d-Fused [1]Benzazepines with Selective in Vitro Antitumor Activity: Synthesis and Structure−Activity Relationships

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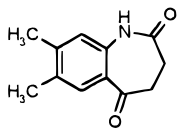
The synthesis of novel quinolino[3,2-*d*][1]benzazepines and pyrido[3,2-*d*][1]benzazepines is described. The in vitro antitumor activity of the compounds has been tested in the antitumor screening of the National Cancer Institute (NCI). Several 2,4-diarylpyrido[3,2-*d*][1]benzazepin-6-ones and -thiones turned out to exhibit considerable cytotoxicity for tumor cells. For studies of SAR within these series, substituents were introduced into the aromatic rings of the parent systems. Compounds from the thiolactam series tended to show higher potency than the corresponding lactams. Prominent compounds with noteworthy activity and remarkable selectivity for renal cancer cell lines are the lactams **10c, 10g**, and **10h** and the corresponding thiolactams **11c**, **11g**, and **11h.** Methylation of the azepine nitrogen leads to complete loss of activity, whereas annelation of a triazolo ring at the lactam site or transformation of the thiolactam function to a thiolactim ether results in decreased antitumor activity and selectivity. Consequently, the secondary lactam or thiolactam structure of the seven-membered ring has to be regarded as essential for selective antitumor activity.

Introduction

The [1]benzazepine-2,5-dione **1** has been described to exhibit anticancer activity when it was screened against Crocker sarcoma 180 in mice.[1] In a previous paper the synthesis of the [1]benzazepine-2,5-diones **2** as analogues of **1** was reported.[2] When **2a** and **2b** were tested in vitro in the disease-oriented antitumor screening panel of the National Cancer Institute (NCI), no antitumor activity was detected. More recently, the spiroannelated [1]benzazepine-2,5-dione **3** was reported to cause considerable growth inhibition on distinct tumor cell lines.[3] On the other hand, little interest has been



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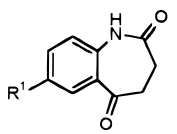
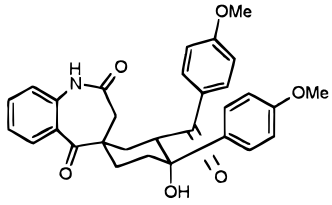


2a (R^1 = H)
2b (R^1 = Br)



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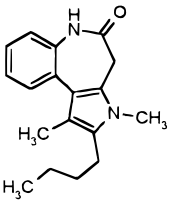

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devoted to the antitumor activity of *d*-fused [1]benzazepin-2-ones. Among the rare examples for structures from this class with putative antitumor activity, the pyrrolo[2,3-*d*][1]benzazepinone **4** is noteworthy, which proved to show weak in vitro antitubuline activity.[4] Our first efforts toward *d*-fused [1]benzazepinones were directed to the quinolino[3,2-*d*][1]benzazepin-6-one **5** and its corresponding thiolactam **6**. The studies were then extended to pyrido[3,2-*d*][1]benzazepin-6-ones **10** and -thiones **11**.

Chemistry

The synthesis of the heterocyclic scaffold of quinolino-[3,2-*d*][1]benzazepines has been described in the literature.[5] The hitherto unknown quinolino[3,2-*d*][1]-benzazepin-6-one **5** was synthesized via a Friedländer condensation[6] employing 2-aminobenzaldehyde in ethanol catalyzed by potassium hydroxide (Scheme 1). Refluxing the lactam **5** with phosphorus pentasulfide in 1,4-dioxane yielded the thiolactam **6**. A satisfactory microanalysis of **6** could not be obtained, presumably because the compound was susceptible to hydrolysis and released hydrogen sulfide upon exposure to air. Upon treatment of **6** with sodium hydride and iodomethane in THF, the thiolactim ether **7** was formed. The synthesis of the pyrido[3,2-*d*][1]benzazepin-6-ones **10** and -thiones **11** was accomplished via routes that have been described in the literature.[7] Hence, the [1]benzazepin-2,5-diones **2** were reacted with 2-propen-1-ones **8** to give the diastereomeric mixtures **9a**−**o** as products of a Michael reaction (Scheme 2). The diastereomers were not separated but cyclized subsequently by means of ammonium ferric sulfate in glacial acetic acid yielding the desired pyrido[3,2-*d*][1]benzazepin-6-ones **10a**−**o**. The hydroxylated derivatives **10p**−**r** were prepared by treatment of the corresponding methoxy-substituted compounds **10k**−**m** with boron tribromide in dichloromethane.[8] Thionation of **10a**−**o** with phosphorus pentasulfide afforded the thiolactams **11a**−**o**. Methylation at the nitrogen of the lactam **10a** was carried out with sodium hydride and iodomethane in boiling toluene (Scheme 3). On the attempted reaction of the tertiary

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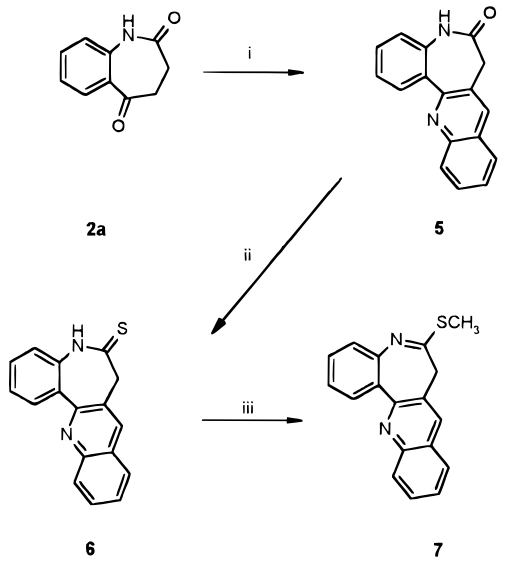
Scheme 1[a]



[a] (i) 2-Aminobenzaldehyde/KOH/EtOH/reflux/1 h; (ii) P_2S_5/$NaHCO_3$/1,4-dioxane/reflux/4 h; (iii) NaH/CH_3I/THF/105 min.

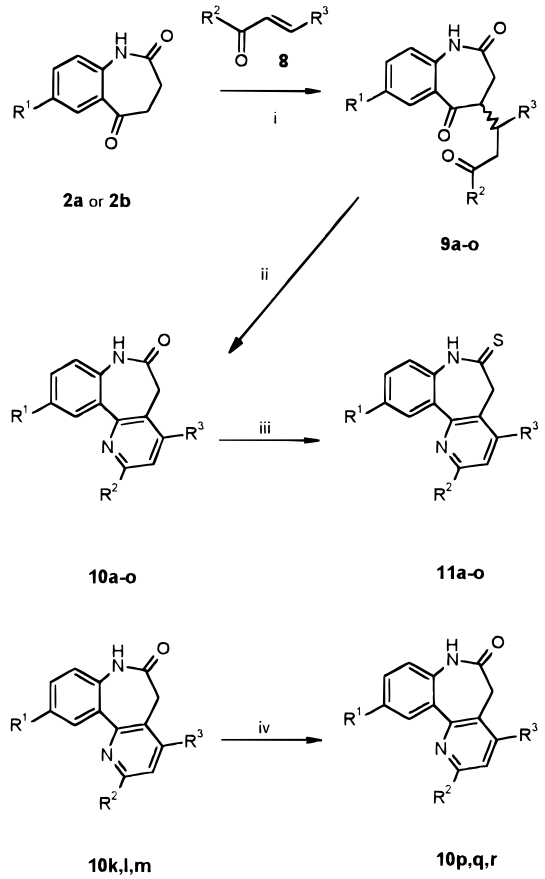
lactam **12** with phosphorus pentasulfide, only poor yields of the thiolactam **13** were obtained. On the other hand, reaction of **12** with Lawesson's reagent[9] in hot toluene gave the N-methylated thiolactam **13** in satisfactory yield. The thiolactim ether **14** was prepared by refluxing the sodium salt of the thiolactam **11a** with iodomethane in THF (Scheme 4).[7] Reaction of **14** with acetic hydrazide in boiling 1-butanol yielded the pyrido-[3,2-*d*][1,2,4]triazolo[4,3-*a*][1]benzazepine **15**.

Results of the Antitumor Screening and Discussion

Compounds **2, 5**−**7**, and **10**−**15** were submitted to the National Cancer Institute for testing against a panel of approximately 60 tumor cell lines. Details of this test system and the information, which is encoded by the activity pattern over all cell lines, have been published.[10] The antitumor activity of a test compound is reported for each cell line by three parameters: log GI_{50} value (GI_{50} = molar concentration of the compound that inhibits 50% net cell growth), log TGI value (TGI = molar concentration of the compound leading to total inhibition of net cell growth), and log LC_{50} value (LC_{50} = molar concentration of the compound leading to 50% net cell death). Furthermore, a meangraph midpoint (MG_MID) is calculated for each of the mentioned parameters, giving an averaged activity parameter over all cell lines. For the calculation of the MG_MID, insensitive cell lines are included with the highest concentration tested. The discovery of compounds with new selectivity patterns is one of the intentions of the screening program. Selectivity of a compound with respect to one or more cell lines of the screen is characterized by a high deviation of the particular cell line parameter compared to the MG_MID value.

Whereas the [1]benzazepine-2,5-diones **2a** and **2b** were inactive in the NCI in vitro antitumor screening, the quinolino[3,2-*d*][1]benzazepine-6-thione **6** showed a modest activity, expressed by a log MG_MID GI_{50} of −4.91. However, the results with the other two structures **5** (log MG_MID GI_{50} = −4.22) and **7** (log MG_MID GI_{50} = −4.04) in this series were disappointing. Therefore, the related 2,4-diphenylpyrido[3,2-*d*][1]-benzazepin-6-one **10a** and the corresponding thiolactam **11a** were tested, which had been reported recently as members of a novel heterocyclic ring system.[7] Both **10a** and **11a** exhibited higher activity than **6**, and namely **11a** showed a moderate selectivity for cell lines from the renal subpanel. This is an interesting feature, because most renal cell carcinoma are not sensitive to a cytostatic therapy. To obtain information about structure−activity relationships, derivatives of **10a** and **11a** were prepared, including compounds with halogen, hydroxy, and methoxy substitution in the phenyl rings.

Scheme 2[a,b]

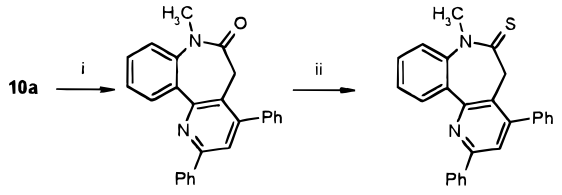


[a] (i) KOH/EtOH/rt/6 h; (ii) $NH_4Fe(SO_4)_2$/NH_4OAc/AcOH/reflux/3 h; (iii) P_2S_5/$NaHCO_3$/1,4-dioxane or THF/reflux/3−6 h; (iv) BBr_3/CH_2Cl_2/rt/18 h.

[b] compounds

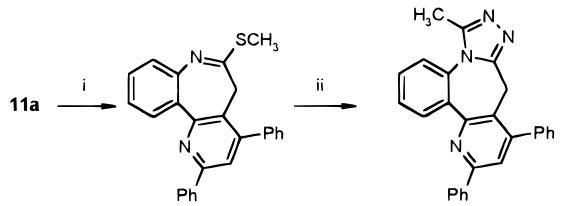
10, **11**	R^1	R^2	R^3
a	H	Ph	Ph
b	H	4-ClPh	Ph
c	H	3-ClPh	Ph
d	H	2-ClPh	Ph
e	H	Ph	4-ClPh
f	H	Ph	3-ClPh
g	H	Ph	4-BrPh
h	Br	Ph	Ph
i	H	2-naphthyl	4-ClPh
j	H	2-naphthyl	Ph
k	H	4-MeOPh	Ph
l	H	Ph	4-MeOPh
m	H	4-MeOPh	4-MeOPh
n	H	Ph	3,4-di-MeOPh
o	H	3,4-(OCH_2O)-Ph	Ph
p	H	4-OH−Ph	Ph
q	H	Ph	4-OHPh
r	H	4-OHPh	4-OHPh

Scheme 3[a]



[a] (i) NaH/CH_3I/reflux/90 min; (ii) Lawesson's reagent/toluene/100 °C/6 h.

Scheme 4[a]



[a] (i) NaH/CH_3I/reflux/90 min; (ii) acetic hydrazide/1-butanol/reflux/5 h.

In both the lactam and the thiolactam series the halogenation in distinct positions enhanced the activity, prominent examples being the 2-(3-chlorophenyl)-substituted derivatives **10c/11c,** the 4-(4-bromophenyl)-substituted compounds **10g/11g**, and the 10-bromo-substituted derivatives **10h/11h**. Shifting the chloro substituent in **10c**/**11c** from the meta to the ortho position (compounds **10d**/**11d**) led to a dramatic decrease of activity (log MG_MID GI_{50} values −4.58 and −4.06, respectively). This loss in potency may be explained by an unfavorable orthogonal position of the 2-phenyl substituent with respect to the pyridine ring, enforced by the ortho substituent. The introduction of methoxy substituents (compounds **10k**−**n** and **11k**−**n**) or phenolic hydroxy functions (**10p**−**r**) into the parent structures failed to improve the activity.

In Table 1, the results for the parent compound **10a** and the most potent compounds **10/11c,g,h** on three renal cancer cell lines (786-0, ACHN, TK-10) are given, which are apparently especially sensitive to the compounds described here. In terms of the log GI_{50} MG_MID value, the compounds exhibited only a modest activity in a range between − 4.4 and − 5.6, which is poor compared to very potent standard compounds such as paclitaxel (−7.9) or doxorubicin (−6.9).[11] On the other hand, a reasonable selectivity for the indicated renal cancer cell lines was found, which is not observed for standard antitumor agents.[11] Selectivity is demonstrated when a compound exhibits a distinctly lower log GI_{50}/log TGI/log LC_{50} value for a particular cell line compared to the corresponding log MG_MID value. The most potent compounds in the lactam and in the thiolactam series turned out to exhibit the highest selectivity on renal cancer cell lines. Furthermore, the more active compounds exhibited a slight selectivity for cell lines from the CNS subpanel. Cell lines from the leukemia and the melanoma subpanel were generally less sensitive to **10** and **11**.

The N-methylated derivatives **12** and **13** were devoid of noteworthy activity in the in vitro screen. A poor activity was retained in the thiolactim ether **14** and in the triazolo annelated compound **15**, but a selectivity for renal cancer cells was not observed with these structures. Hence, the secondary lactam or thiolactam moiety seems to be an important part of the pharmacophor in the series of antitumor agents described here.

Summary

We have developed a new class of compounds with antitumor activity, namely 2,4-diphenylpyrido[3,2-*d*][1]-benzazepin-6-ones **10** and 2,4-diphenylpyrido[3,2-*d*][1]-benzazepine-6-thiones **11**. The compounds show a selectivity for renal cancer cell lines. Structure−activity investigations revealed that halogenation in distinct positions of the parent structures **10a** and **11a** leads to derivatives with enhanced activity and selectivity. A hydrogen at the azepine nitrogen seems to be a necessary requirement for the selectivity for renal cancer cell lines. Structures **10b**, **10c**, **10g**, **10h**, **10i**, **11a**, **11b**, **11c**, **11g**, **11h**, and **11i** have been selected by the NCI for in vivo studies. Further variations of the parent structure are currently carried out to improve both potency and selectivity and to get detailed information on SAR. The mechanism of the antitumor activity is currently investigated.

Experimental Section

Melting points were determined on an electric variable heater (Gallenkamp) and evaluated on a Mettler FP 62 automatic melting point instrument. Elemental analyses were performed in the analytical department of the Institut für Pharmazie, Universität Hamburg. Results obtained were within ±0.4% unless indicated otherwise. Infrared spectra were recorded using KBr pellets on a Pye-Unicam SP 3−200 S, a Philips PU 9712, or a Perkin-Elmer 1660 FTIR spectrometer, respectively. Nuclear magnetic resonance spectra were recorded on a Bruker AC 250 P, a Bruker AMX 400, or a Bruker DRX 500 instrument, respectively, using dimethyl sulfoxide-d_6 as solvent and tetramethylsilane as internal standard. NMR signals are reported in ppm on a δ scale. TLC analyses were carried out on flourescent Polygram Sil G/UV_{254} silica gel plates, using CH_2Cl_2/ethyl acetate (8:2) as eluent. Spots were visualized under 254 nm UV illumination. Compounds **10a, 11a**, and **14** were prepared by literature methods.[7]

5*H*-Quinolino[3,2-*d*][1]benzazepin-6(7*H*)-one (5). A solution of freshly prepared 2-aminobenzaldehyde[6a] (500 mg, 4.1 mmol), **2a**[2] (722 mg, 4.1 mmol), and KOH (1.8 g, 32 mmol) in 12.5 mL of ethanol was refluxed for 1 h. After being cooled to room temperature, the mixture was neutralized with acetic acid and evaporated to dryness under reduced pressure. The residue was redissolved in 40 mL of CH_2Cl_2 and washed four times with water. The organic layer was dried (Na_2SO_4) and evaporated. Crystallization from ethanol yielded yellow crystals (36%): mp 298 °C; IR 3170 (NH), 1690 cm^{-1} (C=O); ^1H NMR (400 MHz) 3.68 (s, 2H), 7.24 (dd, 1H, J = 8.1/1.0 Hz), 7.35 (d"t", 1H, J = 7.6/7.6/1.3 Hz), 7.54 (d"t", 1H, J = 7.6/7.6/1.5 Hz), 7.64 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.77−7.83 (m, 1H), 8.03 (d, 1H, J = 8.1 Hz), 8.09−8.16 (m, 2H), 8.41 (s, 1H, H-8), 10.19 (s, 1H, NH). Anal. C, H, N.

5*H*-Quinolino[3,2-*d*][1]benzazepine-6(7*H*)-thione (6). To a stirred solution of **5** (2.5 g, 9.57 mmol) in 1,4-dioxane (150 mL) under nitrogen at 70 °C were added phosphorus pentasulfide (2.4 g, 10.8 mmol) and subsequently $NaHCO_3$ (3.55 g, 42 mmol). The mixture was refluxed for 4 h and filtered hot through a short silica gel column (Silica gel 100−200, 60 A, ICN). After the column was eluted with 1,4-dioxane (100 mL), the pooled 1,4-dioxane fractions were evaporated to dryness. Recrystallization of the residue yielded yellow crystals (87%): mp 298−300 °C dec; IR 3160 cm^{-1} (NH); ^1H NMR (250 MHz) 4.17 (br s, 2H), 7.30−7.70 (m, 4H), 7.78−7.88 (m, 1H), 8.03−

Table 1. Selected Results of the in Vitro Antitumor Screening[a]

		log GI_{50} [M][b]				log LC_{50} [M][c]			
compd	no. of tests[d]	786-0[e]	ACHN[e]	TK-10[e]	MG_MID[f]	786-0[e]	ACHN[e]	TK-10[e]	MG_MID[f]
10a	1	−5.38	−5.39	−5.61	−5.25	>−4.00	−4.15	>−4.00	−4.08
10c	2	−6.01	−5.94	−5.83	−5.51	−5.27	−4.61	−4.76	−4.27
10g	1	−5.79	−5.40	−6.73	−5.31	−5.02	−4.30	−5.65	−4.21
10h	2	−6.20	−5.90	−6.37	−5.49	−5.32	−4.81	−5.04	−4.31
11c	2	−6.01	−6.21	−6.36	−5.56	−5.32	−4.72	−5.02	−4.27
11g	2	−6.20	−6.06	−5.75	−5.67	−5.35	−5.23	−5.11	−4.60
11h	2	−5.93	−6.13	−5.91	−5.42	−5.15	−5.07	−4.73	−4.22

[a] Data obtained from the NCI's in vitro disease-oriented human tumor cells screen (see refs 10 for details). [b] Log of molar concentration that inhibits 50% net cell growth. [c] Log of molar concentration leading to 50% net cell death. [d] Number of screening experiments carried out by the NCI. The given values are arithmetical means of the results, if more than one experiment was carried out. For reproducibility of results see ref 10a. [e] Renal cancer cell line. [f] MG_MID = meangraph midpoint = arithmetical mean value for all tested cancer cell lines. If the indicated effect was not attainable within the used concentration interval, the highest tested concentration was used for the calculation.

8.21 (m, 3H), 8.43 (s, 1H), 12.28 (s, 1H). Anal. H, N, S; C: calcd, 73.88; found, 72.37.

6-(Methylthio)-7*H*-quinolino[3,2-*d*][1]benzazepine (7). Sodium hydride (8.7 mg, 0.36 mmol, suspension in paraffin) was added to a stirred solution of **6** (100 mg, 0.36 mmol) in THF (15 mL) under nitrogen. After being refluxed for 45 min, the mixture was cooled to room temperature and a solution of iodomethane (51 mg, 0.36 mmol) in THF (1 mL) was added. After being refluxed under nitrogen for further 90 min, the mixture was poured into ice water (30 mL). The precipitate which was formed was filtered and crystallized from toluene to yield colorless crystals (48%): mp 166−167 °C; IR 1635 cm^{-1} (C═N); ^{1}H NMR (250 MHz) 2.42 (s, 3H, SCH_3), 3.61 (s, 2H), 7.29−7.37 (m, 2H), 7.46−7.57 (m, 2H), 7.67−7.76 (m, 1H), 7.85 (d, 1H, J = 8.2 Hz), 7.99 (s, 1H), 8.17−8.29 (m, 2H). Anal. C, H, N, S.

2,4-Diaryl-5*H*-pyrido[3,2-*d*][1]benzazepin-6(7*H*)-ones 10b−o, General Procedure A. A slurry of the appropriate 1*H*-[1]benzazepine-2,5(3*H*,4*H*)-dione **2**[2] (2 mmol), the appropriate 1,3-diarylpropen-1-one **8** (2 mmol) and KOH (11 mg, 0.2 mmol) in ethanol (7 mL) was stirred for 5−20 h. The reaction was monitored by TLC analyses. After the starting material **2** had disappeared (5−20 h), the mixture was adjusted to pH 5 by dropwise addition of acetic acid. The resulting precipitate was filtered off and recrystallized once from ethanol/toluene to yield the solid diastereomeric mixture **9a−o.** To accomplish the ring closure reaction, a mixture of the appropriate Michael adduct **9a−o** (1 mmol), ammonium ferric sulfate dodecahydrate (1 g, 2.07 mmol), and ammonium acetate (1.2 g, 15.67 mmol) was refluxed in glacial acetic acid (7.5 mL) under nitrogen for 3 h. After cooling, the mixture was poured on crushed ice (10 g) and stirred until melting of the ice. The precipitate was collected by filtration, washed with water, and recrystallized from ethanol/toluene.

2-(4-Chlorophenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10b) was prepared following general procedure A in 36% yield from **2a**: colorless crystals; mp 310 °C; IR 3190 (NH), 1670 cm^{-1} (C═O); ^{1}H NMR (400 MHz) 3.36 (br s, 2H, azepine-CH_2), 7.25 (d, 1H, J = 8.1 Hz), 7.37 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.51−7.63 (m, 6H), 7.67 (d, 2H, J = 6.6 Hz), 8.00 (s, 1H, pyridine-H), 8.20 (dd, 1H, J = 6.6/1.5 Hz), 8.29 (d, 2H, J = 8.6 Hz), 10.40 (s, 1H). Anal. C, H, Cl, N.

2-(3-Chlorophenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10c) was prepared following general procedure A in 51% yield from **2a**: colorless crystals; mp 287 °C; IR 3180 (NH), 1690 cm^{-1} (C═O); ^{1}H NMR (400 MHz) 3.39 (br s, 2H), 7.26 (d, 1H, J = 7.6 Hz), 7.38 ("t", 1H, J = 7.1/7.1 Hz), 7.50−7.57 (m, 4H), 7.60 ("t", 2H, J = 6.6/6.6 Hz), 7.68 (d, 2H, J = 7.9 Hz), 8.05 (s, 1H), 8.19−8.26 (m, 2H), 8.31 (s, 1H), 10.42 (s, 1H). Anal. C, H, Cl, N.

2-(2-Chlorophenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10d) was prepared following general procedure A in 58% yield from **2a**: colorless crystals; mp 272 °C; IR 3190 (NH), 1680 cm^{-1} (C═O); ^{1}H NMR (400 MHz) 3.42 (br s, 2H), 7.25 (d, 1H, J = 8.1 Hz), 7.32 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.45−7.68 (m, 10H), 7.75−7.80 (m, 1H) 8.14 (dd, 1H, J = 7.6/1.5 Hz), 10.45 (s, 1H). Anal. C, H, Cl, N.

4-(4-Chlorophenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10e) was prepared following general procedure A in 54% yield from **2a**: colorless crystals; mp 291−292 °C; IR 3190 (NH), 1670 cm^{-1} (C═O); ^{1}H NMR (400 MHz), 3.37 (br s, 2H), 7.26 (d, 1H, J = 8.1 Hz), 7.37 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.44−7.57 (m, 4H), 7.64−7.72 (m, 4H), 7.97 (s, 1H), 8.19−8.26 (m, 3H), 10.42 (s, 1H). Anal. C, H, Cl, N.

4-(3-Chlorophenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10f) was prepared following general procedure A in 33% yield from **2a**: colorless crystals; mp 294 °C; IR 3180 (NH), 1685 cm^{-1} (C═O); ^{1}H NMR (400 MHz) 3.36 (br s, 2H) 7.26 (d, 1H, J = 8.1 Hz), 7.37 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.44−7.57 (m, 4H), 7.60−7.65 (m, 3H), 7.77 (s, 1H), 8.01 (s, 1H), 8.21 (dd, 1H, J = 7.6/1.5 Hz), 8.26 (d, 2H, J = 7.9 Hz), 10.41 (s, 1H). Anal. C, H, Cl, N.

4-(4-Bromophenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10g) was prepared following general procedure A in 35% yield from **2a**: colorless crystals; mp 304 °C; IR 3190 (NH), 1670 cm^{-1} (C═O); ^{1}H NMR (400 MHz) 3.34 (br s, 2H), 7.25 (d, 1H, J = 8.0 Hz), 7.37 ("t", 1H, J = 7.6/7.6 Hz), 7.44−7.57 (m, 4H), 7.63 (d, 2H, J = 8.0 Hz), 7.80 (d, 2H, J = 8.0 Hz), 7.97 (s, 1H), 8.17−8.27 (m, 3H), 10.42 (s, 1H). Anal. C, H, Br, N.

10-Bromo-2,4-diphenyl-5*H*-pyrido[3,2-*d*][1]benzazepin-6(7*H*)-one (10h) was prepared following general procedure A in 31% yield from **2b**: colorless crystals; mp 306 °C; IR 3185 (NH), 1680 cm^{-1} (C═O); ^{1}H NMR (400 MHz) 3.30 (br s, 2H), 7.21 (d, 1H, J = 8.3 Hz), 7.45−7.51 (m, 1H), 7.54 ("t", 3H, J = 7.6/7.6 Hz), 7.60 ("t", 2H, J = 7.6/7.6 Hz), 7.63−7.68 (m, 2H), 7.72 (dd, 1H, J = 8.6/2.5 Hz), 7.99 (s, 1H), 8.23 (d, 2H, J = 7.1 Hz), 8.30 (d, 1H, J = 2.6 Hz), 10.50 (s, 1H). Anal. C, H, Br, N.

4-(4-Chlorophenyl)-2-naphthyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10i) was prepared following general procedure A in 40% yield from **2a**: colorless crystals; mp 290 °C; IR 3180 (NH), 1670 cm^{-1} (C═O); ^{1}H NMR (400 MHz) 3.38 (br s, 2H), 7.27 (d, 1H, J = 8.1 Hz), 7.40 ("t", 1H, J = 7.6/7.6 Hz), 7.53−7.59 (m, 3H), 7.67−7.75 (m, 4H), 7.94−8.00 (m, 1H), 8.03−8.09 (m, 2H), 8.17 (s, 1H), 8.28 (dd, 1H, J = 7.6/1.0 Hz), 8.45 (dd, 1H, J = 8.6/1.5 Hz), 8.81 (s, 1H), 10.45 (s, 1H). Anal. H, Cl, N; C: calcd, 77.93; found, 77.41.

2-Naphthyl-4-phenyl-5*H*-pyrido[3,2-*d*][1]benzazepin-6-(7*H*)-one (10j) was prepared following general procedure A in 26% yield from **2a**: opalescent plates; mp 281−282 °C; IR 3190 (NH), 1670 cm^{-1} (C═O); ^{1}H NMR (400 MHz) 3.42 (br s, 2H), 7.27 (d, 1H, J = 7.1), 7.40 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.52−7.59 (m, 4H), 7.62 ("t", 2H, J = 7.4/7.4 Hz), 7.68−7.75 (m, 2H), 7.94−8.00 (m, 1H), 8.03−8.10 (m, 2H), 8.16 (s, 1H), 8.28 (dd, 1H, J = 7.6/1.5 Hz), 8.45 (dd, 1H, J = 8.6/1.5 Hz), 8.82 (s, 1H), 10.41 (s, 1H). Anal. C; H, N.

2-(4-Methoxyphenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10k) was prepared following general procedure A in 20% yield from **2a**: colorless needles; mp 240 °C dec; IR 3190 (NH), 1670 cm^{-1} (C═O); ^{1}H NMR (400 MHz), 3.34 (br s, 2H), 3.83 (s, 3H, OCH_3), 7.04−7.09 (m, 2H), 7.25 (d, 1H, J = 8.1 Hz), 7.36 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.49−

7.56 (m, 2H), 7.59 ("t", 2H, J = 7.4/7.4 Hz), 7.63−7.68 (m, 2H), 7.89 (s, 1H), 8.16−8.23 (m, 3H), 10.38 (s, 1H). Anal. C, H, N.

4-(4-Methoxyphenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10l) was prepared following general procedure A in 33% yield from **2a**: colorless needles; mp 268 °C; IR 3190 (NH), 1670 cm^{-1} (C═O); ^1H NMR (400 MHz) 3.45 (br s, 2H), 3.86 (s, 3H, OCH_3), 7.15 (d, 2H, J = 9.2 Hz), 7.25 (dd, 1H, J = 7.6/1.0 Hz), 7.36 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.43−7.56 (m, 4H), 7.65 (d, 2H, J = 8.6 Hz), 7.93 (s, 1H), 8.22 (d"t", 3H, J = 8.4/8.4/1.5 Hz), 10.38 (s, 1H). Anal. C, H, N.

2,4-Bis(4-methoxyphenyl)-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10m) was prepared following general procedure A in 42% yield from **2a**: colorless needles; mp 234 °C; IR 3190 (NH), 1675 cm^{-1} (C═O); ^1H NMR (400 MHz), 3.35 (br s, 2H), 3.83 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 7.06 (d, 2H, J = 9.2 Hz), 7.15 (d, 2H, J = 8.7 Hz), 7.25 (d, 1H, J = 7.6 Hz), 7.35 ("t", 1H, J = 7.6/7.6 Hz), 7.51 (d"t", 1H, J = 7.6/7.6/1.5 Hz), 7.62 (d, 2H, J = 8.6 Hz), 7.85 (s, 1H), 8.18 (d, 3H, J = 8.6 Hz), 10.38 (s, 1H). Anal. C, H, N.

4-(3,4-Dimethoxyphenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10n) was prepared following general procedure A in 36% yield from **2a**: colorless needles; mp 297−298 °C; IR 3190 (NH), 1670 cm^{-1} (C═O); ^1H NMR (400 MHz) 3.30 (br s, 2H), 3.86 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 7.14−7.30 (m, 4H), 7.34−7.40 (m, 1H), 7.44−7.56 (m, 4H), 7.96 (s, 1H), 8.23 (d"t", 3H, J = 7.4/7.4/1.5 Hz), 10.39 (s, 1H). Anal. C, H, N.

2-(1,3-Benzodioxol-5-yl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10o) was prepared following general procedure A in 15% yield from **2a**: colorless needles; mp 235 °C; IR 3180 (NH), 1680 cm^{-1} (C═O); ^1H NMR (400 MHz) 3.32 (br s, 2H), 6.10 (s, 2H, methylenedioxy-CH_2), 7.04 (d, 1H, J = 8.1 Hz), 7.25 (dd, 1H, J = 7.6/7.6 Hz), 7.36 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.49−7.56 (m, 2H), 7.59 ("t", 2H, J = 7.1/7.1 Hz), 7.66 (d, 2H, J = 7.1 Hz), 7.79−7.83 (m, 2H), 7.89 (s, 1H), 8.19 (dd, 1H, J = 8.1/1.5 Hz), 10.38 (s, 1H). Anal. C, H, N.

Hydroxylated 2,4-Diaryl-5*H*-pyrido[3,2-*d*][1]benzazepin-6(7*H*)-ones 10p−r, General Procedure B. To a solution of the appropriate methoxy derivative **10k**−**m** in CH_2Cl_2 (10 mL) was added BBr_3. After 18 h of stirring at room temperature, water (10 mL) was added, and stirring was continued for 6 h at room temperature. A solid was formed, which was collected by filtration, washed with water, and recrystallized from ethanol.

2-(4-Hydroxyphenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10p) was prepared following general procedure B from **10k** (425 mg, 1.08 mmol) and BBr_3 (576 mg, 2.3 mmol) in 33% yield: colorless needles; mp >330 °C; IR 3310 (OH), 3220 (NH), 1660 cm^{-1} (C═O); ^1H NMR (400 MHz) 3.35 (br s, 2H), 6.89 (d, 2H, J = 8.0 Hz), 7.24 (d, 1H, J = 8.0 Hz), 7.35 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.49−7.55 (m, 2H), 7.56−7.61 (m, 2H), 7.62−7.67 (m, 2H), 7.83 (s, 1H), 8.06−8.11 (m, 2H), 8.19 (dd, 1H, J = 8.0/1.6 Hz), 9.73 (s, 1H, OH), 10.38 (s, 1H). Anal. C, H, N.

4-(4-Hydroxyphenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10q) was prepared following general procedure B from **10l** (275 mg, 0.7 mmol) and BBr_3 (376 mg, 1.5 mmol) in 38% yield: colorless crystals; mp 303 °C; IR 3260 (OH, NH), 1665 cm^{-1} (C═O); ^1H NMR 3.39 (br s, 2H), 6.96 (d, 2H, J = 8.7 Hz), 7.25 (d, 1H, J = 8.1 Hz), 7.36 (d"t", 1H, J = 7.4/7.4/1.0 Hz), 7.43−7.56 (m, 6H), 7.90 (s, 1H), 8.21 (d"t", 3H, J = 8.1/8.1/1.5 Hz), 9.79 (s, 1H, OH), 10.38 (s, 1H). Anal. C, H, N.

2,4-Bis(4-hydroxyphenyl)-5*H*-pyrido[3,2-*d*][1]-benzazepin-6(7*H*)-one (10r) was prepared following general procedure B from **10m** (211 mg, 0.5 mmol) and BBr_3 (378 mg, 1.51 mmol) in 36% yield: colorless crystals including one C_2H_5-OH per molecule; mp >330 °C; IR 3265 (OH, NH), 1660 cm^{-1} (C═O); ^1H NMR (400 MHz) 1.06 (t, 3H, J = 6.8 Hz, CH_3CH_2-OH), 3.35 (br s, 2H), 3.44 (dq, 2H, J = 6.8/5.1 Hz, CH_3CH_2-OH), 4,34 (t, 1H, J = 5.1 Hz, CH_3CH_2OH), 6.26 (d, 2H, J = 8.7 Hz), 6.95 (d, 2H, J = 8.1 Hz), 7.24 (d, 1H, J = 7.8 Hz), 7.35 ("t", 1H, J = 6.9/6.9 Hz), 7.46−7.54 (m, 3H), 7.77 (s, 1H), 8.06 (d, 2H, J = 8.7 Hz), 8.18 (dd, 1H, J = 7.6/1.0 Hz), 9.72 (s, 1H, OH), 9.77 (s, 1H, OH), 10.35 (s, 1H). Anal. ($C_{25}H_{18}N_2O_3 \cdot C_2H_5OH$) C, H; N: calcd, 6.35; found, 6.83.

2,4-Diaryl-5*H*-pyrido[3,2-*d*][1]benzazepine-6(7*H*)-thiones 11b−o, General Procedure C. A solution of the appropriate lactam **10b**−**o** in THF or 1,4-dioxane was stirred at 50 °C under nitrogen. Phosphorus pentasulfide and after 1 min $NaHCO_3$ were added to the mixture, which was then refluxed under nitrogen, and the reaction was monitored by TLC. If the reaction was not complete after 3 h, addition of the indicated amounts of phosphorus pentasulfide and $NaHCO_3$ was repeated and refluxing was continued for 3 h. After being cooled to room temperature, the mixture was poured onto crushed ice (50 mL) and stirred until the ice melted. The precipitate was filtered, washed with water, and recrystallized from ethanol/toluene.

2-(4-Chlorophenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11b) was prepared following general procedure C from **10b** (198 mg, 0.5 mmol), phosphorus pentasulfide (200 mg, 0.9 mmol), and $NaHCO_3$ (285 mg, 3.4 mmol) in THF (15 mL) in 67% yield: colorless crystals; mp 280 °C; IR 3150 cm^{-1} (NH); ^1H NMR (400 MHz) 3.57 (br s, 1H), 4.19 (br s, 1H), 7.37 (d, 1H, J = 7.6 Hz), 7.47 (d"t", 1H, J = 8.1/8.1/1.0 Hz), 7.51−7.61 (m, 6H), 7.80 (d, 2H, J = 6.6 Hz), 7.99 (s, 1H), 8.19 (dd, 1H, J = 7.6/1.3 Hz), 8.26−8.31 (m, 2H), 12.37 (s, 1H). Anal. C, H, Cl, N, S.

2-(3-Chlorophenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11c) was prepared following general procedure C from **10c** (300 mg, 0.76 mmol), phosphorus pentasulfide (300 mg, 1.35 mmol), and $NaHCO_3$ (430 mg, 5.1 mmol) in THF (25 mL) in 56% yield: colorless crystals; mp 293 °C; IR 3160 cm^{-1} (NH); ^1H NMR (400 MHz) 3.57 (br s, 1H), 4.21 (br s, 1H), 7.38 (d, 1H, J = 8.1 Hz), 7.48 (d"t", 1H, J = 6.6/6.6/1.0 Hz), 7.51−7.61 (m, 6H), 7.80 (d, 2H, J = 6.6 Hz), 8.04 (s, 1H), 8.18−8.25 (m, 2H), 8.30 (s, 1H), 12.38 (s, 1H). Anal. C, H, Cl, N, S.

2-(2-Chlorophenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11d) was prepared following general procedure C from **10d** (396 mg, 1.0 mmol), phosphorus pentasulfide (400 mg, 1.8 mmol), and $NaHCO_3$ (560 mg, 6.66 mmol) in 1,4-dioxane (15 mL) in 70% yield: colorless crystals; mp 320 °C dec; IR 3150 cm^{-1} (NH); ^1H NMR (400 MHz) 3.59 (br s, 1H), 4.24 (br s, 1H), 7.56−7.64 (m, 9H), 7.67 (s, 1H), 7.76−7.81 (m, 3H), 8.13 (dd, 1H, J = 8.1/1.5 Hz), 12.41 (s, 1H). Anal. C, H, Cl, N, S.

4-(4-Chlorophenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11e) was prepared following general procedure C from **10e** (298 mg, 0.75 mmol), phosphorus pentasulfide (294 mg, 1.32 mmol), and $NaHCO_3$ (430 mg, 5.1 mmol) in THF (25 mL) in 77% yield: colorless crystals; mp 270 °C; IR 3140 cm^{-1} (NH); ^1H NMR (400 MHz) 3.59 (br s, 1H), 4.14 (br s, 1H), 7.38 (dd, 1H, J = 8.1/1.0 Hz), 7.44−7.55 (m, 4H), 7.57 (d"t", 1H, J = 7.6/7.6/1.5 Hz), 7.64 (d, 2H, J = 8.7 Hz), 7.81 (d, 2H, J = 8.7 Hz), 7.96 (s, 1H), 8.18−8.26 (m, 3H), 12.39 (s, 1H). Anal. C, H, Cl, N, S.

4-(3-Chlorophenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11f) was prepared following general procedure C from **10f** (324 mg, 0.82 mmol), phosphorus pentasulfide (294 mg, 1.32 mmol), and $NaHCO_3$ (430 mg, 5.1 mmol) in THF (28 mL) in 55% yield: colorless crystals; mp 281 °C; IR 3140 cm^{-1} (NH); ^1H NMR (400 MHz) 3.57 (br s, 1H), 4.12 (br s, 1H), 7.38 (d, 1H, J = 8.1 Hz), 7.44−7.55 (m, 4H), 7.56−7.63 (m, 3H), 7.70−7.77 (m, 1H), 7.93 (s, 1H), 7.99 (s, 1H), 8.21 (dd, 1H, J = 8.2/1.5), 8.25 (d, 2H, J = 7.1 Hz), 12.39 (s, 1H). Anal. C, H, Cl, N, S.

4-(4-Bromophenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11g) was prepared following general procedure C from **10g** (205 mg, 0.46 mmol), phosphorus pentasulfide (294 mg, 1.32 mmol), and $NaHCO_3$ (430 mg, 5.1 mmol) in THF (15 mL) in 61% yield: colorless crystals; mp 302 °C; IR 3150 cm^{-1} (NH); ^1H NMR (400 MHz) 3.58 (br s, 1H), 4.12 (br s, 1H), 7.38 (dd, 1H, J = 8.8/1.1 Hz), 7.45−7.55 (m, 4H), 7.58 (d"t", 1H, J = 7.5/7.5/1.6 Hz), 7.71−7.80 (m, 4H), 7.96 (s, 1H), 8.22 (d"t", 3H, J = 9.0/9.0/1.6 Hz), 12.38 (s, 1H). Anal. C, H, Br, N, S.

10-Bromo-2,4-diphenyl-5*H*-pyrido[3,2-*d*][1]benzazepine-6(7*H*)-thione (11h) was prepared following general procedure C from **10h** (250 mg, 0.57 mmol), phosphorus pentasulfide (224 mg, 1.0 mmol), and $NaHCO_3$ (319 mg, 3.8 mmol) in 1,4-dioxane (15 mL) in 49% yield: colorless crystals; mp 293 °C dec; IR 3140 cm^{-1} (NH); ^1H NMR (400 MHz) 3.61 (br s, 1H), 4.18 (br s, 1H), 7.33 (d, 1H, J = 8.6 Hz), 7.45−7.61 (m, 6H), 7.77 (d, 3H, J = 7.6 Hz), 7.97 (s, 1H), 8.21 (d, 2H, J = 7.1), 8.29 (d, 1H, J = 2.5), 12.42 (s, 1H). Anal. C, H, Br, N, S.

4-(4-Chlorophenyl)-2-naphthyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11i) was prepared following general procedure C from **10i** (200 mg, 0.45 mmol), phosphorus pentasulfide (200 mg, 0.9 mmol), and $NaHCO_3$ (285 mg, 3.4 mmol) in 1,4-dioxane (20 mL) in 52% yield: colorless crystals; mp 325 °C dec; IR 3140 cm^{-1} (NH); ^1H NMR (400 MHz) 3.59 (br s, 1H), 4.15 (br s, 1H), 7.39 (d, 1H, J = 7.6 Hz), 7.51 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.54−7.63 (m, 3H), 7.66 (d, 2H, J = 8.7 Hz), 7.84 (d, 2H, J = 8.7 Hz), 7.95−8.00 (m, 1H), 8.02−8.08 (m, 2H), 8.16 (s, 1H), 8.28 (dd, 1H, J = 8.1/1.5 Hz), 8.43 (dd, 1H, J = 8.7 Hz), 8.81 (s, 1H), 12.40 (s, 1H). Anal. H, Cl, N, S; C: calcd, 75.23; found, 74.78.

2-Naphthyl-4-phenyl-5*H*-pyrido[3,2-*d*][1]benzazepine-6(7*H*)-thione (11j) was prepared following general procedure C from **10j** (500 mg, 1.21 mmol), phosphorus pentasulfide (509 mg, 2.3 mmol), and $NaHCO_3$ (726 mg, 8.6 mmol) in 1,4-dioxane (20 mL) in 66% yield: colorless crystals; mp 295 °C dec; IR 3160 cm^{-1} (NH); ^1H NMR (400 MHz) 3.60 (br s, 1H), 4.23 (br s, 1H), 7.39 (dd, 1H, J = 8.1/1.0 Hz), 7.51 (d"t", 1H, J = 7.6/7.6/1.5 Hz), 7.54−7.63 (m, 6H), 7.83 (d, 2H, J = 7.1 Hz), 7.95−7.99 (m, 1H), 8.03−8.08 (m, 2H), 8.14 (s, 1H), 8.28 (dd, 1H, J = 7.6/1.5 Hz), 8.44 (dd, 1H, J = 8.7 Hz), 8.81 (s, 1H), 12.39 (s, 1H). Anal. H, N, S; C: calcd, 81.28; found, 80.84.

2-(4-Methoxyphenyl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11k) was prepared following general procedure C from **10k** (500 mg, 1.27 mmol), phosphorus pentasulfide (509 mg, 2.3 mmol), and $NaHCO_3$ (726 mg, 8.6 mmol) in 1,4-dioxane (20 mL) in 40% yield: colorless crystals from toluene; mp 282 °C dec; IR 3160 cm^{-1} (NH); ^1H NMR (400 MHz) 3.54 (br s, 1H), 3.83 (s, 3H, OCH_3), 4.19 (br s, 1H), 7.06 (d, 2H, J = 8.4 Hz), 7.37 (d, 1H, J = 7.8 Hz), 7.46 (d"t", 1H, J = 7.8/7.8/1.3 Hz), 7.50−7.60 (m, 4H), 7.77 (d, 2H, J = 6.6 Hz), 7.87 (s, 1H), 8.17−8.22 (m, 3H), 12.35 (s, 1H). Anal. H, N, S; C: calcd, 76.44; found, 75.84.

4-(4-Methoxyphenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11l) was prepared following general procedure C from **10l** (236 mg, 0.6 mmol), phosphorus pentasulfide (294 mg, 1.32 mmol), and $NaHCO_3$ (430 mg, 5.1 mmol) in THF (15 mL) in 61% yield: colorless crystals; mp 302 °C; IR 3140 cm^{-1} (NH); ^1H NMR (400 MHz) 3.56 (br s, 1H), 3.86 (s, 3H, OCH_3), 4.26 (br s, 1H), 7.12 (d, 2H, J = 8.7 Hz), 7.37 (dd, 1H, J = 8.1/1.0 Hz), 7.44−7.60 (m, 5H), 7.78 (d, 2H, J = 8.7 Hz), 7.91 (s, 1H), 8.21 (d"t", 3H, J = 8.6/8.6/1.0 Hz), 12.37 (s, 1H). Anal. C, H, N, S.

2,4-Bis(4-methoxyphenyl)-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11m) was prepared following general procedure C from **10m** (279 mg, 0.66 mmol), phosphorus pentasulfide (294 mg, 1.32 mmol), and $NaHCO_3$ (430 mg, 5.1 mmol) in 1,4-dioxane (15 mL) in 58% yield: colorless crystals; mp 309 °C; IR 3150 cm^{-1} (NH); ^1H NMR (400 MHz) 3.51 (br s, 1H), 3.83 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.23 (br s, 1H), 7.05 (d, 2H, J = 9.2 Hz), 7.12 (d, 2H, J = 8.7 Hz), 7.36 (d, 1H, J = 7.6 Hz), 7.46 ("t", 1H, J = 7.6/7.6 Hz), 7.57 ("t", 1H, J = 7.6/7.6 Hz), 7.76 (d, 2H, J = 8.7 Hz), 7.84 (s, 1H), 8.15−8.22 (m, 3H), 12.35 (s, 1H). Anal. C, H, N, S.

4-(3,4-Dimethoxyphenyl)-2-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11n) was prepared following general procedure C from **10n** (185 mg, 0.44 mmol), phosphorus pentasulfide (200 mg, 0.9 mmol), and $NaHCO_3$ (285 mg, 3.4 mmol) in 1,4-dioxane (15 mL) in 62% yield: colorless crystals; mp 285 °C dec; IR 3200 cm^{-1} (NH); ^1H NMR (400 MHz) 3.56 (br s, 1H), 3.85 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.38 (br s, 1H), 7.13 (d, 1H, J = 8.1 Hz), 7.30 (dd, 1H, J = 8.1/1.5 Hz), 7.35−7.55 (m, 6H), 7.58 (d"t", 1H, J = 7.6/7.6/1.5 Hz), 7.93 (s, 1H), 8.17−8.25 (m, 3H), 12.40 (s, 1H). Anal. C, H, N, S.

2-(1,3-Benzodioxol-5-yl)-4-phenyl-5*H*-pyrido[3,2-*d*][1]-benzazepine-6(7*H*)-thione (11o) was prepared following general procedure C from **10o** (250 mg, 0.62 mmol), phosphorus pentasulfide (294 mg, 1.32 mmol), and $NaHCO_3$ (430 mg, 5.1 mmol) in 1,4-dioxane (15 mL) in 42% yield: colorless crystals; mp 276 °C; IR 3150 cm^{-1} (NH); ^1H NMR (400 MHz) 3.91 (br s, 1H), 4.17 (br s, 1H), 6.10 (s, 2H, methylenedioxy-CH_2), 7.03 (d, 1H, J = 8.1 Hz), 7.36 (d, 1H, J = 7.1 Hz), 7.46 (d"t", 1H, J = 7.6/7.6/1.0 Hz), 7.49−7.60 (m, 4H), 7.77 (d, 2H, J = 8.1 Hz), 7.80 (d, 2H, J = 8.1 Hz), 7.88 (s, 1H), 8.19 (dd, 1H, J = 7.9/1.5 Hz), 12.35 (s, 1H). Anal. C, H, N, S.

7-Methyl-2,4-diphenyl-5*H*-pyrido[3,2-*d*][1]benzazepin-6(7*H*)-one (12). Sodium hydride (13.2 mg, 0.55 mmol) was added to a solution of **10a** (200 mg, 0.55 mmol) in THF (10 mL). After the mixture was refluxed for 75 min, a solution of iodomethane (78 mg, 0.55 mmol) in THF (3 mL) was added, and refluxing was continued for 90 min. After being cooled to room temperature the mixture was poured onto crushed ice (20 g) and stirred until melting of the ice. The precipitate was collected by filtration, washed with water, and recrystallized from ethanol to afford **12** as colorless plates (72%): mp 242 °C; IR 1665 cm^{-1} (C=O); ^1H NMR (400 MHz) 3.24 (d, 1H, J = 13.2 Hz), 3.31 (s, 3H, CH_3), 3.68 (d, 1H, J = 13.2 Hz), 7.42−7.65 (m, 9H), 7.67−7.72 (m, 2H), 7.95 (s, 1H), 8.11 (dd, 1H, J = 8.2/1.5 Hz), 8.24 (d, 2H, J = 7.1 Hz). Anal. C, H, N.

7-Methyl-2,4-diphenyl-5*H*-pyrido[3,2-*d*][1]benzazepine-6(7*H*)-thione (13). Lawesson's reagent[9] (222 mg; 0.55 mmol) was stirred with **12** (362 mg, 1 mmol) in toluene (17 mL) for 6 h at 100 °C. The mixture was filtered hot through a short silica gel column (silica gel 100−200, 60 A, ICN, 2.5 g). After the column was eluted with ethanol (50 mL), the combined organic fractions were evaporated and the residue recrystallized from ethanol yielding **13** as colorless needles (58%): mp 199 °C; IR 3050 cm^{-1} (C−H arom); ^1H NMR (400 MHz) 3.63 (d, 1H, J = 13.2 Hz), 3.75 (s, 3H, CH_3), 4.40 (d, 1H, J = 13.2 Hz), 7.44−7.60 (m, 7H), 7.62−7.70 (m, 2H), 7.75 (d, 2H, J = 6.6 Hz), 7.93 (s, 1H), 8.07 (dd, 1H, J = 7.6/1.0 Hz), 8.24 (dd, 2H, J = 8.1/2.5 Hz). Anal. C, H, N, S.

6-Methyl-10,12-diphenyl-9*H*-pyrido[3,2-*d*][1,2,4]triazolo-[4,3-*a*][1]benzazepine (15). A slurry of acetic hydrazide (370 mg, 0.5 mmol) and **14** (196 mg, 0.5 mmol) in 1-butanol (10 mL) was refluxed for 5 h. The mixture was then evaporated to give a solid residue, which was stirred with water (10 mL), collected by filtration, and recrystallized from ethanol/toluene to yield colorless crystals in 48% yield: mp 268 °C; IR 3060 (C−H arom), 1585 cm^{-1} (C=C arom); ^1H NMR (500 MHz) 3.61 (d, 1H, J = 14.8 Hz), 4.35 (d, 1H, J = 14.8 Hz), 7.43−7.54 (m, 3H), 7.58 ("t", 1H, J = 5.6/5.6 Hz), 7.62−7.79 (m, 7H), 7.94 (s, 1H), 8.22 (d, 2H, J = 5.6 Hz), 8.26 (d, 1H, J = 5.6 Hz). The signal of the CH_3 moiety was not detectable in DMSO-d_6, because it was obscured by the water signal at 3.30 ppm. Therefore, acetone-d_6 was added to disclose the mentioned signal at δ 3.29 ppm (s, 3H, CH_3). Anal. C, H, N.

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Supporting Information Available: log GI_{50} and log LC_{50} values for compounds **2a** and **2b**, **5**−**7**, **10a**−**r**, **11a**−**o**, and **12**−**15**, including the MG_MID values and the results for the renal cancer cells 786-0, ACHN, and TK-10 **(**3 pages**)**. Ordering information is given on any current masthead page.

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