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Received April 12, 1996

Dedicated to the memory of Professor Nicholas Alexandrou

Synthesis of some derivatives of the pyridazino[4,5-*b*][1,5]thiazepine ring system is reported. Thus, 5-benzyl-8-methyl-2-phenyl-2,3,4,5-tetrahydro-5*H*-pyridazino[4,5-*b*][1,5]thiazepin-9(8*H*)-one (**5**) was prepared by an intramolecular *S*-alkylation reaction, whereas the thiazepine ring of sulfone analogue **21**, and that of the novel tricyclic pyrrolidino fused ring system **22** was elaborated by an intramolecular C-alkylation reaction. Unexpected formation of bicyclic pyrido- and thiazine fused pyridazine systems are also discussed.

J. Heterocyclic Chem., **33**, 583 (1996).

Pyridazino[4,5-*b*][1,5]oxazepines and -thiazepines have primarily been of interest as isosteric or structurally related analogues to 4,5-disubstituted pyridazines possessing remarkable biological activities [1,2]. Among the bicyclic derivatives synthesized we have also succeeded to identify some promising lead compounds which formed a rational basis for further synthetic and structure-activity studies. Therefore, synthetic methods permitting efficient derivatization of these ring systems have been required.

In this paper we describe our attempts to prepare some pyridazino[4,5-*b*][1,5]thiazepines having a 2-phenyl or a 2-(4-methoxyphenyl) substituent *via* ring closure reactions of pyridazine intermediates, whereas functionalization of these ring systems at other positions will be reported elsewhere.

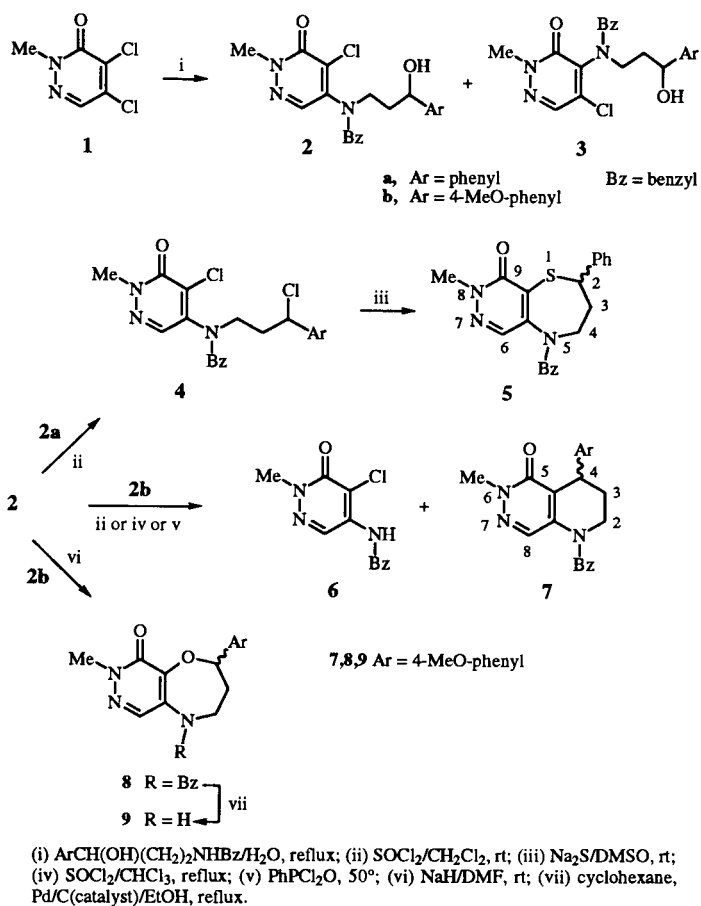
The only described syntheses of pyridazino[4,5-*b*][1,5]-oxazepines and -thiazepines involved cyclizations of *N*-(4-chloro-5-pyridazinyl)-*N*-benzylaminopropanols and *N*-(4-chloro-5-pyridazinyl)-*N*-benzylaminopropyl chlorides by treatment with sodium alcoholate and sodium sulfide, respectively [1,3].

In order to extend the latter ring closure reaction to the aimed 2-phenyl- and 2-(4-methoxyphenyl)pyridazino[4,5-*b*]thiazepines, the suitably aryl substituted pyridazinylaminopropanols were needed. Compounds **2a** and **2b** were prepared as outlined in Scheme 1. Nucleophilic displacement reaction of 4,5-dichloro-2-methyl-3-(2*H*)-pyridazinone (**1**) with 1-phenyl- or 1-(4-methoxyphenyl)benzylaminopropanol, respectively, afforded, as expected [4], two separable regioisomers **2** and **3** in *ca* 2:1 ratios. The choice between the regioisomers was based on ¹H nmr experiments. A significant NOE was obtained between the benzylic and 6-CH protons only in the 5-isomers, *i.e.* compounds **2a** and **2b**. Treatment of **2a** then with thionyl chloride, followed by reacting the resultant **4** with sodium sulfide, provided as an isolable product the desired 2-phenylthiazepine **5** in 38% yield. Fairly unexpectedly, the

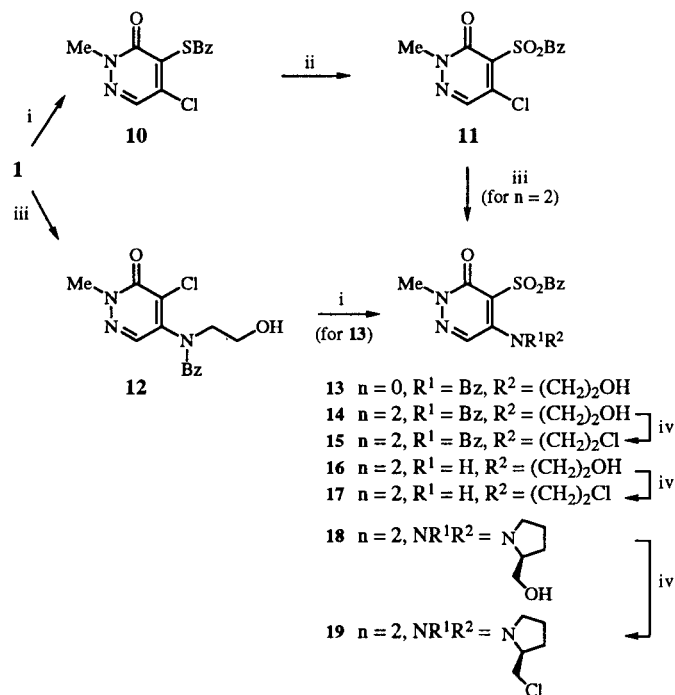
4-methoxy analogue **2b** with various chlorinating agents did not afford the corresponding chloride at all; rather a fragmentation and by a C-C bond formation, a ring closure reaction occurred to give the *N*-dealkylated **6** prepared earlier in another way [5], and the pyrido[2,3-*d*]pyridazine derivative **7** in 33 and 20% yields, respectively [6]. Formation of **7** might proceed *via* an *in situ* formed olefin and/or radical intermediate. In contrast, no anomalous behavior of **2b** was observed when treated with sodium hydride in dimethylformamide. In this reaction the expected oxazepine **8** was obtained which could also be smoothly debenzylated to **9** by catalytic transfer hydrogenation.

Next we turned to another thiazepine ring formation reaction. This approach relied on 4-benzylthio- or 4-benzylsulfonylpyridazinones having a side chain at position 5 suitably functionalized for intramolecular alkylation of the benzylic carbon. Since, reactions of **1** with thiols generally proceeded with excellent regioselectivity (*cf.* [7]), good overall yields were also expected for this route. Conversion of **1** to the 4-benzylsulfonyl-5-chloro derivative **11** was carried out in two steps by the reaction with the *in situ* prepared sodium benzylthiolate in toluene, followed by treatment of the resulting **10**, with 2 equivalents of *m*-chloroperbenzoic acid (*m*-CPBA). Synthesis of **10** was previously described in a multistep route [8]. The 4-benzylsulfonyl-5-(substituted amino)pyridazinones **15**, **17**, **19** possessing a chloroalkyl side chain for the ring closure were then obtained in two straightforward steps *via* the hydroxyethylamino intermediates **14**, **16** and the related (*S*)-hydroxymethylpyrrolidino derivative **18**. The 4-benzylthio-5-hydroxyethylaminopyridazinone **13** was also prepared in two steps from **1**. In this case, however, the nucleophilic displacement reactions were applied in a reverse sequence in order to overbalance the reduced electrophilic reactivity of the monochloropyridazine having an electron-releasing substituent at the *ortho*-position.

Scheme 1

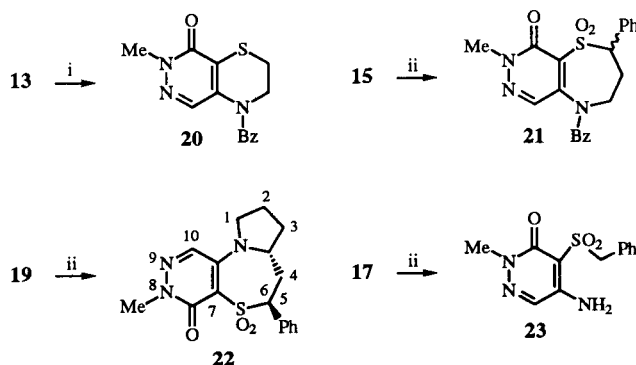


Scheme 2



(i) BzSH/NaH/toluene, rt (for 10) or 80° (for 13); (ii) *m*-CPBA, (2 equivalents)/CH₂Cl₂, rt; (iii) R¹R²NH/H₂O or H₂O-EtOH (for 14 and 18), reflux; (iv) SOCl₂/CH₂Cl₂, reflux.

Scheme 3



(i) SOCl₂/CH₂Cl₂, -10°; (ii) NaH/(CH₃)₂NCHO, rt.

Accordingly, at first the amino substituent was introduced to afford

Table 1 [a]
Analytical Data of Compounds 2-11, 13-23

Compound No.	Method	Yield (%)	Mp (°C) (Solvent)	Formula	Analysis (%) Calcd./Found		
					C	H	N
2a	A	41	oil	C ₂₁ H ₂₂ ClN ₃ O ₂	65.70 65.45	5.78 5.65	10.95 10.67
2b	A	48	45-46	C ₂₂ H ₂₄ ClN ₃ O ₃	63.85 63.59	5.84 5.61	10.15 9.92
3a	A	28	oil	C ₂₁ H ₂₂ ClN ₃ O ₂	65.70 65.83	5.78 5.79	10.95 10.69
3b	A	26	oil	C ₂₂ H ₂₄ ClN ₃ O ₃	63.85 63.60	5.84 5.58	10.15 9.87
4	B	83	oil	C ₂₁ H ₂₁ Cl ₂ N ₃ O	62.69 62.98	5.26 5.41	10.44 10.35
5	C	38	182-183 (<i>i</i> -PrOH)	C ₂₁ H ₂₁ N ₃ OS	69.39 69.12	5.82 5.78	11.56 11.31
6	D	33	180-181 [b]	C ₁₂ H ₁₂ ClN ₃ O	57.71 57.48	4.85 4.78	16.83 16.70
7	D	20	oil	C ₂₂ H ₂₃ N ₃ O ₂	73.10 72.80	6.40 6.23	11.62 11.35
8	E	59	145-146 (EtOH-Et ₂ O)	C ₂₂ H ₂₃ N ₃ O ₃	70.02 69.88	6.10 6.19	11.14 11.08
9	F	46	240 (EtOH)	C ₁₅ H ₁₇ N ₃ O ₃	62.70 62.45	5.96 5.84	14.62 14.38
10	G	74	oil	C ₁₂ H ₁₁ ClN ₂ OS	54.04 54.12	4.16 4.20	10.50 10.44
11	H	88	99-101 (petroleum ether)	C ₁₂ H ₁₁ ClN ₂ O ₃ S	48.24 48.50	3.71 3.42	9.38 9.11
13	G	42	117 (EtOH-Et ₂ O)	C ₂₁ H ₂₃ N ₃ O ₂ S	66.11 66.00	6.07 6.05	11.01 10.98
14	A	88	165-166 (EtOH-Et ₂ O)	C ₂₁ H ₂₃ N ₃ O ₄ S	60.99 60.90	5.60 5.58	10.16 10.18
15	B	95	167-168 (<i>i</i> -PrOH)	C ₂₁ H ₂₂ ClN ₃ O ₃ S	58.39 58.65	5.13 5.20	9.73 9.69
16	A	94	155-156 (H ₂ O)	C ₁₄ H ₁₇ N ₃ O ₄ S	51.99 52.03	5.30 5.26	12.99 12.89
17	B	84	120 (<i>i</i> -PrOH)	C ₁₄ H ₁₆ ClN ₃ O ₃ S	49.19 48.99	4.72 4.55	12.29 12.09
18	A	88	50-54 [c]	C ₁₇ H ₂₁ N ₃ O ₄ S	56.18 55.95	5.82 5.75	11.56 11.47
19	B	77	59 (petroleum ether)	C ₁₇ H ₂₀ ClN ₃ O ₃ S	53.46 53.19	5.28 5.26	11.00 10.88
20	B	61	90-91 (Et ₂ O)	C ₁₄ H ₁₅ N ₃ OS	61.51 61.29	5.53 5.28	15.37 15.19
21	E	65	310-311 (MeOH-Et ₂ O)	C ₂₁ H ₂₁ N ₃ O ₃ S	63.77 63.52	5.35 5.17	10.62 10.49
22	E	31	304-305 (MeOH)	C ₁₇ H ₁₉ N ₃ O ₃ S	59.11 58.86	5.50 5.42	12.16 11.92
23	E	80	248-251 (EtOH)	C ₁₂ H ₁₃ N ₃ O ₃ S	51.61 51.52	4.66 4.66	15.05 14.97

[a] The yields quoted refer only to isolated yields and are unoptimised. [b] Reported mp 183-185° [5]. [c] Hygroscopic.

composition of these enantiomers could cause the observed insignificant optical activity. It is also noteworthy that the presence of diastereomers having the 3*R*,5*R* or 3*S*,5*S* configurations, *i.e.* a *cis* arrangement, could never be detected by nmr or X-ray analyses.

The racemisation might well proceed in the final step of the synthesis of **22** (the precursor **19** definitely shows a characteristic and significant optical activity ($[\alpha]_D^{20} = 65^\circ$, chloroform, *c* = 1) under the strongly basic conditions *via* deprotonation followed a reprotonation.

The deprotonation may be promoted by the neighbouring electron-withdrawing nitrogen, a partial double bond character of the C10a-N11 bond is reflected by the measured short bond length (1.331Å), and by the through space assistance of the 7'-O sulfone oxygen.

In conclusion, we have described the synthesis of novel phenylpyridazino[4,5-*b*][1,5]thiazepines from the readily available 4,5-dichloro-2-methyl-3(2*H*)-pyridazinone (**1**). A new approach to these pyridazine fused compounds was also explored, in which the thiazepine ring was elaborated

Table 2

Crystal Data and Structure Refinement Parameters for Compound **22**

Formula	C ₁₇ H ₁₉ N ₃ O ₃ S
Formula weight	345.41
Crystallization medium	Methanol
Temperature	293 (2) K
Wavelength	1.54180 Å
Crystal system	Orthorhombic
Space group	P b c a
Unit cell dimensions	a = 17.356 (4) Å α = 90° b = 16.492 (5) Å β = 90° c = 11.539 (2) Å γ = 90°
Volume	3302.9 (14) Å ³
Z	8
Density (calculated)	1.389 Mg/m ³
Absorption coefficient	1.924 l mm ⁻¹
F(000)	1456
Crystal size	0.500 x 0.100 x 0.050 mm
Theta range for data collection	5.10 to 75.21°
Index ranges	0 ≤ h ≤ 21, 0 ≤ k ≤ 20, -14 ≤ l ≤ 0
Independent reflections	3374
Absorption correction	None
Refinement method	Full-matrix least-squares on F ²
Data/restraints/parameters	3367/0/223
Goodness-of-fit on F ²	1.035
Final R indices [I > 2 σ(I)]	R1 = 0.0600, wR2 = 0.1469
R indices (all data)	R1 = 0.2507, wR2 = 0.2868
Extinction coefficient	0.0011(2)
Largest diff. peak and hole	0.331 and -0.361 e. Å ⁻³

Table 3

Atomic Coordinates (x 10⁴) and Equivalent Isotropic Displacement Parameters (Å² x 10³)

	x	y	z	U(eq) [Å]
S(6)	3258(1)	6755(1)	894(2)	39(1)
O(7')	3930(3)	6731(3)	1633(4)	50(1)
O(8')	2786(3)	6040(3)	842(5)	61(2)
O(9')	2138(3)	6849(3)	2848(5)	57(2)
N(8)	1483(3)	7961(4)	2225(6)	54(2)
N(9)	1382(4)	8608(4)	1535(7)	69(2)
N(11)	3202(3)	8635(3)	34(5)	40(1)
C(1)	3158(5)	9408(4)	-600(7)	56(2)
C(1')	3791(4)	6198(4)	-1150(6)	39(2)
C(2)	3967(5)	9530(5)	-1024(7)	62(2)
C(2')	4521(4)	5861(4)	-1020(7)	52(2)
C(3)	4464(4)	9122(4)	-142(7)	47(2)
C(3A)	3996(4)	8369(4)	188(6)	38(2)
C(3')	4703(6)	5127(5)	1553(8)	70(3)
C(4)	4194(4)	7641(4)	-563(6)	40(2)
C(4')	4162(6)	4737(5)	-2219(8)	69(3)
C(5)	3569(4)	6983(4)	-559(6)	37(2)
C(5')	3452(5)	5058(5)	-2340(7)	58(2)
C(6A)	2638(3)	7576(4)	1242(6)	38(2)
C(6')	3258(5)	5791(4)	-1820(6)	46(2)
C(7)	2096(4)	7410(4)	2148(7)	45(2)
C(10')	908(5)	7844(6)	3127(9)	85(3)
C(10A)	2624(4)	8328(4)	652(6)	41(2)
C(10)	1924(4)	8774(5)	795(8)	63(2)

[a] U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

route, which was also adaptable to the synthesis of the new tricyclic ring system **22**, may provide an interesting and useful method to various pyridazino[4,5-*b*][1,5]thiazepines.

Table 4

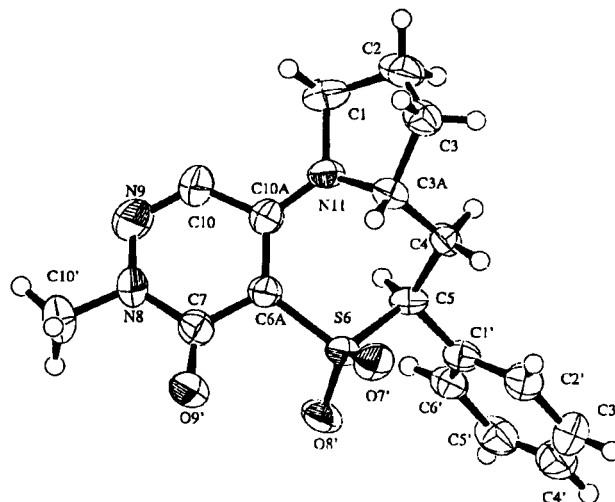
Selected Bond Lengths (Å)

S(6)-O(8')	1.437(5)
S(6)-O(7)	1.445(5)
S(6)-C(6A)	1.777(7)
S(6)-C(5)	1.802(7)
N(8)-N(9)	1.342(9)
N(8)-C(7)	1.403(9)
N(9)-C(10)	1.300(10)
N(11)-C(10A)	1.331(8)
N(11)-C(3A)	1.458(8)
N(11)-C(1)	1.472(8)
C(6A)-C(10A)	1.414(9)
C(6A)-C(7)	1.431(9)
C(10A)-C(10)	1.429(9)

Table 5

Selected Bond Angles (°) and Torsion Angles(°)

O(8')-S(6)-O(7)	117.6(3)	C(10A)-N(11)-C(1)-C(2)	173.5(7)
O(8')-S(6)-C(6A)	106.8(3)	C(3A)-N(11)-C(1)-C(2)	10.0(8)
O(7')-S(6)-C(6A)	112.1(3)	N(11)-C(1)-C(2)-C(3)	-29.5(7)
O(8')-S(6)-C(5)	107.6(3)	C(1)-C(2)-C(3)-C(3A)	37.7(8)
O(7')-S(6)-C(5)	108.2(3)	C(10A)-N(11)-C(3A)-C(4)	87.8(8)
C(6A)-S(6)-C(5)	103.5(3)	C(1)-N(11)-C(3A)-C(4)	-108.4(6)
N(9)-N(8)-C(7)	125.1(6)	C(10A)-N(11)-C(3A)-C(3)	-151.0(6)
C(10)-N(9)-N(8)	117.6(6)	C(1)-N(11)-C(3A)-C(3)	12.8(7)
C(10A)-N(11)-C(3A)	122.2(5)	C(2)-C(3)-C(3A)-C(4)	90.7(7)
C(10A)-N(11)-C(1)	123.8(6)	N(11)-C(3A)-C(4)-C(5)	-44.3(8)
C(3A)-N(11)-C(1)	111.8(6)	C(6')-C(1')-C(5)-S(6)	94.3(6)
C(10A)-C(6A)-S(6)	124.7(5)	C(3A)-C(4)-C(5)-S(6)	47.5(7)
C(7)-C(6A)-S(6)	114.6(5)	O(8')-S(6)-C(5)-C(1')	-42.0(6)
N(11)-C(10A)-C(6A)	125.4(6)	C(6A)-S(6)-C(5)-C(4)	77.6(5)
C(6A)-C(10A)-C(10)	114.2(6)	C(5)-S(6)-C(6A)-C(10A)	-18.3(6)
N(9)-C(10)-C(10A)	125.6(8)	S(6)-C(6A)-C(7)-O(9')	17.3(9)
		S(6)-C(6A)-C(7)-N(8)	-164.1(5)
		C(3A)-N(11)-C(10A)-C(6A)	-20.2(10)
		S(6)-C(6A)-C(10A)-N(11)	-23.0(10)

Figure 1. X-ray Crystallographic Structure of **22**.

by an intramolecular C-C bond formation reaction. This

EXPERIMENTAL

All melting points were determined on a Boetius micro-melting point apparatus, and are uncorrected. The ir spectra were recorded on a Bruker IFS-85 FT-IR spectrometer, unless otherwise stated, in potassium bromide pellets, and frequencies are expressed in cm^{-1} . The nmr spectra were recorded on a Bruker AC-250 FT-NMR spectrometer at 250 MHz (^1H) and 62.9 MHz (^{13}C), at ambient temperature, in the solvent indicated, using the ^2H signal of the solvent as the lock and tetramethylsilane as the internal standard. Chemical shifts are given in ppm (δ) and *J* values in Hz. The signals are designated as follow; s, singlet; d, doublet; t, triplet; m, multiplet; br, broad.

Elemental analyses (C, H, N) were performed on a Carlo Erba Elemental Analyzer Model 1012 apparatus. All analyses and spectroscopic measurements were done by the Analytical Department of Institute for Drug Research. Precoated silica gel plates (Merck) were used for thin layer chromatography. For column-chromatography 70-230 mesh silica gel (MN Kieselgel 60, Macherey Nagel) was applied. Unless otherwise noted all reagents were purchased from commercial suppliers (Aldrich and Fluka) and used as received; solvents (Reanal) were dried and distilled prior to use. Organic extracts were dried over magnesium sulfate. Compounds **1** [10] and **12** [9] were prepared as reported. Of 1-aryl-3-benzylaminopropan-1-ol reagents, which were used for the preparations of compounds **2** and **3**, the 1-(4-methoxyphenyl) derivative was prepared as described [1], whereas the 1-phenyl analogue was obtained using substantially the same method; the details of this procedure are given below.

3-Benzylamino-1-phenylpropan-1-ol.

Step (a): Preparation of ω -Benzylaminopropiophenone.

To a well stirred mixture of ω -chloropropiophenone (1.14 g, 6.76 mmol), anhydrous potassium carbonate (1.86 g, 13.5 mmol) in benzene (25 ml), benzylamine (0.72 g, 6.76 mmol) was added at 60°. After stirring at reflux temperature for 3 hours, the reaction mixture was cooled and treated with water (10 ml). After separation, the organic layer was washed with water (2 x 5 ml) and acidified with 12*N* hydrochloric acid (*pH* = 1). The precipitate was filtered, washed with benzene to give the hydrochloride salt of ω -benzylaminopropiophenone (0.95 g, 51%) as white solid. It had mp 160-162° (this compound was also described by a Mannich reaction, reported mp 163° [14]); ir 3275, 1680; ^1H nmr (dimethyl sulfoxide- d_6): 3.30 (t, 2H, COCH_2), 3.60 (t, 2H, NCH_2), 4.22 (s, 2H, $\text{NCH}_2\text{-Ph}$), 7.40-7.75 (m, 8H, $\text{NCH}_2\text{-Ph}$ and $\text{COPh-}m,p$), 8.00 (d, 2H, $\text{COPh-}o$).

Anal. Calcd. for $\text{C}_{16}\text{H}_{17}\text{NO}\cdot\text{HCl}$: C, 69.63; H, 6.53; N, 5.08. Found: C, 69.30; H, 6.57; N, 5.03.

Step (b): Reduction of ω -Benzylaminopropiophenone.

To a stirred solution of the above hydrochloride (0.95 g, 3.44 mmol) in methanol (42 ml), sodium borohydride (0.65 g, 17.2 mmol) was added portionwise at 15-20°. After stirring at room temperature for 2.5 hours, acetic acid (1.7 ml) and water (34 ml) were carefully added. The methanol was removed *in vacuo*, and the remaining solution was treated with solid sodium carbonate until *pH* = 8. Then the solution was extracted with ethyl acetate (4 x 20 ml). The combined organic layers were washed with water (2 x 20 ml), dried, and evaporated to dryness. The residue was crystallized from petroleum ether to give 3-benzylamino-1-phenylpropan-1-ol (0.54 g, 65%) as white foam, mp 55-56°; ir: 3277; ^1H nmr (deuteriochloroform): 1.85 (m, 2H, COH-CH_2),

2.94 (m, 2H, NCH_2), 3.80 and 3.82 (each d, *J* = 13.5, each 1H, $\text{CH}_2\text{-Ph}$), 4.95 (dd, *J* = 8 and 4, 1H, CH), 7.2-7.4 (m, 10H, Ph).

Anal. Calcd. for $\text{C}_{16}\text{H}_{19}\text{NO}$: C, 79.63; H, 7.93; N, 5.80. Found: C, 79.34; H, 7.89; N, 5.52.

General Procedure for the Synthesis of Compounds **2**, **3**, **14**, **16**, and **18**.

A mixture of **1** (0.82 g, 4.58 mmol), the appropriate amine and solvent (22 ml) was refluxed for the time given.

Product	2	3	14	16	18
Molar ratio (amine/1)	2.5	2.5	3.0	3.0	3.0
Reaction time (hours)	16	16	3	2	2
Solvent	H_2O	H_2O	$\text{H}_2\text{O-EtOH}$ 4:1	H_2O	$\text{H}_2\text{O-EtOH}$ 4:1

The reaction mixture was worked up after cooling to 0° (in the cases of **14** and **18**, ethanol was completely removed before cooling) as follows.

Compounds **2a**, **2b**, **3a**, and **3b**.

To the mixture ethyl acetate (60 ml) was added. The mixture was acidified (*pH* = 3) with 12*N* hydrochloric acid. The aqueous layer was separated and extracted with ethyl acetate (4 x 20 and 4 x 10 ml). The combined organic layers were washed with water (2 x 20 ml), dried, then evaporated to dryness. The residue was subjected to column-chromatography on silica gel using a mixture of chloroform-ethyl acetate (8:2, then 7:3, v/v) as the eluting agent. From the fraction eluted with a mixture of chloroform-ethyl acetate (8:2), the '4-isomers', **3a** and **3b** were obtained, whereas from the fraction eluted with the mixture of chloroform-ethyl acetate (7:3), the '5-isomers' **2a** and **2b** were isolated.

Compounds **14** and **16**.

The mixture was stirred at 0° for 1 hour and the precipitate was collected by suction filtration, then recrystallized to afford pure products.

Compound **18**.

To the mixture ethyl acetate (60 ml) was added, then, the mixture was acidified (*pH* = 3) with 12*N* hydrochloric acid. The aqueous layer was separated and extracted with ethyl acetate (4 x 20 and 4 x 10 ml). The combined organic layers were washed with water (2 x 20 ml), dried, then evaporated to dryness. The residue was triturated with petroleum ether and the precipitate was filtered off to give the product.

5-[*N*-Benzyl-*N*-(3-hydroxy-3-phenyl-1-propyl)amino]-4-chloro-2-methyl-3(2*H*)-pyridazinone (**2a**) and 4-[*N*-Benzyl-*N*-(3-hydroxy-3-phenyl-1-propyl)amino]-5-chloro-2-methyl-3(2*H*)-pyridazinone (**3a**).

These compounds were obtained from the reaction of **1** with 3-benzylamino-1-phenylpropan-1-ol followed by separation by column chromatography.

Compound **2a** was obtained as a yellow oil; ir: 3393, 1618, 1595, 700; ^1H nmr (deuteriochloroform): 2.05 (m, 2H, $\text{CH}_2\text{-CH}_2\text{CH}$), 3.50 (t, 2H, NCH_2CH_2), 3.65 (s, 3H, NCH_3), 4.55 (s, 2H, $\text{NCH}_2\text{-Ph}$), 4.70 (dd, *J* = 8 and 5, 1H, $\text{CH}_2\text{CHOH-Ph}$), 7.10-7.35 (m, 10H, aromatic), 7.50 (s, 1H, 6-CH).

Compound **3a** was obtained as a yellow oil; ir: 3427, 1637, 1572, 943, 700; ^1H nmr (deuteriochloroform): 1.90 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}$), 3.48 (m, 2H, NCH_2CH_2), 3.72 (s, 3H, NCH_3), 4.60

(s, 2H, $\text{NCH}_2\text{-Ph}$), 4.75 (dd, $J = 7$ and 6 , 1H, $\text{CH}_2\text{CHOH-Ph}$), 7.15-7.35 (m, 10H, aromatic), 7.55 (s, 1H, 6-CH).

5-[*N*-Benzyl-*N*-(3-hydroxy-3-(4-methoxyphenyl)-1-propyl)-amino]-4-chloro-2-methyl-3(2*H*)-pyridazinone (**2b**) and 4-[*N*-Benzyl-*N*-(3-hydroxy-3-(4-methoxyphenyl)-1-propyl)amino]-4-chloro-3(2*H*)-pyridazinone (**3b**).

These compounds were obtained from the reaction of **1** with 3-benzylamino-1-(4-methoxyphenyl)propan-1-ol followed by separation by column chromatography.

Compound **2b** was obtained as a yellow solid; ir: 3396, 1612, 1248, 733; ^1H nmr (deuteriochloroform): 2.05 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}$), 3.50 (t, 2H, NCH_2CH_2), 3.68 (s, 3H, NCH_3), 3.78 (s, 3H, OCH_3), 4.58 (s, 2H, $\text{NCH}_2\text{-Ph}$), 4.60 (dd, 1H, $\text{CH}_2\text{CHOH-Ph}$), 6.85 (d, $J = 7$, 2H, $\text{Ph-}m$), 7.18-7.40 (m, 7H, aromatic), 7.55 (s, 1H, 6-CH).

Compound **3b** was obtained as a light yellow oil; ir: 3398, 1615; ^1H nmr (deuteriochloroform): 1.90 (m, 2H, $\text{CH}_2\text{CH}_2\text{-CH}$), 3.45 (m, 2H, NCH_2CH_2), 3.68 (s, 3H, NCH_3), 3.78 (s, 3H, OCH_3), 4.58 (s, 2H, $\text{NCH}_2\text{-Ph}$), 4.65 (dd, 1H, $\text{CH}_2\text{CHOH-Ph}$), 6.82 and 7.20 (each d, each 2H, p -methoxy-Ph), 7.22-7.40 (m, 5H, aromatic), 7.60 (s, 1H, 6-CH).

5-[(*N*-Benzyl-*N*-2-hydroxyethyl)amino]-4-benzylsulfonyl-2-methyl-3(2*H*)-pyridazinone (**14**).

This compound was obtained from **11** and 2-benzylaminoethanol as a yellowish white solid; ir: 3443, 1614, 1578, 1302, 1123, 702; ^1H nmr (deuteriochloroform): 3.30 (t, $J = 7$, 2H, NCH_2CH_2), 3.55 (t, 2H, $\text{CH}_2\text{CH}_2\text{OH}$), 3.75 (s, 3H, NCH_3), 4.62 (s, 2H, $\text{NCH}_2\text{-Ph}$), 4.95 (s, 2H, $\text{SCH}_2\text{-Ph}$), 7.05 (dd, 2H, $\text{Ph-}o$), 7.30 (m, 8H, aromatic), 7.65 (s, 1H, 6-CH).

4-Benzylsulfonyl-5-[*N*-(2-hydroxyethyl)amino]-2-methyl-3(2*H*)-pyridazinone (**16**).

This compound was obtained from **11** and 2-aminoethanol as a white solid; ir: 3420, 3320, 1625, 1600, 1300, 1120, 1065, 695; ^1H nmr (dimethyl sulfoxide- d_6): 3.30 (m, 2H, NCH_2CH_2), 3.40 (m, 2H, $\text{CH}_2\text{CH}_2\text{OH}$), 3.55 (s, 3H, NCH_3), 4.80 (s, 2H, $\text{SCH}_2\text{-Ph}$), 4.95 (t, 1H, OH), 7.20-7.35 (m, 5H, aromatic), 7.85 (s, 1H, 6-CH), 8.28 (t, 1H, NH).

(*S*)-4-Benzylsulfonyl-5-(2-hydroxymethylpyrrolidino)-2-methyl-3(2*H*)-pyridazinone (**18**).

This compound was obtained from **11** and 2(*S*)-hydroxymethylpyrrolidine as a yellowish white solid; ir: 3435, 1620, 1582, 1514, 1300, 1115, 700; ^1H nmr (deuteriochloroform): 1.50-2.15 (m, 4H, 3'- CH_2 and 4'- CH_2), 3.20 (dd, $^3J(\text{H}_a\text{-}5', \text{H}_a\text{-}4') = 6.9$, 1H, 5'- CH_a), 3.98 (ddd, $^2J = 11.8$, $^3J(\text{H}_b\text{-}5', \text{H}_a\text{-}4') = 11.8$, $^3J(\text{H}_b\text{-}5', \text{H}_b\text{-}4') = 6.9$, 1H, 5'- CH_b), 3.44 (dd, 1H, 1'- CH_a), 3.55 (dd, $^2J = 11.9$, $^3J(\text{H}_a\text{-}1', \text{H-}2') = 5.4$, $^3J(\text{H}_b\text{-}1', \text{H-}2') = 3.8$, 1H, 1'- CH_b), 3.66 (s, 3H, NCH_3), 4.30 (m, 1H, 2'-CH), 4.65, and 5.05 (each d, $J = 13.5$, each 1H, $\text{SCH}_2\text{-Ph}$), 7.25 (m, 5H, aromatic), 7.75 (s, 1H, 6-CH); ^{13}C nmr (deuteriochloroform): 25.5 (C-4'), 26.1 (C-3'), 38.9 (NCH_3), 57.8 (C-5'), 60.3 (C-2'), 61.1 ($\text{SCH}_2\text{-Ph}$), 64.4 (C-1'), 107.2 (C-4), 128.3 (C-3", 5"), 128.6 (C-4"), 129.0 (C-1"), 129.1 (C-6), 130.6 (C-2", 6"), 148.7 (C-4), 158.3 (C-3).

General Procedure for the Synthesis of **4**, **15**, **17**, **19** and **20** (Method B).

The appropriate hydroxy compound (1.0 mmole) in dichloromethane (10% solution) (for **6** and **7** no solvent was used) was reacted with thionyl chloride (1.5 mmoles for **15**, **17**, **19**, and **20**;

2.0 mmoles for **4**) in the presence of 4-dimethylaminopyridine (0.10 mmole) as a catalyst (for **4** no catalyst was used).

Product	4	15	17	19	20
Temperature	25°	reflux	reflux	reflux	-10°
Reaction time (hours)	2.5	8	4	5	1

The reaction mixture was then worked up as follows. The solvent was removed *in vacuo*, and the residue was treated with toluene which was evaporated to drive off excess thionyl chloride. The residue obtained was purified to give the product.

Compounds **4**, **17** and **19**.

The above residue was dissolved in dichloromethane and washed successively with water, 5% sodium bicarbonate, then water, and dried. The organic layer was evaporated to dryness. The crude product was triturated with petroleum ether (in the case of **4** and **17**) or subjected to column chromatography using chloroform as the eluting agent for **19**.

Compounds **15** and **20**.

The slurry of the solid residue was triturated with diethyl ether and the crystals which formed were filtered and washed thoroughly with diethyl ether.

5-[*N*-Benzyl-*N*-(3-chloro-3-phenyl-1-propyl)amino]-4-chloro-2-methyl-3(2*H*)-pyridazinone (**4**).

This compound was obtained from **2a** as a yellow oil; ir: 1637, 1593, 698; ^1H nmr (deuteriochloroform): 2.35 (m, 2H, $\text{CH}_2\text{CH}_2\text{CH}$), 3.50 (m, 2H, NCH_2CH_2), 3.75 (s, 3H, NCH_3), 4.60 (s, 2H, $\text{NCH}_2\text{-Ph}$), 4.85 (dd, 1H, $\text{CH}_2\text{CHCl-Ph}$), 7.10-7.40 (m, 10H, aromatic), 7.50 (s, 1H, 6-CH).

5-[(*N*-Benzyl-*N*-2-chloroethyl)amino]-4-benzylsulfonyl-2-methyl-3(2*H*)-pyridazinone (**15**).

This compound was obtained from **14** as a beige solid; ir: 1630, 1578, 1510, 1302, 1119, 733, 702; ^1H nmr (deuteriochloroform): 3.60 (s, 3H, NCH_3), 3.70 (t, $J = 7$, 2H, NCH_2CH_2), 3.80 (t, 2H, $\text{CH}_2\text{CH}_2\text{Cl}$), 4.70 (s, 2H, $\text{NCH}_2\text{-Ph}$), 4.95 (s, 2H, $\text{SCH}_2\text{-Ph}$), 7.10-7.35 (m, 10H, aromatic), 7.90 (s, 1H, 6-CH).

4-Benzylsulfonyl-5-[*N*-(2-chloroethyl)amino]-2-methyl-3(2*H*)-pyridazinone (**17**).

This compound was obtained from **16** as a white solid; ir: 3290, 1636, 1603, 1281, 1103, 706; ^1H nmr (deuteriochloroform): 3.40-3.55 (m, 4H, $\text{NCH}_2\text{CH}_2\text{Cl}$), 3.72 (s, 3H, NCH_3), 4.78 (s, 2H, $\text{SCH}_2\text{-Ph}$), 7.25-7.35 (m, 5H, aromatic), 7.45 (s, 1H, 6-CH), 8.12 (br t, 1H, NH).

(*S*)-4-Benzylsulfonyl-5-(2-chloromethylpyrrolidino)-2-methyl-3(2*H*)-pyridazinone (**19**).

This compound was obtained from **18** as a yellowish white solid; ir: 1628, 1580, 1510, 1304, 1117, 698; ^1H nmr (deuteriochloroform): 1.55-2.40 (m, 4H, 3'- CH_2 and 4'- CH_2), 3.28 (dd, $^3J(\text{H}_a\text{-}5', \text{H}_a\text{-}4') = 6.7$, 1H, 5'- CH_a), 3.94 (ddd, $^2J = 11.3$, $^3J(\text{H}_b\text{-}5', \text{H}_a\text{-}4') = 11.3$, $^3J(\text{H}_b\text{-}5', \text{H}_b\text{-}4') = 5.7$, 1H, 5'- CH_b), 3.46 (dd, 1H, 1'- CH_a), 3.65 (dd, $^2J = 11.7$, $^3J(\text{H}_a\text{-}1', \text{H-}2') = 4.2$, $^3J(\text{H}_b\text{-}1', \text{H-}2') = 6.6$, 1H, 1'- CH_b), 3.66 (s, 3H, NCH_3), 4.55 (m, 1H, 2'-CH), 4.75 and 5.00 (each d, $J = 13.4$, each 1H, $\text{SCH}_2\text{-Ph}$), 7.28 (m, 5H, aromatic), 7.72 (s, 1H, 6-CH); ^{13}C nmr (deuteriochloroform): 25.0 (C-4'), 29.4 (C-3'), 39.1 (NCH_3), 45.3 (C-1'), 56.9 (C-5'), 60.6 (C-2'), 61.6 ($\text{SCH}_2\text{-Ph}$), 107.3 (C-4), 128.3 (C-3", 5"), 128.5 (C-6),

128.6 (C-4"), 130.8 (C-2",6"), 148.7 (C-5), 158.5 (C-3).

4-Benzyl-7-methyl-2,3-dihydro-4*H*-pyridazino[4,5-*b*][1,4]-thiazin-8(7*H*)-one (**20**).

This compound was obtained from **13** as a yellow solid; ir: 1612, 1599, 1344, 870, 728, 698; ¹H nmr (deuteriochloroform): 3.05 (m, 2H, 2-CH₂), 3.65 (m, 2H, 3-CH₂), 3.70 (s, 3H, NCH₃), 4.55 (s, 2H, (NCH₂-Ph), 7.15-7.32 (m, 5H, aromatic), 7.42 (s, 1H, 5-CH); ¹³C nmr (deuteriochloroform): 23.8 (C-2), 39.4 (NCH₂), 49.0 (C3), 55.4 (NCH₂-Ph), 109.9 (C-8a), 126.3 (C-2',6'), 126.5 (C-4'), 127.8 (C-5), 129.0 (C-3',5'), 136.1 (C-1'), 141.5 (C-4a), 158.2 (C-8).

5-Benzyl-8-methyl-2-phenyl-2,3,4,5-tetrahydro-5*H*-pyridazino[4,5-*b*][1,5]thiazepin-9(8*H*)-one (**5**) (Method C).

A solution of sodium sulfide nonahydrate (0.90 g, 3.8 mmoles) in dimethyl sulfoxide (12 ml) was slowly added to a well stirred solution of **4** (0.90 g, 2.3 mmoles) in dimethyl sulfoxide (13 ml), at room temperature under a nitrogen atmosphere, and the reaction mixture was stirred for 0.5 hour. Then it was poured into ice water (90 ml) and stirred at 0° for 4 hours. The yellow precipitate was filtered off, washed successively with water and petroleum ether to give **5** (0.31 g) as a yellowish white solid. This compound had ir: 1612, 1593, 1585, 702; ¹H nmr (deuteriochloroform): 2.04 and 2.35 (each m, each 1H, 3-CH₂), 3.26 (dd, J = 12.5 and 6, 1H, 2-CH), 3.66 (s, 3H, NCH₃), 4.45 and 4.55 (each d, J = 15.5, each 1H, NCH₂-Ph), 4.65 (m, 1H, 4-CH_{2a}), 4.80 (dd, J = 12, J = 6, 1H, 4-CH_{2b}), 7.20-7.40 (m, 11H, aromatic).

5-Benzylamino-4-chloro-2-methyl-3(2*H*)-pyridazinone (**6**) and 1-Benzyl-4-(4-methoxyphenyl)-6-methyl-1,2,3,4-tetrahydro-pyrido[2,3-*d*]pyridazin-5-(6*H*)-one (**7**) (Method D).

A mixture of **2b** (0.25 g, 0.6 mmole) and phenylphosphonic dichloride (1.17 g, 6 mmoles) was stirred at 50° for 8 hours. Ice water (20 ml) was added to the reaction mixture. The solution thus obtained was treated with sodium carbonate until pH = 8, and extracted with chloroform (4 x 10 ml). The combined organic layers were washed with water and dried. The solvent was removed *in vacuo*, and the yellow oily residue which contained compounds **6** and **7**, was subjected to preparative thin layer chromatography (PSC-Fertigplatten, Kieselgel 60F₂₅₄S, Merck) using a mixture of toluene-methanol (9:1, v/v) as the eluent to give pure products (R_f = 0.3 and 0.4 for **6** and **7**, respectively).

Compound **6** (0.03 g) was obtained as a white solid. The ir spectral data of this compound were identical with those of the sample prepared in the authentic way [5].

Compound **7** (0.05 g) was obtained as a yellow oil; ir: 1628, 1595, 1261, 1097, 1026, 800; ¹H nmr (deuteriochloroform): 1.85-1.20 (m, 2H 3-CH₂), 3.05-3.30 (m, 2H, 2-CH₂), 3.65 (s, 3H, NCH₃), 3.75 (s, 3H, OCH₃), 4.35 (br, 1H, 4-CH), 4.60 (s, 2H, NCH₂-Ph), 6.80 and 7.00 (each d, each 2H, *p*-methoxy-Ph), 7.10-7.40 (m, 5H, CH₂-Ph), 7.60 (s, 1H, 8-CH); ¹³C nmr (deuteriochloroform): 28.2 (C-3), 34.4 (C-4), 39.3 (NCH₃), 44.2 (C-2), 54.1 (NCH₂-Ph), 55.2 (OCH₃), 110.2 (C-4a), 113.8 (C-3',5'), 126.2 (C-2",6"), 126.7 (C-4"), 127.6 (C-8), 128.6 (C-2',6'), 129.0 (C-3",5"), 136.4 and 136.7 (C-1' and C-1"), 144.5 (C-8a), 158.0 (C-4'), 160.2 (C-5).

General Procedure for the Synthesis of **8**, **21-23** (Method E).

To a stirred solution of the appropriate chloro compound (5 mmoles) in anhydrous dimethylformamide (25 ml), sodium hydride (14 mmoles for **8** and **22**; 6 mmoles for **21**; and 11

mmoles for **23**) as a 50% oily dispersion was added at 15° (for **21** at 0°) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 4 hours (for **21**, **22**) or 24 hours (for **8**, **23**). The mixture was then quenched over ice water (170 ml), and the product was isolated as follows.

Compound **21**.

The precipitate obtained by quenching the reaction mixture was filtered off and washed successively with water, petroleum ether and diethyl ether, then recrystallized.

Compounds **8**, **22**, **23**.

The aqueous solution was extracted with ethyl acetate (for **8**) or chloroform (for **22**, **23**). The combined organic extracts were washed with water and dried. After evaporation to dryness *in vacuo*, the residue was crystallized.

5-Benzyl-2-(4-methoxyphenyl)-8-methyl-2,3,4,5-tetrahydro-5*H*-pyridazino[4,5-*b*][1,5]oxazepin-9(8*H*)-one (**8**).

This compound was obtained from **13** as a yellowish white solid; ir: 1635, 1600, 1510, 1250; ¹H nmr (deuteriochloroform): 2.10 and 2.40 (each m, each 1H, 3-CH₂), 3.24 (ddd, ³J = 5.5 and 2.7, 1H, 4-CH_a), 3.96 (ddd, ²J = 14.3, ³J = 4.4 and 11.3, 1H, 4-CH_b), 3.70 (s, 3H, NCH₃), 3.80 (s, 3H, OCH₃), 4.48 and 4.54 (each d, J = 16.4, 1H, NCH₂-Ph), 5.28 (dd, 1H, ³J = 4.9 and 11.0, 2-CH), 6.90 and 7.25 (each d, each 2H, *p*-methoxy-Ph), 7.30-7.45 (m, 5H, aromatic), 7.50 (s, 1H, 6-CH).

5-Benzyl-8-methyl-2-phenyl-2,3,4,5-tetrahydro-5*H*-pyridazino[4,5-*b*][1,5]thiazepin-9(8*H*)-one 1,1-Dioxide (**21**).

This compound was obtained from **15** as a beige solid; ir: 1634, 1588, 1582, 1298, 1124, 702; ¹H nmr (dimethyl sulfoxide-*d*₆): 2.10-2.50 (m, 2H, 3-CH₂), 3.50 (s, 3H, NCH₃), 3.60 and 3.92 (each m, each 1H, 4-CH₂), 4.70 (dd, J = 10 and 5, 1H, (2-CH), 4.85 and 4.95 (each d, J = 16, each 1H, NCH₂-Ph), 7.20-7.40 (m, 10H, aromatic), 7.95 (s, 1H, 6-CH); ¹³C nmr (dimethyl sulfoxide-*d*₆): 33.1 (C-3), 39.7 (NCH₃), 52.0 (C-4), 53.9 (NCH₂-Ph), 66.4 (C-2), 114.1 (C-9a), 127.6 (C-2",6"), 128.0 (C-4"), 128.6 (C-3',5'), 128.9 (C-4'), 129.1 (C-3",5"), 129.4 (C-6), 130.3 (C-2',6'), 132.9 (C-1'), 136.7 (C-1"), 149.2 (C-5a), 156.0 (C-9).

3a(*R*),5(*S*)- and 3a(*S*),5(*R*)-8-Methyl-5-phenyl-1,2,3,3a,4,5-hexahydropyrrolo[2',1':4,5]pyridazino[4,5-*b*]-[1,5]thiazepin-7(8*H*)-one 6,6-Dioxide (**22**).

This compound was obtained from **19** as a beige solid; ir: 1628, 1585, 1518, 1294, 1126, 706, 509; ¹H nmr (deuteriochloroform): 2.05-2.20 (m, 4H, 2-CH₂ and 3-CH₂), 2.20 (m, 1H, 4-CH₂), 2.78 (ddd, J = 4.9, 13.3 and 13.3, 1H, 4-CH₂), 3.52 and 3.75 (each m, each 1H, 1-CH₂), 3.68 (s, 3H, NCH₃), 4.36 (dd, J = 5.7, 12.4, 1H, 5-CH), 4.58, m, 1H, 3a-CH), 7.30-7.50 (m, 5H, aromatic), 7.62 (s, 1H, 10-CH).

5-Amino-4-benzylsulfonyl-2-methyl-3(2*H*)-pyridazinone (**23**).

This compound was obtained from **17** as a yellowish white solid; ir: 3427, 1628, 1607, 1285, 1119, 527; ¹H nmr (dimethyl sulfoxide-*d*₆): 3.55 (s, 3H, NCH₃), 4.78 (s, 2H, SCH₂-Ph), 7.25-7.40 (m, 5H, aromatic), 7.50 (s, 1H, 6-CH), 7.7 (br, 2H, NH₂); ¹³C nmr (dimethyl sulfoxide-*d*₆): 38.8 (NCH₃), 59.6 (SCH₂-Ph), 101.6 (C-4), 128.6 (C-3',4',5'), 129.0 (C-1'), 130.9 (C-2',6'), 131.4 (C-6), 149.6 (C-5), 156.9 (C-3).

2-(4-Methoxyphenyl)-8-methyl-2,3,4,5-tetrahydro-5*H*-pyridazino[4,5-*b*][1,5]oxazepin-9(8*H*)-one (**9**) (Method F).

A suspension of **8** (0.38 g, 1 mmole), cyclohexane (0.10 g, 1.2 mmole), and 10% palladium on charcoal catalyst was stirred under reflux for 6 hours. After cooling, the catalyst was filtered off and washed with a mixture of chloroform-methanol (1:1, v/v). The filtrate was evaporated to dryness *in vacuo*, then the residue was suspended in hot ethyl acetate and filtered to give **9** (0.13 g) as a beige solid. This compound had ir: 3273, 1632, 1583, 1516, 1238; ^1H nmr (dimethyl sulfoxide- d_6): 2.05 and 2.28 (each m, each 1H, 3- CH_2), 3.15 and 3.60 (each m, each 1H, 4- CH_2), 3.50 (s, 3H, NCH_3), 3.75 (s, 3H, OCH_3), 4.95 (dd, $J = 10.2$ and 3.2 , 1H, 2-CH), 5.25 (br t, 1H, NH), 6.88 and 7.38 (each d, $J = 7.6$, each 2H, *p*-methoxy-Ph), 7.48 (s, 1H, 6-CH); ^{13}C nmr (dimethyl sulfoxide- d_6): 36.9 (C-3), 39.0 (NCH_3), 42.5 (C-4), 55.2 (OCH_3), 83.3 (C-2), 113.6 (C-3',5'), 127.5 (C-2',6'), 132.6 (C-6), 133.7 and 134.9 (C-1' and C-5a), 139.1 (C-9a), 158.1 (C-4'), 158.9 (C-9).

General Procedure for the Synthesis of **10** and **13** (Method G).

To stirred suspension of a 45% oily dispersion of sodium hydride (1.00 g, 18.8 mmole) in toluene (25 ml), benzylthiol (2.00 g, 16.0 mmole) was added dropwise at room temperature, and the mixture was stirred for 0.5 hour. Then a solution of **1** or **12** (15.0 mmole) in toluene (55 ml) was added dropwise and the reaction mixture was stirred at room temperature for 6.5 hours.

The crystalline material was filtered off, and the filtrate was evaporated to dryness *in vacuo*. Purification by column chromatography with a mixture of ethyl acetate-petroleum ether (1:3, v/v) as eluent afforded the pure product.

4-Benzylthio-5-chloro-2-methyl-3(2H)-pyridazinone (**10**).

This compound (yellow oil) had ir: 1643, 1217, 949, 710; ^1H nmr (deuteriochloroform): 3.65 (s, 3H, NCH_3), 4.10 (s, 2H, $\text{SCH}_2\text{-Ph}$), 7.15-7.35 (m, 5H, aromatic), 7.65 (s, 1H, 6-CH).

4-Benzylthio-5-[(*N*-benzyl-*N*-2-hydroxyethyl)amino]-2-methyl-3(2H)-pyridazinone (**13**).

This compound (yellow solid) had ir: 3432, 1618, 700; ^1H nmr (dimethyl sulfoxide- d_6): 3.35 (t, $J = 7$, 2H, NCH_2CH_2), 3.50 (m, 2H, $\text{CH}_2\text{CH}_2\text{OH}$), 3.60 (s, 3H, NCH_3), 4.15 (s, 2H, $\text{SCH}_2\text{-Ph}$), 4.65 (s, 2H, $\text{NCH}_2\text{-Ph}$), 4.70 (t, 1H, OH), 7.05-7.32 (m, 10H, aromatic), 7.70 (s, 1H, 6-CH).

4-Benzylsulfonyl-5-chloro-2-methyl-3(2H)-pyridazinone (**11**) (Method H).

To a stirred solution of **10** (5.30 g, 20 mmole) in chloroform (100 ml), *meta*-chloroperbenzoic acid (3.45 g, 20 mmole) was

added portionwise at 0° under a nitrogen atmosphere, and the resulting suspension was stirred at 0° for 2 hours. The crystalline material was filtered off and washed with chloroform.

The yellow filtrate was washed successively with 10% sodium bicarbonate and water until $\text{pH} = 6$, then dried. After removal of the chloroform *in vacuo*, the residual solid was recrystallized to give **11** (4.90 g) as a yellow solid. This compound had ir: 1666, 1643, 1323, 1130, 701; ^1H nmr (deuteriochloroform): 3.72 (s, 3H, NCH_3), 4.85 (s, 2H, $\text{SCH}_2\text{-Ph}$), 7.28-7.45 (m, 5H, aromatic), 7.65 (s, 1H, 6-CH).

Acknowledgements.

The authors thank Mrs Á. Forgó-Phur for microanalyses, Ms. K. Balogh for excellent technical assistance, and Mrs. E. Hivessy for careful typing of the manuscript.

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