SELECTIVE AND SIMULTANEOUS DEPROTECTION OF AMINE AND LACTAM FUNCTIONS IN THE SYNTHESES OF PYRIDAZINO[4,5-b]OXAZINONES AND PYRIDAZINO[4,5-b]THIAZINONES
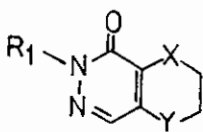
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Abstract - Benzyloxymethyl (BOM) and benzyl (Bz) groups were employed for protection of the amide- and amino-nitrogens in the title compounds. The BOM protective group could be removed selectively or simultaneously with the Bz group depending on the reaction conditions. By catalytic hydrogenation of the fully protected pyridazinooxazinone (**1b**), unexpectedly the 4-methyl derivative (**1e**) could also be prepared. The mechanism for the formation of **1e** is also discussed.

As a part of our studies on structure-activity relationships of pyridazinone derivatives with cardiovascular activities,[1,2] pyridazino[4,5-b]oxazinones and -thiazinones as bicyclic analogues substituted correspondingly at the lactam(7-) and/or amino-(4-) nitrogens have also been considered. An economic and efficient synthetic strategy for selective functionalization of these positions required to elaborate a simple procedure for selective or simultaneous protection/deprotection of the lactam and amino functions. Furthermore, temporary blocking of these positions has been shown to be a prerequisite to form the oxazine moiety by ring closure.[3] We describe here our preparative results as well as some mechanistic aspects of this work.

As selectively and simultaneously removable protective groups for the lactam- and amino-nitrogens, benzyloxymethyl (BOM) and benzyl (Bz) groups were considered.

1: X=O, Y=NR^2 a: R^1=H, R^2=Bz   e: R^1=H, R^2=CH$_3$

2: X=S, Y=NR^2 b: R^1=BOM, R^2=Bz   f: R^1=CH$_2$OH, R^2=Bz

3: X=NR^2, Y=O   c: R^1=R^2=H   g: R^1=CH$_3$, R^2=H

4: X=NR^2, Y=S   d: R^1=BOM, R^2=H   h: R^1=CH$_3$, R^2=Bz

Thus, the desired bicyclic derivatives (**1b-4b**) were synthesized starting from 2-benzyloxymethyl-4,5-dichloro-3(2*H*)-pyridazinone (**5**)[4] as shown in Scheme 1.

Scheme 1
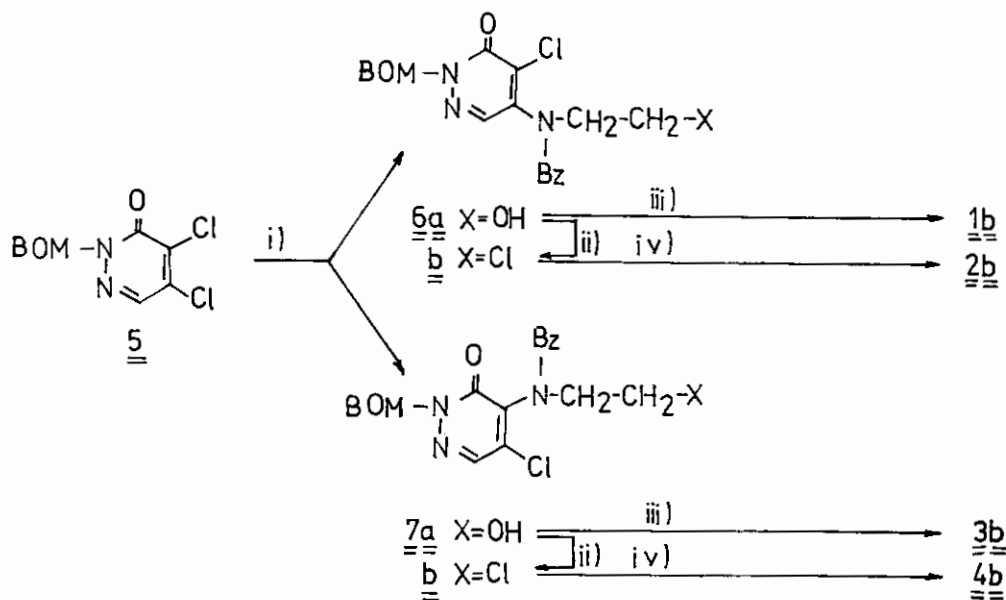
i: BzNHCH$_2$CH$_2$OH/H$_2$O or toluene, reflux; ii: SOCl$_2$/CH$_2$Cl$_2$, reflux; iii: NaOEt/EtOH, reflux; iv: Na$_2$S/EtOH, reflux

At first **5** was allowed to react with *N*-benzylaminoethanol in water or toluene affording **6a** and **7a** in a ratio of *ca.* 10 or 2.5, respectively. After separation of the isomers by column chromatography, reaction with thionyl chloride gave the corresponding 2-chloroethylamino derivatives (**6b**) and (**7b**). The ring closure of the hydroxyethylamino and chloroethylamino precursors to oxazinones and thiazinones,

respectively, was then easily achieved by treatment with sodium ethoxide or sodium sulfide, respectively, in ethanol. Cleavage of the lactam BOM group of **1b-3b** could *selectively* be performed in benzene or toluene by using BBr_3 at 25 °C or $AlCl_3$ at reflux temperature. (Scheme 2)

Scheme 2
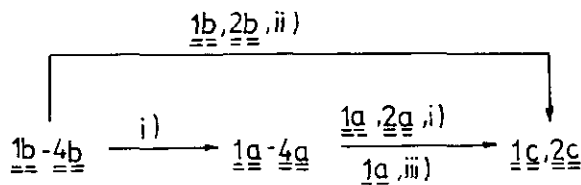
i: BBr_3/benzene or toluene, 25 °C, for **4b** -10 °C or $AlCl_3$/toluene,reflux;
ii: H_3PO_3/PhOH, 150 °C; iii: H_2/Pd-C/MeOH/H^+, 25 °C

In the case of **4b**, BBr_3 completely removed both protective groups at 25 °C, and a selective cleavage of the BOM group could only be achieved at -10 °C. It seems therefore that the selectivity of these reactions is also dependent on the position of the N-Bz group. By removing the BOM group, cleavage of the N-Bz group could be retarded as in **1b-3b**, by electronic effect of the 8-OMZ_2 ($MZ_2=BBr_2$, $AlCl_2$) group formed *in situ* by reaction of the BOM-lactam moiety with the Lewis acid, or it might be simultaneously facilitated by the neighbouring effect of the 8-OMZ_2 group acting as a Lewis acid, from steric and electronic reasons, as in **4b**. When **1a**, the "BOM-deprotected" derivate of **1b**, was treated with $AlCl_3$ in toluene at reflux temperature, the debenzylation proceeded smoothly supporting the above explanation on a dramatic role of the $OAlCl_2$ group in deactivating the N-Bz group toward debenzylation. As such a deactivating group may not be formed in the case of **1a**, the debenzylation of this compound is not hindered at all.

Both protective groups were removed from **1b** and **2b** by heating in phosphoric acid at 150 °C in the presence of phenol,[5] and compounds (**1c**) and (**2c**), respectively, could be isolated. Catalytic hydrogenation of **1b** with palladium on charcoal in methanol resulted in different products depending on the reaction time as depicted in Scheme 3.

When the reaction was stopped after a short period of time (*ca.* 5 min), compound (**1d**) could be isolated in the yield of ≈20 % besides unreacted starting material. When the reaction had been conducted to the calculated hydrogen consumption, and then the mixture was immediately worked up, **1c** could be obtained in good yield. Finally, when the reaction mixture had been set aside for several days before working up, quite surprisingly, the 4-methyl derivative (**1e**) was the only isolable product. The position of the methyl group in this compound was unambigously proved by ^{1}H nmr data as comparing to the 7-methyl derivative (**1g**) synthesized in the authentic way.[6] As expected, a nOe

between methyl and 5-CH signals was observed only in **1e**.

Scheme 3
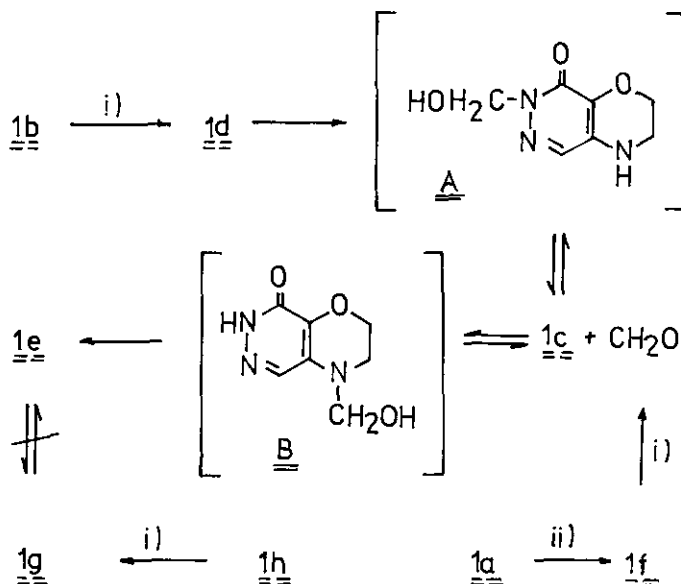
i: H_2/Pd-C/MeOH/H^+, 25 °C; ii: CH_2O/H_2O, reflux

Scheme 3 also shows a working hypothesis for the formation of **1e**. Hydrogenolysis of the *N*-BOM derivative (**1b**) affords the *N*-CH_2OH derivative (**A**), similarly as it has already been described for pyrroles.[7] In our case, the intermediate (**A**) formed may however be expected[8] to undergo a rearrangement to the 4-CH_2OH derivative (**B**) *via* elimination-addition steps. Intermediate (**B**) is then converted to the 4-methyl derivative (**1e**) by reduction of the 4-CH_2OH group. In agreement with these proposals, in a separate experiment, the 4-Bz-7-CH_2OH derivative (**1f**), which in turn was found to easily decompose to **1a**, gave **1e** under conditions employed for **1b**. Furthermore, **1e** could also be obtained by treatment of **1c** with formaldehyde.

The intermolecular nature of the rearrangement was also proved. In a crossover experiment, catalytic hydrogenation of **1b** in the presence of morpholine afforded **1c** and *N*-methylmorpholine as only products, while formation of **1e** could not be detected.[9]

Though, the rearrangement reaction, could also involve the migration of the BOM group, as it has been observed for a BOM-triazole derivative,[10] but in our case, all findings support the mechanism proposed above and are against the migration of the BOM group.

In conclusion, these results indicate that in the synthesis of pyridazinooxazinones, and -thiazinones, and

possibly in relating compounds as well, the BOM and Bz groups represent a powerful combination for a selective and simultaneous protection of the lactam and amine functions in a variety of preparative manipulations.

EXPERIMENTAL

Melting points were determined on a Boetius apparatus and are uncorrected. The ir spectra were recorded in potassium bromide pellets on a Bruker IFS 85 spectrophotometer. The ^{1}H nmr spectra were recorded on a Bruker AC-250 spectrometer at ambient temperature using TMS as internal reference. DNOE experiments were performed with the Bruker microprogram.

Synthesis of compounds (1g), [6] (1h)[11] and (5)[4] were performed according to the quoted literatures. Analytical and spectroscopic data of the new compounds are collected in *Table 1* and *Table 2*, respectively.

Synthesis of 5-(N-benzyl-N-2-hydroxyethylamino)-2-benzyloxymethyl-4-chloro-3(2H)-pyridazinone (6a) and 4-(N-benzyl-N-2-hydroxyethylamino)-5-chloro-3(2H)-pyridazinone (7a).

Method I. A mixture of 25.9 g (0.09 mol) of 5 and 41.1 g (0.27 mol) of 2-N-benzylaminoethanol in 300 ml of water was stirred under reflux for 11 h. The cold mixture was acidified to pH 3 with 36 % aqueous HCl and extracted with EtOAc. The organic layers were washed with water and dried over anhydrous Na_2SO_4. The solvent was evaporated *in vacuo* and the crude oil was chromatographed on silica gel using $CHCl_3$ as eluent to give 1.55 g (4%) of 7a. Further elution with an 1:1 mixture of $CHCl_3$-EtOAc afforded 14.75 g (41%) of 6a.

Method II. A similar procedure was followed as decribed in method I using 2-N-benzylaminethanol and 5 in a molar ratio of 10. As solvent toluene (270 ml) was used instead of water. The reaction mixture was stirred under reflux for 11 h and was worked up as described in Method I to give 15.45 g (43%) 6a and 7.55 g (21%) 7a.

Synthesis of 4-benzyl-7-benzyloxymethyl-3,4-dihydro-2H-pyridazino[4,5-b][1,4]oxazin-8(7H)-one (1b) and 4-benzyl-6-benzyloxymethyl-3,4-dihydro-2H-pyridazino[4,5-b][1,4]oxazin-5(6H)-one (3b).

Method III. A solution of sodium ethoxide prepared from 0.14 g (0.06 mol) of sodium in 75 ml of ethanol and 8.5 g (0.02 mol) of 6a or 7a was stirred under reflux for 11 h (6a) or 3 h (7a), then the precipitate was filtered off and washed with EtOH. The filtrate was evaporated *in vacuo* and the residue was taken up in water and extracted with EtOAc. The organic layer was washed with water and dried over anhydrous Na_2SO_4. The solvent was evaporated *in vacuo* and the crude oil was chromatographed on silica gel using 9:1 mixture of $CHCl_3$-EtOAc as eluent for 1b and $CHCl_3$ for 3b.

Table I

Physical and analytical data of compounds (1a-f, 2a-c, 3a-b, 4a-c, 5b-c)

Compd	Method	Yield %	mp(°C) (cryst. from)	Molecular formula	Analysis (Calcd/Found)		
					C	H	N
1a	VI/1	61	225-226 (i-PrOH)	$C_{13}H_{13}N_3O_2$	64.18 64.33	5.38 5.31	17.27 17.00
1b	IV	60	oil	$C_{21}H_{21}N_3O_3$	69.47 69.35	5.83 6.00	11.57 11.40
1c	IX	80[a] 75[b]	>300	$C_6H_7N_3O_2 \cdot H_2O \cdot HCl$	34.78 34.85	4.80 4.63	20.29 20.05
	VIII	47	>300	$C_6H_7N_3O_2$	47.05 46.97	4.60 4.35	27.42 27.33
1d	IX	20	142-143	$C_{14}H_{15}N_3O_3$	61.53 61.48	5.53 5.41	15.37 15.23
1e	IX	87	220-230	$C_7H_9N_3O_2 \cdot HCl$	41.32 41.52	4.95 4.96	20.64 20.74
	X	32	218-219	$C_7H_9N_3O_2$	49.12 49.28	4.86 5.02	24.56 24.72
1f	XI	71	115-118	$C_{14}H_{15}N_3O_3 \cdot 0.5H_2O$	59.56 59.44	5.70 5.60	14.88 14.64
2a	VI/1 VII	54 40	235-240 (i-PrOH)	$C_{13}H_{13}N_3OS$	60.20 60.32	5.05 5.00	16.20 16.12
2b	V	43	oil	$C_{21}H_{21}N_3O_2S$	66.46 66.38	5.58 5.65	11.07 11.23
2c	VIII	45	280-285	$C_6H_7N_3OS$	42.60 42.58	4.17 4.20	24.84 24.67
3a	VI/1	66	164-165	$C_{13}H_{13}N_3O_2$	64.18 64.38	5.38 5.42	17.27 17.41
3b	IV	55	oil	$C_{21}H_{21}N_3O_3$	69.47 69.40	5.83 5.81	11.57 11.35
4a	VI/2	77	163-164	$C_{13}H_{13}N_3OS$	60.20 60.09	5.05 5.10	16.20 16.35
4b	V	41	oil	$C_{21}H_{21}N_3O_2S$	66.46 66.32	5.58 5.62	11.07 10.92
4c	VI/1	59	222-224	$C_6H_7N_3OS$	42.60 42.65	4.17 4.10	24.84 24.96
6a	I/II	41/43	oil	$C_{21}H_{22}N_3O_3Cl$	63.13 62.95	5.55 5.58	10.52 10.43
7a	I/II	4/21	oil		62.90	5.45	10.40
6b	III	65	oil	$C_{21}H_{21}N_3O_2Cl_2$	60.29 60.09	5.06 4.92	10.04 9.93
7b	III	43	oil		60.14	5.00	10.14

[a] from 1a; [b] from 1b

Table II

The ir(KBr) and ^{1}H-nmr data of compounds (1a-f, 2a-c, 3a-b, 4a-c, 6a-b, 7a-b)

Compd	ir(cm^{-1}) ν C=O (amid-I)	N-CH$_2$ 2H	X-CH$_2^c$ 2H	PhCH$_2$N s,2H	PhCH$_2$O s,2H	OCH$_2$ s,2H	Ar^{d,e} m	CH s,1H	other signals
1a^a	1634	3.40 t (4.5)	4.25 (4.5)	4.50	–	–	7.30^d	7.60	12.10(br s, 1H, 7-NH)
1b^a	1639	3.30 m	4.20 m	4.45	4.65	5.45	7.30^e	7.60	–
1c^b	1630	3.35 m	4.10 m	–	–	–	–	7.50	6.50(br s, 1H, 4-NH) 12.00(br s, 1H, 7-NH)
1d^a	1612	3.40 m	4.20 m	–	4.70	5.50	7.30^d	7.55	5.45(s, 1H, 4-NH)
1e^b	1634	3.35 m	4.20 m	–	–	–	–	7.80	2.90(s, 3H, 4-CH$_3$) 12.40(br s, 1H, 7-NH)
1f^b	1605-1633(br)	3.50 t (4.5)	4.30 t (4.5)	4.55	–	5.50^d (5.50)	7.30^d	7.65	4.80(br s, 1H, 7-CH$_2$-OH)
2a^b	1614	3.00 m	3.65 m	4.75	–	–	7.30^d	7.70	12.35(br s, 1H, 7-NH)
2b^a	1622	3.10 m	3.70 m	4.60	4.75	5.55	7.30^e	7.55	–
2c^b	1637	2.95 m	3.55 m	–	–	–	–	7.45	7.25(s, 1H, 4-NH)
3a^b	1637	3.15 br s	4.80 br s	4.80	–	–	7.30^d	7.60	12.55(s, 1H, 6-NH)
3b^a	1636	3.15 t (4)	3.95 t (4)	4.75^f	4.80^f	5.60	7.35^e	7.55	–
4a^a	1639	2.80 m	3.40 m	4.90	–	–	7.35^d	7.45	11.30(br s, 1H 6-NH)
4b^a	1634	2.85 m	3.35 m	4.70^f	4.75^f	5.60	7.30^e	7.50	–
4c^b	1634	2.95 m	3.60 m	–	–	–	–	7.40	6.95(s, 1H, 4-NH)
6a^a	1624	3.62 t (5.5)	3.84 t (5.5)	4.69^f	4.73^f	5.48	7.15^e	7.55	–
6b^a	1649	3.50 m	3.70 m	4.60	4.70	5.50	7.30^e	7.70	–
7a^a	1647	3.60^{f}m	3.60^{f}m	4.55^f	4.60^f	5.40	7.15^e	7.50	–
7b^a	1651	3.55^{f}m	3.70^{f}m	4.60	4.70	5.55	7.30^e	7.65	–

Solvent [a] CDCl$_3$ [b] DMSO-d$_6$; [c] X=O: 1a-f; 3a-b; 6a-b; X=S: 2a-c; 4a-c; X=Cl: 7a-b; intensity of [d] 5H [e] 10H; [f] overlapping signals.

Synthesis of 5-(N-benzyl-N-2-chloroethylamino)-2-benzyloxymethyl-4-chloro-3(2H)-pyridazinone (**6b**) *and 4-(N-benzyl-N-2-chloroethylamino)-2-benzyloxymethyl-4-chloro-3(2H)-pyridazinone* (**7b**).

Method IV. A solution of 8 g (0.02 mol) of **6a** or **7a** in 80 ml of dry CH_2Cl_2 was treated with 4.76 g (0.04 mol) of thionyl chloride and a catalytic amount of 4-(N,N-dimethylamino)pyridine (DMAP). The mixture was heated under reflux for 5 h. Then excess of thionyl chloride and the solvent were removed *in vacuo.* The residue was taken up in 100 ml of water and extracted with EtOAc. The organic layers were washed subsequently with water, 5% aqueous solution of $NaHCO_3$, and once again with water. After evaporation to dryness, the residue was triturated with petroleum ether (bp 40-70 °C) to give the product.

Synthesis of 4-benzyl-7-benzyloxymethyl-3,4-dihydro-2H-pyridazino[4,5-b][1,4]thiazin-8-(7H)-one (**2b**) *and 4-benzyl-6-benzyloxymethyl-3,4-dihydro-2H-pyridazino[4,5-b][1,4]thiazin-5(6H)-one* (**4b**).

Method V. A suspension of 6.38 g (0.015 mol) of **6b** or **7b** and 7.3 g (0.03 mol) of sodium sulfide nonahydrate in 130 ml of EtOH under nitrogen atmosphere was heated under reflux for 4 h (**6b**) or for 2 h (**7b**). The precipitate was filtered off, washed with EtOH, and the filtrate was evaporated *in vacuo.* The residue was cromatographed on silica gel using a 95:5 mixture of $CHCl_3$:EtOAc as eluent. An analytical sample of **2b** was purified by preparative thin layer chromatography on Kieselgel $60F_{254}S$ using a 9:1 mixture of toluene-MeOH as eluent.

Selective cleavage of the N-BOM group with boron tribromide: Preparation of 4-benzyl-3,4-dihydro-2H-pyridazino[4,5-b][1,4]oxazinones (**1a, 3a**) *and -thiazinones* (**2a, 4a**).

Preparation of **1a, 2a, 3a.** *Method VI/1.* To a solution of 3 mmol of the *N*-BOM derivatives (**1b-3b**), respectively in 30 ml of benzene, 1.5 g (6 mmol) of boron tribromide were added under stirring at 10 °C. The reaction mixture was stirred for 1 h at room temperature. Then 20 ml of MeOH were added under cooling and the mixture was stirred for 30 min at room temperature. The low boiling fractions were removed *in vacuo.* The residue was boiled with 100 ml of water for 1 h. The cold solution was extracted with $CHCl_3$, the organic layers were washed with water then with 5% aqueous solution of $NaHCO_3$ and water. After evaporation to dryness *in vacuo*, the residue was recrystallized to give compounds (**1a, 2a**) or cromatographed on silica gel using an 1:1 mixture of $CHCl_3$-EtOAc as eluent to give compound (**3a**).

Preparation of **4a.** *Method VI/2.* A solution of 0.38 g (1 mmol) of **4b** in 8 ml of toluene was stirred with 0.3 g (1.2 mmol) of boron tribromide at -10 °C for 30 min. The reaction mixture was worked up as described in Method VI/1.

Selective cleavage of the N-BOM group with aluminium trichloride. Preparation of **2a**. *Method VII.* 0.38 g of **2b** (1 mmol) were added to a solution of 0.67 g (5 mmol) of anhydrous aluminium trichloride in 8 ml of dry toluene with stirring and the mixture was stirred under reflux for 2 h, then cooled. Ice-water was added and the solution was extracted with CHCl3. The organic layers were washed with water, 5% aqueous solution of NaHCO3, and then with water again. After evaporation *in vacuo*, the residue was purified by preparative thin layer chromatography on Kieselgel 60 $F_{254}S$ using a 8:2 mixture of toluene-MeOH as eluent.

Simultaneous cleavage of N-BOM and N-Bz groups
Preparation of 3,4-dihydro-2H-pyridazino[4,5-b][1,4]oxazin-8(7H)-one (**1c**) *and -thiazin-8(7H)-one (**2c**)*
Method VIII. A mixture of 0.38 g (1 mmol) of the appropriate compound (**1b**) or (**2b**) and 0.1 g (1.1 mmol) of PhOH in 2.5 ml of 85% phosporic acid was heated under stirring for 3 h. Ice-cold water was then added to the cold mixture and filtered. The filtrate was adjusted to pH 8 with powdered Na2CO3 and the solution was evaporated *in vacuo* to dryness.
The residue was stirred with an 1:1 mixture of hot CHCl3-MeOH, filtered and evaporated. The residue was dissolved in a cold 1:1 mixture of CHCl3-MeOH, and filtered. The filtrate was evaporated to dryness and the residue was washed with ether.

Preparation of 3,4-dihydro-2H-pyridazino[4,5-b][1,4]oxazin-8(7H)-one (**1c**), *its 7-benzyloxymethyl* (**1d**) *and 4-methyl* (**1e**) *derivatives.*

Method IX/1. In a Parr apparatus, a solution of 2 mmol of **1a**, **1b** or **1f**, respectively in 15 ml of MeOH was acidified to pH 3 with 36 % aqueous HCl. The reaction mixture was hydrogenated with 0.4 g of 10 % palladium on charcoal catalyst at room temperature. After the calculated hydrogen consumption had been reached, the catalyst was filtered off and the filtrate was evaporated to dryness. The residue was triturated with ether to give the hydrochloric salt of **1c**.
When the reaction of **1b** was stopped after 5 min and worked up as above, and the residue was chromatographed on silica gel with EtOAc, compound (**1d**) could be isolated besides the starting material.
When the reaction mixture of **1b** or **1f** was set aside under hydrogen for 2 days, and worked up as above, compound (**1e**) in the form of hydrochloric salt could be isolated.
Method IX/2. In a Parr apparatus, a solution of 0.19 g (1 mmol) of **1c**.HCl and 0.1 ml of 36% aqueous solution of formaldehyde in 8 ml of MeOH was hydrogenated in the presence of 0.2 g of 10 % palladium on charcoal at room temperature. The mixture was worked up as described in method IX/1 after 2 days to give **1e** in the form of hydrochloric salt.
Method X. A solution of 0.36 g (1 mmol) of **1b** and 4.9 g (60 mmols) of cyclohexene in 5 ml of EtOH was refluxed in the presence of 0.1 g of 10 % palladium on charcoal for 12 h. The cold mixture was

filtered off, the filtrate was evaporated to dryness, and the residue was chromatographed on silica gel using EtOAc as eluent to give **1e**.

*The reaction of **1a** with formaldehyde. Preparation of 4-benzyl-7-hydroxymethyl-3,4-dihydro-2H-pyridazino[4,5-b][1,4]oxazin-8(7H)-one (**1f**)*

Method XI. A mixture of 0.33 g (1.36 mmol) of **1a** in 1 ml of 36 % aqueous solution of formaldehyde was stirred under reflux for 3 h. After cooling the precipitate was filtered off, washed with water and dried to give **1f**.

ACKNOWLEDGEMENTS

REFERENCES AND NOTES

1.   P. Mátyus, J. Kosáry, E. Kasztreiner, N. Makk, E. Diesler, K. Czakó, G. Rabloczky, L. Jaszlits, E. Horváth, Z. Tömösközi, G. Cseh, E. Horváth, and P. Arányi, *Eur. J. Med. Chem.*, 1992, **27**, 107.

2.   PCT Int. Appl. WO-92 12,137

3.   I. Varga, G. Jerkovich, and P. Mátyus, *J. Heterocycl. Chem.*, 1991, **28**, 493, and reference cited therein.

4.   Compound (**5**) has been used for the synthesis of BOM-imidazo[4,5-*d*]pyridazinone derivatives. Removing of the BOM group could be achieved by treatment with BCl_3 at -78 °C.
      R. P. Gagnier, M. J. Halat, and B. A. Otter, *J. Heterocycl. Chem.*, 1984, **21**, 481.
      BBr_3 was used for removing of BOM and Bz groups from 1,3-disubstituted uracils.
      N. G. Kundu, R. P. Hertzberg, and S. J. Hannon, *Tetrahedron Lett.*, 1980, **21**, 1109.

5.   G. F. Field, W. J. Zally, L. H. Sternbach, and J. F. Blount, *J. Org. Chem.*, 1976, **41**, 3853.

6.   Japan Pat. Appl. Kokai, 7802497 (1978) (*Chem. Abstr.*, 1978, **88**, 190873z).

7.   M. J. Anderson and J. K.Groves, *Tetrahedron Lett.*, **1971**, 3165.

8.   It has already been shown that 2-hydroxymethyl-3(2*H*)-pyridazinones decompose easily.
      H. Gregory, J. Hills, and L. F. Wiggins, *J. Chem. Soc.*, 1949, 1248.

9.   The reaction mixture was quantitatively and qualitatively analyzed by gc and tlc, respectively, using a sample of *N*-methylmorpholine (Aldrich).

10.   J. H. Jones and P. B. Wyatt, *J. Chem. Res. (S)*, 1987, 396.

11.   T. Matsuo, Y. Tsukamoto, T. Takagi, and M. Sato, *Chem. Pharm. Bull.*, 1982, **30**, 832.