

Full Paper

# An Efficient Synthesis and Reactions of Novel Indolylpyridazinone Derivatives with Expected Biological Activity

Samar A. Abubshait

Chemistry Department, Girls College of Science, P.O. Box 838, Dammam-31113, Saudi Arabia, Tel: (+966) 504988846, Fax: (+966) 38681088; E-mail: abu\_sa\_005@yahoo.com

Received: 29 October 2006; in revised form: 9 December 2006 / Accepted: 18 December 2006 / Published: 10 January 2007

Abstract: Reaction of 4-anthracen-9-yl-4-oxo-but-2-enoic acid (1) with indole gave the corresponding butanoic acid 2. Cyclocondensation of 2 with hydrazine hydrate, phenyl hydrazine, semicarbazide and thiosemicarbazide gave the pyridazinone derivatives 3a**d**. Reaction of **3a** with POCl<sub>3</sub> for 30 min gave the chloropyridazine derivative **4a**, which was used to prepare the corresponding carbohydrate hydrazone derivatives 5a-d. Reaction of chloropyridazine 4a with some aliphatic or aromatic amines and anthranilic acid gave 6a-f and 7, respectively. When the reaction of the pyridazinone derivative 3a with POCl<sub>3</sub> was carried out for 3 hr an unexpected product 4b was obtained. The structure of 4b was confirmed by its reaction with hydrazine hydrate to give hydrazopyridazine derivative 9, which reacted in turn with acetyl acetone to afford 10. Reaction of 4b with methylamine gave 11, which reacted with methyl iodide to give the trimethylammonium iodide derivative 12. The pyridazinone 3a also reacted with benzene- or 4-toluenesulphonyl chloride to give 13a-b and with aliphatic or aromatic aldehydes to give **14a-g**. All proposed structures were supported by IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, and MS spectroscopic data. Some of the new products showed antibacterial activity.

**Keywords**: Substituted pyridazinones, chloropyridazine, anthracene, indole, antibacterial activity.

#### Introduction

In recent years a substantial number of 6-aryl-3-(2*H*)-pyridazinones have been reported to possess antimicrobial [1, 2], potent analgesic [3], anti-inflammatory [3-7], antifeedant [8], herbicidal [9], antihypertensive [10-12] and antiplatelet activities [13-15], anticancer effects [16] and other anticipated biological [17] and pharmacological properties [18, 19]. In particular, a large number of indolylpyridazinone derivatives are well known as antimicrobial agents [1, 20], intermediates for drugs and agrochemicals [21, 22], antiphlogistics [23], antipyretics [24], inflammation inhibitors [25], blood platelet aggregation inhibitors, cardiovascular and antihypertensive agents [26]. As part of our program aimed at utilizing  $\beta$ -aroylpropionic acid derivatives containing the indole moiety as starting materials for the synthesis of pyridazine and pyridazinone derivatives, these reports of interesting biological activities prompted us to synthesize a new series of 6-anthracenepyridazinones containing indolyl moieties through the nucleophilic addition of indole to 6-anthracene-4-oxo-2-butenoic acid, followed by cyclocondensation of the resulting adduct to give the corresponding dihydropyridazinone and to screen some of these new compounds for antibacterial activity.

#### **Results and Discussion**

4-Anthracen-9-yl-4-oxo-but-2-enoic acid (1) was prepared following a reported procedure [1, 27]. Reaction of 1 with indole in dry benzene gave 4-anthracen-9-yl-2-(1*H*-indol-3-yl)-4-oxo-butyric acid (2). Cyclocondensation of 2 with hydrazine hydrate, phenyl hydrazine, semicarbazide and thiosemicarbazide in dry benzene [28-31] gave 6-anthracen-9-yl-4-(1*H*-indol-3-yl)-4,5-dihydro-2*H*-pyridazin-3-one, 6-anthracen-9-yl-4-(1*H*-indol-3-yl)-2-phenyl-4,5-dihydro-2*H*-pyridazin-3-one, 3-anthracen-9-yl-5-(1*H*-indol-3-yl)-6-oxo-5,6-dihydro-4*H*-pyridazine-1-carboxylic acid amides **3a-d**, respectively (Scheme 1). Physical properties, mass spectral data and elemental analyses for the synthesized compounds **1-3d** are given in Table 1.





Compound	<b>M.P.</b> (°C)	Mol. Formula	M.W.	Analysis % Calc./ Found			
No	Cryst. solvent	Mol. weight	from MS	С	Н	Ν	S
1	215-217	$C_{18}H_{12}O_3$	276.08	78.25	4.38		
	Ethanol	276.29		78.20	4.35		
2	223	$C_{26}H_{19}NO_3$	393.14	79.37	4.87	3.56	
	Benzene	393.43		79.35	4.82	3.53	
<b>3</b> a	122	$C_{26}H_{19}N_{3}O$	389.15	80.18	4.92	10.79	
	Benzene	389.45		80.20	4.72	10.59	
3b	270	$C_{32}H_{23}N_{3}O$	465.18	82.56	4.98	9.03	
	Benzene	465.54		82.58	4.94	9.06	
3c	145	$C_{27}H_{20}N_4O_2$	432.16	74.98	4.66	12.96	
	Benzene	432.47		75.01	4.70	13.00	
3d	160	$C_{27}H_{20}N_4OS$	448.14	72.30	4.49	12.49	7.15
	Benzene	448.54		72.37	4.53	12.52	7.20

Table 1. Physical properties, mass spectral data and elemental analyses for compounds 1-3.

Reaction of pyridazinone **3a** with POCl<sub>3</sub> for 30 min gave the chloropyridazine derivative **4a** [32], which reacted with carbohydrate hydrazones of ribose, glucose, galactose and lactose in ethanol to give hydrazonopyradazine derivatives **5a-d** [6, 12]. Mixing chloropyridazine **4a** with aliphatic or aromatic amines, namely methylamine, ethylamine, aniline, sulphanilinic acid,  $\alpha$ -naphthylamine or diphenylamine in dry benzene gave pyridazine derivatives **6a-f** [7, 12, 33]. In addition, **4a** reacted with anthranilic acid in dry benzene to give **7** (Scheme 2) [1, 30, 32]. Physical properties, mass spectral data and elemental analyses for all newly synthesized compounds **4a-7** are listed in Table 2.



Scheme 2.

Comment		Mal Essentia		Analyzia % Cala / Faund			
Compound	<b>M.P.</b> (°C)	Mol. Formula	<b>WI.W.</b>	Analys	18 % Ca	alc./ Fou	ina
No	Cryst. solvent	Mol. Weight	from MS	С	Η	Ν	S
<b>4</b> a	200	$C_{26}H_{16}ClN_3$	405.10	76.94	3.97	10.35	
	Benzene	405.88		76.99	3.94	10.33	
<b>4b</b>	152	$C_{18}H_{11}ClN_2$	290.06	74.36	3.81	9.64	
	Benzene	290.75		74.40	3.85	9.66	
5a	360	$C_{31}H_{27}N_5O_4$	533.56	69.78	5.10	13.13	
	Ethanol	533.58		69.82	5.15	13.17	
5b	315	$C_{32}H_{29}N_5O_5$	563.60	68.19	5.19	12.43	
	Ethanol	563.60		68.23	5.23	12.40	
5c	348	$C_{32}H_{29}N_5O_5$	563.60	68.19	5.19	12.43	
	Ethanol	563.60		68.14	5.23	12.44	
5d	138-140	$C_{38}H_{39}N_5O_{10}$	725.24	62.89	5.42	9.65	
	Ethanol	725.74		62.93	5.46	9,63	
6a	147	$C_{27}H_{20}N_4$	400.17	80.98	5.03	13.99	
	Benzene	400.47		80.95	5.08	14.02	
6b	210	$C_{28}H_{22}N_4$	414.18	81.13	5.35	13.52	
	Benzene	414.50		81.20	5.40	13.56	
6с	156	$C_{32}H_{22}N_4$	462.54	83.09	4.79	12.11	
	Benzene	462.54		83.12	4.74	12.09	
6d	286	$C_{32}H_{22}N_4O_3S$	542.14	70.83	4.09	10.33	5.91
	Benzene	542.61		70.79	4.00	10.00	5.94
6e	199	$C_{36}H_{24}N_4$	512.22	84.35	4.72	10.93	
	Benzene	512.60		84.40	4.76	10.95	
6f	236	$C_{38}H_{26}N_4$	538.22	84.73	4.87	10.40	
	Benzene	538.64		84.77	4.82	10.46	
7	130	$C_{33}H_{20}N_4O$	488.16	81.13	4.13	11.47	
	Benzene	488.54		81.16	4.17	11.50	

Table 2. Physical properties, mass spectral data and elemental analyses for compounds 4-7.

Surprisingly, when the reaction of **3a** with POCl<sub>3</sub> was carried out for 3 hr an unexpected product, 6-anthracen-9-yl-6-chloropyridazine (**4b**), was obtained via dearylation and substitution of the hydroxyl group by chlorine [20] (Scheme 2). The structure of **4b** was proven by the similarity of its melting point to that of an authentic sample which was independently prepared by the reaction of 4-anthracen-9-yl-4-oxo-but-2-enoic acid (**1**) with hydrazine hydrate in dry benzene and treatment of the resulting pyridazinone **8** with POCl<sub>3</sub> for 30 min to give **4b** (Scheme 3) [1, 5, 7, 30, 31]. Reaction of chloropyridazine **4b** with hydrazine hydrate in boiling benzene [34] gave the hydrazinopyridazine derivative **9**, whose structure was inferred from its infrared spectrum. The structure of **9** was further confirmed by its reaction with acetyl acetone in boiling methanol that gave 3-anthracen-9-yl-6-(3,5-dimethylpyrazol-1-yl) pyridazine (**10**) [5, 6, 14, 32]. As a point of interest, it was observed that reaction of **4b** with methylamine at 140 °C afforded **11**. On the other hand, when compound **11** was reacted with excess CH<sub>3</sub>I in methanol the quaternary ammonium iodide derivative **12** was formed (Scheme 3). Physical properties, mass spectral data and elemental analyses for all newly synthesized compounds **8-12** are given in Table 3.



Table 3. Physical properties, mass spectral data and elemental analyses for compounds 8-12.

Compound	<b>M.P.</b> (°C)	Mol. Formula	M.W.	Analysis % Calc./ Found			
No	Cryst. solvent	Mol. Weight	from MS	С	Н	Ν	S
8	165	$C_{18}H_{12}N_2O$	272.30	79.39	4.44	10.29	
	Benzene	272.30		79.42	4.40	10.32	
9	230	$C_{18}H_{14}N_4$	286.12	75.50	4.93	19.57	
	Benzene	286.33		75.50	4.90	19.59	
10	210	$C_{23}H_{18}N_4$	350.15	78.83	5.18	15.99	
	Methanol	350.42		78.88	5.15	16.02	
11	126	$C_{19}H_{15}N_3$	285.12	79.98	5.30	14.73	
	Methanol	285.34		80.02	5.28	14.77	
12	150	$C_{21}H_{20}N_{3}I$	314.17	57.15	4.57	9.52	
	Methanol	441.31		57.10	4.52	9.58	

The reaction of pyridazinone **3a** with benzene/4-toluenesulfonyl chloride and anhydrous  $K_2CO_3$  in dry acetone at reflux for 24 hr gave 6-anthracen-9-yl-4-(1*H*-indol-3-yl)-2-(benzenesulfonyl or 4-toluenesulfonyl)-4,5-dihydro-2*H*-pyridazin-3-ones **13a** and **13b**, respectively. Pyridazinone **3a** also reacted with same aliphatic and aromatic aldehydes namely formaldehyde, acetaldehyde, benzaldehyde, 2-hydroxybenzaldehyde, 4-hydroxybenzaldehyde, 2-methoxybenzaldehyde, 4-methoxybenzaldehyde, 2,4-dimethoxybenzaldehyde, 2-hydroxynapthaldehyde and furfuraldehyde to give pyridazinone derivatives **14a-j**, respectively (Scheme 4). Physical properties, mass spectral data and elemental analyses for all new compounds **13a-14j** are given in Table 4.



Table 4. Physical properties, mass spectral data and elemental analyses for compounds 13-14.

Compound	M.P. (°C)	Mol. Formula	M.W.	Analysis % Calc./ Found			nd
No	Cryst. solvent	Mol. Weight	from MS	С	Н	Ν	S
13a	154	C <sub>32</sub> H <sub>23</sub> N <sub>3</sub> O <sub>3</sub> S	529.15	72.57	4.38	7.93	6.05
	Benzene	526.61		72.50	4.41	7.90	6.00
13b	177	$C_{33}H_{25}N_3O_3S$	543.16	72.91	4.64	7.73	5.90
	Benzene	543.64		72.95	4.68	7.77	5.93
14a	260	$C_{27}H_{19}N_{3}O$	401.15	80.78	4.77	10.47	
	Benzene	401.46		80.74	4.79	10.41	
14b	288	$C_{28}H_{21}N_{3}O$	415.17	80.94	5.09	10.11	
	Benzene	415.49		80.89	5.13	10.07	
14c	360	$C_{33}H_{23}N_{3}O$	477.18	83.00	4.85	8.80	
	Benzene	477.56		83.03	4.88	8.85	
14d	350	$C_{33}H_{23}N_3O_2$	493.18	80.31	4.70	8.51	
	Benzene	493.55		80.40	4.73	8.53	
14e	264	$C_{33}H_{23}N_3O_2$	493.18	80.31	4.70	8.51	
	Benzene	493.55		80.37	4.75	8.55	
14f	196	$C_{34}H_{25}N_3O_2$	507.19	80.45	4.96	8.28	
	Benzene	507.58		80.49	4.92	8.22	
14g	202	$C_{34}H_{25}N_3O_2$	507.19	80.45	4.96	8.28	
	Benzene	507.58		80.49	5.10	8.26	
14h	94	$C_{35}H_{27}N_3O_3$	537.61	78.19	5.06	7.82	
	Benzene	537.61		78.22	5.10	7.85	
14i	230	$C_{37}H_{25}N_3O_2$	543.19	81.75	4.64	7.73	
	Benzene	543.61		81.80	4.68	7.70	
14j	328	$C_{31}H_{21}N_3O_2$	467.16	79.64	4.53	8.99	
	Benzene	467.16		79.66	4.55	9.11	

#### Molecules 2007, 12

#### **Biological Screening**

The activities of some of the prepared compounds against representative Gram positive and negative bacteria were tested by the disk diffusion method [1, 8, 35]. The results are listed in Table 5. From the data it is clear that compounds **6b**, **14i** possess high activity against both types of bacteria, while compound **6c** displays low activity. Compounds **1** and **6b** possess high activity, compounds **2**, **3a-3d**, **4a**, **5a**, **5d**, **14g**, **14i** possess moderate activity and compounds **6c** and **13a** possess less activity against Gram positive strains. As far as Gram negative microorganisms are concerned, compound **14i** showed high activity, while compounds **1**, **2**, **3a**, **3b**, **3d**, **4a**, **5a**, **5d**, **6b**, **13a** and **14g** all displayed moderate activity and **3c** and **6c** possess less activity against such microorganisms.

Compound	Gram posit	ive bacteria	Gram negative bacteria			
No	Staph. aureus	Staph. epidermis	E. coli	Pr. vulgaris		
1	+++	+++	+	++		
2	++	++	++	++		
<b>3</b> a	+	+++	++	++		
3b	++	+++	++	++		
3c	++	++	+	+		
3d	++	++	++	+		
<b>4</b> a	++	++	++	+		
5a	++	++	++	+		
5d	++	++	+++	+		
6b	++	++++	++	++		
6c	++	+	+	+		
13a	+	++	++	++		
14g	+++	+	++	++		
14i	+++	++	+++	++		

Table 5. Antibacterial activity of select compounds\*

\* Solvent: DMF,  $[c] = 250 \ \mu g \ mL^{-1}$ . Ratings: + = less active (inhibition zone 1-5 mm); ++ = more active (inhibition zone 5-10 mm), +++ = more active (inhibition zone 10-15 mm); ++++ = highly active (inhibition zone 15-20 mm); reference substance for Gram positive and Gram negative bacteria: ampicillin.

## Conclusions

A novel synthesis of some new indolylpyridazinone derivatives by cyclocondensation of indolylbutyric acid **2** with hydrazine hydrate and its derivatives to give pyridazinone derivatives **3a-d** is described. The reactions of pyridazinone **3a** with  $PCl_5/POCl_3$ , arylsulphonyl chloride derivatives and aliphatic or aromatic aldehydes were studied, as were the behaviors of chloropyridazine derivatives towards hydrazine hydrate, carbohydrate hydrazones and aliphatic or aromatic amines. The structures of all new synthesized compounds were established from their spectral data and elemental analysis. Additionally, the antimicrobial activity of selected compounds against Gram positive and negative bacteria is reported.

#### Acknowledgements

I thank Dr. Malka Mehsen in Girls College of Science, Dammam, Saudi Arabia for performing the biological tests

#### **Experimental**

#### General

Melting points were determined on Reichert hot stage microscope and are uncorrected. IR spectra were measured with a Nicolet Magna 520 instrument, using potassium bromide disks; results are given in cm<sup>-1</sup>. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were recorded at 200 and 90.56 MHz, respectively, in DMSO- $d_6$  on a JEOL JNM-GX270 spectrometer. The chemical shifts are reported in parts per million (ppm) downfield from internal tetramethylsilane (TMS). Electron impact MS spectra were obtained on a JEOL JMS-HX 100 instrument at 70 eV. Elemental microanalysis was done on a Carlo Erba analyzer model 110. Suitable crystals were grown by slow crystallization from methanol, ethanol and benzene.

#### 4-Anthracen-9-yl-4-oxo-but-2-enoic acid (1)

Compound **1** was prepared following the literature procedure [1, 20, 27]. It was obtained in 85% yield as white crystals; IR (cm<sup>-1</sup>): 1608 (C=C), 1662 (ketone C=O), 1699 (acid C=O), 3054, 2970, 2927, 2869 (C-H), 4200-3400 (acid OH); <sup>1</sup>H-NMR: 7.20-8.50 (m, 11H, Ar-H and vinyl), 11 (br, 1H, COOH); <sup>13</sup>C-NMR: 127-144 (16C, Ar and vinyl), 170, 188.10 (2C, acid and ketone <u>C</u>=O). Its physical properties, mass spectral data and elemental analysis are given in Table 1.

#### 4-Anthracen-9-yl-2-(1H-indol-3-yl)-4-oxo-butyric acid (2).

Indole (10 mmol) was added to a solution of 4-anthracen-9-yl-4-oxo-but-2-enoic acid (**1**, 10 mmol) in dry benzene (10 mL) and the reaction mixture was refluxed for 6 hr. The solid that separated on cooling was recrystallized from benzene to give compound **2** as white crystals, yield 80%; IR (cm<sup>-1</sup>): 1618 (C=C), 1674 (ketone C=O), 1708 (acid C=O), 3030, 3070, 2926, 2853 (C-H), 3414 (indole N-H); <sup>1</sup>H-NMR: 3.40 (d, 2H, CH<sub>2</sub>), 4.04 (t, 1H, CH), 6.51 (s, 1H, indole CH), 7.02-7.91 (m, 13H, Ar-H), 10.08 (br, 1H, NH), 11.10 (br, 1H, COOH); <sup>13</sup>C-NMR: 40-41 (2C, <u>CH<sub>2</sub>-CH</u>), 112.50-136.50 (21C, Ar), 123 (1C, indole <u>C-NH</u>), 175.30, 198.90 (2C, acid and ketone <u>C</u>=O). Physical properties, mass spectral data and elemental analysis for compound **2** are given in Table 1.

#### General method for the preparation of **3a-d**:

Hydrazine hydrate derivatives (10 mmol) were added to a solution of 2 (10 mmol) in dry benzene (5 mL) and the resulting reaction mixture was refluxed for 6 hr. The solid that separated on cooling was recystallized from benzene to give compounds **3a-d**. Their physical properties, mass spectral data and elemental analysis are given in Table 1.

#### 6-Anthracen-9-yl-4-(1H-indol-3-yl)-4,5-dihydro-2H-pyridazin-3-one (3a).

Obtained from hydrazine hydrate and **2** as white needles, yield 81%; IR (cm<sup>-1</sup>): 1604 (C=C),1635 (C=N), 1671 (pyridazinone C=O), 3080, 3010, 3054, 2957 (C-H), 3100-3272 (-OH), 3411-3375 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 3.35 (d, 2H, CH<sub>2</sub>), 4.36 (t, 1H, CH), 6.81 (s, 1H, indole CH), 6.90-7.91 (m, 13H, Ar-H), 10.9-12.40 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 33.80-40.10 (2C, <u>CH<sub>2</sub>-CH</u>), 111.20-136 (21C, Ar), 123 (1C, indole <u>C</u>-NH), 153.34 (1C, <u>C</u>=N-N), 170 (1C, C=O).

#### 6-Anthracen-9-yl-4-(1H-indol-3-yl)-2-phenyl-4,5-dihydro-2H-pyridazin-3-one (3b).

Obtained from phenyl hydrazine and **2** as white crystals, yield 79%; IR (cm<sup>-1</sup>): 1605 (C=C), 1640 (C=N), 1674 (pyridazinone C=O), 3054, 3070, 2923, 2869 (C-H), 3400-3411 (indole N-H); <sup>1</sup>H-NMR: 3.35 (d, 2H, CH<sub>2</sub>), 4.05 (t, 1H, CH), 6.80-7.82 (m, 19H, Ar-H), 11.02 (br, 1H, indole NH); <sup>13</sup>C-NMR: 33.80-40.10 (2C, <u>C</u>H<sub>2</sub>-<u>C</u>H), 111.20-136 (26C, Ar), 123 (1C, indole <u>C</u>-NH), 141.20 (1C, <u>C</u>-N-N), 153.34 (1C, <u>C</u>=N-N), 170 (1C, pyridazinone <u>C</u>=O).

### 3-Anthracen-9-yl-5-(1H-indol-3-yl)-6-oxo-5,6-dihydro-4H-pyridazine-1-carboxylic acid amide (3c).

Obtained from semicarbazide and **2** as a white solid, yield 75%; IR (cm<sup>-1</sup>): 1605 (C=C), 1638 (C=N), 1650 (amide C=O), 1678 (pyridazinone C=O), 3070, 3054, 2926(C-H), 3320-3410 (indole and amide N-H, NH<sub>2</sub>); <sup>1</sup>H-NMR: 3.34(d, 2H, CH<sub>2</sub>), 4.05(t, 1H, CH), 4.50(br, 2H, NH<sub>2</sub>), 6.81-7.80(m, 14H, Ar-H), 11.02(br, 1H, indole NH); <sup>13</sup>C-NMR: 33.80-41.07 (2C, <u>CH<sub>2</sub>-CH</u>), 112.11-136 (21C, Ar), 123.80 (1C, indole <u>C</u>-NH), 157.36 (1C, <u>C</u>=N-N), 175,189 (2C, pyridazinone and amide <u>C</u>=O).

# 3-Anthracen-9-yl-5-(1H-indol-3-yl)-6-oxo-5,6-dihydro-4H-pyridazine-1-carbothioic acid amide (3d).

Obtained from thiosemicarbazide and **2** as white needles, yield 87%; IR (cm<sup>-1</sup>): 1270 (C=S), 1604 (C=C), 1640 (C=N), 1704 (pyridazinone C=O), 3057, 3030, 2959(C-H), 3350-3453 (indole and carbothioic acid amide N-H, NH<sub>2</sub>); <sup>1</sup>H-NMR: 3.34 (d, 2H, CH<sub>2</sub>), 4.05 (t, 1H, CH), 4.50 (br, 2H, NH<sub>2</sub>), 7.04-8.30 (m, 14H, Ar-H), 11.02 (br, 1H, indole NH); <sup>13</sup>C-NMR: 33.80-41.07 (2C, <u>CH<sub>2</sub>-CH</u>), 111.56-133.41 (21C, Ar), 122.83 (1C, indole <u>C</u>-NH), 155 (1C, <u>C</u>=N-N), 177 (1C, pyridazinone <u>C</u>=O), 183 (1C, <u>C</u>=S).

#### 3-(6-Anthracen-9-yl-3-chloropyridazin-4-yl)-1H-indole (4a).

POCl<sub>3</sub> (5 mL) was added to **3a** (10 mmol) and the reaction mixture was heated on oil bath for 30 min, set aside to cool and then poured onto crushed ice (60 g), filtered, washed well with water and recrystallized from benzene to give **4a** as a brown solid, yield 81%; IR (cm<sup>-1</sup>): 756 (C-Cl), 1605 (C=C), 1640 (C=N), 3057, 3047, 2923, 2869 (C-H), 3391 (indole N-H); <sup>1</sup>H-NMR: 7.30-8.30 (m, 15H, Ar-H), 10.90 (br, 1H, indole NH); <sup>13</sup>C-NMR: 111.10-135 (23C, Ar), 123 (1C, indole <u>C</u>-NH), 152 (1C, N-N=<u>C</u>-Cl), 160 (1C, <u>C</u>=N-N). Physical properties, mass spectral data and elemental analysis for compound **4a** are given in Table 2.

#### 3-Anthracen-9-yl-6-chloropyridazine (4b).

*Method A:*  $POCl_3$  (5 mL) was added to **3a** (10 mmol) and the reaction mixture was heated on oil bath for 3hr, then set-aside poured on to 60 g crushed ice, filtered, washed well with water and recrystallized from benzene to give **4b** as a brown solid, yield 81%.

*Method B:* POCl<sub>3</sub> (5 mL) was added to **8** (10 mmol) and the reaction mixture was heated on oil bath for 30 min, then set-aside poured on to 60 g crushed ice, filtered, washed well with water and recrystallized from benzene to give **4b** as a brown solid, yield 87%; IR (cm<sup>-1</sup>): 752 (C-Cl), 1605 (C=C), 1648 (C=N), 3057, 3028 (C-H); <sup>1</sup>H-NMR: 7.32-8.28 (m, 11H, Ar-H); <sup>13</sup>C-NMR: 111-132 (16C, Ar), 151 (1C, N-N=<u>C</u>-Cl), 158 (1C, <u>C</u>=N-N). Physical properties, mass spectral data and elemental analysis for compound **4b** are given in Table 2.

# General procedure for the reaction of chloropyridazine **4a** with carbohydrate hydrazones.

The appropriate carbohydrate hydrazone (1 mmol) was added to a mixture of **4a** (1 mmol) in ethanol (5 mL) and the reaction mixture was refluxed for 6 hr. The solid that separated on cooling was recystallized from ethanol to give compounds **5a-d**. Physical properties, mass spectral data and elemental analysis for compounds **5a-d** are given in Table 2.

(2*R*,3*S*,4*S*)-5-{[6-Anthracen-9-yl-4-(1H-indol-3-yl)pyridazin-3-yl]hydrazono}pentane-1,2,3,4,-tetraol (**5a**).

Ribose hydrazone gave compound **5a** as an orange solid, yield 57%; IR (cm<sup>-1</sup>): 1605 (C=C), 1615 (N=N), 1657 (C=N), 3060, 2967, 2926, 2869 (C-H), 3430-3250 (indole and hydrazone N-H, NH-N=C), 3750-3250 (O-H); <sup>1</sup>H-NMR: 3.32-3.50 (m, 3H, aliphatic CH-OH), 3.68 (d, 2H, aliphatic CH<sub>2</sub>-OH), 3.90 (s, 1H, NH-N), 4.85 (br, 4H, OH), 7- 8.27 (m, 15H, Ar-H), 7.53 (s, 1H, CH=N), 10.90 (br, 1H, indole NH); <sup>13</sup>C-NMR: 60.9-74.60 (4C, aliphatic <u>C</u>-O), 111-138.70 (23C, Ar), 122.60 (1C, indole <u>C</u>-NH), 148-154 (2C, <u>C</u>=N-N), 159.20 (1C, N-<u>C</u>=N).

# (2*R*,3*R*,4*R*,5*S*)-6-{[6-Anthracen-9-yl-4-(1H-indol-3-yl)pyridazin-3-yl]-hydrazono}-hexane-1,2,3,4,5-pentaol (**5b**).

Glucose hydrazone gave compound **5b** as a yellow solid, yield 52%; IR (cm<sup>-1</sup>): 1600 (C=C), 1637 (C=N), 3060, 2960, 2925 (C-H), 3414-3197 (indole and hydrazone N-H), 3625-3620 (O-H); <sup>1</sup>H-NMR: 3.30-3.44 (m, 4H, aliphatic CH-OH), 3.68 (m, 2H, aliphatic CH<sub>2</sub>-OH), 3.90 (s, 1H, NH-N), 4.85 (br, 5H, OH), 6.80-8.50 (m, 15H, Ar-H), 7.53 (s, 1H, CH=N), 10.90 (br, 1H, indole NH); <sup>13</sup>C-NMR: 62.10-73.90 (5C, aliphatic <u>C</u>-O), 111-148.70 (23C, Ar), 122.80 (1C, indole <u>C</u>-NH), 148.60-154.7 (2C, <u>C</u>=N-N), 164 (1C, N-<u>C</u>=N).

# (2*R*,3*S*,4*R*,5*S*)-6-{[6-Anthracen-9-yl-4-(1*H*-indol-3-yl)pyridazin-3-yl]hydrazono}-hexane-1,2,3,4,5-pentaol (**5c**).

Galactose hydrazone gave compound **5c** as a white solid, yield 55%; IR (cm<sup>-1</sup>): 1565 (HN-N=C), 1605 (C=C), 1640 (C=N), 3057, 2960, 2923, 2890 (C-H), 3460-3412 (indole and hydrazone N-H), 3629-3400 (O-H); <sup>1</sup>H-NMR: 2.50-3.48 (m, 4H, aliphatic CH-OH), 3.60 (m, 2H, aliphatic CH<sub>2</sub>-OH), 3.91 (s, 1H, NH-N), 4.85 (br, 5H, OH), 7.00-8.10 (m, 15H, Ar-H), 7.51 (s, 1H, CH=N), 10.91 (br, 1H, indole NH); <sup>13</sup>C-NMR: 61.10-73.90 (5C, aliphatic <u>C</u>-O), 111-148.70 (23C, Ar), 122 (1C, indole <u>C</u>-NH), 148.60-154.70 (2C, <u>C</u>=N-N), 159.20 (1C, N-<u>C</u>=N).

# 6-{[6-Anthracen-9-yl-4-(1H-indol-3-yl)pyridazin-3-yl]hydrazono}-3-(3,4,5-trihydroxy-6-hydroxy-methyltetrahydropyran-2-yloxy)-hexane-1,2,4,5-tetraol (**5d**).

Lactose hydrazone gave compound **5d** as a white solid, yield 58%; IR (cm<sup>-1</sup>): 1570 (HN-N=C), 1605 (C=C), 1638 (C=N), 3057, 2960, 2923(C-H), 3412-3412 (indole and hydrazone N-H), 3635-3390 (O-H); <sup>1</sup>H-NMR: 2.99-3.76(m, 9H, aliphatic CH-OH), 3.66-3.68 (m,4H, aliphatic CH<sub>2</sub>-OH), 3.90 (s, 1H, NH-N), 4.85 (br, 8H, OH), 7.00-8.50 (m, 15H, Ar-H), 7.50 (s, 1H, CH=N), 10.90 (br, 1H, indole, NH); <sup>13</sup>C-NMR: 62.50-72.10 (10C, aliphatic <u>C</u>-O), 96.50 (1C, O-<u>C</u>-O), 111-148.70 (23C, Ar), 122 (1C, indole <u>C</u>-NH), 148.60-154.70 (2C, <u>C</u>=N-N), 159.20 (1C, N-<u>C</u>=N).

### General reaction of chloropyridazine 4a with aliphatic or aromatic amines

The aliphatic or aromatic amine (1 mmol) was added to a mixture of **4a** (1 mmol) in dry benzene (5 mL) and the reaction mixture was heated in oil bath for 6 hr. The solid that separated on cooling was recrystallized from benzene to give compounds **6a-f**. Their physical properties, mass spectral data and elemental analysis are given in Table 2.

# [6-Anthracen-9-yl-4-(1H-indol-3-yl)-pyridazin-3-yl]-methylamine (6a).

Methylamine gave **6a** as a white solid, yield 67%; IR (cm<sup>-1</sup>): 1619 (C=C), 1637 (C=N), 3054, 3030, 2957, 2923 (C-H), 3413-3406 (indole and secondary amine N-H); <sup>1</sup>H-NMR: 0.83 (s, 3H, CH<sub>3</sub>), 3.89 (br, 1H, secondary amine NH), 7.05-7.90 (m, 15H, Ar-H), 11.12 (br, 1H, indole NH); <sup>13</sup>C-NMR: 37.50 (1C, N-<u>C</u>H<sub>3</sub>), 111-136 (23C, Ar), 123 (1C, indole <u>C</u>-NH), 148.60 (1C, N-<u>C</u>=N), 159.2 (1C, <u>C</u>=N-N).

#### [6-Anthracen-9-yl-4-(1H-indol-3-yl)-pyridazin-3-yl]-ethylamine (6b).

Ethylamine gave **6b** as a brown solid, yield 52%; IR (cm<sup>-1</sup>): 1617 (C=C), 1635 (C=N), 3054, 2967, 2925, 2869 (C-H), 3429-3410 (indole N-H and secondary amine N-H); <sup>1</sup>H-NMR: 0.85 (t, 3H, CH<sub>3</sub>), 1.60 (m, 2H, CH<sub>2</sub>), 3.89 (br, 1H, secondary amine NH), 7.05-8.00 (m, 15H, Ar-H), 11.10 (br, 1H, indole NH); <sup>13</sup>C-NMR: 16.20 (1C, <u>C</u>H<sub>3</sub>), 44.20 (1C, N-<u>C</u>H<sub>2</sub>), 111-136 (23C, Ar), 123.41 (1C, indole <u>C</u>-NH), 151.10 (1C, <u>C</u>=N-N), 160.10 (1C, N-<u>C</u>=N).

[6-Anthracen-9-yl-4-(1H-indol-3-yl)-pyridazin-3-yl]-phenylamine (6c).

Aniline gave **6c** as white needles, yield 72%; IR (cm<sup>-1</sup>): 1617 (C=C), 1638 (C=N), 3057, 2982, 2973, 2869 (C-H), 3429-3400 (indole N-H and secondary amine N-H); <sup>1</sup>H-NMR: 3.89 (br, 1H, secondary amine NH), 6.80-8.30 (m, 20H, Ar-H), 11.10 (br, 1H, indole NH); <sup>13</sup>C-NMR: 111-148 (29C, Ar), 123 (1C, indole <u>C</u>-NH), 150.10 (1C, <u>C</u>=N-N), 160.5 (1C, N-<u>C</u>=N).

#### 4-[6-Anthracen-9-yl-4-(1H-indol-3-yl)-pyridazin-3-ylamino] benzenesulfonic acid (6d).

Sulphanilic acid gave **6d** as a gray solid, yield 51%; IR (cm<sup>-1</sup>): 1160, 1423 (SO<sub>2</sub>), 1601 (C=C), 1631 (C=N), 3057, 2960, 2920 (C-H), 3390 (indole and secondary amine N-H), 3200-3100 (O-H); <sup>1</sup>H-NMR: 3.89 (br, 1H, secondary amine NH), 6.00-8.50 (m, 19H, Ar-H), 11.10 (br, 1H, indole NH), 14.90 (br, 1H, SO<sub>3</sub>H); <sup>13</sup>C-NMR: 111-148.70 (27C, Ar), 133.50 (1C, <u>C</u>-S), 124 (1C, indole <u>C</u>-NH), 148.60 (1C, <u>C</u>=N-N), 150.50 (1C, -NH-Ph), 159 (1C, N-<u>C</u>=N).

#### [6-Anthracen-9-yl-4-(1H-indol-3-yl)-pyridazin-3-yl]-naphthalen-1-yl amine (6e).

α-Naphthylamine gave **6e** as a light brown solid, yield 58%; IR (cm<sup>-1</sup>): 1616 (C=C), 1640 (C=N), 3054, 2999, 2973 (C-H), 3429-3401 (indole and secondary amine N-H); <sup>1</sup>H-NMR: 3.89 (br, 1H, secondary amine NH), 6.70-8.27 (m, 22H, Ar-H), 11.10 (br, 1H, indole NH); <sup>13</sup>C-NMR: 109.40-141.60 (33C, Ar), 122 (1C, indole <u>C</u>-NH), 148.60 (1C, <u>C</u>=N-N), 161.20 (1C, N-<u>C</u>=N).

#### [6-Anthracen-9-yl-4-(1H-indol-3-yl)-pyridazin-3-yl] diphenylamine (6f).

Diphenylamine gave **6f** as a dark brown solid, yield 51%; IR: 1617 (C=C), 1635 (C=N), 3057, 2982, 2973 (C-H), 3410 (indole N-H); <sup>1</sup>H-NMR: 6.72-8.50 (m, 25H, Ar-H), 11.10 (br, 1H, indole NH); <sup>13</sup>C-NMR: 111-136 (33C, Ar), 122.50 (1C, indole <u>C</u>-NH), 142.90 (2C, N-<u>C</u>), 150 (1C, <u>C</u>=N-N), 160 (1C, N-<u>C</u>=N).

#### 2-Anthracen-9-yl-4-(1H-indol-3-yl)-1,9-a,10-triaza-anthracen-9-one (7).

Anthranilic acid (1 mmol) was added to a mixture of **4a** (1 mmol) in dry benzene (5 mL) and the reaction mixture was refluxed for 6 hr. The solid that separated on cooling was recystallized from benzene to give **7** as a brown solid, yield 65%; IR: 1600 (C=C), 1638 (C=N), 1665 (C=O), 3050, 2959, 2925, 2869 (C-H), 3410-3290 (indole N-H); <sup>1</sup>H-NMR: 7.10-8.60 (m, 19H, Ar-H), 12 (br, 1H, indole NH); <sup>13</sup>C-NMR: 111-147.70 (29C, Ar), 122 (1C, indole <u>C</u>-NH), 155.50 (1C, <u>C</u>=N-N), 160 (1C, N-<u>C</u>=N), 170 (1C, N-<u>C</u>=O).

#### 6-Anthracen-9-yl-2H-pyridazin-3-one (8).

Hydrazine hydrate (1 mmol) was added to a solution of 4-anthracen-9-yl-4-oxo-but-2-enoic acid (1, 1 mmol) in dry benzene (10 mL) and the reaction mixture was refluxed for 6 hr. The solid that separated after concentration and cooling was recrystallized from benzene to give  $\mathbf{8}$  as white needles,

#### Molecules 2007, 12

yield 85%; IR (cm<sup>-1</sup>): 1604 (C=C), 1630 (C=N), 1670 (C=O), 3070, 3030, 2957 (C-H), 3411-3357 (indole N-H); <sup>1</sup>H-NMR: 6.50-8.60 (m, 11H, Ar-H), 10.20 (br, 1H, pyridazinone NH); <sup>13</sup>C-NMR: 111-135.70 (16C, Ar), 155 (1C, <u>C</u>=N-N), 168 (1C, <u>C</u>=O).

#### 6-Anthracen-9-yl-pyridazin-3-yl) hydrazine (9).

Hydrazine hydrate (1 mmol) was added to a solution of **4b** (1 mmol) in dry benzene (10 mL) and the reaction mixture was refluxed for hr. The solid that separated was recrystallized from dry benzene to give **9** as buff crystals, yield 70%; IR (cm<sup>-1</sup>): 1605 (C=C), 1181 (C=N), 3054, 3015, 2958 (C-H), 3327-3139 (hydrazine NHNH<sub>2</sub>); <sup>1</sup>H-NMR: 3.89-10 (br, 3H, NH-NH<sub>2</sub>), 6.59-8.30 (m, 11H, Ar-H); <sup>13</sup>C-NMR: 111-137 (16C, Ar), 158 (1C, <u>C</u>=N-N), 160 (1C, N-<u>C</u>=NHNH<sub>2</sub>).

#### 3-Anthracen-9-yl-6-(3,5-dimethylpyrazol-1-yl)pyridazine (10).

Acetylacetone (1 mmol) was added to a mixture of **9** (1 mmol) in methanol (10 mL) and the reaction mixture was refluxed for 5 hr. The solid that separated after cooling was recrystallized from methanol to give **10** as yellow crystals, yield 62%; IR (cm<sup>-1</sup>): 1604 (C=C), 1635 (C=N), 3050, 2959, 2925, 2869 (C-H); <sup>1</sup>H-NMR: 2.93 (s, 6H, 2CH<sub>3</sub>), 6.50-8.270 (m, 12H, Ar-H); <sup>13</sup>C-NMR: 14.20 (2C, 2CH<sub>3</sub>), 111-135 (17C, Ar), 148 (2C, <u>C</u>=N), 155 (1C, <u>C</u>=N-N), 160 (1C, N-<u>C</u>=N).

#### 6-Anthracen-9-yl-3-methylamino-pyridazine (11).

Methylamine (1 mmol) was added to a mixture of **4b** (1 mmol) and the reaction mixture was heated for 4 hr on an oil-bath at 140 °C; then cooled and triturated with methanol. The solid that separated was recrystallized from methanol to give **11** as white crystals, yield 56%; IR (cm<sup>-1</sup>): 1604 (C=C), 1635 (C=N), 3050, 2959, 2925, 2869 (C-H), 3412-3412 (indole and hydrazone N-H); <sup>1</sup>H-NMR: 2.50 (d, 3H, CH<sub>3</sub>), 6.30-8.32 (m, 11H, Ar-H), 4.20 (br, 1H, amine NH); <sup>13</sup>C-NMR: 35.30 (1C, CH<sub>3</sub>), 113-135 (16C, Ar), 155.60 (1C, <u>C</u>=N-N), 159 (1C, N-<u>C</u>=N).

#### (6-Anthracen-9-yl-pyridazin-3-yl)trimethylammonium iodide (12).

Excess methyl iodide (5 mL) was added to a mixture of **11** (1 mmol) in methanol (10 mL) and the reaction mixture was refluxed for 8 hr. After evaporation of all the solvent, the solid residue was recrystallized from methanol to give **12** as white crystals, yield 85%; IR (cm<sup>-1</sup>): 1604 (C=C), 1635 (C=N), 3050, 2959, 2925, 2869 (C-H), 3412-3412 (N-N); <sup>1</sup>H-NMR: 2.89 (s, 9H, 3CH<sub>3</sub>), 7.39-8.30 (m, 11H, Ar-H); <sup>13</sup>C-NMR: 52 (3C, N-CH<sub>3</sub>), 125.30-135.10 (16C, Ar), 148 (1C, <u>C</u>=N-N), 159 (1C, N-<u>C</u>=N).

#### 6-Anthracen-9-yl-2-benzenesulfonyl-4-(1H-indol-3-yl)-4,5-dihydro-2H-pyridazin-3-one (13a).

Benzenesulfonyl chloride (1 mmol) was added to a mixture of **3a** (1 mmol), anhydrous  $K_2CO_3$  (1 mmol) in dry acetone (5 mL) and the reaction mixture was refluxed for 24 hr. The solid that separated on cooling was recystallized from benzene to give **13a** as a white solid, yield 75%; IR (cm<sup>-1</sup>): 1337-

# 6-Anthracen-9-yl-4-(1H-indol-3-yl)-2-(toluene-4-sulfonyl)-4,5-dihydro-2H-pyridazin- 3-one (13b).

4-Toluenesulfonyl chloride (1 mmol) was added to a mixture of **3a** (1 mmol), anhydrous K<sub>2</sub>CO<sub>3</sub> (1 mmol) in dry acetone (5 mL) and the reaction mixture was refluxed for 24 hr. The solid that separated on cooling was recystallized from benzene to give **13b** as a white solid, yield 73%; IR (cm<sup>-1</sup>): 1337-1173 (SO<sub>2</sub>), 1616 (C=C), 1637 (C=N), 1670 (pyridazinone C=O), 3054, 2957, 2923, 2869 (C-H), 3406 (indole N-H); <sup>1</sup>H-NMR: 2.10 (s, 3H, CH<sub>3</sub>), 2.30 (t, 1H, CH<sub>2</sub>), 3.70 (t, 1H, CH), 6.80-8.43 (m, 19H, Ar-H), 10.02 (br, 1H, indole NH); <sup>13</sup>C-NMR: 20.90 (1C, <u>C</u>H<sub>3</sub>), 34.20 (1C, <u>C</u>H<sub>2</sub>), 43.90 (1C, <u>C</u>H-CO), 111-142 (27C, Ar), 123 (1C, indole <u>C</u>-NH,), 157 (1C, <u>C</u>=N-N), 178 (1C, pyridazinone <u>C</u>=O).

# General reaction of pyridazinone 3a with some aliphatic or aromatic aldehydes

Aliphatic or aromatic aldehyde (1 mmol) was added to a mixture of **3a** (1 mmol), NaOH (10%) in ethanol (5 mL) and the reaction mixture was refluxed for 6 hr. The solid that separated on cooling was recystallized from benzene to give **14a-j**. Their physical properties, mass spectral data and elemental analysis are given in Table 4.

# 6-Anthracen-9-yl-4-(1H-indol-3-yl)5-methylene-4,5-dihydro-2H-pyridazin-3-one (14a).

Formaldehyde gave **14a** as an orange solid, yield 53%; IR (cm<sup>-1</sup>): 1615 (C=C), 1637 (C=N), 1671 (pyridazinone C=O), 3054, 2957, 2925, 2869 (C-H), 3400-3413 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 3.36 (s, 2H, CH<sub>2</sub>), 4.40 (s, 1H, pyridazinone CH), 7.04-8.50 (m, 14H, Ar-H), 11.02 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 51 (1C, pyridazinone <u>C</u>H), 111-142 (23C, Ar and vinyl), 122 (1C, indole <u>C</u>-NH), 155 (1C, <u>C</u>=N-N), 170 (1C, pyridazinone <u>C</u>=O).

# 6-Anthracen-9-yl-5-ethylidene-4-(1H-indol-3-yl)-4,5-dihydro-2H-pyridazin-3-one (14b).

Acetaldehyde gave **14b** as an orange solid, yield 58%; IR (cm<sup>-1</sup>): 1617 (C=C), 1637 (C=N), 1667 (pyridazinone C=O), 3054, 2957, 2925, 2869 (C-H), 3400-3414 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 1.70 (d, 3H, CH<sub>3</sub>), 3.36 (m, 1H, vinyl CH), 4.40 (s, 1H, pyridazinone CH), 6.67-8.22 (m, 14H, Ar-H), 11.02 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 12- 52.50 (2C, pyridazinone <u>C</u>H<sub>3</sub>, <u>C</u>H), 111-140 (23C, Ar and vinyl), 122.80 (1C, indole <u>C</u>-NH), 155.60 (1C, <u>C</u>=N-N), 170 (1C, pyridazinone <u>C</u>=O).

# 6-Anthracen-9-yl-5-benzylidene-4-(1H-indol-3-yl)-4,5-dihydro-2H-pyridazin-3-one (14c).

Benzaldehyde gave **14c** as an orange solid, yield 62%; IR (cm<sup>-1</sup>): 1616 (C=C), 1637 (C=N), 1671 (pyridazinone C=O), 3054, 2957, 2925, 2869(C-H), 3400-3412 (pyridazinone and indole N-H); <sup>1</sup>H-

NMR: 3.36 (s, 1H, vinyl CH), 4.40 (s, 1H, pyridazinone CH), 7.20-8.20 (m, 19H, Ar-H), 11.02 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 52.40 (1C, pyridazinone <u>C</u>H), 111-137 (29C, Ar and vinyl), 122 (1C, indole <u>C</u>-NH,), 155.60 (1C, <u>C</u>=N-N), 168 (1C, pyridazinone <u>C</u>=O).

#### 6-Anthracen-9-yl-5-(2-hydroxybenzylidene)-4-(1H-indol-3-yl)-4,5-dihydro-2H-pyridazin-3-one (14d).

2-Hydroxybenzaldehyde gave **14d** as a brown solid, yield 60%; IR (cm<sup>-1</sup>): 1619 (C=C), 1637 (C=N), 1681 (pyridazinone C=O), 3059, 2959, 2927, 2870 (C-H), 3250-3500 (O-H), 3400-3411 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 3.37 (s, 1H, vinyl CH), 4.40 (s, 1H, pyridazinone CH), 6.62-8.52 (m, 18H, Ar-H), 5.50 (br, 1H, OH), 11.01 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 52 (1C, pyridazinone <u>C</u>H), 111-136.10 (28C, Ar and vinyl), 122.80 (1C, indole <u>C</u>-NH), 155.60 (1C, <u>C</u>=N-N), 156(1C, -<u>C</u>-OH), 168 (1C, pyridazinone <u>C</u>=O).

#### 6-Anthracen-9-yl-5-(4-hydroxybenzylidene)-4-(1H-indol-3-yl)-4,5-dihydro-2H-pyridazin-3-one (14e).

4-Hydroxybenzaldehyde gave **14e** as a buff solid, yield 72%; IR (cm<sup>-1</sup>): 1595 (C=C), 1640 (C=N), 1674 (pyridazinone C=O), 3054, 2957, 2925, 2869 (C-H), 3250-3500 (O-H), 3400-3414 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 3.37 (s, 1H, vinyl CH), 4.40 (s, 1H, pyridazinone CH), 5.67 (br, 1H, OH), 6.44-8.17 (m, 18H, Ar-H), 11.02 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 53 (1C, pyridazinone <u>C</u>H), 111-136 (28C, Ar and vinyl), 122.80 (1C, indole <u>C</u>-NH), 155.60 (1C, <u>C</u>=N-N), 157.50 (1C, <u>C</u>-OH), 168 (1C, pyridazinone <u>C</u>=O).

#### 6-Anthracen-9-yl-4-(1H-indol-3-yl)-5-(2-methoxybenzylidene)-4,5-dihydro-2H-pyridazin-3-one (14f).

2-Methoxybenzaldehyde gave **14f** as a brown solid, yield 50%; IR (cm<sup>-1</sup>): 1590 (C=C), 1641 (C=N), 1671 (pyridazinone C=O), 3059, 2958, 2935, 2835 (C-H), 3410-3424 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 3.36 (s, 1H, vinyl CH), 3.70(s, 3H, -OCH<sub>3</sub>), 4.40 (s, 1H, pyridazinone CH), 6.58-8.28 (m, 18H, Ar-H), 11.02 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 52.40 (1C, pyridazinone <u>C</u>H), 56 (1C, O-<u>C</u>H<sub>3</sub>), 111-138 (28C, Ar and vinyl), 122.80 (1C, indole <u>C-</u>NH,), 155.60 (1C, <u>C</u>=N-N), 159.70 (1C, <u>C</u>-OCH<sub>3</sub>), 168 (1C, pyridazinone <u>C</u>=O,).

#### 6-Anthracen-9-yl-4-(1H-indol-3-yl)-5-(4-methoxybenzylidene)-4,5-dihydro-2H-pyridazin-3-one (14g).

4-Methoxybenzaldehyde gave **14g** as a brown solid, yield 72%; IR (cm<sup>-1</sup>): 1613 (C=C), 1637 (C=N), 1669 (pyridazinone C=O), 3054, 2957, 2925, 2869 (C-H), 3400-3412 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 3.37 (s, 1H, vinyl CH), 3.74 (s, 3H, OCH<sub>3</sub>), 4.37 (s, 1H, pyridazinone CH), 6.86-7.80 (m, 18H, Ar-H), 10.02, 11.02 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 52 (1C, pyridazinone <u>C</u>H,), 56 (1C, O<u>C</u>H<sub>3</sub>), 111-136 (28C, Ar and vinyl), 122.80 (1C, indole <u>C</u>-NH), 155.60 (1C, <u>C</u>=N-N), 161 (1C, <u>C</u>-OCH<sub>3</sub>), 168 (1C, pyridazinone <u>C</u>=O,).

6-Anthracen-9-yl-5-(2,4-dimethoxybenzylidene)-4-(1H-indol-3-yl-4,5-dihydro-2H-pyridazin-3-one (14h).

2,4-Dimethoxybenzaldehyde gave **14h** as an orange solid, yield 51%; IR (cm<sup>-1</sup>): 1601 (C=C), 1636 (C=N), 1669 (pyridazinone C=O), 3059, 2958, 2923, 2855 (C-H), 3410-3424 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 3.36 (s, 1H, CH), 3.75 (s, 6H, -OCH<sub>3</sub>), 4.40 (s, 1H, pyridazinone CH), 6.48-7.98 (m, 17H, Ar-H), 10.52 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 52 (1C, pyridazinone <u>C</u>H), 56.27 (2C, O-<u>C</u>H<sub>3</sub>), 98-151 (27C, Ar and vinyl), 122 (1C, indole <u>C</u>-NH,), 155.60 (1C, <u>C</u>=N-N), 160-162 (2C, <u>C</u>-O-CH<sub>3</sub>), 168 (1C, pyridazinone <u>C</u>=O).

6-Anthracen-9-yl-5-(2-hydroxynaphthalen-1-yl-methylene)-4-(1H-indol-3-yl)-4,5-dihydro-2H-pyridazin-3-one (14i).

2-Hydroxynaphthaldehyde gave **14i** as a brown solid, yield 58%; IR (cm<sup>-1</sup>): 1619 (C=C), 1637 (C=N), 1681 (pyridazinone C=O), 3059, 2959, 2927, 2870 (C-H), 3250-3500 (O-H), 3400-3411 (pyridazinone and indole N-H); <sup>1</sup>H-NMR: 3.85 (s, 1H, vinyl CH), 4.40 (s, 1H, pyridazinone CH), 6.47-7.95 (m, 20H, Ar-H), 5.62 (br, 1H, OH), 10.21 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 52.40 (1C, pyridazinone <u>C</u>H), 111-137 (32C, Ar and vinyl), 122.80 (1C, indole <u>C</u>-NH), 155.60 (1C, <u>C</u>=N-N), 156 (1C, -<u>C</u>-OH), 170 (1C, pyridazinone <u>C</u>=O).

6-Anthracen-9-yl-5-furan-2-yl-methylene-4-(1H-indol-3-yl)-4,5-dihydro-2H-pyridazin-3-one (14j).

Furfuraldehyde gave **14j** as a brown solid, yield 59%; IR (cm<sup>-1</sup>): 1616 (C=C), 1637 (C=N), 1670 (pyridazinone C=O), 3054, 2957, 2925, 2869 (C-H), 3400-3412 (pyridazinone and indole N-H), 1200 (C-O-C); <sup>1</sup>H NMR: 3.39 (s, 1H, vinyl CH), 4.37 (s, 1H, pyridazinone CH), 6.30-8.55 (m, 17H, Ar-H), 11.02 (br, 2H, pyridazinone and indole NH); <sup>13</sup>C-NMR: 51 (1C, pyridazinone <u>C</u>H, ), 111-136 (25C, Ar and vinyl), 122.80 (1C, indole <u>C</u>-NH), 145-155.3 (2C, furan O-<u>C</u>), 155.60 (1C, <u>C</u>=N-N), 168 (1C, pyridazinone <u>C</u>=O).

# References

- 1. Sayed, G.H.; Sayed, M.A.; Mahmoud, M.R.; Shaaban, S.S. Synthesis and Reactions of New Pyidazinone Derivatives of Expected Antimicrobial Activities. *Egypt. J. Chem.* **2002**, *45*, 767-776.
- 2. Katrusiak, A.; Katrusiak, A.; Baloniak, S. Reactivity of 6-Chloro-4- and 5-Hydrazino-2- Phenyl-3(2*H*)-Pyridazinones with Vilsmeier Reagent. *Tetrahedron* **1994**, *50*, 12933-12940.
- 3. Okcelik, B.; Unlu, S.; Banoglu, E.; Kupeli, E.; Yesilada, E.; Sahin, M.F. Investigation of New Pyridazinone Derivatives for the Synthesis of Potent Analgesic and Anti-Inflammatory Compounds with Cyclooxygenase Inhibitory Activity. *Arch. Pharm. Pharm. Med. Chem.* **2003**, *336*, 406-412.
- 4. Dogruer, D.S.; Sahin, M.F.; Kupeli, E.; Yesilada, E. Synthesis and Analgesic and Anti-Inflammatory Activity of New Pyridazinones. *Turk. J. Chem.* **2003**, *27*, 727-738.

- 5. Frolov, E.B.; Lakner, F.J.; Khvat, A.V.; Ivachtchenko, A.V. An Efficient Synthesis of Novel 1,3oxazolo [4,5-*d*] Pyridazinones. *Tetrahedron Lett.* **2004**, *45*, 4693-4696.
- Banoglu, E.; Akoglu, C.; Unlu, S.; Kupeli, E.; Yesilada, E.; Sahin, M.F. Amide Derivatives of [6-(5-Methyl-3-phenylpyrazole-1-yl)-3(2*H*)-Pyridazinone-2-yl]acetic Acids as Potential Analgesic anti-Inflammatory Compounds. *Arch. Pharm. Pharm. Med. Chem.* 2004, 337, 7-14.
- 7. Gokce, M.; Dogruer, D.; Sahin, F. Synthesis and Antinociceptive Activity of 6-Substituted-3pyridazinone Derivatives. *Il Farmaco* **2001**, *56*, 233-237.
- 8. Cao, S.; Qian, X.; Song, G.; Chai, B.; Jiang, Z. Synthesis and Antifeedant Activity of New Oxadiazolyl 3(2H)-pyridazinones. J. Agric. Food Chem. 2003, 51, 152-155.
- 9. Piaz, V.D.; Ciciani, G.; Giovannoni, M.P. 5-Acetyl-2-Methyl-4-Nitro-6-Phenyl-3(2*H*)-Pyriazinone: Versatile Precursor to Hetero-Condensed Pyridazinones. *Synthesis* **1994**, 669-671.
- Ogretir, C.; Yarligan, S.; Demirayak, S. Spectroscopic Determination of Acid Dissociation Constants of Some Biologically Active 6-Phenyl-4,5-Dihydro-3(2H)-Pyridazinone Derivatives. J. Chem. Eng. Data 2002, 47, 1396-1400.
- Barbaro, R.; Betti, L.; Botta, M.; Corelli,F.; Giannaccini, G.; Maccari, L.; Manetti, F.; Strappaghetti, G.; Corsano, S. Synthesis Biological Evaluation and Pharmacophore Generation of New Pyridazinone Derivatives with Affinity Toward α<sub>1</sub>- and α<sub>2</sub>- Adrenoceptors. *J. Med. Chem.* 2001, 44, 2118-2132.
- 12. Sircar, I. Synthesis of New 1,2,4-Triazolo[4,3-b]pyridazines and Related Compound. J. Heterocyclic Chem. **1985**, 22, 1045-1048.
- Coelho, A.; Sotelo, E.; Fraiz, N.; Yanez, M.; Laguna, R.; Cano, E.; Ravina, E. Pyridazines. Part 36: Synthesis and Antiplatelet Activity of 5-Substituted-6-Phenyl-3(2*H*)- Pyridazinones. *Bioorg. Med. Chem. Lett.* 2004, *14*, 321-324
- Sotelo, E.; Centeno, N.B.; Rodrigo, J.; Ravina, E. Pyridazine Derivatives. Part 27: A joint Theoretical and Experimental approach to the Synthesisi of 6-Phenyl-4,5-disubstituted-3(2H)Pyridazinones. *Tetrahedron Lett.* 2002, 58, 2389-2395.
- Sotelo, E.; Fraiz, N.; Yanez, M.; Terrades, V.; Laguna, R.; Cano, E.; Ravina, E. Pyridazines. Part XXIX: Synthesis and Platelet Aggregation Inhibition Activity of 5-Substituted-6-Phenyl-3(2*H*)-Pyridazinones Novel Aspects of their Biological Action. *Bioorg. Med. Chem.* 2002, *10*, 2873-2882.
- 16. Malinka, W.; Redzicka, A.; Lozach, O. New Derivatives of Pyrrolo[3,4-*d*]Pyridazinone and their Anticancer Effects. *Il Farmaco* **2004**, *59*, 457-462.
- Youssef, A.S.; Marzouk, M.I.; Madkour, H.M.F.; El-Soll, A.M.A.; El-Hashash, M.A. Synthesis of some heterocyclic systems of anticipated biological activities via 6-aryl-4-pyrazol-1-yl-pyridazin-3-one. *Can. J. Chem.* 2005, *83*, 251-259.
- 18. Sotelo, E.; Pita, B.; Ravina, E. Pyridazines. Part 22:<sup>1</sup> Highly Efficient Synthesis of Pharmacologically Useful 4-Cyano-6-Phenyl-5-Substituted-3(2*H*)-Pyridazinones. *Tetrahedron Lett.* **2000**, *41*, 2863-2866.
- 19. Sotelo, E.; Coelho, A.; Ravina, E. Pyridazine Derivatives 32<sup>1</sup>): Stille-Based Approaches in the Synthesis of 5-Substituted-6-Phenyl-3(2*H*)-Pyridazinones. *Chem. Pharm. Bull.* **2003**, *51*, 427-430.
- 20. Kassab, R.R. Simple Synthesis and Reactions of Some New Pyridazinono Derivatives and their Antimicrobial Activity. *Egypt. J. Chem.* **2002**, *45*, 1055-1073.

- 21. Toshiki, S.; Hiroshi, Y. Jpn. Kokai Tokkyo Koho JP 01,100,157, **1989**; [Chem Abstr. **1989**, 111, 153626 u].
- 22. Masanori, S.; Toshiharu, O.; Hiroko, T. Jpn. Kokai Tokkyo Koho JP 01,31,763, **1989**; [Chem Abstr. **1989**, 111, 15623 r].
- 23. Tsutomu, F.; Yoichiro, N.; Tomokayu, G.; Amid Kazuimasa, Y. Jpn. Kokai Tokkyo Koho JP 61,148,160, **1987**; [Chem Abstr. **1987**, 106, 50037 v].
- 24. John, B.E.; James C.N.; Bayer, A.C. *Eur. Pat. Appl.* EP 409,027, **1991**; [*Chem. Abstr.* **1991**, *114*, 228729 c].
- 25. Kamat, G.A.; Joshi, G.R.; Gadaginamath, S.G. Proc. Indian Acad. Sci. Chem. Sci. 1993, 105, 189.
- Halasz, B.D.; Monsieurs, K.; Elias, O.; Karolyhazy, L.; Tapolcsanyi, P.; Maes, B.U.; Riedl, Z.; Hajos, G.; Dommisse, R.A.; Lemiere, G.L.; Kosmrlj, J.; Matyus, P. Synthesis of 5*H*-Pyridazino[4,5-*b*]Indoles and their benzofurane analogues utilizing an intramolecular Heck-Type Reaction. *Tetrahedron.* 2004, 60, 2283-2291.
- Sayed, G.H.; El-Kady, M.Y.; Abd Elhalim, M.S. Synthesis and Reactions of Some α–aryl-(4bromobenzoyl)propionic acids. *Indian J. Chem.* 1981, 20, 845-848.
- Sayed, G.H.; Hamed, A.A.; Meligi, G.A.; Boraie, W.E.; Shafik, M. The Use of 4-(3,4-Dichlorophenyl)-4-Oxo-2-(4-Antipyrinyl)-Butonoic Acid in the Preparation of Some New Heterocyclic Compounds With Expected Biological Activity. *Molecules* 2003, 8, 322-332.
- 29. Toth, G.; Molnar, S.; Tamas, T.; Borbely, I. An Efficient Synthesis of 4,5-Dihydro-3(2*H*)-Pyridazinone Derivative. *Synth. Commun.* **1997**, 27, 3513-3524.
- Sayed, G.H.; Sayed, M.A.; Shaaban, S.S.; Mahmoud, M.R. Synthesis and Reactions of 4-(p-Bromophenyl)-4-Oxo-2-(4-Antipyrinyl)Butanoic Acid and Some Unexpected Products. *Egypt. J. Chem.* 2000, 43, 17-29.
- 31. Coates, W.J.; McKillop, A. One Pot Preparation of 6-Substituted 3(2*H*)-Pyridazinones from Ketones. *Synthesis* **1993**, 334-342.
- Kassab, R.R.; Sayed, G.H.; Radwan, A.M.; Abd El-Azzez, N. Some reactions with (biphenyl)-4-(5-oxo-1,3-diphenyl-2-pyrazolin-4-yl)-4,5-dihydropyridazin-3-(2H)ones. *Rev. Roum. Chim.* 2001, 46, 649-655.
- Jaihne, H.; Sayed, A.; Zaher, H.A.; Sherif, O. Reaction of 3-Chloro- and 3-Hydrazino-6-(p-tolyl)pyridazines. *Indian J. Chem.* 1977, 250-251.
- El-Hashash, M.A.; Amine, M.S.; Soliman, F.M.; Morsi, M.A. Behavior of aroylacyclic acids toward hydrazine hydrate and some on the cyclized products. *J. Serb. Chem. Soc.* 1992, 57, 563-569.
- Chung, K.T.; Chen, S.C.; Wong, T.Y.; Wei, C.I. Effects of Benzidine and Benzidine Analogues on Growth of Bacteria Including *Azotobacter Vinelandii*. *Environ. Toxicol. Chem.* 1998, 17, 271-275.

Sample Availability: Available from the author.

© 2007 by MDPI (http://www.mdpi.org). Reproduction is permitted for noncommercial purposes.