many 2-benzoylindole derivatives **IV** exhibited strong cytotoxicity with IC_{50} values of ≤ 1 to ≥ 0.02 μg/mL (**6**, **7**, **9**, **12**−**14**, **16**−**20**, **23**−**25**, **33**−**35**, **40**) or <0.02 μg/mL (**1**−**3**, **8**, **11**, **21**, **36**). From all other 2-aroylindole derivatives tested, only the two 5-methylindole species **50** and **52**, the 1-naphthyl-species **70**, the 4-isochinolinyl derivative **72**, and the N-alkylated species **81** showed noteworthy cytotoxic activity (Tables 2−4). In general, all precursor compounds except **8b**, **9b**, and **36b** proved to be inactive. However, removal of the N-phenylsulfo-

Table 1. Tubulin-Inhibitory Activity and In Vitro Cytotoxicity of 2-Aroylindole Analogs **1**−**40**, **42**, **44**, and **50**−**52**



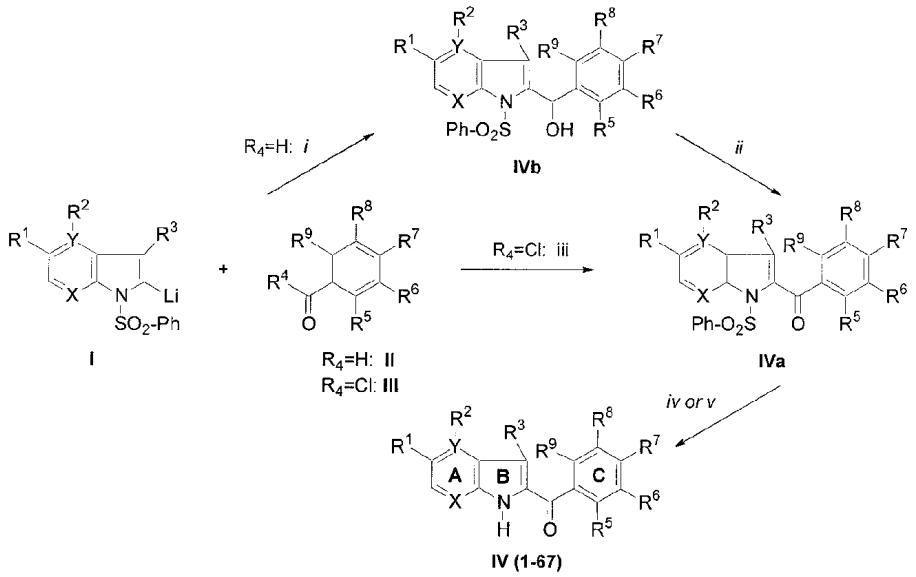
compd	R^1	R^5	R^6	R^7	R^8	R^9	ITP[a] IC_{50} [μM]	HeLa/KB[b] IC_{50} [μM]	SK-OV-3[b] IC_{50} [μM]
1	OCH_3	H	H	H	H	H	0.53	0.068	0.68
2	OCH_3	OCH_3	H	H	H	H	1.29	0.036	0.11
3	OCH_3	H	OCH_3	H	H	H	0.53	0.011	0.011
4	OCH_3	H	H	OCH_3	H	H	NE[c]	11.4	11.4
5	OCH_3	OCH_3	OCH_3	H	H	H	>10[d]	6.4	3.2
6	OCH_3	OCH_3	H	OCH_3	H	H	5.6	0.10	1.03
7	OCH_3	H	OCH_3	OCH_3	H	H	0.81	1.32	1.64
8	OCH_3	H	OCH_3	H	OCH_3	H	0.81	0.019	0.019
9	OCH_3	OCH_3	OCH_3	OCH_3	H	H	≥10	0.059	0.088
10	OCH_3	OCH_3	OCH_3	H	OCH_3	H	NE	8.79	9.37
11	OCH_3	H	OCH_3	OCH_3	OCH_3	H	0.99	0.029	0.058
12	OCH_3	CH_3	H	H	H	H	4.8	1.21	0.38
13	OCH_3	H	H	CH_3	H	H	1.5	0.38	1.88
14	OCH_3	CH_3	H	H	CH_3	H	5.2	0.72	0.72
15	OCH_3	H	OCH_2Ph	H	H	H	NE	>8.6	>8.6
16	OCH_3	H	OH	H	H	H	0.66	0.22	0.22
17	OCH_3	H	$O(CO)(CH_2)_2CH_3$	H	H	H	0.85	0.27	0.24
18	OCH_3	H	OCF_3	H	H	H	1.7	0.27	0.21
19	OCH_3	H	SCF_3	H	H	H	≥10	0.88	0.63
20	OCH_3	H	SCF_2H	H	H	H	2.1	0.39	0.36
21	OCH_3	H	CF_3	H	H	H	1.5	0.03	0.03
22	OCH_3	NO_2	H	H	H	H	>10	>10.8	>10.8
23	OCH_3	NH_2	H	H	H	H	6.7	3.76	3.76
24	OCH_3	H	NO_2	H	H	H	0.85	0.10	0.10
25	OCH_3	H	NH_2	H	H	H	0.99	0.34	0.23
26	OCH_3	CH_3	NO_2	H	H	H	>10	>10.3	>10.3
27	OCH_3	CH_3	NH_2	H	H	H	>10	11.4	11.4
28	OCH_3	NO_2	OCH_3	H	H	H	>10	>9.8	>9.8
29	OCH_3	H	H	CH_2CH_3	H	H	≥10	8.9	11.5
30	OCH_3	H	H	$CH_2CH_2CH_3$	H	H	>10	>10.9	>10.9
31	OCH_3	H	H	$C(CH_3)_3$	H	H	NE	>10.4	>10.4
32	OCH_3	H	H	$O(CH_2)_4CH_3$	H	H	NE	>9.5	>9.5
33	OCH_3	H	H	Cl	H	H	5.0	3.50	1.75
34	OCH_3	H	H	Br	H	H	4.3	0.91	0.91
35	OCH_3	F	H	H	H	H	1.0	0.37	0.74
36	OCH_3	H	F	H	H	H	0.39	0.026	0.015
37	OCH_3	H	H	F	H	H	n.d.	5.57	7.43
38	OCH_3	F	H	H	H	F	NE	6.96	8.70
39	OCH_3	Cl	H	H	H	F	>10	>10.5	>10.5
40	OCH_3	H	Cl	Cl	H	H	2.5	0.10	0.10
42	H	OCH_3	H	H	H	H	>10	>12.7	>12.7
44	H	H	OCH_3	OCH_3	OCH_3	H	NE	6.42	9.64
50	CH_3	OCH_3	H	H	H	H	3.5	0.38	0.75
51	CH_3	H	OCH_3	H	H	H	>10	>12.1	>12.1
52	CH_3	H	OCH_3	OCH_3	OCH_3	H	0.86	0.03	0.03
colchicine								0.023	0.020

[a] ITP = inhibition of tubulin polymerization. [b] IC_{50} values were determined in the initial screening from XTT proliferation assays, after incubation with test compound for 48 h. A detailed analysis of the antitumor activity of selected compounds **1**−**3**, **6**, **9**, **11**, **23**, **24**, **34**, and **40** is summarized in Table 4. Each experiment was performed at least in duplicate. [c] No effect was observed at a concentration up to 10 μM. [d] Weak inhibitory activity.

nyl-protection group yielding compounds **8**, **9**, and **36** resulted in 40- to 100-fold higher activity (Table 1).

In terms of SAR information, substituting the indole structure (azaindole-derivatives **60**−**67**) yielded inactive compounds, except **64** and **65** with low cytotoxicity. The substitution of C by N at the 5-methoxyindole-C4- (**64**−**67**) or 5-methoxyindole-C7-position (**60**−**63**) results in conformational changes in the relative positions of the aromatic rings A and C, which might be responsible for this loss of activity. However, also some simple changes in the indole-substitution pattern (**41**−**59**) generally resulted in loss of activity. The N-alkylated compounds **77**−**81** depicted reduced cytotoxicity in comparison to their parent compound **1**. In summary, these results from the cellular cytotoxicity screen suggested that the 5-methoxyindole group seems to be beneficial for potent antitumor activity. It is noteworthy, that the 5-methylindole derivative **51** is inactive, whereas its cognate 5-methoxyindole derivative **3** showed the highest antiproliferative activity of all compounds tested so far (IC_{50} ≤ 0.0032 nM). In contrast, the 3,4,5-trimethoxybenzoylindole derivatives **11** (on the basis of 5-methoxyindole) and **52** (on the basis of 5-methylindole) are cytotoxic with comparable potency. In the biochemical tubulin polymerization assay, however, a surprising difference in the IC_{50} values of these substances could be noted. The 5-methylindole compound **52** was about 11-fold more active in inhibiting tubulin polymerization than the 5-methoxyindole derivative **11** (see next section for details).

Scheme 1. Synthesis of 2-Aroylindole Derivatives IV and the Respective Precursors **IVa**/**IVb**[a]



Ia X=Y=C, R^1=OCH_3, R^2=R^3=H

Ib X=Y=C, R^1=CH_3, R^2=R^3=H

Ic X=Y=C, R^1=OCH_2Ph, R^2=R^3=H

Id X=Y=C, R^1=R^3=H, R^2=OCH_3

Ie X=Y=C, R^1=R^2=H, R^3=CH_3

If X=Y=C, R^1=R^2=R^3=H

Ig X=N, Y=C, R^1=R^2=R^3=H

Ih X=C, Y=N, R^1=OCH_3, R^2=R^3=H

IVa	IVb	IV	X, Y, R^1, R^2, R^3, R^5, R^6, R^7, R^8, R^9
1a	**1b**	**1**	X=Y=C, R^2=R^3=R^5=R^6=R^7=R^8=R^9=H, R^1=OCH_3
2a	**2b**	**2**	X=Y=C, R^2=R^3=R^6=R^7=R^8=R^9=H, R^1=R^5=OCH_3
3a	**3b**	**3**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=R^6=OCH_3
4a	**4b**	**4**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=R^7=OCH_3
5a		**5**	X=Y=C, R^2=R^3=R^7=R^8=R^9=H, R^1=R^5=R^6=OCH_3
6a	**6b**	**6**	X=Y=C, R^2=R^3=R^6=R^8=R^9=H, R^1=R^5=R^7=OCH_3
7a		**7**	X=Y=C, R^2=R^3=R^5=R^8=R^9=H, R^1=R^6=R^7=OCH_3
8a		**8**	X=Y=C, R^2=R^3=R^5=R^7=R^9=H, R^1=R^6=R^8=OCH_3
9a		**9**	X=Y=C, R^2=R^3=R^8=R^9=H, R^1=R^5=R^6=R^7=OCH_3
10a		**10**	X=Y=C, R^2=R^3=R^7=R^9=H, R^1=R^5=R^6=R^8=OCH_3
11a		**11**	X=Y=C, R^2=R^3=R^5=R^9=H, R^1=R^6=R^7=R^8=OCH_3
12a		**12**	X=Y=C, R^2=R_3=R_6=R_7=R_8=R_9=H, R_1=OCH_3, R_5=CH_3
13a		**13**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_3, R^7=CH_3
14a		**14**	X=Y=C, R^2=R^3=R^6=R^7=R^9=H, R^1=OCH_3, R^5=R^8=CH_3
15a	**15b**	**15**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_3, R^6=OCH_2Ph
16a		**16**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_3, R^6=OH
17a		**17**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_3, R^6=$O(CO)(CH_2)_2CH_3$
18a		**18**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_3, R^6=OCF_3
19a		**19**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_3, R^6=SCF_3
20a		**20**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_3, R^6=SCF_2H
21a		**21**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_3, R^6=CF_3
22a		**22**	X=Y=C, R^2=R^3=R^6=R^7=R^8=R^9=H, R^1=OCH_3, R^5=NO_2
		23	X=Y=C, R^2=R^3=R^6=R^7=R^8=R^9=H, R^1=OCH_3, R^5=NH_2
24a		**24**	X=Y=C, R^2=R^3=R^6=R^7=R^8=R^9=H, R^1=OCH_3, R^6=NO_2
		25	X=Y=C, R^2=R^3=R^6=R^7=R^8=R^9=H, R^1=OCH_3, R^6=NH_2
26a		**26**	X=Y=C, R^2=R^3=R^7=R^8=R^9=H, R^1=OCH_3, R^5=CH_3, R^6=NO_2
		27	X=Y=C, R^2=R^3=R^7=R^8=R^9=H, R^1=OCH_3, R^5=CH_3, R^6=NH_2
28a		**28**	X=Y=C, R^2=R^3=R^7=R^8=R^9=H, R^1=OCH_3, R^5=NO_2, R^6=OCH_3
29a		**29**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_3, R^7=CH_2CH_3
30a		**30**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_3, R^7=$CH_2CH_2CH_3$
31a		**31**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_3, R^7=$C(CH_3)_3$
32a		**32**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_3, R^7=$O(CH_2)_4CH_3$

Scheme 1. (Continued)

33a	**33**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_3, R^7=Cl	**51a**	**51**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=CH_3, R^6=OCH_3
34a	**34**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_3, R^7=Br	**52a**	**52**	X=Y=C, R^2=R^3=R^5=R^9=H, R^1=CH_3, R^6=R^7=R^8=OCH_3
35a	**35**	X=Y=C, R^2=R^3=R^6=R^7=R^8=R^9=H, R^1=OCH_3, R^5=F	**53a**	**53**	X=Y=C, R^2=R^3=R^5=R^6=R^7=R^8=R^9=H, R^1=OCH_2Ph
36a	**36**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_3, R^6=F	**54a**	**54**	X=Y=C, R^2=R^3=R^4=R^7=R^8=R^9=H, R^1=OCH_2Ph, R^5=OCH_3
37a	**37**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_3, R^7=F	**55a**	**55**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_2Ph, R^6=OCH_3
38a	**38**	X=Y=C, R^2=R^3=R^6=R^7=R^8=H, R^1=OCH_3, R^5=R^9=F	**56a**	**56**	X=Y=C, R^2=R^3=R^5=R^6=R^8=R^9=H, R^1=OCH_2Ph, R^7=OCH_3
39a	**39**	X=Y=C, R^2=R^3=R^6=R^7=R^8=H, R^1=OCH_3, R^5=Cl, R^9=F	**57a**	**57**	X=Y=C, R^2=R^3=R^5=R^9=H, R^1=OCH_2Ph, R^6=R^7=R^8=OCH_3
40a	**40**	X=Y=C, R^2=R^3=R^5=R^8=R^9=H, R^1=OCH_3, R^6=R^7=Cl	**58a**	**58**	X=Y=C, R^2=R^3=R^5=R^7=R_8=R_9=H, R^1=OCH_2Ph, R^6=Cl
41a	**41**	X=Y=C, R^1=R^2=R^3=R^5=R^6=R^7=R^8=R^9=H	**59a**	**59**	X=Y=C, R^2=R^3=R^5=R^7=R^8=R^9=H, R^1=OCH_2Ph, R^7=Cl
42a	**42**	X=Y=C, R^1=R^2=R^3=R^6=R^7=R^8=R^9=H, R^5=OCH_3	**60a**	**60**	X=N, Y=C, R^1=R^2=R^3=R^6=R^7=R^8=R^9=H, R^5=OCH_3
43a	**43**	X=Y=C, R^1=R^2=R^3=R^6=R^8=R^9=H, R^5=R^7=OCH_3	**61a**	**61**	X=N, Y=C, R^1=R^2=R^3=R^5=R^7=R^8=R^9=H, R^6=OCH_3
44a	**44**	X=Y=C, R^1=R^2=R^3=R^5=R^9=H, R^6=R^7=R^8=OCH_3	**62a**	**62**	X=N, Y=C, R^1=R^2=R^3=R^6=R^8=R^9=H, R^5=R^7=OCH_3
45a	**45**	X=Y=C, R^1=R^2=R^6=R^7=R^8=R^9=H, R^3=CH_3, R^5=OCH_3	**63a**	**63**	X=N, Y=C, R^1=R^2=R^3=R^5=R^9=H, R^6=R^7=R^8=OCH_3
46a	**46**	X=Y=C, R^1=R^2=R^5=R^7=R^8=R^9=H, R^3=CH_3, R^6=OCH_3	**64a**	**64**	X=C, Y=N, R^3=R^6=R^7=R^8=R^9=H, R^1=R^5=OCH_3
47a	**47**	X=Y=C, R^1=R^2=R^6=R^8=R^9=H, R^3=CH_3, R^5=R^7=OCH_3	**65a**	**65**	X=C, Y=N, R^3=R^5=R^7=R^8=R^9=H, R^1=R^6=OCH_3
48a	**48**	X=Y=C, R^1=R^2=R^5=R^9=H, R^3=CH_3, R^6=R^7=R^8=OCH_3	**66a**	**66**	X=C, Y=N, R^3=R^6=R^8=R^9=H, R^1=R^5=R^9=OCH_3
49a	**49**	X=Y=C, R^1=R^3=R^5=R^7=R^8=R^9=H, R^2=R^6=OCH_3	**67a**	**67**	X=C, Y=N, R^3=R^5=R^9=H, R^1=R^6=R^7=R^8=OCH_3
50a	**50**	X=Y=C, R^2=R^3=R^6=R^7=R^8=R^9=H, R^1=CH_3, R^5=OCH_3			

[a] Reactions and conditions: *i*: procedure A (THF, −78 °C); *ii*: procedure B (PDC, CH_2Cl_2, R. T.); *iii*: procedure C (THF, −78 °C); *iv*: procedure D (NaOH, EtOH, reflux); *v*: procedure E (TBAF, THF/MeOH 1/1, reflux).

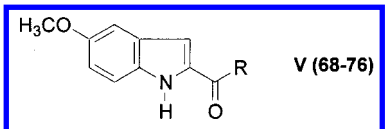
Many active compounds were found among the 2-benzoyl-5-methoxyindole derivatives **1**−**40** with the 3-methoxyphenyl derivative **3** being the most active. In general, single substitutions at the phenyl-3-position (R^6) resulted in a number of active compounds (e.g., **3**, **15**, **16**, **17**−**21**, **24**, **25**, and **36**). However, only the 3-fluorophenyl- (**36**) and the 3-methoxyphenyl derivative (**3**) showed higher cytotoxic activity than the unsubstituted compound **1**; their effect is similar to that of paclitaxel, the standard agent for treatment of advanced breast and ovarian cancer.

By comparing the effect of electron-donating or -withdrawing groups at the phenyl-3-position (R^6), no clear influence can be noted. For example, compound **3** with the electron-donating 3-OCH_3 and compound **36** with the electron-withdrawing 3-F are both high cytotoxic compounds. In contrast, **25** with the electron donating NH_2-substituent at the phenyl-3-position is less cytotoxic than **24** with the electron-withdrawing NO_2 group at the same position.

Cell Cycle Specific Mode of Action, Effect on Tubulin Polymerization and GTPase Activity in Vitro. Compounds **1**, **3**, and **11** were selected for mode-of-action studies to elucidate the molecular target leading to cytotoxicity. By using fluorescence activated cell sorting (FACS) analysis, a concentration-dependent arrest of U373 human astrocytoma cells in the G2/M phase with 4N chromosomes was observed (Figure 1A/B), correlating nicely with the cytoxicity against this cell line (Table 2). From this result, we hypothesized that 2-aroylindoles are acting in a cell cycle specific manner by interfering with the mitotic spindle apparatus. To prove this hypothesis, selected compounds were tested for inhibition of $\alpha\beta$ tubulin polymerization. As summarized in Tables 1−5, with the exception of **6**, **7**, **9**, and **19** all compounds having significant cytotoxicity inhibited tubulin polymerization with $IC_{50} < 10\ \mu M$. Thus, we conclude that the spindle apparatus formed by tubulin $\alpha\beta$ heterodimers is the cellular target of 2-aroylindoles. For compounds **6**, **7**, **9**, and **19**, showing only marginal inhibition of tubulin polymerization ($IC_{50} \geq 10\ \mu M$), the cytotoxic effect might be explained by a target different from tubulin. Nevertheless, in general the IC_{50} values determined in the cellular cytotoxicity and biochemical polymerization assay did correlate. One exception is compound **3**, being highly cytotoxic but less active in inhibition of tubulin polymerization as compared to **8** and **36**. In contrast to the cellular assay, the dynamic range of the biochemical assay is narrow, and 50−100 times higher concentrations are needed to achieve the same half-maximal biological effect. Most likely, the intracellular milieu and compound concentration, which is effected by the efficiency of cellular uptake, as well as the target concentration within the cell are quite different from the in vitro situation and not easily transferable. Since similar results were obtained with the well-known tubulin inhibitory drugs paclitaxel and vincristine,[19] this phenomenon is not limited to 2-aroylindol derivatives. Again, as with the investigation of cytotoxicity, no electronic effect of the substituents at the phenyl ring can be noted: compound **24** (R^6=NO_2) resulted in nearly the same IC_{50} value as compound **25** (R^6=NH_2).

The assembly of microtubules requires GTP hydrolysis, catalyzed by the GTPase activity of β-tubulin.[7] All tubulin inhibitors studied so far are GTPase effectors,

Scheme 2. 5-Methoxy-2-aroylindole Derivatives **V** (**68**−**76**)



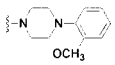
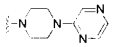
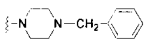
Compd.	R=
68	cyclopropyl
69	cyclobutyl
70	1-naphtyl
71	2-pyridinyl
72	4-isochinolinyl
73	
74	
75	
76	

Table 2. Cell Cycle Arrest and Cyctotoxicity of Analogs **1**, **3**, and **11** in U373 Astrocytoma Cells[a]

compd	U373 proliferation IC_{50} [nM]	U373 cell cycle IC_{50} [nM]
1	74	62.7
3	28	10.7
11	73	36.1

[a] The IC_{50} values for compounds **1**, **3** and **11** were calculated from respective dose−response curves for cytotoxicity or cell-cycle arrest (Figure 1).

either stimulating or inhibiting GTP hydrolysis.[22,23] Since preliminary experiments with [^{3}H]colchicine showed that **1** bound to β-tubulin with the same potency than colchicine [IC_{50} [colchicine] 0.53 μM vs IC_{50} [**1**] 0.51 μM; compound **3** (IC_{50} 0.28) bound even a bit better], we studied the effect of **1** on GTPase hydrolysis by using highly purified tubulin free of contaminating GTPase activity. Whereas colchicine or nocodazole stimulated and vincristine inhibited GTP hydrolysis, **1** had no significant effect at 1 and 10 μM concentration (Table 3). In summary, these results confirmed that 2-aroylindoles are constituting a new class of cell cycle specific small molecule tubulin inhibitors with high cytotoxicity toward cancer cells.

Table 3. Effect of **1** and Well-Known Tubulin-Inhibitory Agents on GTPase Activity of ss-Tubulin[a]

	β-tubulin GTPase activity[a]	
compound	10 μM	1 μM
DMSO (0 °C)	0.12	
DMSO (37 °C)	3.3	
colchicine	10.1	6.7
nocodazole	9.0	4.9
vincristine	0.09	5.3
taxol	1.4	3.3
1	3.5	3.2

[a] β-Tubulin GTPase activity is shown as the quotient of GDP/GTP concentrations, determined by phosphorimager analysis. Tubulin polymerization was induced by 1 M glutamate and incubation for 2 h at 37 °C. All compounds were added before starting the polymerization reaction.

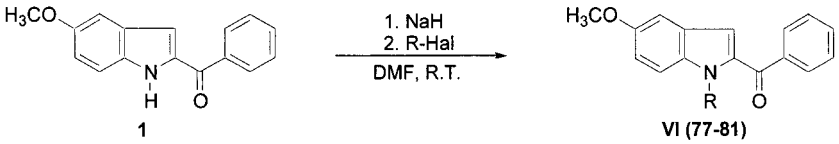
Table 4. Mean Cytotoxic Activity for Selected, Most Active Compounds[a]

compound	mean IC_{70} [μg/mL]	compound	mean IC_{70} [μg/mL]
1	0.22	**24**	1.40
2	0.35	**34**	2.56
3	0.27	**40**	1.34
6	1.74	**50**	2.03
9	0.73	**52**	1.17
11	0.17	**70**	0.88
23	1.44	**81**	2.95

[a] Cytoxicity of 16 selected 2-aroylindoles was studied using a panel of human tumor cell lines, namely, MCF-7, MAXF 401NL (breast), HT29 (colon), GXF 251L (stomach), LXFA 529L, LXF 66NL, LXFL 629L, MEXF 462NL, MEXF 462NL, MEXF 514L (skin/melanocyten), OVCAR3 (ovary), RXF 393NL, RXF 944L (renal), and UXF 1138L (soft tissue). The mean IC_{70} values in [μg/mL] are shown.

Antiangiogenic Activity. It is well-known, that tubulin inhibitors such as combretastatin-A4 phosphate are tumor vascular-targeting agents, aimed at a rapid and extensive shut-down of the established tumor

Scheme 3. Preparation of N-Alkylated Derivatives **VI** (**77**−**81**) (procedure F)



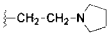
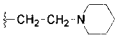
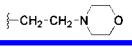
Compd.	R=
77	$CH_2CH_2N(CH_3)_2$
78	$CH_2CH_2CH_2N(CH_3)_2$
79	
80	
81	

Table 5. In Vivo Tumor Activity and Toxicity Data for **1**[a]

tumor desig.	dose [mg/kg]	sched	route	opt. T/C (d) [%]	GD 200% [d]	BWC [%]	drug rel. deaths [%]
MEXF 989	100	d1−5, 8−12	o.	**34** (28)	4.8	+11	0
	200	d1−5, 8−12	p.o.	**19** (17)	12.9	+3	0
RXF 944LX	100	d1−5, 8−12	o.	100 (1)	−0.4	+11	0
	200	d1−5, 8−12	p.o.	100 (1)	−0.4	+1	0

[a] Opt. T/C (d): Optimum tumor weight of treated animals/control animals in % (deviation); GD 200%: growth delay until tumor doubling in days; BWC: medium maximum body weight change in %; group size: 6−12 tumors.

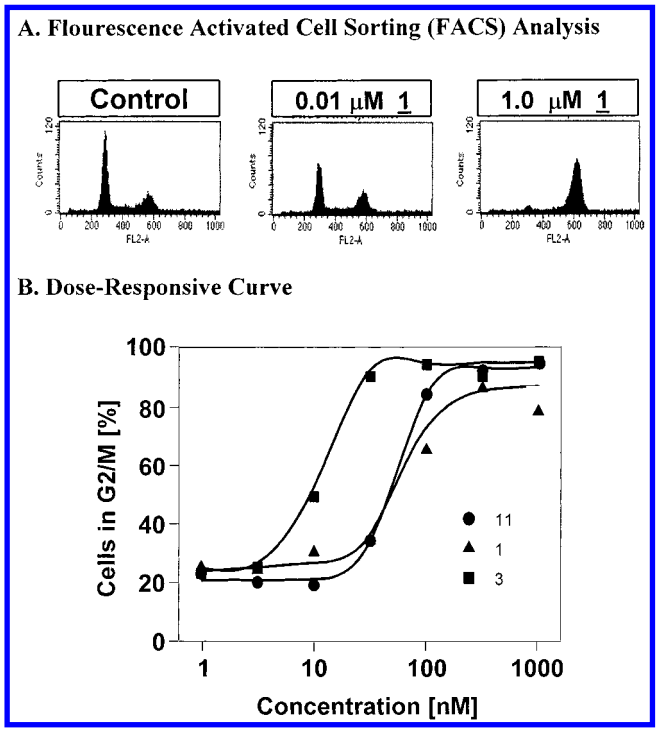


Figure 1. Cell cycle arrest of U373 astrocytoma cells induced by 2-aroylindole analogues **1**, **3**, and **11**. The distribution of U373 astrocytoma cells within the cell cycle was analyzed by FACS as described in Materials and Methods. Selected FACS histograms of cells treated with DMSO or **1** are shown in A (at 0, 0.01, and 1 μM, 17, 30, and 78% of all cells are in G2/M), the dose−response-curves for **1**, **3**, and **11** are shown in B. IC_{50} values for arresting cells in G2/M as well as cytotoxicity are summarized in Table 2.

vasculature, leading to tumor cell necrosis.[12] Thus, a variety of 2-aroylindoles (Figure 2) were tested for their in vivo antiangiogenic activity in the chick embryo chorioallantoic membrane (CAM) assay.[24] An agarose pellet containing the compound was placed on the germination layer of artificially incubated fertilized hens' eggs, and after 24 h the development of new blood vessels was determined under the stereo microscopically. For evaluation of antiangiogenic effects, a score system was defined,[25] and the compounds were classified due to their respective effect on the chorioallantoic membrane. Compounds **7** and **25** exhibited strong antiangiogenic activity, whereas **28** and **61** had almost no activity. Therefore, the antiangiogenic effect might be explained by a target different from tubulin. As far as the most cytotoxic compound **1** (weak anti-angiogenic effect) is concerned, substitution at the *meta*-position in the phenyl ring seemed to be beneficial for anti-angiogenic activity. However, the most potent compound in the tubulin polymerization assay, **36**, resulted in the CAM-assay in membrane irritation in more than 80% of the eggs with more than 50% of the embryos dying. As many compounds (**1**, **16**, **3**, **18**, and **65**) were not

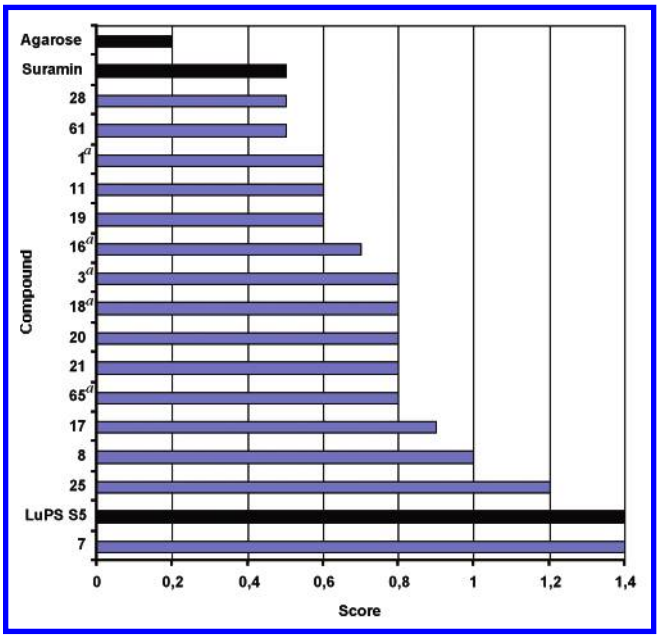


Figure 2. Antiangiogenic potency of selected compounds in the CAM test. The CAM test was performed as described in Materials and Methods. For evaluation of the antiangiogenic effect, a score system was used:

Score		Effects observed
0:	No effect	- none
0.5:	Very weak effect	- no capillary-free area
		- area with reduced density of capillaries around the pellet not larger than the area of the pellet
1:	Weak to medium effect	- small capillary-free area or area with significantly reduced density of capillaries
		- effects not larger than double the size of the pellet
2:	Strong effect	- capillary-free area around the pellet at least double the size of the pellet

As a negative control, CAMs were treated with agarose solution only; suramin **A** (50 μg/pellet) served as a positive control. The β-1,4-galactan sulfate LuPS S5[25] as a potent antiangiogenic compound is shown, too. Each experiment was performed at least in duplicate. All samples were tested at the concentration of 50 μg/pellet. Footnote a: substance was tested in suspension; due to diffusion processes, the standard deviation was 0.3.

easily soluble in the agarose buffer and thus had to be tested in suspension, some score-values have a large standard deviation (up to 0.3) due to variable diffusion processes, which have to be considered in these specific cases.

In Vivo Activity against Human Tumor Xenografts. To evaluate whether the potent in vitro

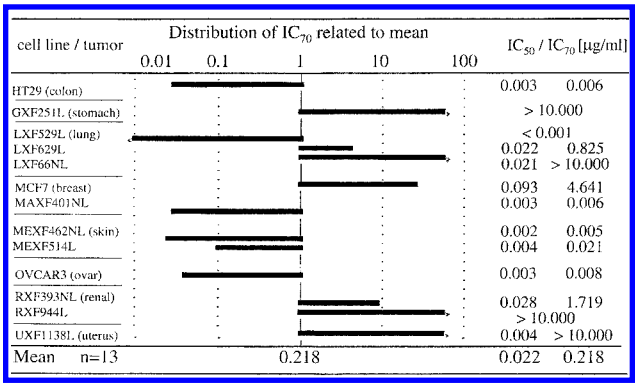


Figure 3. Chemosensitivity profile of compound **1** against human tumor cell lines. Bars to the left represent more sensitive; bars to the right more resistant tumor lines.

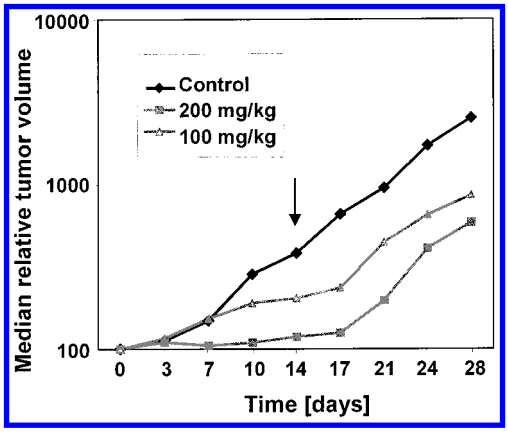


Figure 4. In vivo activity of **1** in the human MEXF 989 melanoma xenograft model. Drug was given daily orally on days 1−5 and 8−12. The therapy was well tolerated at the dose administered, and no toxicity (0/6) nor body weight loss were seen. The arrow indicates the termination of therapy. The optimal T/C in the 200 mg/kg group was 19%, corresponding to a 81% inhibition of tumor growth as compared to the vehicle control.

activity of 2-aroylindole derivatives can be translated into anticancer efficacy in human tumor xenografts in vivo, compound **1**, which was one of the most potent agents in the propidium iodide assay (Table 4), was selected. The in vitro chemosensitive profile (Figure 3) for compound **1** showed different cytotoxicities of **1** in a panel of human tumor cell lines. Melanomas (2/2), ovarian (1/1), and colon (1/1) cancers were the more sensitive, and gastric (1/1), lung (2/3), and renal (2/2) cancers were the more resistant tumor types. According to this in vitro chemosensitive profile, the human melanoma xenograft MEXF 989 was selected as a potentially sensitive tumor type. Additionally, the human hypernephroma xenograft RXF 944L was employed, too.

For oral dosing, 100 and 200 mg/kg **1** were administered Qd×5 over 2 weeks (Table 5). Both p.o. dosages were very well tolerated and showed no signs of toxicity (0/6) or body weight loss. Treatment with **1** resulted in growth inhibition of 81% of control at 200 mg/kg/day and 66% at 100 mg/kg/day in the human melanoma xenograft model MEXF 989 (Figure 4). The renal cell carcinoma RXF 944, however, was resistant toward therapy with compound **1**.

Conclusions

In conclusion, we have identified (5-methoxy-1*H*-2-indolyl)-phenyl-methanones as a novel class of highly potent anticancer agents and, by targeting microtubules, leading to mitotic catastrophy and finally apoptotic cell death. Although interfering with the colchicine binding site of β-tubulin, they do not affect β-tubulin GTPase activity. Selected compounds are as active as paclitaxel, the standard tubulin inhibitor used for advanced cancer treatment, and depicted antiangiogenic activity, too. Being orally bioavailable with marked in vivo antitumor activity, certain 2-aroylindoles may have potential for clinical development as anticancer drugs.

Experimental Section

Chemicals and Biologicals. General chemicals, XTT as well as tubulin inhibitors paclitaxel, vincristine, colchicine, and nocodazole were purchased from Sigma (Munich, Germany), and glutamate monohydrate was from Merck (Darmstadt, Germany). α[^{32}P]GTP was obtained from Amersham Pharmacia (Freiburg, Germany).

Human Tumor Cell Lines. The cell lines SKOV3 (ovary/HTB-77), KB/HeLa (cervix/CCL-17), U373 (astrocytoma/HTB-17), CCL HT29 (colon adenocarcinoma/HTB-38), and MACL MCF7 (breast adenocarcinoma/HTB-22) were obtained from ATCC. The cell line OVCAR3 (ovarian adenocarcinoma) is from the NCI tumor cell repository.[26,27] The cell lines MAXF 401NL (papillary breast adenocarcinoma), GXF 251L (stomach adenocarcinoma), LXFE 66NL (lung epidermoid carcinoma), LXFL 529L (large cell lung cancer), LXFA 629L (adenocarcinoma), MEXF 462NL (amelanotic melanoma), MEXF 514L (melanotic melanoma), MEXF 989 (amelanotic melanoma), RXF 944L (renal hypernephroma), RXF 393NL (renal hypernephroma), and UXF 1138L (carcinoma of the *corpus uteri*) were established at the University of Freiburg/Oncotest GmbH, Freiburg.

Cytotoxicity Assays. The compounds were dissolved in dimethyl sulfoxide (DMSO) at a final concentration of 1 mg/mL and stored at −20 °C or, alternatively, 8 °C. The XTT (sodium 3′-[1-(phenylaminocarbonyl)-3,4-tetrazolium]bis(4-methoxy-6-nitro)benzene sulfonic acid hydrate) assay was used as described[28] to determine proliferation by quantification of cellular metabolic activity. Half-maximal inhibition constants (IC_{50}) or estimates thereof were obtained by nonlinear regression analysis (program GraphPad Prism).

A modified propidium iodide (PI) assay, quantifying dead cells by staining of DNA and RNA, was applied for determination of cytotoxicity toward the human tumor cell panel.[29] Growth inhibition was expressed as treated/control × 100 (% T/C); inhibiting concentrations (IC) were determined by plotting compound concentration versus cell viability. Mean IC_{50} and IC_{70} values were calculated for each individual cell line. For compound **1**, a chemosensitivity profile was determined (Figure 3).

From all IC_{70} values, the mean IC_{70} was calculated according to the formula:

$$\text{mean } IC_{50,70} = {}_{10}\left(\frac{\sum_{x=1}^{n} \log (IC_{50/70})_x}{10}\right)$$

with x = value of specific tumor cell line and n = total number of tumor cell lines studied. If IC_{50} or IC_{70} values could not be determined within the examined concentration range, the lowest or highest concentration studied was used for calculation.

Flow Cytometry. U373 cells (5×10^6 cells) were exposed to the cytotoxic agents for 24 h at 37 °C, briefly treated with trypsin and collected by centrifugation. After the cells were washed twice with PBS, they were fixed in 80% v:v methanol

for 30 min on ice. Subsequently, cells were washed three times with PBS containing 0.1% saponin and incubated with PBS/saponin buffer containing 20 μg/mL propidium iodide and 1 mg/mL RNAse A for 30 min at 37 °C. Now, cells were washed once again with PBS/saponin and then resuspended in PBS. The DNA content of the cells was determined using fluorescence-activated cell sorting (FACS) with a Calibur flow cytometer (Becton Dickinson, Heidelberg, Germany). The number of cells in G2/M phase was calculated using Mod Fit LT cell cycle analysis software (VERITY). Data points were connected, and the respective IC_{50} value was calculated using a nonlinear regression program (GraphPad Prism).

Human Tumor Xenograft Experiments. For animal experiments, **1** was dissolved in DMSO and diluted with PBS containing 0.05% v:v Tween 80 to obtain a final DMSO concentration of 10%. Six to eight-week-old outbred nude mice of NMRI genetic background were used for all experiments. The animals were bred in-house and kept under laminar air flow on natural day light cycles. Diet (altromin, Lage, Germany) and water were provided ad libitium and room temperature (25 ± 2 °C) as well as humidity (60 ± 10%) were maintained. The gender of the mice was chosen according to the gender of the patients from which the tumors were originally derived. For the experiments the RXF944L and MEXF989 tumor xenograft models were selected and engrafted from tumors in serial passage growing s.c. in nude mice. Fragments of approximately 25 mg were implanted s.c. in both flanks of the animals. When the tumors were clearly palpable and had reached a volume of 100−200 mm^3, animals (6−12 tumors) were randomly allocated into treatment groups. Tumor growth was followed twice weekly by serial caliper measurement. Tumor volumes were calculated using the formula length × $width^2/2$, where length (*a*) is the largest dimension, and width (*b*) is the smallest dimension perpendicular to the length ($ab^2/2$).[30] Data evaluation was performed using specifically designed software by plotting relative tumor volume against time. Relative tumor volumes were calculated for each single tumor by dividing the tumor volume on day X by the tumor volume on day 0 at the time of randomization. Tumor doubling time of test and control groups was defined as the period required to double the initial tumor volume (200%). Growth curves were analyzed in terms of maximal tumor inhibition (treated/control, T/C, calculated as median tumor weight of treated divided by median tumor weight of control animals × 100) and growth delay (the difference in days to double the initial tumor volume of the test minus the control groups). Statistical data analysis was performed using nonparametrical Mann−Whitney statistics. Median relative tumor volumes of each treatment group were compared to those of the control group. Human tumors growing s.c. in nude mice were treated orally with doses of 100 and 200 mg/kg/day **1** on days 1−5 and 8−12. The drug doses and treatment schedule used proved to be well tolerated in nontumor bearing nude mice prior to initiation of tumor experiments.

CAM Assay for Antiangiogenic Potency. All preliminary steps were performed at approximately 60 °C. Test compounds were dissolved in a 2.5% aq agarose solution (final concentration: 1−20 mg/mL). For the preparation of the pellets, 10 μL of these solutions were applied dropwise on circular Teflon supports of 3 mm in diameter and then cooled to room temperature at once. After incubation at 37 °C and relative humidity of 80% for 65−70 h, the fertilized hens' eggs were positioned in a horizontal position and rotated several times. Before the opening on the snub side, 10 mL of albumin were aspirated from a hole on the pointed side. At two-third of the height (from the pointed side), the eggs were traced with a scalpel, and the shells were removed with forceps. The aperture (cavity) was covered with keep-fresh film, and the eggs were incubated at 37 °C at a relative humidity of 80% for 75 h. When the formed chorioallantoic membrane (CAM) had approximately a diameter of 2 cm, one pellet (1 pellet/egg) was placed on it. The eggs were incubated for 1 day and subsequently evaluated under the stereo microscope. For every test compound, 15−20 eggs were utilized and for the evaluation of the antiangiogenic effect, a score system was used (see Figure 2).

Tubulin Polymerization Assay. The assay was basically performed according to Bollag et al.[31] Tubulin heterodimers with MAPs (0.8 mg/mL; 80 μg/assay), isolated by cycles of polymerization and depolymerization from fresh bovine brain, were incubated with test compounds (4 μg/mL in the initial screening, different concentrations in the final IC_{50} determination scheme) in PEM (100 mM PIPES, 1 mM EGTA, 1 mM $MgCl_2$) buffer pH 6.6 containing 1 mM GTP in a total volume of 100 μL at 37 °C for 1 h. Samples (75 μL) were then transferred to a 96-well Millipore Multiscreen Durapore hydrophilic 0.22 μm pore size filtration plate. Recovered microtubules on the filters were stained with 50 μL amido black solution (0.1% w/v naphthol blue black (Sigma), 45% v:v methanol, 10% v/v acetic acid) for 2 min. Vacuum was applied and unbound dye was removed by two additions of 200 μL destain solution (90% v/v methanol, 2% v/v acetic acid). The microtubule bound dye was then eluted by incubation with 200 μL elution solution (25 mM NaOH, 0.05 mM EDTA, 50% v/v ethanol) for 20 min. 160 μL elution solution were then transferred to a 96-well plate, and the absorbance was measured at 600 nm using the Wallac Victor Multilabel counter (PerkinElmer, Freiburg).

Tubulin GTPase Assay. The tubulin GTPase assay was performed with slight modifications according to Roychowdhury et al.[32] Highly purified, lyophilized MAP-free bovine brain tubulin (Cytoskeleton Inc./Denver, USA) was reconstituted in PEM (100 mM PIPES, 1 mM EGTA, 1 mM $MgCl_2$) buffer pH 6.6 and stored in aliquots at −80 °C. The reaction mixture used for the GTPase assay contained 1 mg/mL tubulin, 1 mM $MgCl_2$, 100 μM α[^{32}P]GTP (specific activity 3000 Ci/mmol), and 1 M monosodium glutamate in PEM buffer. Test compounds, dissolved in 10% v/v DMSO, were added prior to addition of glutamate and α[^{32}P]GTP (final 1% DMSO). Tubulin polymerization was started by incubation at 37 °C for 1 h and terminated by addition of sodium dodecyl sulfate at 1% final concentration. GTP hydrolysis was measured by thin-layer chromatography of the reaction mixture using polyethyleneimine-(PEI) cellulose plates. The chromatograms were developed with 0.35 M $(NH_4)_2CO_3$. Chromatography plates were exposed to X-ray films and quantified by phosphorimager analysis using a Fuji BAS-1800II device.

Synthesis. Elemental Analyses: Analytical Lab. University Regensburg. − mp: Büchi 512, Reichert hot-stage microscope. − IR: FT, Nicolet 510. − ^{1}H-NMR: Bruker 250 (250 MHz). − MS: Varian MAT 311A (EI, 70 eV). All reactions were carried out under nitrogen and dried over self-indicating silica gel, concentrated H_2SO_4 and KOH.

Procedure A: Synthesis of Substituted (1-Phenylsulfonyl-1*H*-2-indolyl)-phenylmethanoles (IVb): *n*-Butyllithium (9.9 mL, 15.9 mmol in hexane) was added dropwise to a solution of anhydrous diisopropylamine (2.23 mL, 15.9 mmol) in dry THF (15 mL) at −78 °C. After the sample was stirred for 10 min, the mixture was allowed to warm to 0 °C, and then it was stirred for 30 min. A solution of the appropriate 1-phenylsulfonyl indole (14.0 mmol) in dry THF (22 mL) was added within 10 min, and the reaction mixture was kept stirring at 0 °C for 30 min. Then the solution of the respective (1-phenylsulfonyl-1*H*-2-indolyl)lithium so obtained was cooled to −78 °C again, and the aldehyde **III** (4.39 g, 15.4 mmol) in dry THF (15 mL) was added slowly. After the sample was warmed to room-temperature overnight, the mixture was poured into 1% aq HCl (100 mL), and the organic layer was separated. The water layer was extracted with ethyl acetate (3 × 50 mL), and the combined organic layers were washed successively with bicarbonate and brine. After the sample was dried (Na_2SO_4), the solvent was evaporated under reduced pressure to leave a foamy solid, which was subjected to column chromatography (SiO_2; ethyl acetate/hexane 4/1) or recrystallized from ethanol, yielding the product as light yellowish crystals. Thus, compounds **1b**−**4b**, **6b**, **15b**, and **72b** were prepared.

(5-Methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-phenyl-methanol (1b): colorless crystals, 86%, mp 51−52 °C. IR (KBr): 3429, 3064, 2937, 2834, 1615, 1368, 1159 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.72 (s, 3H), 6.15−6.18 (m, 1H, exchangeable), 6.37−6.39 (m, 1H), 6.60 (s, 1H), 6.86−6.9 (m, 1H), 7.06−7.07 (m, 1H), 7.28−7.39 (m, 5H), 7.47−7.53 (m, 2H), 7.60−7.67 (m, 1H), 7.73−7.76 (m, 2H), 7.84−7.87 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 393 (63) [$M^{+\bullet}$], 251 (100), 236 (13), 224 (21), 105 (61), 77 (44). Anal. ($C_{22}H_{19}NO_4S$) C, H, N.

2-Methoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanol (2b): light red crystals, 41%, mp 75−76 °C. IR (KBr): 3414, 3068, 2961, 2836, 1603, 1589, 1368, 1177 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.70 (s, 3H), 3.75 (s, 3H), 6.10−6.12 (m, 1H, exchangeable), 6.68−6.77 (m, 2H), 6.86−6.91 (m, 2H), 6.94−7.05 (m, 3H**),** 7.45−7.49 (m, 1H), 7.54−7.70 (m, 3H), 7.86−7.95 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 423 (27) [$M^{+\bullet}$], 281 (35), 135 (100), 77 (34). Anal. ($C_{23}H_{21}NO_5S$) C, H, N.

3-Methoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanol (3b): light yellow crystals, 68%, mp 121−122 °C. IR (KBr): 3435, 3095, 2958, 2836, 1605, 1358, 1160 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.72 (s, 6H), 6.16−6.18 (m, 1H, exchangeable), 6.34−6.36 (m, 1H), 6.56 (s, 1H), 6.84−6.95 (m, 4H), 7.06−7.07 (m, 1H), 7.23−7.29 (m, 1H), 7.47−7.53 (m, 2H), 7.61−7.67 (m, 1H), 7.79−7.79 (m, 2H), 7.85−7.88 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 423 (72) [$M^{+\bullet}$], 266 (100), 250 (23), 135 (45), 77 (27). Anal. ($C_{23}H_{21}NO_5S$) C, H, N.

4-Methoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanol (4b): light red crystals, 77%, mp 78−79 °C. IR (KBr): 3442, 3068, 2935, 2836, 1513, 1474, 1368, 1175 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.72 (s, 3H), 3.74 (s, 3H), 6.03−6.05 (m, 1H, exchangeable), 6.31−6.33 (m, 1H), 6.63 (s, 1H), 6.85−6.90 (m, 3H), 7.06−7.07 (m, 1H), 7.23−7.29 (m, 2H), 7.45−7.51 (m, 2H), 7.60−7.73 (m, 3H), 7.83−7.87 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 423 (27) [$M^{+\bullet}$], 281 (100), 265 (18), 250 (17), 173 (18), 135 (31), 77(25). Anal. ($C_{23}H_{21}NO_5S$) C, H, N.

2,4-Dimethoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanol (6b): colorless crystals, 61%, mp 119−120 °C. IR (KBr): 3450, 3002, 2941, 2836, 1591, 1508, 1364, 1179 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.69 (s, 3H), 3.73 (s, 3H), 3.78 (s, 3H), 5.75−5.77 (m, 1H, exchangeable), 6.15 (s, 1H), 6.51−6.60 (m, 3H), 6.85−6.89 (m, 1H), 7.00−7.01 (m, 1H), 7.26−7.29 (m, 1H), 7.51−7.68 (m, 3H), 7.84−7.90 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 453 (23) [$M^{+\bullet}$], 311 (60), 284 (25), 173 (67), 165 (100), 77 (39). Anal. ($C_{24}H_{23}NO_6S$) C, H, N.

3-Benzyloxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanol (15b): colorless crystals, 72%, mp 61 °C. IR (KBr): 3440, 3064, 2937, 2834, 1609, 1486, 1368 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.71 (s, 3H), 5.05 (s, 2H), 6.16−6.18 (m, 1H), 6.32−6.35 (m, 1H), 6.55 (s, 1H), 6.86−6.87 (m, 1H), 6.89−6.98 (m, 3H), 7.04−7.05 (m, 1H), 7.21−7.51 (m, 8H), 7.60−7.66 (m, 1H), 7.72−7.76 (m, 2H), 7.84−7.88 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 499 (20) [$M^{+\bullet}$], 359 (13), 267 (17), 250 (25), 91 (100), 77 (30). Anal. ($C_{29}H_{25}N_{O5}S$) C, H, N.

4-Isochinolinyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanol (72b): colorless crystals, 64%, mp 138−139 °C. IR (KBr): 3424, 3060, 2958, 2834, 1623, 1590, 1505, 1366, 1177 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.72 (s, 3H), 6.46−6.49 (m, 1H), 6.57 (s, 1H), 6.92−6.96 (m, 1H), 7.06−7.10 (m, 2H), 7.53−7.59 (m, 2H), 7.66−7.74 (m, 2H), 7.78−7.84 (m, 1H), 7.89−7.95 (m, 3H), 8.05−8.09 (m, 1H), 8.17−8.20 (m, 1H), 8.28 (s, 1H), 9.29 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 444 (41) [$M^{+\bullet}$], 302 (100), 286 (28), 271 (26), 156 (29), 128 (37), 77 (40). Anal. ($C_{25}H_{20}N_2O_4S$) C, H, N.

Procedure B: Preparation of (1-phenylsulfonyl-1*H*-indolyl)-phenyl-methanones (IVa) from IVb: PDC (pyridinium dichromate) (11.66 g, 31.0 mmol) and PTFA (pyridinium trifluoroacetate) (2.48 g, 155 mmol) were added to a solution of the (1-phenylsulfonyl-1*H*-indolyl)methanol derivative **IVb** (6.2 mmol) in 40 mL of dry CH_2Cl_2. When the oxidation was completed (2 h to 3 weeks, TLC-control), solid chromium waste was removed by filtration through SiO_2. Evaporation of the solvent left a foamy material, which was purified by column chromatography on silica gel with CH_2Cl_2 as eluent or recrystallized from ethyl acetate/light petrol (4:1) leading to light yellow cristals. Thus, compounds **1a**−**4a**, **6a**, **15a**, and **72a** were prepared.

Procedure C: Preparation of (1-Phenylsulfonyl-1*H*-2-indolyl)-phenyl-methanones (IVa) by reaction of (1-phenylsulfonyl-1*H*-indolyl)-2-lithium with Carboxylic Acid Chlorides: At −78 °C a solution of the respective (1-phenylsulfonyl-1*H*-indolyl)-2-lithium (**I**) (5.0 mmol) was added to the appropriate benzoic acid chloride (**II**) (5.5 mmol) in dry THF (15.0 mL). The mixture was allowed to warm to room-temperature overnight, hydrolyzed with aqueous $NaHCO_3$ (300 mL; 2%), extracted with ethyl acetate (3 × 50 mL), and the combined organic layers were dried (Na_2SO_4). Column chromatography (SiO_2/CH_2Cl_2) or crystallization from ethyl acetate/light petrol (4:1) afforded the products as colorless to faintly yellowish crystals. Thus, compounds **5a**, **7a**−**14a**, and **16a**−**71a** were prepared.

(5-Methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-phenyl-methanone (1a): colorless needles, 61%, mp 148 °C. IR (KBr): 3064, 3008, 2964, 2838, 1663, 1613, 1598, 1368, 1164 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3 H), 7.09−7.14 (m, 1H), 7.19−7.21 (m, 2H), 7.57−7.65 (m, 4H), 7.68−7.77 (m, 2H), 7.88−7.96 (m, 5H). EI-MS (70 eV); *m*/*z* (%): 391 (82) [$M^{+\bullet}$], 250 (100), 236 (8), 222 (14), 207 (20), 179 (24), 105 (32), 77 (51). Anal. ($C_{22}H_{17}NO_4S$) C, H, N.

2-Methoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (2a): colorless crystals, 62%, mp 179 °C. IR (KBr): 3067, 3015, 2985, 2936, 1648, 1596, 1474, 1374, 1167 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.67 (s, 3H), 3.75 (s, 3H), 7.01 (s, 1H), 7.06−7.21 (m, 4H), 7.55−7.74 (m, 5H), 7.90−7.96 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 421 (100) [$M^{+\bullet}$], 280 (58), 265 (49), 249 (90), 160 (78), 135 (56), 77 (86). Anal. ($C_{23}H_{19}NO_5S$) C, H, N.

3-Methoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (3a): colorless needles, 67%, mp 181 °C. IR (KBr): 3083, 3014, 2958, 2842, 1663, 1603, 1366, 1152 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 3.84 (s, 3H), 7.10−7.14 (m, 1H), 7.19−7.22 (m, 2H), 7.29−7.34 (m, 1H), 7.40−7.64 (m, 5H), 7.69−7.76 (m, 1H), 7.89−7.96 (m, 3 H). EI-MS (70 eV); *m*/*z* (%): 421 (72) [$M^{+\bullet}$], 280 (100), 265 (20), 249 (31), 135 (20), 77 (49). Anal. ($C_{23}H_{19}NO_5S$) C, H, N.

4-Methoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (4a): beige crystals, 64%, mp 129−130 °C. IR (KBr): 3066, 3002, 2937, 2937, 1611, 1512, 1370, 1162 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 3.80 (s, 3H), 6.16 (s, 1H), 6.88−6.93 (m, 1H), 7.01−7.04 (m, 2H), 7.12−7.40 (m, 8H), 7.55−7.61 (m, 1H), 7.82−7.86 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 421 (72) [$M^{+\bullet}$], 357 (22), 280 (100), 252 (32), 173 (42), 135 (56), 77 (57). Anal. ($C_{23}H_{19}NO_5S$): C, H, N.

2,3-Dimethoxyphenyl-(5-methoxy-1-phenylsulfonyl-1-*H*-2-indolyl)-methanone (5a): colorless crystals, 80%, mp 128 °C. IR (KBr): 3081, 3004, 2941, 2838, 1663, 1615, 1368, 1171 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.57 (s, 3H), 3.75 (s, 3H), 3.87 (s, 3H), 7.06−7.24 (m, 5H), 7.32−7.35 (dd,1.7, 8.1 Hz, 1H), 7.59−7.65 (m, 2H), 7.69−7.76 (m, 1H), 7.91−8.00 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 451 (49) [$M^{+\bullet}$], 311 (29), 279 (100), 264 (33), 160 (32), 77 (27). Anal. ($C_{24}H_{21}NO_6S$) C, H, N.

2,4-Dimethoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (6a): colorless crystals, 53%, mp 62−64 °C. IR (KBr): 3046, 2943, 2943, 1653, 1601, 1573, 1370, 1165 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.64 (s, 3H), 3.75 (s, 3H), 3.88 (s, 3H), 6.64−6.69 (m, 2H), 6.92 (s, 1H), 7.02−7.07 (m, 1H), 7.13−7.14 (m, 1H), 7.57−7.74 (m, 4H), 7.85−7.95 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 451 (100) [$M^{+\bullet}$], 311 (74), 295 (40), 279 (76), 264 (34), 173 (97), 165 (72), 160 (62), 77 (72). Anal. ($C_{24}H_{21}NO_6S$) C, H, N.

3,4-Dimethoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (7a): light red crystals, 58%, mp 75 °C (dec). IR (KBr): 3068, 3004, 2939, 2838, 1652, 1615, 1596, 1513, 1372, 1175 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 3.83 (s, 3H), 3.87 (s, 3H), 7.06−7.17 (m, 4H), 7.43−7.71 (m, 5H), 7.91−7.95 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 451 (89) [$M^{+\bullet}$], 387 (18), 310(63), 279 (100), 264 (39), 165 (32), 77 (70), 51 (24). Anal. ($C_{24}H_{21}NO_6S$) C, H, N.

3,5-Dimethoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (8a): light red crystals, 64%, mp 122−123 °C (dec). IR (KBr): 3087, 2968, 2838, 1667, 1594, 1368, 1179 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 3.80 (s, 6H), 6.97 (s, 2H), 7.08−7.22 (m, 3H), 7.57−7.63 (m, 2H), 7.67−7.74 (m, 1H), 7.88−7.96 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 451 (38) [M$^{+\bullet}$], 311 (100), 295 (27), 279 (27), 264 (17), 77 (40). Anal. ($C_{24}H_{21}NO_6S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1*H*-2-indolyl-(2,3,4-trimethoxyphenyl)-methanone (9a): colorless crystals, 45%, mp 57−59 °C. IR (KBr): 3103, 3000, 2944, 2840, 1656, 1615, 1495, 1372, 1175 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.63 (s, 3H), 3.76 (s, 3H), 3.77 (s, 3H), 3.90 (s, 3H), 6.95−7.09 (m, 3H), 7.14−7.15 (m, 1H), 7.37−7.40 (m, 1H), 7.58−7.75 (m, 3H), 7.88−7.98 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 481 (67) [M$^{+\bullet}$], 341, 309 (100), 294 (26), 195 (19), 181 (44), 173 (37), 160 (60), 77 (30). Anal. ($C_{25}H_{23}NO_7S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1*H*-2-indolyl-(2,3,5-trimethoxyphenyl)-methanone (10a): colorless crystals, 78%, mp 79−81 °C. IR (KBr): 3465, 3004, 2942, 2836, 1642, 1603, 1368, 1171 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.56 (s, 3H), 3.74 (s, 3H), 3.75 (s, 3H), 3.90 (s, 3H), 6.74 (s, 1H), 6.88 (m, 1H), 6.99−7.04 (m, 1H), 7.11−7.12 (m, 1H), 7.24 (s, 1H), 7.55−7.71 (m, 3H), 7.83−7.93 (m, 3H). EI-MS (70 eV); *m*/*z* (%):481 (47) [M$^{+\bullet}$], 341 (35), 325 (21), 309 (100), 294 (38), 168 (34), 160 (30), 77 (39). Anal. ($C_{25}H_{23}NO_7S$) C, H, N.

3,4,5-Trimethoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (11a): colorless crystals, mp 140−142 °C. IR (KBr): 3098, 2996, 2942, 1653, 1584 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.78 (s, 3H), 3.81 (s, 3H), 3.82 (s, 6H), 7.10−7.25 (m, 5H), 7.60−7.78 (m, 3H), 7.95−8.00 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 481 (100) [M$^{+\bullet}$], 341 (60), 309 (62), 294 (18), 173 (17). Anal. ($C_{25}H_{23}NO_7S$) C, H, N.

2-Methylphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (12a): colorless crystals, 30%, mp 149−153 °C. IR (KBr): ν = 1659, 1472, 1368, 748, 725 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.49 (s, 3H), 3.75 (s, 3H), 7.08−7.18 (m, 3H), 7.25−7.49 (m, 3H), 7.47−7.76 (m, 4H), 7.89−7.93 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 405 (41) [M$^{+\bullet}$], 264 (100). Anal. ($C_{23}H_{19}NO_4S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1-*H*-2-indolyl-(4-methylphenyl)-methanone (13a): colorless needles, 77%, mp 126−127 °C. IR (KBr): 3074, 2962, 2836, 1648, 1605, 1586, 1368, 1177 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.43 (s, 3H), 3.77 (s, 3H), 7.08−7.13 (m, 1H), 7.17−7.19 (m, 2H), 7.39−7.42 (m, 2H), 7.57−7.64 (m, 2H), 7.68−7.74 (m, 1H), 7.78−7.81 (m, 2H), 7.88−7.95 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 405 (90) [M$^{+\bullet}$], 341, 264 (100), 250 (23), 236 (18), 119 (46), 91 (34), 77 (37), 51 (12). Anal. ($C_{23}H_{19}NO_4$) C, H, N.

2,5-Dimethylphenyl-(5-methoxy-1-phenylsulfonyl-1-*H*-2-indolyl)-methanone (14a): colorless crystals, 80%, mp 164 °C. IR (KBr): 3068, 3027, 2989, 2927, 2834, 1665, 1615, 1532, 1372, 1180 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.24 (s, 3H), 2.44 (s, 3H), 3.77 (s, 3H), 7.09−7.20 (m, 4H), 7.27−7.35 (m, 2H), 7.59−7.65 (m, 2H), 7.70−7.77 (m, 1H), 7.91−7.97 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 419 (35) [M$^{+\bullet}$], 278 (100), 263 (25), 248 (17), 234 (11), 105 (9), 77 (21). Anal. ($C_{24}H_{21}NO_4S$) C, H, N.

3-Benzyloxyphenyl-(5-Methoxy-1-phenylsulfonyl-1-*H*-2-indolyl)-methanone (15a): colorless crystals, 63%, mp 121 °C. IR (KBr): 3448, 3068, 2935, 2836, 1659, 1594, 1366, 1183 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 5.18 (s, 2H), 7.08−7.12 (m, 1H), 7.15−7.16 (m, 2H), 7.31−7.51 (m, 9H), 7.54−7.62 (m, 2H), 7.66−7.73 (m, 1H), 7.87−7.84 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 497 (17) [M$^{+\bullet}$], 357 (22), 91 (100), 77 (26). Anal. ($C_{29}H_{23}NO_5S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1*H*-2-indolyl-(3-trifluoromethoxyphenyl)-methanone (18a): colorless crystals, 55%, mp 188−192 °C. IR (KBr): 1656, 1477, 1453, 1329, 734, 589 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.70 (s, 3H), 6.92−6.97 (m, 2H), 7.12 (s, 1H), 7.41−7.95 (m, 10H). EI-MS (70 eV); *m*/*z* (%): 475 (99) [M$^{+\bullet}$], 334 (100). Anal. ($C_{23}H_{16}F_3NO_5S$) C, H, N.

3-(Trifluoromethylthio)phenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (19a): colorless powder, 76%, mp 123−124 °C. IR (KBr): 3070, 3006, 2940, 2842, 1669, 1339, 1220 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.83 (s, 3H), 6.94 (d, 0.8 Hz, 1H), 6.99 (dd, 2.6 Hz, 0.5 Hz, 1H), 7.12 (d, 2.6 Hz, 1H), 7.44−7.61 (m, 4H), 7.88−8.10 (m, 5H), 8.25 (m,1H). EI-MS (70 eV); *m*/*z* (%): 491 (52) [M$^{+\bullet}$], 287 (19), 249 (100), 234 (29), 146 (54), 77 (34), 28 (22). Anal. ($C_{23}H_{16}F_3NO_4S_2$) C, H, N.

3-(Difluoromethylthio)phenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (20a): colorless crystals, 42%, mp 188−195 °C. IR (KBr): 1649, 1481, 1387, 765, 562 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.70 (s, 3H), 6.92−7.92 (m, 14H). EI-MS (70 eV); *m*/*z* (%): 473 (30) [M$^{+\bullet}$]. Anal. ($C_{23}H_{17}F_2NO_4S_2$): C, H, N.

3-Trifluoromethylphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (21a): colorless crystals, 29%, mp 175−177 °C. IR (KBr): 1670, 1474, 1449, 1331, 812, 725, 596, 575 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.70 (s, 3H), 6.92−7.02 (m, 2H), 7.49 (s, 1H), 7.48−7.99 (m, 10H). EI-MS (70 eV); *m*/*z* (%): 457 (7) [M$^{+\bullet}$], 318 (14), 141 (24). Anal. ($C_{23}H_{16}F_3NO_4S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1-*H*-2-indolyl-(2-nitrophenyl)-methanone (22a): beige needles, 47%, mp 190−191 °C. IR (KBr): 3070, 3012, 2935, 2838, 1673, 1650, 1613, 1532, 1320, 1352, 1169 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 7.19−7.24 (m, 3H), 7.64−7.80 (m, 4H), 7.86−7.94 (m, 2H), 8.05−8.13 (m, 3H), 8.16−8.23 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 436 (24) [M$^{+\bullet}$], 134 (100), 104 (57), 77 (41). Anal. ($C_{22}H_{16}N_2O_6S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1-*H*-2-indolyl-(3-nitrophenyl)-methanone (24a): beige needles, 53%, mp 228−230 °C. IR (KBr): 3074, 2838, 1659, 1613, 1326, 1368, 1167 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.78 (s, 3 H), 7.14−7.22 (m, 2H), 7.39 (s, 1H), 7.58−7.64 (m, 2H), 7.69−7.76 (m, 1H), 7.86−8.00 (m, 4H), 8.30−8.95 (m, 2H), 8.55−8.59 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 436 (87) [M$^{+\bullet}$], 372 (9), 295 (25), 249 (100), 234 (37), 206 (24), 178 (22), 150 (18), 141 (16), 77 (59). Anal. ($C_{22}H_{16}N_2O_6S$): C, H, N.

5-Methoxy-1-phenylsulfonyl-1-*H*-2-indolyl-(2-methyl-3-nitrophenyl)-methanone (26a): colorless crystals, 73%, mp 210−211 °C. IR (KBr): 3085, 2971, 2838, 1659, 1615, 1530, 1322, 1356, 1167 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.48 (s, 3H), 3.77 (s, 3H), 7.15−7.22 (m, 2H), 7.31 (s, 1H), 7.52−7.76 (m, 5H), 7.93−7.99 (m, 3H), 8.08−8.11 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 450 (100) [M$^{+\bullet}$], 310 (20), 292 (22), 262 (36), 77 (22). Anal. ($C_{23}H_{18}N_2O_6S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1-*H*-2-indolyl-(3-methoxy-2-nitrophenyl)-methanone (28a): light yellow crystals, 55%, mp 180 °C. IR (KBr): 3068, 2973, 2842, 1669, 1650, 1605, 1580, 1538, 1374, 1178 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 3.98 (s, 3H), 7.16−7.21 (m, 2H), 7.33−7.39 (m, 2H), 7.60−7.74 (m, 5H), 7.89−7.99 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 466 (46) [M$^{+\bullet}$], 326 (29), 302 (88) 164 (100), 125 (43), 77 (99). Anal. ($C_{23}H_{18}N_2O_7S$) C, H, N.

4-Ethylphenyl-(5-methoxy-1-phenylsulfonyl-1-*H*-2-indolyl)-methanone (29a): colorless crystals, 52%, mp 107−108 °C. IR (KBr): 3070, 2970, 2836, 1656, 1605, 1586, 1370, 1162 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.23 (t, J = 7.6 Hz, 3H), 2.73 (q, J = 7.6 Hz, 2 H), 3.77 (s, 3H), 7.11 (dd, J = 2.6, 9.1 Hz, 1H), 7.18−7.19 (m, 2H), 7.42−7.45 (m, 2H), 7.57−7.64 (m, 2H), 7.68−7.75 (m, 1H), 7.81−7.84 (m, 2H), 7.89−7.95 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 419 (100) [M$^{+\bullet}$], 355 (20), 279(97), 250 (50), 234 (32), 133 (45), 77 (62), 51 (15). Anal. ($C_{25}H_{23}NO_4S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1-*H*-2-indolyl-(4-propylphenyl)-methanone (30a): colorless crystals, 67%, mp 112−114 °C. IR (KBr): 3070, 2970, 2935, 2838, 1652, 1605, 1586, 1370, 1177 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.43 (s, 3H), 3.77 (s, 3H), 7.08−7.13 (m, 1H), 7.17−7.19 (m, 2H), 7.39−7.42 (m, 2H), 7.57−7.64 (m, 2H), 7.68−7.74 (m, 1H), 7.78−7.81 (m, 2H), 7.89−7.95 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 433 (100) [M$^{+\bullet}$], 369 (32), 292 (82), 264 (33), 250 (64), 234 (30), 220 (37), 147 (42), 91 (25), 77 (57). Anal. ($C_{25}H_{23}NO_4S$) C, H, N.

4-*tert*-Butylphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (31a): colorless crystals, mp 161−163 °C. IR (KBr): 3071, 2973, 2867, 1670, 1603, cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.33 (s, 9H), 3.77 (s, 3H), 7.08−7.19 (m, 3H), 7.57−7.76 (m, 5H), 7.82−7.91 (m, 5H). EI-MS (70 eV); *m*/*z*

(%): 447 (58) [$M^{+\bullet}$], 383 (14), 307 (87), 250 (80), 77 (89), 57 (100). Anal. ($C_{26}H_{25}NO_4S$) C, H, N.

4-Pentyloxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (32a): colorless crystals, mp 118−120 °C. IR (KBr): 3063, 2956, 2869, 1638, 1601 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 0.90 (t, J = 6.9 Hz, 3H), 1.30−1.45 (m, 4H), 1.75 (quint, J = 6.8 Hz, 2H), 3.77 (s, 3H), 4.10 (t, J = 6.5 Hz, 2H), 7.06−7.18 (m, 5H), 7.55−7.75 (m, 3H), 7.83−7.94 (m, 5H). EI-MS (70 eV); *m*/*z* (%): 477 (84) [$M^{+\bullet}$], 413 (41), 337 (54), 336 (63), 266 (100). Anal. ($C_{27}H_{27}NO_5S$) C, H, N.

4-Chlorophenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (33a): colorless crystals, mp 146−148 °C. IR (KBr): 3085, 2938, 1660, 1586 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 7.09−7.20 (m, 2H), 7.26 (d, J = 0.5 Hz, 1H), 7.56−7.75 (m, 5H), 7.85−7.97 (m, 5H). EI-MS (70 eV); *m*/*z* (%): 425 (90) [$M^{+\bullet}$], 361 (16), 284 (68), 249 (100), 234 (27), 139 (40). Anal. ($C_{22}H_{16}ClNO_4S$) C, H, N.

4-Bromophenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (34a): colorless crystals, mp 145−148 °C. IR (KBr): 3081, 2959, 2834, 1659, 1613 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.95−7.20 (m, 2H), 7.26−7.27 (m, 1H), 7.57−7.64 (m, 2H), 7.68−7.75 (m, 1H), 7.81−7.96 (m, 7H). EI-MS (70 eV); *m*/*z* (%): 469 (43) [$M^{+\bullet}$], 405 (10), 328 (19), 249 (100), 234(39). Anal. ($C_{22}H_{16}BrNO_4S \times 0.15\ CH_2Cl_2$): calcd. C 55.07, H 3.40, N 2.90; found C 55.16, H 3.79, N 2.76.

2-Fluorophenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (35a): colorless crystals, 29%, mp 199−205 °C. IR (KBr): 1613, 1472, 1449, 1205, 1173, 725, 602 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.70 (s, 3H), 6.92−6.96 (m, 1H), 7.11−7.13 (m, 1H), 7.44−7.68 (m, 5H), 7.85−7.95 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 409 (54) [$M^{+\bullet}$], 268 (72), 141 (48). Anal. ($C_{22}H_{16}FNO_4S$) C, H, N.

3-(Fluoromethylthio)phenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (36a): colorless crystals, 47%, mp 149 °C. IR (KBr): 1676, 1491, 1342, 1298, 733, 524 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 7.09−7.19 (m, 2H), 7.27 (s, 1H), 7.56−7.73 (m, 7H), 7.85−7.95 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 409 (62) [$M^{+\bullet}$], 268 (100). Anal. ($C_{22}H_{16}FNO_4S_2$) C, H, N.

4-Fluorophenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (37a): colorless crystals 44%, mp 123−128 °C. IR (KBr): 1672, 1599, 1472, 1219, 1159, 725, 598 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.70 (s, 3H), 6.91−6.96 (m, 1H), 7.08−7.76 (m, 9H), 7.81−7.99 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 409 (54) [$M^{+\bullet}$], 268 (72), 141 (48). Anal. ($C_{22}H_{16}FNO_4S$) C, H, N.

2,6-Difluorphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (38a): colorless crystals, 29%, mp 124 °C. IR (KBr): 1674, 1466, 1217, 1175, 723, 598, 565 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.81 (s, 3H), 6.92−7.14 (m, 5H), 7.40−7.60 (m, 4H), 7.95−7.98 (m, 2H), 8.00−8.01 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 427 (57) [$M^{+\bullet}$], 286 (100), 141 (33). Anal. ($C_{22}H_{15}F_2NO_4S$) C, H, N.

2-Chloro-6-fluorophenyl-(5-methoxy-1-phenylsulfonyl-1-*H*-2-indolyl)-methanone (39a): beige crystals, 27%, mp 130 °C. IR (KBr): 3014, 2958, 2834, 1679, 1605, 1530, 1372, 1177, 1221, 1048 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 7.21−7.26 (m, 2H), 7.37 (s, 1H), 7.39−7.51 (m, 2H), 7.61−7.79 (m, 4H), 8.02−8.10 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 443 (80) [$M^{+\bullet}$], 379 (9), 303 (62), 267 (100), 252 (46), 224 (31), 157 (41), 130 (21), 77 (61). Anal. ($C_{22}H_{15}ClFNO_4S$) C, H, N.

3,4-Dichlorophenyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (40a): colorless crystals, mp 141−144 °C. IR (KBr): 3091, 3008, 2929, 2836, 1663, 1615 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.78 (s, 3H), 7.10−7.21 (m, 2H), 7.33 (s, 1H), 7.56−7.75 (m, 3H), 7.80−7.98 (m, 5H), 8.04 d, J = 1.8 Hz, 1H). EI-MS (70 eV); *m*/*z* (%): 459 (58) [$M^{+\bullet}$], 395 (9), 318 (27), 283 (100), 268 (27), 173 (26). Anal. ($C_{22}H_{15}Cl_2NO_4S$) C, H, N.

1-Phenylsulfonyl-1*H*-2-indolyl-phenyl-methanone (41a): colorless crystals, mp 142−143 °C. IR (KBr): 3071, 1661, 1599, 1533, 1364, 1342 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 7.29−7.41 (m, 2H), 7.49−7.80 (m, 8H), 7.91−8.09 (m, 5H). EI-MS (70 eV); *m*/*z* (%): 361 (68) [$M^{+\bullet}$], 297 (37), 220 (100), 192 (30), 165 (34), 105(39), 77 (95). Anal. ($C_{21}H_{15}NO_3S$) C, H, N.

2-Methoxyphenyl-(1-phenylsulfonyl-1*H*-2-indolyl)-methanone (42a): colorless crystals, mp 141−143 °C. IR (KBr): 3070, 3008, 2940, 1640, 1595 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.85 (s, 1H), 6.95−7.07 (m, 2H), 7.23−7.30 (m, 1H), 7.40−7.69 (m, 7H), 8.09−8.17 (M, 3H). EI-MS (70 eV); *m*/*z* (%): 391 (100) [$M^{+\bullet}$], 250 (49), 219 (77), 130 (83), 77 (93). Anal. ($C_{22}H_{17}NO_4S$): C, H, N.

2,4-Dimethoxyphenyl-(1-phenylsulfonyl-1*H*-2-indolyl)-methanone (43a): colorless crystals, mp 66−68 °C. IR (KBr): 3060, 2996, 2930, 1634, 1597 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.73 (s, 3H); 3.88 (s, 3H), 6.46−6.58 (m, 2H), 6.79 (s, 1H), 7.22−7.58 (m,6H), 7.53−7.58 (m, 1H), 8.40−8.52 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 421 (84) [$M^{+\bullet}$], 281 (72), 249 (53), 165 (100), 130 (82), 77 (90). Anal. ($C_{23}H_{19}NO_5S$) C, H, N.

3,4,5-Trimethoxyphenyl-(1-phenylsulfonyl-1*H*-2-indolyl)-methanone (44a): colorless crystals, mp 152−153 °C. IR (KBr): 3073, 3058, 2971, 1646, 1584 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.88 (s, 6H), 3.97 (s, 3H), 6.95 (s, 1H), 7.25−7.37 (m, 3H), 7.43−7.65 (m, 5H), 8.11−8.17 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 451 (100) [$M^{+\bullet}$], 387 (9), 311 (78), 295 (30), 279 (44). Anal. ($C_{24}H_{21}NO_6S$) C, H, N.

2-Methoxyphenyl-(3-methyl-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (45a): colorless crystals, 51%, mp 167−169 °C. IR (KBr): 1657, 1573, 1451 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.07 (s, 3H), 3.57 (s, 3H), 7.05−7.93 (m, 13H). EI-MS (70 eV); *m*/*z* (%): 405 (100) [$M^{+\bullet}$], 264 (70). Anal. ($C_{23}H_{19}NO_4S$) C, H, N.

3-Methoxyphenyl-(3-methyl-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (46a): colorless crystals, 43%, mp 113 °C. IR (KBr): 1660, 1588, 1448, 1233, 1116, 793, 734 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.12 (s, 3H), 3.81 (s, 3H), 7.25−8.00 (m, 13H). EI-MS (70 eV); *m*/*z* (%): 405 (91) [$M^{+\bullet}$], 264 (100). Anal. ($C_{23}H_{19}NO_4S$): C, H, N.

2,4-Dimethoxyphenyl-(3-methyl-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (47a): colorless crystals, 34%, mp 155−157 °C. IR (KBr): 1663, 1546, 1482, 1149, 1306, 765, 694 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.49 (s, 3H), 3.58 (s, 3H), 3.86 (s, 3H), 6.60−6.69 (m, 2H), 7.24−7.65 (m, 7H), 7.79−7.97 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 435 (100) [$M^{+\bullet}$], 294 (71). Anal. ($C_{24}H_{21}NO_5S$) C, H, N.

3,4,5-Trimethoxyphenyl-(3-methy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (48a): pale beige powder, 83%, mp 149.5−151 °C. IR (KBr): 3068, 3020, 2942, 2836, 1648, 1611, 1592, 1366 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 2.18 (s, 3H), 3.86 (s, 6H), 3.95 (s, 3H), 7.23 (s, 2H), 7.25−7.55 (m, 6H), 7.85−7.90 (m, 2H), 8.08 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 465 (68) [$M^{+\bullet}$], 324 (49), 293 (100), 278 (31), 195 (44), 28 (76). Anal. ($C_{25}H_{23}NO_6S \times 0.33\ H_2O$): calcd. C 63.68, H 5.06, N 2.97; found C 63.52, H 4.99, N 2.76.

3-Methoxyphenyl-(4-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (49a): colorless crystals, 74%, mp 132 °C (dec). IR (KBr): 3062, 2943, 2842, 1652, 1611, 1592, 1366 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.82 (s, 3H), 3.85 (s, 3H), 6.86−6.89 (m, 1H), 7.15 (m, 1H), 7.27−7.32 (m, 1H), 7.38−7.50 (m, 4H), 7.59−7.65 (m, 3H), 7.69−7.73 (m, 1H), 7.94−7.98 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 421 (42) [$M^{+\bullet}$], 357 (7), 280 (100), 265 (36), 250 (22), 135 (17), 121(24), 77 (48). Anal. ($C_{23}H_{19}NO_5S$) C, H, N.

2-Methoxyphenyl-(5-methyl-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (50a): colorless crystals, 48%, mp 157−158 °C. IR (KBr): 1652, 1586, 1232, 1115 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.34 (s, 3H), 3.64 (s, 3H), 7.00 (s, 1H), 7.05−7.31 (m, 3H), 7.42 (s, 1H), 7.54−7.72 (m, 5H), 7.87−7.96 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 405 (100) [$M^{+\bullet}$], 264 (49). Anal. ($C_{23}H_{19}NO_4S$) C, H, N.

3-Methoxyphenyl-(5-methyl-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (51a): colorless crystals, 39%, mp 124−127 °C. IR (KBr): 1657, 1554, 1236, 1165 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.36 (s, 3H), 3.82 (s, 3H), 7.21 (s, 1H), 7.28−7.74 (m, 9H), 7.90−7.95 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 405 (56) [$M^{+\bullet}$], 264 (100). Anal. ($C_{23}H_{19}NO_4S$) C, H, N.

3,4,5-Trimethoxyphenyl-(5-methy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (52a): pale beige powder, 63%, mp 152−153 °C. IR (KBr): 3060, 2996, 2838, 1648, 1611, 1592,

1366 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 2.44 (s, 3H), 3.88 (s, 6H), 3.96 (s, 3H), 6.88 (d, 0.8 Hz, 1H), 7.26 (s, 2H), 7.20−7.38 (m, 2H), 7.45−7.64 (m, 3H), 8.01 (m, 1H), 8.06−8.11 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 465 (100) [M$^{+\bullet}$], 401 (30), 324 (73), 293 (93), 278 (37), 195 (24), 28 (80). Anal. ($C_{25}H_{23}NO_6S \times 0.25\ H_2O$): calcd. C 63.88, H 5.04, N 2.98; found C 63.92, H 5.04, N 2.74.

5-Benzyloxy-1-phenylsulfonyl-1*H*-2-indolyl-phenylmethanone (53a): colorless crystals, mp 205−207 °C. IR (KBr): 3179, 2977, 1654, 1599 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.10 (s, 2H), 7.15−7.45 (m, 8H), 7.55−7.80 (m, 6H), 7.85−8.00 (m, 5H). EI-MS (70 eV); *m*/*z* (%): 467 (30) [M$^{+\bullet}$], 376 (18), 236 (18), 141 (23), 91 (100). Anal. ($C_{28}H_{21}NO_4S \times 0.2$ ethyl acetate): calcd. C 71.30, H 4.70, N 2.89; found C 71.13, H 4.65, N 2.86.

5-Benzyloxy-1-phenylsulfonyl-1*H*-2-indolyl-(2-methoxyphenyl)-methanone (54a): colorless crystals, mp 114.5−116 °C. IR (KBr): 3066, 2940, 2842, 1652, 1599, 1168 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.68 (s, 3H), 4.99 (s, 2H), 6.71 (d, *J* = 0.8 Hz, 1H), 6.92 (m, 2H), 7.06 (dd, *J* = 9.1 Hz, *J* = 2.6 Hz, 1H), 7.25−7.60 (m, 11H), 7.97−8.02 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 497 (19) [M$^{+\bullet}$], 266 (17), 135 (28), 91 (100). Anal. ($C_{29}H_{23}NO_5S$) C, H, N.

5-Benzyloxy-1-phenylsulfonyl-1*H*-2-indolyl-(3-methoxyphenyl)-methanone (55a): grey powder, mp 129−131 °C. IR (KBr) 3066, 2948, 2842, 1659, 1545, 1175 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.79 (s, 3H), 5.01 (s, 2H), 6.80 (d, *J* = 0.8 Hz, 1H), 6.97 (dd, *J* = 2.5 Hz, *J* = 0.3 Hz, 1H), 7.08 (dd, *J* = 9.1 Hz, *J* = 2.5 Hz, 1H), 7.09 (ddd, *J* = 8.1 Hz, *J* = 2.5 Hz, *J* = 1.4 Hz, 1H), 7.23−7.62 (m, 12H), 7.92−7.99 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 497 (15) [M$^{+\bullet}$], 357 (14), 266 (20), 91 (100). Anal. ($C_{29}H_{23}NO_5S$) C, H, N.

5-Benzyloxy-1-phenylsulfonyl-1*H*-2-indolyl-(4-methoxyphenyl)-methanone (56a): colorless crystals, mp 70−72 °C. IR (KBr): 3067, 3033, 2925, 1653, 1599 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 5.09 (s, 2H), 7.07−7.46 (m, 10H), 7.55−7.75 (m, 3H), 7.84−7.94 (m, 5H). EI-MS (70 eV); *m*/*z* (%): 497 (24) [M$^{+\bullet}$], 357 (20), 266 (23), 158 (39), 91 (100). Anal. ($C_{29}H_{23}NO_5S$) C, H, N.

5-Benzyloxy-1-phenylsulfonyl-1*H*-2-indolyl-(3,4,5-trimethoxyphenyl)-methanone (57a): colorless crystals, mp 150−152 °C. IR (KBr): 3066, 2938, 2873, 1659, 1611 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.80 (s, 3H), 3.81 (s, 6H), 5.10 (s, 2H), 7.17−7.46 (m, 10H), 7.58−7.71 (m, 3H), 7.94−8.00 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 557 (19) [M$^{+\bullet}$], 466 (9), 417 (22), 294 (42), 195 (31), 91 (100). Anal. ($C_{31}H_{27}NO_7S$) C, H, N.

5-Benzyloxy-1-phenylsulfonyl-1*H*-2-indolyl-(3-chlorophenyl)-methanone (58a): colorless crystals, mp 150−152 °C. IR (KBr): 3087, 2860, 1657, 1566 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.11 (s, 2H), 7.19−7.48 (m, 8H), 7.58−7.99 (m, 10H). EI-MS (70 eV); *m*/*z* (%): 501 (18) [M$^{+\bullet}$], 410 (6), 361 (7), 141 (19), 91 (100). Anal. ($C_{28}H_{20}ClNO_4S$) C, H, N.

5-Benzyloxy-1-phenylsulfonyl-1*H*-2-indolyl-(4-chlorophenyl)-methanone (59a): colorless crystals, mp 63−65 °C. IR (KBr): 3064, 2871, 1661, 1588 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.11 (s, 2H), 7.18−7.48 (m, 8H), 7.57−7.71 (m, 5H), 7.86−7.98 (m, 5H). EI-MS (70 eV); *m*/*z* (%): 501 (7) [M$^{+\bullet}$], 361 (5), 270 (6), 141 (14), 91 (100). Anal. ($C_{28}H_{20}ClNO_4S$) C, H, N.

2-Methoxyphenyl-(1-phenylsulfonyl-1*H*-(pyrrolo[2,3-b]-pyridin-2-yl))-methanone (60a): beige crystals, mp 124−125 °C. IR (KBr): 3066, 2945, 2842, 1636, 1600, 1392, 1182 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.61 (s, 3H), 6.64 (dd, *J* = 7.9 Hz, *J* = 1.0 Hz, 1H), 6.82−7.08 (m, 2H), 6.99 (dd, *J* = 7.5 Hz, *J* = 1.6 Hz, 1H), 7.16 (dd, *J* = 7.9 Hz, *J* = 4.7 Hz, 1H), 7.41−7.77 (m, 4H), 7.79 (dd, *J* = 7.9 Hz, *J* = 1.7 Hz), 8.36−8.40 (m, 2H), 8.49 (dd, *J* = 4.7 Hz, *J* = 1.7 Hz, 1H). EI-MS (70 eV); *m*/*z* (%): 392 (43) [M$^{+\bullet}$], 251 (25), 131 (73), 77 (100). Anal. ($C_{21}H_{16}N_2O_4S$) × 1/2 Et_2O: calcd. C 64.29, H 4.54, N 6.81; found C 6.27, H 4.27, N 6.58.

3-Methoxyphenyl-(1-phenylsulfonyl-1*H*-(pyrrolo[2,3-b]-pyridin-2-yl))-methanone (61a): colorless crystals, mp 138−140 °C. IR (KBr): 3031, 2964, 2836, 1656, 1605, 1256 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.80 (s, 3H), 6.76 (s, 1H), 6.82−7.08 (m, 2H), 7.12 (dddd, *J* = 8.2 Hz, *J* = 2.6 Hz, *J* = 1.1 Hz, *J* = 0.3 Hz, 1H), 7.20 (dd, *J* = 8.0 Hz, *J* = 4.8 Hz, 1H), 7.33 (ddd, *J* = 8.2 Hz, *J* = 8.0 Hz, *J* = 0.3 Hz, 1H), 7.10−7.18 (m, 2H), 7.35−7.50 (m, 3H), 7.84 (dd, *J* = 8.0 Hz, *J* = 1.7 Hz), 8.27−8.35 (m, 2H), 8.53 (dd, *J* = 4.8 Hz, *J* = 1.7 Hz, 1H). EI-MS (70 eV); *m*/*z* (%): 392 (64) [M$^{+\bullet}$], 251 (100), 135 (27), 77 (96). Anal. ($C_{21}H_{16}N_2O_4S$) C, H, N.

2,4-Dimethoxyphenyl-(1-phenylsulfonyl-1*H*-(pyrrolo-[2,3-b]pyridin-2-yl))-methanone (62a): light beige powder, mp 180−190 °C (dec). IR (KBr): 3064, 3016, 2968, 2838, 1611, 1586, 1339 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.30 (s, 3H), 3.78 (s, 3H), 6.28 (s, 1H), 6.34 (d, *J* = 2.5 Hz, 1H), 6.56 (dd, *J* = 8.6 Hz, *J* = 2.4 Hz, 1H), 7.14 (dd, *J* = 7.9 Hz, *J* = 4.8 Hz, 1H), 7.30−7.40 (m, 2H), 7.44−7.50 (m, 2H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.73 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz), 8.05−8.18 (m, 1H), 8.44 (dd, *J* = 4.8 Hz, *J* = 1.6 Hz, 1H). EI-MS (70 eV); *m*/*z* (%): 422 (65) [M$^{+\bullet}$], 405 (30), 254 (24), 165 (27), 138 (100). Anal. ($C_{22}H_{18}N_2O_5S$) × 1/3 H_2O: calcd. C 61.67, H 4.39, N 6.54; found C 61.79, H 4.37, N 6.25.

3,4,5-Trimethoxyphenyl-(1-phenylsulfonyl-1*H*-(pyrrolo-[2,3-b]pyridin-2-yl))-methanone (63a): pale yellow powder, mp 180−181 °C. IR (KBr): 3060, 2973, 1653, 1584, 1344 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.88 (s, 6H), 3.97 (s, 3H), 6.84 (s, 1H), 7.25−7.31 (m, 2H), 7.29 (s, 2H), 7.53−7.68 (m, 3H), 8.42−8.47 (m, 2H), 8.44 (dd, *J* = 4.8 Hz, *J* = 1.6 Hz, 1H). EI-MS (70 eV); *m*/*z* (%): 452 (100) [M$^{+\bullet}$], 312 (75), 281 (39), 77 (42). Anal. ($C_{23}H_{20}N_2O_6S$) C, H, N.

2-Methoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-yl)-methanone (64a): colorless crystals, 44%, mp 197−198 °C. IR (KBr): 3095, 2975, 2838, 1659, 1595, 1376, 1171 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.83 (s, 3H), 3.85 (s, 3H), 6.90−6.93 (m, 1H), 6.96 (s, 1H), 7.09−7.18 (m, 2H), 7.59−7.66 (m, 4H), 7.71−7.78 (m, 1H), 7.96−7.80 (m, 2H), 8.31−8.35 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 422 (100) [M$^{+\bullet}$], 281 (38), 250 (51), 161 (56), 135 (44), 77 (68). Anal. ($C_{22}H_{18}N_2O_5S$) C, H, N.

3-Methoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-yl)-methanone (65a): colorless crystals, 66%, mp 147−149 °C. IR (KBr): 3089, 2946, 2840, 1663, 1596, 1376, 1169 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.84 (s, 3H), 3.88 (s, 3H), 6.95−6.99 (m, 1H), 7.25 (s, 1H), 7.31−7.36 (m, 1H), 7.42−7.55 (m, 3H), 7.62−7.69 (m, 2H), 7.74−7.80 (m, 1H), 7.97−8.01 (m, 2H), 8.36−8.40 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 422 (51) [M$^{+\bullet}$], 281 (100), 265 (14), 135 (24), 77 (55). Anal. ($C_{22}H_{18}N_2O_5S$) C, H, N.

2,4-Dimethoxyphenyl-(5-methoxy-1-phenylsulfonyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-yl)-methanone (66a): colorless crystals, 14%, mp 132 °C. IR (KBr): 3062, 2944, 2852, 1634, 1582, 1366, 1171 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.60 (s, 3H), 3.84 (s, 3H), 3.87 (s, 3H), 6.63−6.69 (m, 2H), 6.85−6.89 (m, 2H), 7.59−7.76 (m, 4H), 7.64−7.99 (m, 2H), 8.27−8.31 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 452 (83) [M$^{+\bullet}$], 311 (100), 280 (78), 173 (92), 77 (37). Anal. ($C_{23}H_{20}N_2O_6S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-yl-(3,4,5-trimethoxyphenyl)-methanone (67a): colorless crystals, 73%, mp 190−191 °C. IR (KBr): 3072, 2946, 2840, 1659, 1580, 1374, 1174 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.82 (s, 9H), 3.89 (s, 3H), 6.96−6.99 (m, 1H), 7.23 (s, 2H), 7.29 (s, 1H), 7.64−7.70 (m, 3H), 7.75−7.80 (m, 1H), 8.01−8.05 (m, 2H), 8.39−8.43 (m, 1H). EI-MS (70 eV); *m*/*z* (%): 482 (94) [M$^{+\bullet}$], 342 (100), 326 (22), 310 (49), 77 (46). Anal. ($C_{24}H_{22}N_2O_7S$) C, H, N.

Cyclopropyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (68a): colorless crystals, mp 118−120 °C. IR (KBr): 3064, 2934, 1669, 1615 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.05−1.14 (m, 4H), 2.63−2.74 (m, 1H), 3.70 (s, 3H), 7.08−7.20 (m, 2H), 7.49−7.72 (m, 4H), 7.85−7.99 (m, 3H). EI-MS (70 eV); *m*/*z* (%): 355 (100) [M$^{+\bullet}$], 287 (40), 214 (51), 146 (39), 77 (38). Anal. ($C_{19}H_{17}NO_4S$) C, H, N.

Cyclobutyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (69a): colorless crystals, mp 146−147 °C. IR (KBr): 3023, 2990, 2944, 1676, 1615 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.72−2.34 (m, 6H), 4.06 (quint, *J* = 8.3 Hz, 1H), 7.08−7.19 (m, 2H), 7.39 (d, *J* = 0.5 Hz, 1H), 7.57−7.75 (m, 3H),

7.90−7.97 (m, 3H). EI-MS (70 eV); *m/z* (%): 369 (85) [$M^{+\bullet}$], 314 (30), 287 (15), 229 (28), 174 (100). Anal. ($C_{20}H_{19}NO_4S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1*H*-2-indolyl-(1-naphthalenyl)-methanone (70a): colorless crystals, mp 225−228 °C. IR (KBr): 3071, 3008, 2961, 1652, 1613 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 7.11−7.23 (m, 3H), 7.56−7.79 (m, 7H), 7.92−7.99 (m, 3H), 8.07−8.12 (m, 1H), 8.20−8.27 (m, 1H), 8.60−8.67 (m, 1H). EI-MS (70 eV); *m/z* (%): 441 (24) [$M^{+\bullet}$], 300 (100), 257 (19), 228 (12). Anal. ($C_{26}H_{19}NO_4S$) C, H, N.

5-Methoxy-1-phenylsulfonyl-1*H*-2-indolyl-(2-pyridinyl)-methanone (71a): colorless crystals, 75%, mp 207 °C. IR (KBr): 3073, 2966, 2836, 1671, 1615, 1584, 1370, 1169 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 7.04−7.09 (m, 1H), 7.16−7.17 (m, 1H), 7.27 (s, 1H), 7.53−7.59 (m, 2H), 7.63−7.72 (m, 2H), 7.79−7.85 (m, 3H), 8.05−8.16 (m, 2H), 8.70−8.73 (m, 1H). EI-MS (70 eV); *m/z* (%): 492 (9) [$M^{+\bullet}$], 251 (100), 208 (11), 179 (9), 77 (15). Anal. ($C_{21}H_{16}N_2O_4S$) C, H, N.

4-Isochinolinyl-(5-methoxy-1-phenylsulfonyl-1*H*-2-indolyl)-methanone (72a): yellow crystals, 36%, mp 189−190 °C. IR (KBr): 3064, 2962, 2836, 1652, 1615, 1569, 1362, 1175 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.78 (s, 3H), 7.16−7.21 (m, 2H), 7.37 (s, 1H), 7.60−7.67 (m, 2H), 7.71−7.77 (m, 1H), 7.82−8.03 (m, 5H), 8.31−8.34 (m, 1H), 8.59−8.64 (m, 2H), 9.58 (s, 1H). EI-MS (70 eV); *m/z* (%): 442 (34) [$M^{+\bullet}$], 301 (100), 285 (14), 258 (25), 77 (27). Anal. ($C_{25}H_{18}N_2O_4S$) C, H, N.

Removal of the Phenylsulfonyl Protection Group to Form (1*H*-2-Indolyl)-phenyl-methanones (IV): Procedure D: The N-protected methanone derivative **IVa** (1.8 mmol) was heated in ethanol (40 mL) and 10% aq NaOH (20 mL) under reflux for 12 h. After the sample was cooled, the solution was poured into brine (100 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure to leave the crude product, which was subjected to column chromatography (SiO_2; CH_2Cl_2). Thus, compounds **1**−**21**, **28**−**34**, **36**, **37**, **40**−**76** were prepared.

Procedure E: A mixture of the N-protected methanone derivative **IVa** (1.8 mmol) and TBAF (tetrabutylammonium fluoride trihydrate) (0.79 g, 2.5 mmol) in THF/MeOH 1:1 (20 mL) was gently refluxed. When TLC indicated that the reaction was completed (30 min − 4 h), part of the solvent was removed to allow precipitation of the yellow product. Thus, compounds **22**, **24**, **26**, **35**, **38**, and **39** were prepared.

General Procedure for the Preparation of the Amino Compounds 23, 25, and 27: The respective nitro compound (**22**, **24**, or **26**) (1.7 mmol) was dissolved in dry methanol (5 mL). 10% Pd/C (0.4 g) was added, and the flask was connected to a balloon, filled with dry hydrogen. The mixture was stirred for 24 h at room temperature. When TLC analysis proved that the reaction was completed, the mixture was filtered and the solvent was removed in vacuo. The residue was purified by chromatography (SiO_2, CH_2Cl_2) to give the desired amino compound.

5-Methoxy-1*H*-2-indolyl-phenyl-methanone (1): light yellow needles, 90%, mp 162 °C. IR (KBr): 3311, 2836, 1625, 1600 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 6.96−7.03 (m, 2H), 7.15−7.16 (m, 1H), 7.39−7.43 (m, 1H), 7.56−7.72 (m, 3H), 7.90−7.94 (m, 2H), 11.86 (br. s, 1H). EI-MS (70 eV); *m/z* (%): 251 (100) [$M^{+\bullet}$]. Anal. ($C_{16}H_{13}NO_2$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(2-methoxyphenyl)-methanone (2): beige crystals, 87%, mp 127 °C. IR (KBr): 3303, 3070, 2964, 2834, 1620, 1524 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.73 (s, 3H), 3.75 (s, 3H), 6.67 (s, 1H), 6.93−6.98 (m, 1H), 7.04−7.10 (m, 2H), 7.17−7.21 (m, 1H), 7.35−7.41 (m, 2H), 7.50−7.57 (m, 1H), 11.77 (s, 1H). EI-MS (70 eV); *m/z* (%): 281 (100) [$M^{+\bullet}$], 263 (14), 173 (27), 161 (29), 77 (19). Anal. ($C_{17}H_{15}NO_3$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(3-methoxyphenyl)-methanone (3): yellow crystals, 8%, mp 147−148 °C. IR (KBr): 3294, 3066, 2962, 2834, 1630, 1605, 1576 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 3.86 (s, 3H), 6.96−7.01 (m, 1H), 7.05−7.06 (m, 1H), 7.16−7.17 (m, 1H), 7.22−7.27 (m, 1H), 7.38−7.42 (m, 2H), 7.47−7.51 (m, 2H), 11.85 (s, 1H). EI-MS (70 eV); *m/z* (%): 281 (100) [$M^{+\bullet}$], 266 (23), 158 (19), 130 (14). Anal. ($C_{17}H_{15}NO_3$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(4-methoxyphenyl)-methanon (4): beige crystals, 86%, mp 165 °C. IR (KBr): 3276, 3062, 2956, 2836, 1625, 1572, 1509 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 3.88 (s, 3H), 6.94−6.99 (m, 1H), 7.02−7.03 (m, 1H), 7.09−7.16 (m, 3H), 7.39−7.41 (m, 1H), 7.92−7.98 (m, 2H), 11.78 (s, 1H). EI-MS (70 eV); *m/z* (%): 281 (100) [$M^{+\bullet}$], 173 (54), 158 (42), 77 (13). Anal. ($C_{17}H_{15}NO_3$) C, H, N.

2,3-Dimethoxyphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (5): yellow crystals, 88%, mp 172−173 °C. IR (KBr): 3317, 2943, 2840, 1629, 1580, 1268 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.67 (s, 3H), 3.72 (s, 3H), 3.87 (s, 3H), 6.68−6.69 (m, 1H), 6.94−7.01 (m, 2H), 7.08−7.09 (m, 1H), 7.15−7.26 (m, 2H), 7.35−7.38 (m, 1H), 11.82 (br. s, 1H). EI-MS (70 eV); *m/z* (%): 311 (100) [$M^{+\bullet}$], 293 (35), 280 (27), 119 (23). Anal. ($C_{18}H_{17}NO_4$) C, H, N.

2,4-Dimethoxyphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (6): colorless crystals, 81%, mp 160−161 °C. IR (KBr): 3286, 2960, 2836, 1623, 1599, 1501 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.74 (s, 3H), 3.75 (s, 3H), 3.86 (s, 3H), 6.61−6.66 (m, 1H), 6.71 (s, 2H), 6.92−6.96 (m, 1H), 7.08−7.09 (m, 1H), 7.34−7.42 (m, 2H), 11.69 (br. s, 1H). EI-MS (70 eV); *m/z* (%): 311 (86) [$M^{+\bullet}$], 280 (6), 173 (100), 165 (18). Anal. ($C_{18}H_{17}NO_4$) C, H, N.

3,4-Dimethoxyphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (7): yellow crystals, 59%, mp 187 °C. IR (KBr): 3298, 3089, 2964, 2834, 1596, 1515 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 3.85 (s, 3H), 3.87 (s, 3H) 6.93−6.97 (m, 1H), 7.06 (s, 1H), 7.11−7.14 (m, 2H), 7.37−7.40 (m, 1H), 7.46−7.47 (m, 1H), 7.59−7.64 (m, 1H), 11.77 (br. s, 1H). EI-MS (70 eV); *m/z* (%): 311 (100) [$M^{+\bullet}$], 173 (60), 158 (32), 130 (14). Anal. ($C_{18}H_{17}NO_4$) C, H, N.

3,5-Dimethoxyphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (8): yellow needles, 67%, mp 141−142 °C. IR (KBr): 3309, 3008, 2943, 2840, 1611, 1592 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 3.82 (s, 6H), 6.78−6.80 (m, 1H), 6.98−7.00 (m, 3H), 7.07 (s, 1H), 7.15−7.16 (m, 1H), 7.37−7.40 (m, 1H), 11.83 (br. s, 1H). EI-MS (70 eV); *m/z* (%): 311 (100) [$M^{\bullet+}$], 296 (21), 158 (22), 130 (11). Anal. ($C_{18}H_{17}NO_4$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(2,3,4-trimethoxyphenyl)-methanone (9): yellow crystals, 85%, mp 156 °C. IR (KBr): 3298, 3064, 2941, 2842, 2833, 1623, 1596, cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 6H), 3.80 (s, 3H), 3.88 (s, 3H), 6.76 (s, 1H), 6.90−6.99 (m, 2H), 7.10−7.12 (m, 1H), 7.21−7.25 (m, 1H), 7.36−7.39 (m, 1H), 11.77 (br. s, 1H). EI-MS (70 eV); *m/z* (%): 341 (100) [$M^{\bullet+}$], 323 (23), 173 (55), 161 (37). Anal. ($C_{19}H_{19}NO_5$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(2,3,5-trimethoxyphenyl)-methanone (10): yellow crystals, 84%, mp 198 °C. IR (KBr): 3355, 3068, 2954, 2834, 1686, 1636, 1528 cm^{-1}.^{1}H-NMR (DMSO-d_6): δ 3.72 (s, 3H), 3.73 (s, 6H), 3.88 (s, 3H), 6.75−6.76 (m, 1H), 6.82 (s, 1H), 6.90−6.95 (m, 1H), 7.02 (s, 1H), 7.07−7.08 (m, 1H), 7.33−7.36 (m, 1H), 11.67 (br. s., 1H). EI-MS (70 eV); *m/z* (%): 341 (100) [$M^{\bullet+}$], 323 (41), 310 (17), 173 (36), 168 (89), 161 (33). Anal. ($C_{19}H_{19}NO_5$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(3,4,5-trimethoxyphenyl)-methanone (11): yellow crystals, mp 210−211 °C. IR (KBr): 3291, 3073, 2952, 1605, 1574 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 3.79 (s, 3H), 3.88 (s, 6H), 6.95−7.00 (m, 1H), 7.14−7.17 (m, 2H), 7.22 (s, 2H), 7.38−7.42 (m, 1H), 11.85 (s, 1H). EI-MS (70 eV); *m/z* (%): 341 (100) [$M^{\bullet+}$], 310 (6), 195 (5), 173 (32), 158 (14). Anal. ($C_{19}H_{19}NO_5$) C, H, N.

5-Methoxy-1*H*-2-indolyl(2-methylphenyl)-1-methanone (12): yellow crystals, 83%, mp 120 °C. IR (KBr): 3309, 1742, 1634 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.30 (s, 3H), 3.72 (s, 3H), 6.67 (s, 1H), 6.44−6.99 (m, 1H), 7.08−7.09 (m, 1H), 7.42−7.52 (m, 5H), 11.85 (s, 1H). EI-MS (70 eV); *m/z* (%): 265 (100) [$M^{+\bullet}$], 250 (25), 158 (9). Anal. ($C_{17}H_{15}NO_2$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(4-methylphenyl)-methanone (13): light yellow needles, 56%, mp 200 °C. IR (KBr): 3295, 3066, 2968, 2838, 1624, 1609, 1522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.42 (s, 3H), 3.75 (s, 3H), 6.96 (dd, J = 2.4, 9.0

Hz, 1H), 7.01 (s, 1H), 7.14 (d, J = 2.4 Hz, 1H), 7.37−7.41 (m, 3H), 7.81 (s, 1H), 7.84 (s, 1H), 11.81 (br. s, 1H). EI-MS (70 eV); m/z (%): 265 (100) [$M^{+\bullet}$], 250 (22), 130 (10), 91 (12). Anal. ($C_{17}H_{15}NO_2$) C, H, N.

2,5-Dimethylphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (14): yellow needles, 64%, mp 152−153 °C. IR (KBr): 3328, 3060, 2993 2833, 1634, 1620, 1522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.26 (s, 3H), 2.34 (s, 3H), 3.74 (s, 3H), 6.70 (d, J = 3.9 Hz, 1H), 6.98 (dd, J = 2.4, 9.0 Hz, 1H), 7.11 (d, J = 2.4 Hz, 1H), 7.22−7.41 (m, 4H), 11.82 (br. s, 1H). EI-MS (70 eV); m/z (%): 279 (100) [$M^{+\bullet}$], 262 (26), 132 (13), 77 (7). Anal. ($C_{18}H_{17}NO_2$) C, H, N.

3-Benzyloxyphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (15): light yellow crystals, 92%, mp 150−151 °C. IR (KBr): 3294, 3068, 2956, 2832, 1629, 1600, 1528 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 5.22 (s, 2H), 6.88−6.89 (m, 1H), 6.95−6.99 (m, 1H), 7.10−7.11 (m, 1H), 7.30−7.50 (m, 10H), 11.82 (br. s, 1H). EI-MS (70 eV); m/z (%): 357 (32) [$M^{\bullet+}$], 266 (4), 91 (100). Anal. ($C_{23}H_{19}NO_3$) C, H, N.

3-Hydroxyphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (16): Compound **17** (1.00 g, 2.8 mmol) was dissolved in THF/methanol 1/1 (20 mL). Ammonium formate (0.5 g, 8 mmol) and 10% Pd/C (0.8 g) was added and the reaction mixture was stirred at 70 °C for 2 h. The catalyst was removed by filtration through a Celite pad and washed with dry methanol (10 mL). The filtrate was washed successively with sat. sodium bicarbonate solution (40 mL) and water (3 × 30 mL), and the product was extracted with CH_2Cl_2 (3 × 30 mL). After the sample was dried (Na_2SO_4), evaporation left the desired alcohol, which was recrystallized from ethyl acetate/ether/petrol ether.

light yellow crystals, 74%, mp 167−168 °C. IR (KBr). ν 3363, 3288, 3070, 2960, 2833, 1619, 1590, 1522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.94−7.07 (m, 3H), 7.15 (m, 1H), 7.28−7.29 (m, 1H), 7.31−7.40 (m, 3H), 9.83 (s, 1H), 11.80 (br. s, 1H). EI-MS (70 eV); m/z (%):267 (100) [$M^{+\bullet}$], 252 (41), 174 (10), 158 (21), 130 (29), 121 (23), 93 (22), 65 (26). Anal. ($C_{16}H_{13}NO_3$) C, H, N.

(3-(5-Methoxy-1*H*-2-indolylcarbonyl)phenyl)propanoate (17): Butanoic acid (0.11 g, 1.0 mmol) and pyridin (1 mL) were added to a solution of **16** in dry ethyl acetate (20 mL). After the sample was stirred for 4 h at room temperature, the mixture was quenched with concentrated hydrochloric acid (5 mL) on ice (20 mL), and the product was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried ($NaSO_4$), and the solvent was removed under reduced pressure. The residue was chromatographed (SiO_2, CH_2Cl_2) to give the title compound, which was crystallized from CH_2Cl_2/hexane.

yellow crystals, 86%, mp. 124 °C. IR (KBr): 3299, 2964, 2842, 1760, 1627, 1586, 1522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 0.95−1.01 (t, J = 7.4 Hz, 3H), 1.61−1.75 (m, J = 7.4, 7.3 Hz, 2H), 2.57−2.63 (t, J = 7.3 Hz, 2H), 3.76 (s, 3H), 6.96−7.04 (m, 2H), 7.15−7.16 (m, 1H), 7.37−7.45 (m, 2H), 7.59−7.66 (m, 2H), 7.78−7.83 (m, 1H), 11.90 (br. s, 1H). EI-MS (70 eV); m/z (%): 337 (95) [$M^{+\bullet}$], 267 (94), 71 (75), 43 (100). Anal. ($C_{20}H_{19}NO_4$): C, H, N.

5-Methoxy-1*H*-2-indolyl-(3-trifluoromethoxyphenyl)-methanone (18): yellow crystals, 31%, mp 145−149 °C. IR (KBr): 3294, 1631, 1533, 1289, 841 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.97−7.04 (m, 2H), 7.14−7.16 (m, 1H), 7.38−7.41 (m, 1H), 7.66−7.79 (m, 3H), 7.92−7.96 (m, 1H), 11.92 (s, 1H). EI-MS (70 eV); m/z (%): 335 (100) [$M^{+\bullet}$]. Anal. ($C_{17}H_{12}F_3NO_3$) C, H, N.

3-(Trifluoromethylthio)phenyl-(5-methoxy-1*H*-2-indolyl)-methanone (19): yellow crystals, 48%, mp >145 °C. IR (KBr): 3291, 1652, 1518, 1323, 1176, 754 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.97−7.03 (m, 2H), 7.14−7.15 (m, 1H), 7.38−7.42 (m, 1H), 7.72−7.78 (m, 1H), 8.00−8.03 (m, 1H), 8.10−8.14 (m, 2H), 11.94 (s, 1H). EI-MS (70 eV); m/z (%): 351 (100) [$M^{+\bullet}$]. Anal. ($C_{17}H_{12}F_3NO_2S$) C, H, N.

3-(Difluoromethylthio)phenyl-(5-methoxy-1*H*-2-indolyl)-methanone (20): yellow crystals, 54%, mp 128−129 °C. IR (KBr): 3305, 1647, 1514, 1302, 748 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.96−7.04 (m, 2H), 7.14−7.15 (m, 1H), 7.38−8.04 (m, 5H), 7.60 (t, SCHF2, JHF = 55.73 Hz, 1H), 11.92 (s, 1H). EI-MS (70 eV); m/z (%): 333 (100) [$M^{+\bullet}$]. Anal. ($C_{17}H_{13}F_2NO_2$ S) C, H, N.

3-Trifluoromethylphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (21): yellow crystals, 24%, mp 193−195 °C. IR (KBr): 3307, 1622, 1526, 764 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.74 (s, 3H), 6.96−7.03 (m, 2H), 7.15−7.16 (m, 1H), 7.38−7.42 (m, 1H), 7.78−7.85 (m, 1H), 8.02−8.05 (m, 1H), 8.13 (s, 1H), 8.18−8.22 (m, 1H), 11.96 (s, 1H). EI-MS (70 eV); m/z (%): 319 (100) [$M^{\bullet+}$], 304 (37), 173 (15), 145 (20). Anal. ($C_{17}H_{12}F_3NO_2$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(2-nitrophenyl)-methanone (22): yellow crystals, 40%, mp 185−187 °C. IR (KBr): 3299, 3072, 2985, 2838, 1609, 1530, 1345 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.73 (s, 3H), 6.69 (s, 1H), 7.01 (dd, J = 2.4, 9.0 Hz, 1H), 7.07−7.08 (m, 1H), 7.40 (d, J = 9.0 Hz, 1H), 7.79−7.95 (m, 3H), 8.23−8.27 (m, 1H), 12.04 (br. S, 1H). EI-MS (70 eV); m/z (%): 296 (65) [$M^{\bullet+}$], 162 (100), 134 (22), 104 (37), 76 (17). Anal. ($C_{16}H_{12}N_2O_4$) C, H, N.

2-Aminophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (23): yellow needles, 83%, mp 144−145 °C. IR (KBr): 3486, 3311, 3062, 2952, 2830, 1615, 1584 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3 H), 6.60−6.67 (m, 3H), 6.83−6.96 (m, 3H), 7.15 (d, J = 2.4 Hz, 1H), 7.26−7.41 (m, 2H), 7.82−7.86 (m, 1H), 11.69 (br. s, 1H). EI-MS (70 eV); m/z (%): 266 (100) [$M^{\bullet+}$], 238 (49), 223 (26), 195 (14), 120 (17), 92 (21), 84 (32). Anal. ($C_{16}H_{14}N_2O_2$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(3-nitrophenyl)-methanone (24): yellow crystals, 85%, mp 221−222 °C. IR (KBr): 3326, 3089, 2950, 2832, 1603, 1520, 1343 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 6.98−7.03 (m, 1H), 7.11−7.15 (m, 2H), 7.39−7.43 (m, 1H), 7.84−7.90 (m, 1H), 8.31−8.35 (m, 1H), 8.48−8.52 (m, 1H), 8.59−8.61 (m, 1H), 12.00 (br. s, 1H). EI-MS (70 eV); m/z (%): 296 (100) [$M^{\bullet+}$], 281 (31), 174 (23), 119 (14). Anal. ($C_{16}H_{12}N_2O_4$) C, H, N.

3-Aminophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (25): orange crystals, 79%, mp 221−222 °C. IR (KBr): 3419, 3327, 3056, 2997, 2833, 1619, 1600, 1490 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3 H), 5.39 (s, 2H), 6.80−6.84 (m, 1H), 6.93−7.05 (m, 3H), 7.10−7.22 (m, 3H), 7.36−7.39 (m, 1H), 11.75 (s, 1H). EI-MS (70 eV); m/z (%): 266 (100) [$M^{+\bullet}$], 251 (17), 158 (16), 130 (14), 92 (16). Anal. ($C_{16}H_{14}N_2O_2$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(2-methyl-3-nitrophenyl)-methanone (26): yellow crystals, 55%, mp 199−200 °C. IR (KBr): 3340, 3076, 2935, 2833, 1622, 1524, 1358 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.36 (s, 3H), 3.74 (s, 3 H), 6.74 (s, 1H), 6.99−7.03 (m, 1H), 7.09−7.10 (m, 1H), 7.39−7.42 (m, 1H), 7.58−7.64 (m, 1H), 7.81−7.85 (m, 1H), 8.08−8.12 (m, 1H), 12.02 (br. s, 1H). EI-MS (70 eV); m/z (%): 310 (100) [$M^{+\bullet}$], 293 (14), 147 (14), 119 (12). Anal. ($C_{17}H_{14}N_2O_4$) C, H, N.

3-Amino-2-methylphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (27): brown crystals, 56%, mp 163−165 °C. IR (KBr): 3431, 3317, 3074, 2935, 2840, 1617, 1590 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.97 (s, 3H), 3.72 (s, 3H), 5.08 (s, 2H), 6.63−6.67 (m, 2H), 6.77−6.81 (m, 1H), 6.93−7.09 (m, 3H), 7.27−7.38 (m, 1H), 11.75 (s, 1H). EI-MS (70 eV); m/z (%): 280 (100) [$M^{+\bullet}$], 265 (19), 106 (17). Anal. ($C_{17}H_{16}N_2O_2$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(3-methoxy-2-nitrophenyl)-methanone (28): yellow crystals, 83%, mp 212 °C (dec). IR (KBr): 3332, 3101, 3004, 2956, 2844, 1615, 1603, 1524, 1354 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.76 (s, 3H), 3.98 (s, 3 H), 6.94 (m, 1H), 7.02 (dd, J = 2.4, 9.0 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H), 7.39 (d, J = 9.0 Hz, 1H), 7.44−7.48 (m, 1H), 7.60−7.64 (m, 1H), 7.73−7.79 (m, 1H), 11.98 (br. s, 1H). EI-MS (70 eV); m/z (%): 326 (42) [$M^{+\bullet}$], 162 (100), 119 (20), 76 (13). Anal. ($C_{17}H_{14}N_2O_5$) C, H, N.

4-Ethylphenyl-(5-methoxy-1*H*-indol-2-yl)-methanone (29): yellow crystals, 52%, mp 154−155 °C. IR (KBr): ν = 3317, 2833, 1613, 1601, 1522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.25 (t, J = 7.6 Hz, 3H), 2.73 (q, J = 7.6 Hz, 2H), 3.77 (s, 3H), 6.98 (dd, J = 2.4, 9.0 Hz, 1H), 7.04 (s, 1H), 7.15 (d, J = 2.4 Hz, 1H), 7.38−7.44 (m, 3H), 7.85 (s, 1H), 7.88 (s, 1H), 11.82 (br. s, 1H). EI-MS (70 eV); m/z (%): 279 (100) [$M^{+\bullet}$], 264 (20), 250 (40), 158 (41), 130 (25). Anal. ($C_{19}H_{19}NO_2$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(4-propylphenyl)-methanone (30): yellow needles, 70%, mp 145−146 °C. IR (KBr): 3299, 3068, 3035, 2989, 2833, 1624, 1609, 1524 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 0.94 (t, J = 7.3 Hz, 3H), 1.66 (m, 2H), 2.68 (t, J = 7.6 Hz, 2H), 3.77 (s, 3H), 6.98 (dd, J = 2.4, 9.9 Hz, 1H), 7.04 (s, 1H), 7.16 (d, J = 2.4 Hz, 1H), 7.39−7.42 (m, 3H), 7.84 (s, 1H), 7.88 (s, 1H), 11.82 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 293 (100) [M$^{+\bullet}$], 278 (15), 250 (46), 158 (40), 130 (24), 91 (13). Anal. ($C_{19}H_{19}NO_2$) C, H, N.

4-*tert*-Butylphenyl-(5-methoxy-1*H*-2-indolyl)-methanone (31): yellow crystals, mp 204−207 °C. IR (KBr): 3293, 3129, 3006, 2965, 1605, 1522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.35 (s, 9H), 3.76 (s, 3H), 6.95−7.06 (m, 3H), 7.40 (d, J = Hz, 1H), 7.58−7.64 (m, 2H), 7.84−7.91 (m, 2H), 11.82 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 307 (100) [M$^{+\bullet}$], 292 (17), 250 (15), 174 (11), 158 (12). Anal. ($C_{20}H_{21}NO_2$) C, H, N.

5-Methoxy-1*H*-2-indolyl-(4-pentyloxyphenyl)-methanone (32): yellow crystals, mp 139−141 °C. IR (KBr): 3290, 3064, 2930, 1624, 1601 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 0.90 (t, J = 6.9 Hz, 3H), 1.30−1.47 (m, 4H), 1.75 (quint, J = 6.9 Hz, 2H), 3.77 (s, 3H), 4.09 (t, J = 6.8 Hz, 2H), 6.93−7.04 (m, 2H), 7.07−7.17 (m, 3H), 7.40 (m, 1H), 7.89−7.96 (m, 2H), 11.75 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 337 (100) [M$^{+\bullet}$], 267 (9), 173 (37), 158 (17). Anal. ($C_{21}H_{23}NO_3$) C, H, N.

4-Chlorophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (33): yellow crystals, mp 191−193 °C. IR (KBr): 3305, 3067, 2952, 1629, 1591 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.96−7.07 (m, 2H), 7.15 (d, J = 2.3 Hz, 1H), 7.40 (d, J = 9.0 Hz, 1H), 7.62−7.69 (m, 2H), 7.90−7.97 (m, 2H), 11.90 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 285 (100) [M$^{+\bullet}$], 270 (30), 158 (18), 139 (16). Anal. ($C_{16}H_{12}ClNO_2$) C, H, N.

4-Bromophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (34): yellow crystals, mp 188−190 °C. IR (KBr): 3305, 3052, 2950, 1630, 1588 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.97−7.06 (m, 2H), 7.14 (d, J = 2.4 Hz, 1H), 7.41 (d, J = 9.0 Hz, 1H), 7.76−7.89 (m, 4H), 11.90 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 329 (100) [M$^{+\bullet}$], 314 (28), 250 (13), 207 (19), 158 (30). Anal. ($C_{16}H_{12}BrNO_2$) C, H, N.

2-Fluorophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (35): yellow crystals, 30%, mp 145 °C. IR (KBr): 3313, 1632, 1526, 1231, 754 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.73 (s, 3H), 6.84 (s, 1H), 6.96−7.00 (m, 1H), 7.10−7.11 (m, 1H), 7.33−7.43 (m, 3H), 7.60−7.71 (m, 2H), 11.94 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 269 (100) [M$^{+\bullet}$], 254 (36), 123 (19). Anal. ($C_{16}H_{12}FNO_2$) C, H, N.

3-Fluorophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (36): yellow crystals, 49%, mp 154−156 °C. IR (KBr): 3319, 1630, 1519, 1234, 752 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.95−7.00 (m, 1H), 7.05 (s, 1H), 7.13−7.14 (m, 1H), 7.37−7.40 (m, 1H), 7.48−7.77 (m, 4H), 11.88 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 269 (100) [M$^{+\bullet}$]. Anal. ($C_{16}H_{12}FNO_2$) C, H, N.

4-Fluorophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (37): yellow crystals, 88%, mp 168 °C. IR (KBr): 3397, 1626, 1601, 1588, 1236, 762 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.95−7.03 (m, 2H), 7.13−7.14 (m, 1H), 7.37−7.43 (m, 3H), 7.96−8.02 (m, 2H), 11.85 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 269 (100) [M$^{+\bullet}$], 254 (34), 123 (21). Anal. ($C_{16}H_{12}FNO_2$) C, H, N.

2,6-Difluorophenyl-(5-methoxy-1-1*H*-2-indolyl)-methanone (38): yellow crystals, 59%, mp 165−172 °C. IR (KBr): 3336, 1626, 1234, 793 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.72 (s, 3H), 6.88 (s, 1H), 6.99−7.04 (m, 1H), 7.09−7.11 (m, 1H), 7.25−7.41 (m, 3H), 7.60−7.73 (m, 1H), 12.07 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 287 (100) [M$^{+\bullet}$], 272 (24), 158 (18). Anal. ($C_{16}H_{11}F_2NO_2$) C, H, N.

2-Chloro-6-fluorophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (39): yellow crystals, 32%, mp 168−170 °C. IR (KBr): 3328, 3078, 2958, 2834, 1618, 1528 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.73 (s, 3H), 6.81 (s, 1H), 7.03 (dd, J = 2.5, 9.0 Hz, 1H), 7.10 (d, J = 2.5 Hz, 1H), 7.37−7.53 (m, 3H), 12.09 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 303 (100) [M$^{+\bullet}$], 288 (19), 158 (24), 130 (20). Anal. ($C_{16}H_{11}NO_2ClF$) C, H, N.

3,4-Dichlorophenyl-(5-methoxy-1*H*-2-indolyl)-methanone (40): yellow crystals, mp 190−192 °C. IR (KBr): 3316, 2988, 2830, 1620, 1549 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.80 (s, 3H), 6.93−7.18 (m, 4H), 7.80−7.92 (m, 2H), 8.03−8.12 (m, 1H), 11.95 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 319 (100) [M$^{+\bullet}$], 304 (31), 241 (10), 173 (16), 130 (15). Anal. ($C_{16}H_{11}Cl_2NO_2$ × 0.4 CH_2Cl_2) C, H, N.

1*H*-2-Indolyl-phenyl-methanone (41): yellow crystals, mp 145−147 °C. IR (KBr): 3314, 3081, 1669, 1616 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 7.08−7.16 (m, 2H), 7.29−7.37 (m, 1H), 7.48−7.75 (m, 5H), 7.91−7.97 (m, 2H), 11.90 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 221 (100) [M$^{+\bullet}$], 204 (13), 144 (36), 89 (28), 77 (30). Anal. ($C_{15}H_{11}NO$) C, H, N.

1*H*-2-Indolyl-(2-methoxyphenyl)-methanone (42): yellow crystals, mp 129−130 °C. IR (KBr): 3305, 3064, 1634, 1620, 1595 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 6.76−6.79 (m, 1H), 7.02−7.11 (m, 2H), 7.17−7.33 (m, 2H), 7.39−7.58 (m, 3H), 7.64 (d, J = 7.9 Hz, 1H), 11.91 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 251 (100) [M$^{+\bullet}$], 233 (73), 204 (32), 131 (69), 89 (50). Anal. ($C_{16}H_{13}NO_2$ × 0.5 ethyl acetate): calcd. C 73.20, H 5.80, N 4.74; found C 72.97, H 5.48, N 4.92.

1*H*-2-Indolyl-(2,4-dimethoxyphenyl)-methanone (43): yellow crystals, mp 134−135 °C. IR (KBr): 3313, 3060, 2946, 1617, 1591 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.83 (s, 3H), 3.89 (s, 3H), 6.53−6.58 (m, 2H), 6.93−6.97 (m, 1H), 7.10−7.18 (m, 1H), 7.25−7.68 (m, 4H), 9.25 (bs, 1H). EI-MS (70 eV); *m*/*z* (%): 281 (100) [M$^{+\bullet}$], 263 (46), 250 (10), 165 (32), 143 (48), 131 (25). Anal. ($C_{17}H_{15}NO_3$ × 0.25 ethyl acetate): calcd. C 71.27, H 5.65, N 4.62; found C 71.19, H 5.44, N 4.81.

1*H*-2-Indolyl-(3,4,5-trimethoxyphenyl)-methanone (44): yellow crystals, mp 148−150 °C. IR (KBr): 3319, 3011, 2942, 1619, 1582 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.95 (s, 6H), 3.96 (s, 3H), 7.15−7.22 (s, 2H), 7.25−7.28 (m, 2H), 7.35−7.52 (m, 2H), 7.72−7.78 (m,1H), 9.31 (bs, 1H). EI-MS (70 eV); *m*/*z* (%): 311 (100) [M$^{+\bullet}$], 296 (8), 168 (15), 144 (17). Anal. ($C_{18}H_{17}NO_4$ × 0.25 ethyl acetate): calcd. C 68.46, H 5.75, N 4.20; found C 68.11, H 5.39, N 4.42.

2-Methoxyphenyl-(3-methyl-1*H*-2-indolyl)-methanone (45): pale yellow-reddish crystals, 62%, mp 152−153 °C. IR (KBr): 3319, 1637, 1562 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.99 (s, 3H), 3.71 (s, 3H), 7.00−7.63 (m, 8H), 11.39 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 265 (100) [M$^{+\bullet}$], 250 (34). Anal. ($C_{17}H_{15}NO_2$) C, H, N.

3-Methoxyphenyl-(3-methyl-1*H*-2-indolyl)-methanone (46): pale yellow-reddish crystals, 80%, mp 131 °C. IR (KBr): 3340, 1636, 1524 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.25 (s, 3H), 3.81 (s, 3H), 7.04−7.10 (m, 1H), 7.19−7.52 (m, 6H), 7.64−7.67 (m, 1H), 11.44 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 265 (100) [M$^{+\bullet}$], 158 (14). Anal. ($C_{17}H_{15}NO_2$) C, H, N.

2,4-Dimethoxyphenyl-(3-methyl-1*H*-2-indolyl)-methanone (47): pale yellow crystals, 33%, mp 124−126 °C. IR (KBr): 3327, 1629, 1572 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.07 (s, 3H), 3.70 (s, 3H), 3.84 (s, 3H). 6.62−6.69 (m, 2H), 6.99−7.06 (m, 1H), 7.21−7.28 (m, 2H), 7.37−7.40 (m, 1H), 7.58−7.63 (m, 1H), 11.30 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 295 (100) [M$^{+\bullet}$], 165 (23). Anal. ($C_{18}H_{17}NO_3$) C, H, N.

3,4,5-Trimethoxyphenyl-(3-methyl-1*H*-2-indolyl)-methanone (48): pale yellow crystals, 6%, mp 138−144 °C. IR (KBr): 3324, 1639, 1534 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.32 (s, 3H), 3.76 (s, 3H), 3.82 (s, 6H), 7.05 (s,2H) 7.06−7.10 (m, 1H), 7.24−7.28 (m, 1H), 7.30−7.7.44 (m, 1H), 7.64−7.68 (m, 1H), 11.44 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 325 (100) [M$^{+\bullet}$], 294 (35). Anal. ($C_{19}H_{19}NO_4$) C, H, N.

4-Methoxy-1*H*-2-indolyl-(3-methoxyphenyl)-methanone (49): yellow needles, 90%, mp 148 °C. IR (KBr): 3315, 3060, 2941, 2838, 1615, 1574 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.84 (s, 3H), 3.87 (s, 3H), 6.53−6.56 (m, 1H), 7.02−7.08 (m, 2H), 7.20−7.27 (m, 2H), 7.35−7.37 (m, 1H), 7.48−7.51 (m, 2H), 12.00 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 281 (100) [M$^{+\bullet}$], 266 (35), 158 (28), 130 (21), 77 (15). Anal. ($C_{17}H_{15}NO_3$) C, H, N.

2-Methoxyphenyl-(5-methyl-1*H*-2-indolyl)-methanone (50): pale yellow crystals, 85%, mp 165−167 °C. IR (KBr): 3325, 1638, 1574 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.33 (s, 3H), 3.72 (s, 3H), 6.65 (s, 1H), 7.02−7.19 (m, 3H), 7.33−

7.40 (m, 3H), 7.48−7.55 (m, 1H), 11.78 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 265 (100) [M$^{+\bullet}$], 158 (12). Anal. ($C_{17}H_{15}NO_2$) C, H, N.

3-Methoxyphenyl-(5-methyl-1*H*-2-indolyl)-methanone (51): pale yellow crystals, 25%, mp 192−202 °C. IR (KBr): 3316, 1632, 1516 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.42 (s, 3H), 3.82 (s, 3H), 7.05−7.17 (m, 2H), 7.23−7.25 (m, 1H), 7.30−7.47 (m, 3H), 7.87−7.88 (m, 1H), 8.05 (s, 1H), 11.92 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 265 (66) [M$^{+\bullet}$], 158 (100). Anal. ($C_{17}H_{15}NO_2$) C, H, N.

3,4,5-Trimethoxyphenyl-(5-methyl-1*H*-2-indolyl)-methanone (52): pale yellow crystals, 60%, mp 202−203 °C. IR (KBr): 3315, 1627, 1522, 1028, 841, 756 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.36 (s, 3H), 3.76 (s, 3H), 3.86 (s, 6H), 7.11−7.15 (m 2H), 7.20 (s, 2H), 7.36−7.39 (m, 1H), 7.47 (s, 1H), 11.82 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 325 (100) [M$^{+\bullet}$], 168 (34), 158 (32). Anal. ($C_{19}H_{19}NO_4$) C, H, N.

5-Benzyloxy-1*H*-2-indolyl-phenyl-methanone (53): yellow crystals, mp 187−188 °C. IR (KBr): 3299, 3031, 2861, 1600, 1570 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.10 (s, 2H), 7.00−7.10 (m, 2H), 7.22−7.50 (m, 6H), 7.54−7.72 (m, 4H), 7.88−7.94 (m, 2H); 11.90 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 327 (60) [M$^{+\bullet}$], 236 (100), 158 (15), 130 (17), 105 (22), 91 (98). Anal. ($C_{22}H_{17}NO_2$ × 0.15 ethyl acetate): calcd. C 79.70, H 5.39, N 4.11; found C 79.79, H 5.32, N 4.24.

5-Benzyloxy-1*H*-2-indolyl-(2-methoxyphenyl)-methanone (54): colorless powder, mp 150−151 °C. IR (KBr): 3276, 3069, 2937, 2836, 1628, 1518 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.83 (s, 3H), 5.08 (s, 2H), 6.82 (d, J = 1.2 Hz, 1H), 7.01−7.10 (m, 4H), 7.28−7.52 (m, 8H), 9.18 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 357 (67) [M$^{+\bullet}$], 268 (87), 158 (71), 91 (100). Anal. ($C_{23}H_{19}NO_3$) C, H, N.

5-Benzyloxy-1*H*-2-indolyl-(3-methoxyphenyl)-methanone (55): colorless powder, mp 153−154 °C. IR (KBr): 3303, 3062, 2905, 2861, 1629, 1520 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.89 (s, 3H), 5.10 (s, 2H), 7.04−7.18 (m, 4H), 7.30−7.49 (m, 8H), 7.56 (m, 1H), 9.24 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 357 (67) [M$^{+\bullet}$], 268 (87), 158 (71), 91 (100). Anal. ($C_{23}H_{19}NO_3$) C, H, N.

5-Benzyloxy-1*H*-2-indolyl-(4-methoxyphenyl)-methanone (56): yellow crystals, mp 155−157 °C. IR (KBr): 3318, 3017, 2929, 1622, 1589 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.85 (s, 3H), 5.08 (s, 2H), 6.96−7.50 (m, 11H), 7.91 (s, 1H), 7.97 (s, 1H), 11.80 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 357 (78) [M$^{+\bullet}$], 266 (100), 158 (70) 135 (28), 130 (29), 91 (91). Anal. ($C_{23}H_{19}NO_3$ × 0.5 ethyl acetate): calcd. C 74.79, H 5.77, N 3.49; found C 74.73, H 5.24, N 3.77.

5-Benzyloxy-1*H*-2-indolyl-(3,4,5-trimethoxyphenyl)-methanone (57): yellow crystals, mp 165−167 °C. IR (KBr): 3299, 3067, 2977, 1605, 1582 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 3.87 (s, 6H), 5.08 (s, 2H), 7.02−7.07 (m, 1H), 7.13−7.16 (m, 1H), 7.20−7.49 (m, 9H), 11.81 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 417 (61) [M$^{+\bullet}$], 326 (90), 158 (67), 130 (28), 91 (100). Anal. ($C_{25}H_{23}NO_5$) C, H, N.

5-Benzyloxy-1*H*-2-indolyl-(3-chlorophenyl)-methanone (58): yellow crystals, mp 163−165 °C. IR (KBr): 3301, 3062, 2861, 1629, 1566 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.10 (s, 2H), 7.02−7.50 (m, 8H), 7.57−7.98 (m, 5H), 11.95 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 361 (39) [M$^{+\bullet}$], 270 (37), 207 (8), 91 (100). Anal. ($C_{22}H_{16}ClNO_2$ × 0.4 CH_2Cl_2): calcd. C 67.97, H 4.28, N 3.54; found C 67.51, H 4.42, N 3.53.

5-Benzyloxy-1*H*-2-indolyl-(4-chlorophenyl)-methanone (59): yellow crystals, mp 188−190 °C. IR (KBr): 3303, 3035, 2859, 1618, 1589 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 5.10 (s, 2H), 7.02−7.11 (m, 2H), 7.22−7.49 (m, 7H), 7.65 (m, 2H), 7.93 (m, 2H), 11.92 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 361 (28) [M$^{+\bullet}$], 270 (31), 207 (6), 139 (9), 91 (100). Anal. ($C_{22}H_{16}ClNO_2$) C, H, N.

(1*H*-Pyrrolo[2,3-b]pyridin-2-yl)-(2-methoxyphenyl)-methanone (60): beige crystals, mp 211−213 °C. IR (KBr): 3250−2700, 3079, 2980, 2838, 1646, 1602, 1578 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.84 (s, 3H), 6.88 (d, J = 2.1 Hz, 1H), 7.01−7.10 (m, 2H), 7.17 (dd, J = 8.0 Hz, J = 4.7 Hz, 1H), 7.40−7.56 (m, 2H), 8.03 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 8.82 (dd, J = 4.7 Hz, J = 1.6 Hz, 1H), 12.49 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 252 (100) [M$^{+\bullet}$], 234 (35), 135 (34), 133 (52), 77 (31). Anal. ($C_{15}H_{12}N_2O_2$) C, H, N.

(1*H*-Pyrrolo[2,3-b]pyridin-2-yl)−(3-methoxyphenyl)-methanone (61): colorless crystals, mp 166−168 °C. IR (KBr): 3250−2700, 3066, 2971, 2890, 2834, 1644, 1605, 1578 cm^{-1}. ^{1}H-NMR (CDCl3): δ 3.91 (s, 3H), 7.14 (d, J = 2.1 Hz, 1H), 7.18 (ddd, J = 8.2 Hz, J = 2.6 Hz, J = 1.1 Hz, 1H), 7.21 (dd, J = 8.0 Hz, J = 4.7 Hz, 1H), 7.46 (ddd, J = 8.2 Hz, J = 7.6 Hz, J = 0.4 Hz, 1H), 7.52 (dd, J = 2.6 Hz, J = 1.4 Hz, 1H), 7.61 (ddd, J = 7.6 Hz, J = 1.4 Hz, J = 1.1 Hz, 1H), 8.11 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 8.83 (dd, J = 4.7 Hz, J = 1.6 Hz, 1H), 12.52 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 252 (100) [M$^{+\bullet}$], 237 (16), 211 (29), 145 (29), 77 (11). Anal. ($C_{15}H_{12}N_2O_2$ × 1/6 H_2O): calcd. C 70.58, H 4.87, N 10.97; found C 70.62, H 4.93, N 10.95.

(1*H*-Pyrrolo[2,3-b]pyridin-2-yl)−(2,4-dimethoxyphenyl)-methanone (62): colorless powder, mp 206−210 °C (dec). IR (KBr): 3300−2700, 3289, 3068, 2967 1634, 1609, 1559 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.30 (s, 3H), 3.78 (s, 3H), 6.28 (s, 1H), 6.34 (d, J = 2.5 Hz, 1H), 6.56 (dd, J = 8.6 Hz, J = 2.4 Hz, 1H), 7.14 (dd, J = 7.9 Hz, J = 4.8 Hz, 1H), 7.30−7.40 (m, 2H), 7.44−7.50 (m, 2H), 7.71 (d, J = 8.6 Hz, 1H), 7.73 (dd, J = 7.9 Hz, J = 1.6 Hz, 1H), 8.05−8.18 (m, 1H), 8.44 (dd, J = 4.8 Hz, J = 1.6 Hz, 1H). EI-MS (70 eV); *m*/*z* (%): 282 (100) [M$^{+\bullet}$], 264 (38), 165 (46), 150 (17), 132 (34). Anal. ($C_{16}H_{14}N_2O_3$) C, H, N.

(1*H*-Pyrrolo[2,3-b]pyridin-2-yl)−(3,4,5-trimethoxyphenyl)-methanone (63): colorless crystals, mp 204−206 °C. IR (KBr): 3250−2700, 3068, 2962, 2836, 1642, 1605, 1586 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.96 (s, 6H), 3.98 (s, 3H), 7.16 (d, J = 1.9 Hz, 1H), 7.23 (dd, J = 8.0 Hz, J = 4.7 Hz, 1H), 7.30 (s, 2H), 8.13 (dd, J = 4.7 Hz, J = 1.6 Hz, 1H), 8.82 (dd, J = 4.7 Hz, J = 1.6 Hz, 1H), 12.70 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 312 (100) [M$^{+\bullet}$], 297 (16), 281 (25), 145 (16). Anal. ($C_{17}H_{16}N_2O_4$) C, H, N.

2-Methoxyphenyl-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-yl)-methanone (64): colorless needles, 53%, mp 190 °C. IR (KBr): 3294, 3076, 2944, 2840, 1627, 1600, 1522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 3.83 (s, 3H), 6.64 (s, 1H), 6.77−6.81 (m, 1H), 7.04−7.10 (m, 1H), 7.17−7.21 (m, 1H), 7.39−7.43 (m, 1H), 7.50−7.54 (m, 1H), 7.76−7.80 (m, 1H), 12.02 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 282 (100) [M$^{+\bullet}$], 263 (31), 251 (11), 173 (26), 162 (26), 135 (23), 77 (30). Anal. ($C_{16}H_{14}N_2O_3$) C, H, N.

3-Methoxyphenyl-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-yl)-methanone (65): light yellow crystals, 77%, mp 150 °C. IR (KBr): 3297, 3074, 2983, 2836, 1623, 1522 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.85 (s, 3H), 3.87 (s, 3H), 6.80−6.84 (m, 1H), 7.04 (s, 1H), 7.23−7.27 (m, 1H), 7.39−7.40 (m, 1H), 7.49−7.56 (m, 2H), 7.79−7.83 (m, 1H), 12.10 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 282 (100) [M$^{+\bullet}$], 253 (29), 173 (13), 145 (14), 135 (20), 77 (17). Anal. ($C_{16}H_{14}N_2O_3$) C, H, N.

2,4-Dimethoxyphenyl(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-yl)-methanone (66): colorless needles, 46%, mp 100 °C (dec). IR (KBr): 3299, 3095, 3004, 2970, 2840, 1607, 1520 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.75 (s, 3H), 3.84 (s, 3H), 3.85 (s, 3H), 6.61−6.65 (m, 1H), 6.69−6.71 (m, 2H), 6.75−6.78 (m, 1H), 7.41−7.44 (m, 1H), 7.74−7.78 (m, 1H), 11.92 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 312 (100) [M$^{+\bullet}$], 294 (37), 265 (16), 138 (36), 77 (13). Anal. ($C_{17}H_{16}N_2O_4$) C, H, N.

3,4,5-Trimethoxyphenyl-(5-methoxy-1*H*-pyrrolo[3,2-*b*]-pyridin-2-yl)-methanone (67): light yellow needles, 68%, mp 233 °C. IR (KBr): 3303, 2943, 2838, 1623, 1582, 1506 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.77 (s, 3H), 3.88 (s, 9H), 6.79−6.83 (m, 1H), 7.15 (s, 1H), 7.23 (s, 2H), 7.79−7.83 (m, 1H), 12.08 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 342 (100) [M$^{+\bullet}$], 175 (11). Anal. ($C_{18}H_{18}N_2O_5$) C, H, N.

Cyclopropyl-(5-methoxy-1*H*-2-indolyl)-methanone (68): yellow crystals, mp 205−207 °C. IR (KBr): 3307, 2965, 1634, 1526 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 0.97−1.08 (m, 4H), 2.76−2.87 (m, 1H), 3.77 (s, 3H), 6.91−6.97 (m, 1H), 7.11−7.15 (m, 1H), 7.31−7.42 (m, 2H), 11.6 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 215 (100) [M$^{+\bullet}$], 200 (21), 174 (22), 172 (8), 119 (19). Anal. ($C_{13}H_{13}NO_2$) C, H, N.

Cyclobutyl-(5-methoxy-1*H*-2-indolyl)-methanone (69): yellow crystals, mp 175−179 °C. IR (KBr): 3299, 3066, 2938, 1642, 1524 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.75−2.35 (m, 6H), 3.76 (s, 3H), 3.97−4.12 (m, 1H), 6.89−6.96 (m, 1H), 7.10−7.18 (m, 2H), 7.32−7.38 (m, 1H), 11.55 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 229 (100) [$M^{+\bullet}$], 201 (9), 186 (10), 174 (70), 146 (12). Anal. ($C_{14}H_{15}NO_2$) C, H, N.

(5-Methoxy-1*H*-2-indolyl)-1-naphthalenyl-methanone (70): yellow crystals, mp 174−175 °C. IR (KBr): 3301, 3050, 1611, 1574, 1518 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.72 (s, 3H), 6.76 (s, 1H), 6.98−7.12 (m, 2H), 7.40−7.47 (m, 1H), 7.53−7.70 (m, 3H), 7.82−7.89 (m, 1H), 8.03−8.20 (m, 3H), 12.02 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 301 (100) [$M^{+\bullet}$], 300 (47), 284 (13); 158 (11), 127 (26). Anal. ($C_{20}H_{15}NO_2$) C, H, N.

(5-Methoxy-1*H*-indol-2-yl)-2-pyridinyl-methanone (71): yellow crystals, 65%, mp 201 °C. IR (KBr): 3328, 3067, 1649 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.73 (s, 3H), 7.98−8.04 (m, 1H), 8.12−8.22 (m, 2H), 8.31−8.39 (m, 2H), 8.53−8.60 (m, 1H), 8.69−8.71 (m, 1H), 8.83−8.85 (m, 1H), 11.84 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 252 (100) [$M^{+\bullet}$], 237 (18), 173 (88), 158 (49), 77 (13). Anal. ($C_{15}H_{12}N_2O_2$) C, H, N.

4-Isoquinolinyl-(5-methoxy-1-*H*-2-indolyl)-methanone (72): yellow crystals, 75%, mp 228−230 °C. IR (KBr): 3058, 2952, 2827, 1630, 1503 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.73 (s, 3H), 6.88 (m, 1H), 6.98−7.03 (m, 1H), 7.09−7.10 (m, 1H), 7.40−7.44 (m, 1H), 7.75−7.90 (m, 2H), 8.10−8.13 (m, 1H), 8.26−8.30 (m, 1H), 8.83 (s, 1H), 9.53 (s, 1H), 12.07 (br. s, 1H). EI-MS (70 eV); *m*/*z* (%): 302 (100) [$M^{+\bullet}$], 287 (13), 128 (22). Anal. ($C_{19}H_{14}N_2O_2$) C, H, N.

General Procedure for the Preparation of the 5-Methoxy-1*H*-2-indolecarboxamides 73−76: The respective piperazine derivative (2.0 mmol) was dissolved in diethyl ether (15 mL). A solution of 0.49 g (2.33 mmol) 5-methoxy-1*H*-2-indolecarboxylic acid chloride in benzene (10 mL) was added, and the reaction mixture was stirred for 20 h at room temperature. The mixture was poured in 5% aq NaOH (100 mL), and the product was extracted with ethyl acetate (150 mL). After the sample was dried (Na_2SO_4), 95% of the solvent was removed in vacuo and the residue was treated with diethyl ether (50 mL). The resulting colorless crystals were collected by filtration and washed with diethyl ether.

***N*-4-(2-Methoxyphenyl)perhydro-1-pyrazinyl-5-methoxy-1*H*-2-indolecarboxamide (73):** colorless crystals, mp 186.189 °C. IR (KBr): 3284, 2836, 1601 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.98−3.05 (m, 4H), 3.75 (s, 3H), 3.80 (s, 3H), 3.83−3.95 (m, 4H), 6.72−6.77 (m, 1H), 6.82−7.08 (m, 6H), 7.29−7.37 (m, 1H), 11.45 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 365 (39) [$M^{+\bullet}$], 216 (7), 175 (34), 162 (100), 134 (29). Anal. ($C_{21}H_{23}N_3O_3$ × 0.33 ethyl acetate): calcd. C 67.95, H 6.55, N 10.65; found C 67.74, H 6.21, N 10.98.

***N*-4-(2-Pyrazinyl)perhydro-1-pyrazinyl-5-methoxy-1*H*-2-indolecarboxamide (74):** colorless crystals, mp 180−183 °C. IR (KBr): 3268, 2834, 1598 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 3.67−3.76 (m, 4H), 3.77 (s, 3H), 3.83−3.94 (m, 4H), 6.74−6.79 (m, 1H), 6.86 (dd, J1 = 2.5 Hz, J2 = 8.9 Hz, 1H), 7.08 (d, *J* = 2.5 Hz, 1H), 7.32 (d, *J* = 8.9 Hz, 1H), 7.88 (d, *J* = 2.6 Hz, 1H), 8.12 (dd, J1 = 2.6 Hz, J2 = 1.5 Hz, 1H), 8.35 (d, *J* = 1.5 Hz, 1H), 11.48 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 337 (100) [$M^{+\bullet}$], 216 (12), 190 (32), 174 (60), 134 (42). Anal. ($C_{18}H_{19}N_5O_2$ × 0.15 CH_2Cl_2): calcd. C 62.26, H 5.56, N 20.00; found C 62.51, H 5.43, N 20.21.

***N*-4-Methylperhydro-1-pyrazinyl-5-methoxy-1*H*-2-indolecarboxamide (75):** colorless crystals, mp 155−157 °C. IR (KBr): 3237, 2994, 1600 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.21 (s, 3H), 2.37 (t, *J* = 5.1 Hz, 4H), 3.68−3.79 (m, 7H), 6.65−6.70 (m, 1H), 6.80−6.88 (m, 1H), 7.03−7.09 (m, 1H), 7.28−7.36 (m, 1H), 11.43 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 273 (28) [$M^{+\bullet}$], 174 (17), 119 (15), 99 (21), 70 (100). Anal. ($C_{15}H_{19}N_3O_2$ × 0.2 CH_2Cl_2): calcd. C 62.88, H 6.74, N 14.47; found C 63.03, H 6.72, N 14.06.

***N*-4-Phenylmethylperhydro-1-pyrazinyl-5-methoxy-1*H*-2-indolecarboxamide (76):** colorless crystals, mp 164−166 °C. IR (KBr): 3245, 2938, 1603 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.43 (t, *J* = 5.9 Hz), 4H), 3.52 (s, 2H), 3.70−3.80 (m, 7H), 6.68−6.70 (m, 1H), 6.80−6.87 (m, 1H), 7.04−7.07 (m, 1H), 7.23−7.38 (m, 6H), 11.40 (s, 1H). EI-MS (70 eV); *m*/*z* (%): 349 (28) [$M^{+\bullet}$], 216 (15), 174 (30), 146 (74), 91 (100). Anal. ($C_{21}H_{23}N_3O_2$ × 0.2 ethyl acetate): calcd. C 71.34, H 6.76, N 11.45; found C 71.69, H 6.66, N 11.68.

Procedure F: Preparation of N-Substituted Derivatives 77−81: At 0 °C, sodium hydride (60% suspension in paraffin oil) (80 mg, 2.0 mmol) was added to **1** (0.35 g, 1.4 mmol) in 10 mL of anhydrous THF. After 30 min, the alkyl chloride (5.0 mmol) was added, and the reaction mixture was stirred for 10 h at room temperature. Water was carefully added, and the mixture was poured into sat. sodium bicarbonate solution (50 mL). The organic layer was separated, the aqueous layer was extracted with ethyl acetate (3 × 15 mL), and the combined organic layers were dried (Na_2SO_4). Removal of the solvent resulted in yellow crystals that were subjected to flash chromatography (SiO_2; ethyl acetate/hexane).

(5-Methoxy-1-(2-dimethylaminoethyl)-1*H*-2-indolyl)-phenyl-methanone (77): yellow wax, mp 38−40 °C. IR (KBr): 3023, 2948, 2822, 1638, 1597 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.10 (s, 6H), 2.51 (t, *J* = 6.7 Hz, 2H), 3.76 (s, 3H), 4.61 (t, *J* = 6.7 Hz, 2H), 6.85 (s, 1H), 7.01−7.09 (m, 1H), 7.13−7.18 (m, 1H), 7.53−7.73 (m, 4H), 7.82−7.87 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 322 (7) [$M^{+\bullet}$], 264 (1), 251 (6), 58 (100). Anal. ($C_{20}H_{22}N_2O_2$) C, H, N.

(5-Methoxy-1-(3-dimethylaminopropyl)-1*H*-2-indolyl)-phenyl-methanone (78): yellow wax, mp 51−52 °C. IR (KBr): 3050, 2927, 1643, 1597, 1576 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.86 (quint, *J* = 6.9 Hz, 2H), 2.08 (s, 6H), 2.19 (t, *J* = 6.9 Hz, 2H), 3.75 (s, 3H), 4.55 (t, *J* = 7.0 Hz, 2H), 6.90 (s. 1H), 7.02−7.08 (m, 1H),7.17 (d, *J* = 3.6 Hz, 1H), 7.53−7.72 (m, 4H), 7.82−7.88 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 336 (31) [$M^{+\bullet}$], 265 (57), 160 (18), 84 (30), 72 (19), 58 (100). Anal. ($C_{21}H_{24}N_2O_2$ × 0.4 ethyl acetate): calcd. C 73.03, H 7.38, N 7.54; found C 72.75, H 7.23, N 7.71.

(5-Methoxy-1-(2-pyrrolidinoethyl)-1*H*-2-indolyl)-phenyl-methanone (79): yellow wax, mp 68−71 °C. IR (KBr): 3066, 2971, 2956, 1638, 1578 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.43−1.54 (m, 4H), 2.37−2.48 (m, 4 H), 2.69 (t, *J* = 6.5 Hz, 2H), 4.63 (t, *J* = 6.5 Hz, 2H), 6.83 (s, 1H),7,00−7.07 (m, 1H), 7.14−7.18 (m, 1H), 7.52−7.73 (m, 4H), 7.83−7.89 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 348 (14) [$M^{+\bullet}$], 97 (6), 84 (100). Anal. ($C_{22}H_{24}N_2O_2$) C, H, N.

(5-Methoxy-1-(2-piperidinoethyl)-1*H*-2-indolyl)-phenyl-methanone (80): yellow wax, mp 55−57 °C. IR (KBr): 3067, 2929, 2834, 1636, 1597 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 1.20−1.34 (m, 6H), 2.23−2.35 (m, 4H), 2.53 (t, *J* = 6.5 Hz, 2H), 3.75 (m, 3H), 4.65 (t, *J* = 6.5 Hz, 2H), 6.83 (s, 1H),7,00−7.07 (m, 1H), 7.14−7.18 (m, 1H), 7.52−7.73 (m, 4H), 7.83−7.89 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 362 (9) [$M^{+\bullet}$], 251 (2), 99 (8), 98 (100). Anal. ($C_{23}H_{26}N_2O_2$ × 0.15 ethyl acetate): calcd. C 75.45, H 7.30, N 7.46; found C 75.44, H 7.22, N 7.57.

(5-Methoxy-1-(2-morpholinoethyl)-1*H*-2-indolyl)-phenyl-methanone (81): yellow wax, mp 66−68 °C. IR (KBr): 3071, 2965, 2942, 1630, 1597 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.32 (t, *J* = 4.8 Hz, 4H), 2.52 (t, *J* = 6.2 Hz, 2H), 3.31 (t, *J* = 4.8 Hz, 4H), 4.65 (t, *J* = 6.2 Hz, 2H), 6.85 (s, 1H), 7.00−7.06 (m, 1H), 7.13−7.18 (m, 1H), 7.54−7.74 (m, 4H), 7.85−7.92 (m, 2H). EI-MS (70 eV); *m*/*z* (%): 364 (6) [$M^{+\bullet}$], 287 (3), 259 (8), 146 (8), 100 (100). Anal. ($C_{22}H_{24}N_2O_3$ × 0.15 ethyl acetate): calcd. C 71.88, H 6.73, N 7.42; found C 71.93, H 6.70, N 7.62.

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Supporting Information Available: Combustion analytical data, tubulin-inhibitory activity data, and in vitro cytotoxicity data of all prepared compounds that have not been presented in Table 1 because of inactivity or very weak

activity. This material is available free of charge via the Internet at http://pubs.acs.org.

Note Added after ASAP Posting

The headings in Table 1 were not aligned with their corresponding columns in the version released ASAP on 11/17/2001. The correct alignment has been incorporated in this version, posted 12/13/2001.

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