Preparation and Structures of Isoindolone- or Pyrimidone-Condensed Heterocycles Containing a Hydroxy Group on a Cyclohexane or Norbornane Moiety

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Abstract: With DL-valinol, 3-amino-1-propanol and *o*-aminothiophenol, aroyl(bi/tri)cyclic lactones **1** and **2** were cyclized to isoindole- **4-6, 8, 9,** pyrimidinone- **10** or thiazepine- **7** condensed heterocycles. The ketal lactone **3** furnished the benzthiazoloisoindole **9** and mixtures of epimeric hydroxyphthalazinoquinazolinones **11** and **12**. The structures were established by means of ^{1}H and ^{13}C NMR spectroscopy and in some cases by X-ray crystallography.

Keywords: Cycloalkane lactones, Isoindolones, 1,3-oxazines, Thiazoles, Stereostructure, NMR, X-ray.

INTRODUCTION

We have recently developed a method with which to synthetize (bi)cycloalkane aroyl lactones and ketal lactones [1], which seemed to be applicable as starting compounds for the preparation of derivatives with the hydroxy group at different sites on the saturated carbocycle. Our first attempts focused on the hydrolysis and hydrazonolysis of the lactones, which resulted in hydroxylated products on a preparative scale [2]. Until recently, no simple method was known for the introduction of a hydroxy group onto a saturated ring. The results emphasized the advantageous features of this reaction. The literature procedures [3-7] for preparation of the starting synthons involved either electrophilic addition following lactonization and elimination of the undesired group or oxidation with perbenzoic acid [8] and lithiation [9,10]. Epoxidation on the olefinic bond [11,12] or the photolysis and reduction of nitrosamines [13] are not general routes to hydroxy-substituted derivatives.

In the present paper, our earlier-developed procedure is extended by reacting the lactones **1-3** with bifunctional reagents: aminoalcohols, 2-aminothiophenol and *diexo*- norbornane-2-aminocarbohydrazides.

RESULTS AND DISCUSSION

In the presence of PTSA as catalyst, *cis*-2-toluoylcyclohexane lactone **1** was refluxed with 2-amino-3-methylbutan-1-ol or 3-amino-1-propanol in xylene to yield the saturated 7-hydroxyoxazolo- **4** and 8-hydroxy[1,3]oxaz-ino[2,3-*a*]isoindolone **5**. Through the reaction of **1** and *o*-aminothiophenol, a mixture of two products was obtained: the partially saturated isoindolo[1,2-*b*]benzthiazolone **6** and dibenzo[*b,f*][1,4]thiazepine **7**, which were separated by column chromatography and their structures established by means of NMR spectroscopic methods. For the formation of **7**, the amino attacks on the oxo group, giving a Schiff base; the thiol then reacts at the cyclohexane α-carbon. The intermediate is stabilized by the formation of OH and formyl groups, the latter subsequently being eliminated (Scheme **1**).

A compound analogous to **7**, clothiapine, was synthetized earlier [13], and partially saturated thiazepines are also known in the literature [14]. With 3-amino-1-propanol, *diendo*-norbornanelactone **2** cyclizes to the saturated methano-8-hydroxy-1,3-oxazinoisoindolone **8** (Scheme **2**). From lactone **1**, with *diexo*-3-aminonorbornane-2-carbohydrazide, the pentacyclic methano-2-hydroxyphthalazinoquinazolinone **10** was obtained (Scheme **3**).

On opening with 2-aminophenyl-1-mercaptan, ketal lactone **3** yielded the tetracyclic 3-hydroxy-benzthiazoloisoindolone **9** (Scheme **3**). In the reaction of **3** with *diexo*-3-aminobicyclo[2.2.1]heptane-2-carbohydrazide, different mixtures of the pentacyclic hydroxyphthalazinopyrimidinone isomers **11** and **12** were isolated after purification by column chromatography. The X-ray data revealed that the products contain a 3-hydroxy group on a *cis*-condensed cyclohexane ring, *equatorial* [86(1)%] for **11** (Fig. **1**) and *axial* [72(1)%] for **12**. These mixtures are thermodynamically stable and the products could not be separated in pure form.

To summarize, the reactions of lactones **1** or **2** and ketal lactone **3** [12] with bidentate nucleophiles can be utilized for the transannulational hydroxylation of cyclohexane- or

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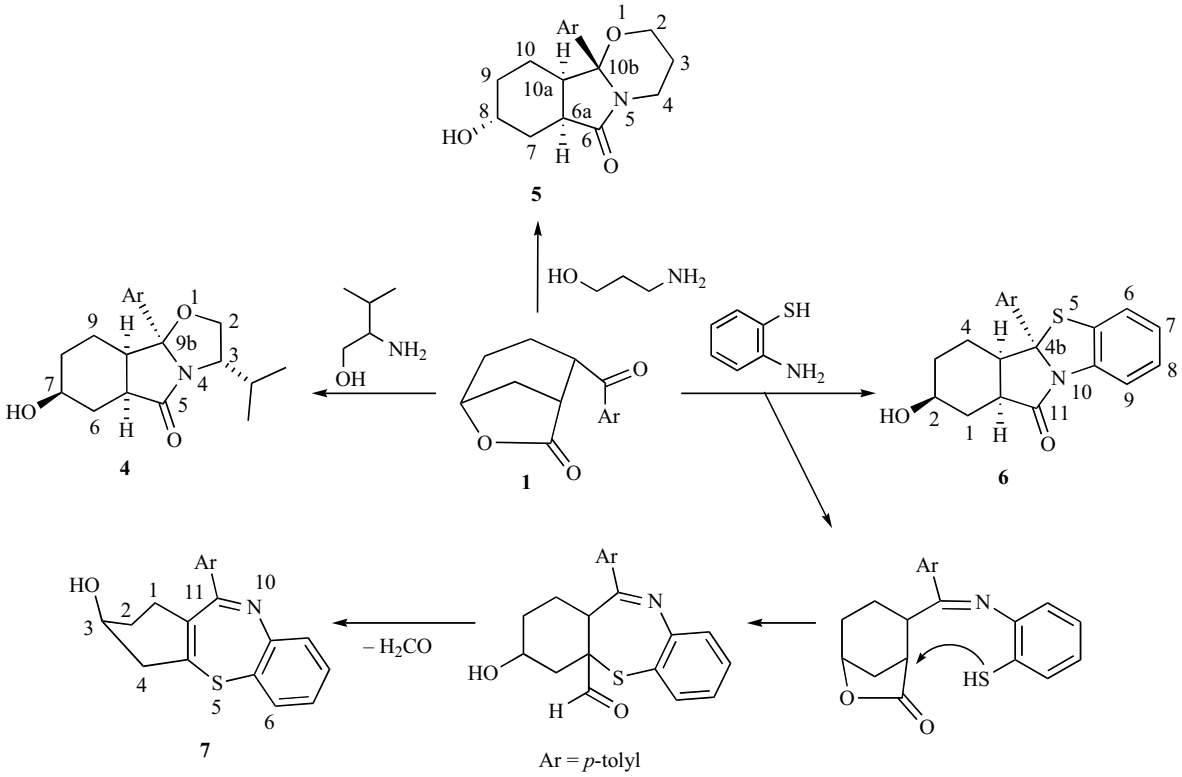
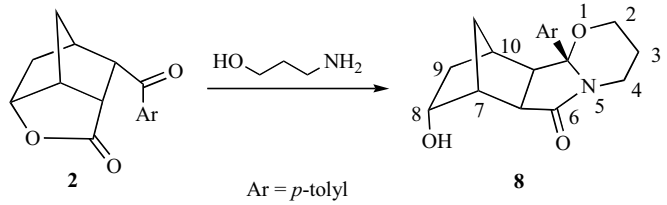
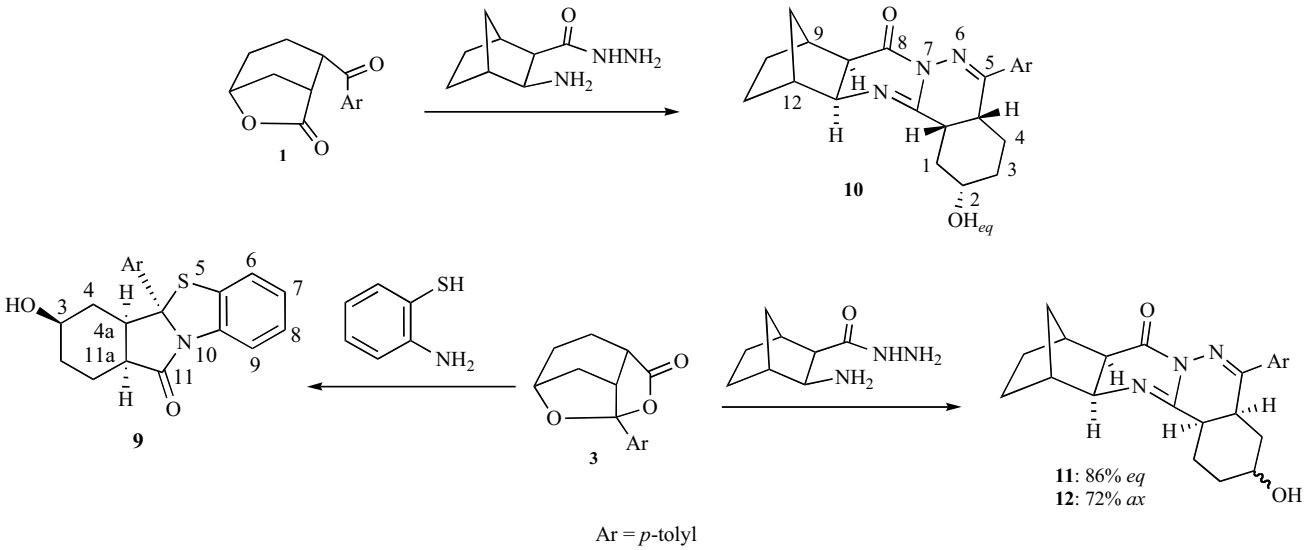


Scheme 1.



Scheme 2.



Scheme 3.

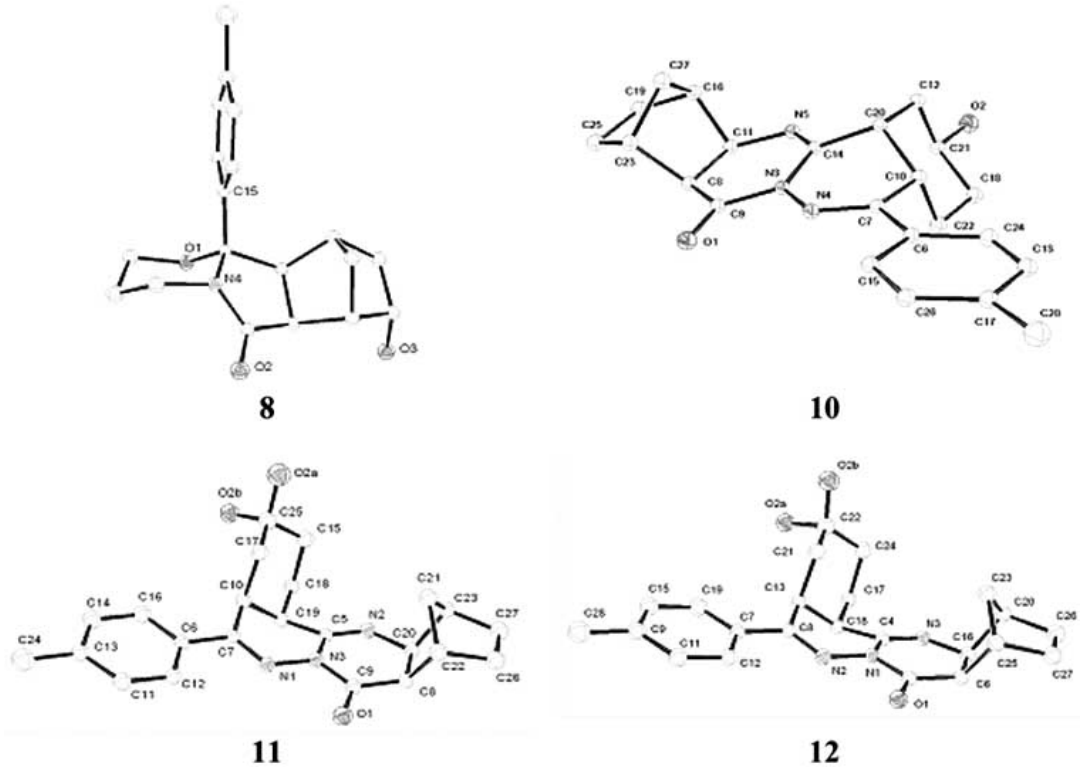


Fig. (1). ORTEP perspective views of compounds **8, 10-12**.

Table 1. Characteristic IR Frequencies[a] and ^{1}H NMR Data[b] of Compounds 4-11[c]

Compound	νOH	νC=O	γC$_{Ar}$H	CH$_3$	CH$_2$[d]	CH[e]	CH[f]	CH[g]	2',6'- H	3',5'- H	CH$_2$[i]	CH(CO)[j]	CH–N=[k]
	Band	Band	Band	s(3H)	Cyclohexane/ene				Tolyl(2×2H)[h]		2×d(2×1H)	Norbornane Ring	
4	3480	1701	810	2.37	1.2- 2.3	2.40	3.05	3.99	7.34	7.19	–	–	–
5	3425[l]	1701	814	2.38[m]	0.7- 2.1	2.37[m]	2.88	3.87	7.13, 7.40	7.19, 7.26	–	–	–
6	3485	1703	814	2.32[m]	1.4-2.5[m]	2.80	2.85	4.08	7.22	7.14	–	–	–
7	3363	–	839[l]	2.45[m]	1.8-3.0[m]	–	–	4.25	7.35	7.28	–	–	–
8	3360	1677	814	2.39	0.8-1.9[m]	2.36	3.44	4.24	7.04, 7.43	7.18, 7.29	0.94, 1.24[l]	3.44	2.36
9	3440	1690	805	2.31[m]	1.2-2.4[m]	2.92	2.78	3.58	7.21	7.14	–	–	–
10	3330	1704[l]	827	2.38	1.2-2.1	3.3	2.87	3.77[m]	7.64	7.30	1.21, 1.36	2.77	3.77[m]
11	3265[o]	1710[l]		2.38[m]	1.2-2.9[m]	3.06	2.95	3.92	7.78	7.22	1.26, 1.40[n]	2.79	3.79

[a]In KBr discs (cm^{-1}). Further bands, *v*NH: 3500-2500, very broad, in overlap with the *v*OH (**11**); *v*C-O: 1032 (**4**), 1061 (**5**), 1064 (**6**), 1068 and 1046 (**7**), 1058 (**8**), 1073 (**9**), 968 (**10**), 1079 (**11**); [b]In $CDCl_3$ solution (in DMSO-d_6 for **10**) at 500 MHz. Chemical shifts in ppm (δ_{TMS} = 0 ppm), coupling constants in Hz. Further signals: CH$_3$ (*i*-Pr, **4**): 0.74, 1.11, 2×d, *J* = 6.7; CH (*i*-Pr, **4**): 1.33 m; OCH$_2$, 2×dd: 3.60 and 4.33, *J* = 8.5, 7.4 and 7.0 (**4**), 3.67 and 3.76, *J* = 12.3, 2.3 and 5.0 (**5**, **8**); NCH$_2$, dd + dt: *J* = 13.2, 3.6 and 5.2 (**5**, **8**), NCH, m (1H): 3.68 (**4**); CH (norbornene, 2×~s (2×1H): 1.24[m] and 2.65 (**8**, Pos. 7, 10), 2.38[m]; Condensed benzene ring, 3-H$^{\cdot}$: 7.04 (**6**, **9**), 7.13 (**7**), 4$^{\cdot}$-H: 7.03 ± 0.02, 5$^{\cdot}$-H: 7.12 ± 0.02 (coalesced with the d of 3',5'-H for **6**), 6$^{\cdot}$-H: 7.86 (**6**, **9**), 7.55 (**7**); [c]Assignments were supported by HMQC, HMBC (except for **11**), DIFFNOE (for **4**, **6-9**), for **5, 8, 9, 11** also by 2D-COSY measurements; [d]Multiplets, total intensity: 6H, 4H (**8**): norbornane-CH$_2$ (Pos. 9) and CCH$_2$C (Pos. 3), 8H (**5**): in overlap with CCH$_2$C (Pos. 3), with norbornane-CH$_2$ (Pos. 10, 11); [e]CH bound to C$_{quat}$Ar, td (**4**, **6**, **9**, **11,** *J* = 11.5 and 6.2 for **4**, 12.5 and 5.6 for **9**), d, *J* = 8.1 (**8**) and m (**10**); [f]CH bound to C=O (**4**-**9**) or C(N)=N dt, *J* = 6.5, 2.2 (**4**), 7.5, 5.5 (**5**), t, *J* = 6.2 (**6**), 5.6 (**9**), d, *J* = 8.1 (**8**), 8.7 (**10**, **11**); [g]**C**H(OH) group, broad m for **4**, **7** and **8**, Δ*v*: 5 Hz (**4**), tt, *J* = 5.7, 2.9 (**5**), qi, *J* = ~3 (**6**), 11.3, 3.7 (**9**), d, *J* = 8.7 (**11**); [h]2×~d, *J* = 8.0 (**4**, **8**, **10**, **11**), one (**6**, **7**) or both (**9**) broadened, ~d and dd for **5**; [i]Bridging CH$_2$ in norbornene, *J* = 10.8 (**8**, **11**), 10.5 (**10**); [j]d, *J* = 8.1 (**8**), 8.7 (**10**, **11**); [k]Vicinal to quaternary C(tolyl) for (**8**), d, *J* = 8.1, for **11** dd, *J* = 8.6, 2.5; [l]Split band with the second maximum at 3395 (**5**), 829 (**7**), and 1672 (**11**), probably coupled with *v*C=O (**11**); [m]Overlapped signals; [n]In overlap with one m of the two vicinal norbornane-CH$_2$ groups; [o]Hidden by the signal of the solvent.

diexo-norbornane-fused heterocycles. The opening of the ketal lactone **3**, however, led to a mixture of conformers, separation of which did not succeed.

Structure

The spectral data (IR and ^{1}H and ^{13}C NMR) prove the structures given in Tables **1** and **2**.

In compound **4**, the carbonyl is attached *axially* to the cyclohexane, in accordance with our earlier experience [15,16], which points to similar *cis*-annelated perhydroisoindolones. This is unambiguous from the triple doublet split (td) of 9a-H and confirms the *axial* orientation of this H and the *equatorial* position for 5a-H (in the CHCO group): only one *diaxial* coupling (9H$_{ax}$,9a-H) is present. DIFFNOE measurements proved the sterically close arrangement of the *or-*

Table 2. ^{13}C NMR Chemical Shifts[a] of Compounds 4-11[b,c]

Compound	C-Tyl	C=O	C-1	C-2	C-3	C-4	C-5	C-6	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'	CH_3	C-1"	C-2",6"	C-3",5"	C-4"
			Cyclohexane/ene[d] or Norbornane[e] Ring						Condensed Aromatic Ring[f]							Tolyl (Tyl) Group			
4	102.4	180.5	48.6	41.9	29.6	64.9	29.9	17.0	–	–	–	–	–	–	21.47	139.5	125.6	129.5	139.6
5	96.2	179.7	43.5	39.7	31.5	66.0	30.0	19.8	–	–	–	–	–	–	21.5	133.9	127.5[g]	129.3[g]	138.4
6	87.0	175.1	48.2	41.8	29.7	64.4	30.2	22.0	131.1	134.7	116.7	125.7	126.1	123.1	21.4	142.5	124.5	129.8	138.3
7	122.9	–	107.4	123.6	31.3	68.0	31.9	19.9	135.6	131.3	123.9	122.8	124.9	113.3	21.5	129.33	130.1	129.26	137.4
8	97.3	179.9	53.4	43.4	45.6	71.6	39.1	40.0	–	–	–	–	–	–	21.5	134.4	127.76[g]	129.0[g]	138.3
9	85.7	172.9	48.2	42.8	21.3	32.0	69.3	38.7	130.5	134.3	116.3	125.5	125.8	122.8	21.1	142.1	124.1	129.5	138.1
10	158.2	165.1	62.5	49.9	44.2	29.9	26.5	46.1	34.8	36.6	31.9	22.4	66.1	33.4	21.8	133.4	127.6	129.8	140.2
11[h]	?	?	63.1	49.9	44.9	29.2	26.8	46.2	35.8	36.3	34.7	24.9	65.1	35.5	21.7	?	126.7	129.8	?

[a]In ppm (δ_{TMS} = 0 ppm) at 125.7 MHz. Solvent: $CDCl_3$ (for **10** DMSO-d_6). Further signals, CH_3 (*i*-Pr, **4**): 19.2 and 21.49; C**C**H$_2$C: 25.3 (**5**), 25.8 (**8**); CH_2(norbornane): 33.2 (**8**), 34.8 (**10** and **11**); NCH_2: 38.0 (**5** and **8**); OCH_2: 73.1(**4**), 62.4 (**5**), 62.8 (**8**), NCH: 61.3; [b]Assignments were supported by DEPT (except for **11**), HMQC and also HMBC (except for **11**) measurements; [c]Here, C-1,1',1",2,2',4" indicate the substituted carbons, C-1 bound to the C-tolyl group and the N atom for the cyclohexane ring and norbornane, and C-1' to the S atom; [d]For **4-6**, **9**/**7**; [e]For **8**, **10-11**; [f]For **10-11** cyclohexane; [g]Due to hindered rotation of the tolyl group, two separated lines. The counterparts of the lines given in the Table are at 128.9 and 130.3 (**5**), 127.82 and 130.6 (**8**); [h]Due to the very poor solubility, the ^{13}C NMR shifts of protonated carbons were determined from the HMQC measurements. The same possibility, of course, does not exist for quaternary carbon atoms.

tho tolyl-H's and the annelational H's (5a,9a-H), and also of the former H's and the isopropyl methyl-H's. The hydroxy group must be *axial* (*cis* to the carbonyl), because the geminal CH exibits a narrow signal ($\Delta\nu \approx 5$ Hz), which demonstrates its *equatorial* position. In **4**, a stable 7-membered intramolecular H-bridge can exist. This is supported by the higher νOH frequency (3480 cm^{-1} for **4** and 3485 cm^{-1} for **6**, as compared with 3360-3440 cm^{-1} for the further compounds) and the sharp contour of the νOH band [17]. The stereostructure for **4** is given in Scheme **1** and Fig. (**2**).

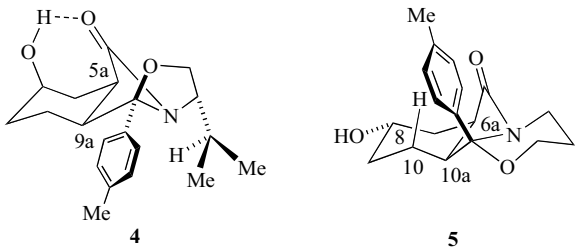


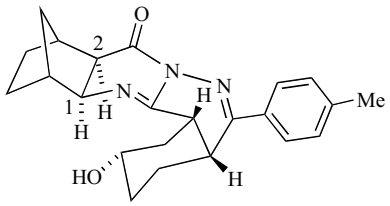
Fig. (2).

Compound **5** has a skeleton analogous to that of **4** (*cis*-annelated perhydroisoindolone) as indicated by the similar sums of the carbon chemical shifts of the cyclohexane ring (230.5 ppm for **5**, and 231.9 ppm for **4**). For *trans* annelation, a significantly higher value would be expected [18a]. Furthermore, the shifts of the annelational carbons are also similar [43.5 and 39.7 ppm (**5**) and 48.6 and 41.9 ppm (**4**)]; either smaller, while higher values would be expected for a *trans*-annelated structure [18a]. In accord with this, the couplings of CHCO (6a-H) are all smaller (≤ 7.5 Hz) than the data characteristic of a *diaxial* interaction (≥ 9-10 Hz). The OH must be *equatorial*: the geminal H (8-H) gives a triple triplet signal due to the two *diaxial* and two *axial-equatorial* couplings with the neighbouring H's. NOE was not observed between the aromatic and annelational H's, and the *axial* 10-methylene-H is much more shielded than in **4** because of the anisotropic shielding of the tolyl group [18b], which is near to the H in question and consequently *trans* to the annelational H's (Fig. **2**).

Similar values of the shifts of the hydroxy-substituted and annelational carbons of the cyclohexane ring, and also the narrow CH(OH) signal (2-H), suggest analogous stereo structures for **6** and **4**. The same holds for the skeleton of **9**. Similarly as in **4**, the sterically close positions of the annelational H's 4a,11a-H and the *ortho*-tolyl H's were demonstrated by the DIFFNOE results. The position (Pos. 3) of the hydroxy group, however, is different in **9**. It is *equatorial* as in **5** and the geminal H gives a triple triplet signal. The ^{13}C NMR shifts of the annelational carbons and the ^{1}H NMR chemical shifts are very similar to those observed for **6**, which (in accordance with the DIFFNOE measurements) supports the analogous orientation of the tolyl group, and hence the postulated structure of **9** (Scheme **3**).

As compound **7** contains only one chiral centre, this precludes the possibility of the formation of different isomers. From the presence of only one methyne carbon (DEPT measurement) and (besides twelve aromatic carbons) three further sp^2-type carbons, the structure depicted in Scheme **1** follows.

The X-ray stereostructures of **8**, **10** and **11** show that the norbornane annelations to the condensed heteroring are *diexo,* due to the doublet split of the signal of the annelational H's, in accord with our "splitting rule" [19, 20]. In *diendo* isomers, the dihedral angles of the latter and their CH neighbours (Pos. 7 and 10 in **8** and Pos. 9 and 12 in **10** and **11**) are ~30°; consequently, a further split leads to the double doublet split of the signals of the annelational H's in question. In the *diexo* compounds, these dihedral angles are ~90°; no split occurs, and only the interaction of annelational H's leads to a doublet, as observed for **8**, **10** and **11**. Due to the distorted skeleton of **11** (as a consequence of the crowded steric structure), the 12,12a-H interaction leads to a small splitting, resulting in a dd. The *exo* 9-H of **8** gives a ddd split. The *J*(8-H,9-H) interaction (4.8 Hz) is evidence [21] of the *exo* position of 8-H and thus an *endo* OH (in Pos. 8). This is in accord with the X-ray results (Fig. **1**), the latter also confirming the close-lying position of the tolyl group relative to the bridging CH_2 in the norbornane moiety. (The



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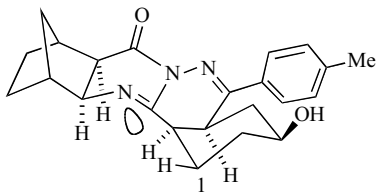

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Fig. (3).

DIFFNOE results were not convincing because of signal overlaps).

For **11**, the *cis* annelation of the cyclohexanole to the pyridazine follows from the splittings of the annelational H signals. Further supporting data are the relatively small carbon shifts of the annelational carbons [18a], which are very similar to those measured for **10**. Thus, *diexo* and *cis* annelations are present in **10** and **11**. In both compounds, the position of the hydroxy group is unambiguous because of the structures of the starting materials. The equatorial position (*trans* to the annelational H's in the cyclohexane ring) of the OH group in **11** follows from the ^{1}H NMR signal of the geminal H, which is a sextet with a half signal width of ~25 Hz. Due to the very similar chemical shifts in the ^{1}H and ^{13}C NMR spectra of the CH(OH) group for **10** and **11**, the *equatorial* orientation of the OH group is also unambiguous in **10**. A strikingly large difference was observed for a methylene-H in the cyclohexane of **11**. While all six such H's gave signals in the interval 1.2-2.2 ppm for **10**, as did five of them in **11**, the sixth in **11** gave a signal at 2.83 ppm. The significant downfield shift of this H (1*eq*-H) can be explained by the anisotropy of the lone electron pair on the N atom [18c] (*cf.* Fig. **3**). This arrangement requires the same positions for the two annelational H's in each of the pyrimidone and the pyridazine (the four annelational H's must lie on the same side of the skeleton: *αααα*; Scheme **3** and Figs. (**1** and **3**) as the annelation (*cis*) of the cyclohexane and the orientation (*eq*) of the OH group are identical in **10** and **11**, and the above-mentioned downfield signal of a CH_2 group (at ~2.83 ppm) is absent in the ^{1}H NMR spectrum of **10**. In this compound, two each of the annelational H's must lie opposite to the skeleton (*ααββ* configuration) and the angle made by the C–1*ax*-H bond to the plane of the :N=C–C moiety is ~60° (Fig. **3**).

Because of the poor solubility, the NMR spectra of compound **12** provided only dubious results. Here, the stereostructure was determined by X-ray diffraction (Fig. **1**).

EXPERIMENTAL

IR spectra were run in KBr disks on a Bruker IFS-55 FT-spectrometer controlled by Opus 3.0 software. The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution in 5 mm tubes at RT, on a Bruker DRX-500 spectrometer at 500.13 (^{1}H) and 125.76 (^{13}C) MHz, with the deuterium signal of the solvent as the lock and TMS as internal standard. The standard Bruker micro program NOEMULT to generate NOE [22] and to get DIFFNOE spectra [18d, 23] was used with a selective pre-irradiation time. DEPT spectra [24] were run in a standard manner [25], using only a Θ = 135 C pulse to separate the CH/CH_3 and CH_2 lines phased "up" and "down", respectively. The 2D-COSY [26a,27a], HMQC [26b,27b] and HMBC [28,29] spectra were obtained by using the standard Bruker pulse programs COSY-45 INV4GSSW and INV4GSLRNDSW.

General Procedure for Preparation of Compounds 4-12

A mixture of **1** or **3** (1.22 g, 5 mmol) or **2** (1.28 g, 5 mmol), a bidentate nucleophile (DL-valinol 0.77 g, 1-amino-3-propanol 0.56 g, 2-aminothiophenol 0.94 g, 7.5 mmol) or *diexo*-3-aminobicylo[2.2.1]heptane-2-hydrazide (1.27 g, 7.5

Table 3. Physical and Analytical Data on Compounds 4-12

Compd.	Mp. (°C)	Yield (%)	Formula (Mw.)	Analysis					
				Found %			Calcd %		
				C	H	N	C	H	N
4	154-156[a]	43	$C_{20}H_{27}NO_3$ (329.44)	72.15	8.45	4.05	72.92	8.26	4.25
5	176-178[a]	52	$C_{18}H_{23}NO_3$ (301.39)	72.45	7.82	4.51	71.73	7.69	4.65
6	165-167[a]	28	$C_{21}H_{21}NO_2S$ (351.47)	71.05	6.55	3.81	71.77	6.02	3.99
7	178-180[b]	13	$C_{20}H_{19}NOS$ (321.44)	74.28	5.72	4.15	74.73	5.96	4.36
8	252-254[c]	47	$C_{19}H_{23}NO_3$ (313.40)	72.11	7.12	4.58	72.82	7.40	4.47
9	204-205[b]	36	$C_{21}H_{21}NO_2S$ (351.47)	71.99	6.11	3.87	71.77	6.02	3.99
10	241-243[d]	32	$C_{23}H_{27}N_3O_2$ (377.49)	72.70	7.38	10.88	73.18	7.21	11.13
11	276-277[b]	16	$C_{23}H_{27}N_3O_2$ (377.49)	73.59	7.05	11.18	73.18	7.21	11.13
12	296-297[b]	17	$C_{23}H_{27}N_3O_2$ (377.49)	73.01	7.46	10.79	73.18	7.21	11.13

Crystallization solvent: [a]Et_2O. – [b]EtOAc. – [c]EtOH. – [d]*i*-Pr_2O.

mmol), and 0.04 g PTSA in xylene (15 mL) was refluxed for 10 h. Monitoring by TLC: aluminium sheets, silica gel 60 F_{254}, EtOAc–*n*-hexane 2:1 for **4, 6, 7** and **9**, EtOAc for **5, 8, 10, 11** and **12**, developed in iodine vapour. After evaporation, the residue was dissolved in $CHCl_3$, transferred to a silica gel column (Kieselgel 60 Merck, 0.040-0.063 mm) and eluted with EtOAc-*n*-hexane (2:1) for **4** and **9**, *n*-hexane-EtOAc (2:1) for **10**, *n*-hexane-EtOAc (1:1) for **6** and **7**, and EtOAc for **5, 8, 11** and **12**. The residues of the eluates were crystallized. Data on compounds **4-12** are listed in Table **3**.

X-Ray Study

The crystallographic data were collected at 173 K with a Nonius-Kappa CCD area detector diffractometer with graphite-monochromatized Mo-K_α radiation (λ = 0.71073 Å). φ and ω rotation scans and the DENZO-SMN ν0.93.0 software package [30] were used.

Crystal Data for 8

$C_{19}H_{23}NO_3$, M_r = 313.38, triclinic, space group *P*-1 (no. 2), a = 8.2662(4), b = 10.7774(5), c = 10.7966(5) Å, α = 62.872(2), β = 70.659(3), γ = 85.255(2)°, V = 805.05(7) Å^3, T = 173 K, Z = 2, μ(Mo-K_α) = 0.087 mm^{-1}. 3017 unique reflections (R_{int} = 0.031) were used. The final $wR(F^2)$ was 0.105 (all data) and $R[F^2 > 2\sigma(F^2)]$ = 0.042.

Crystal Data for 10

$C_{23}H_{27}N_3O_2$, M_r = 377.48, monoclinic, space group $P2_1/n$ (no. 14), a = 8.6411(3), b = 12.6208(6), c = 17.2917(6) Å, β = 90.836(2)°, V = 1885.59(13) Å^3, T = 173 K, Z = 4, μ(Mo-K_α) = 0.086 mm^{-1}. 3468 unique reflections (R_{int} = 0.035) were used in the calculations. The final $wR(F^2)$ was 0.107 (all data)and $R[F^2 > 2\sigma(F^2)]$ = 0.042.

Crystal Data for 11

$C_{23}H_{27}N_3O_2$, *M*r = 377.48, triclinic, space group *P*-1 (no. 2), a = 9.5765(10), b = 9.8653(8), c = 10.7500(11) Å, α = 80.164(5), β = 72.851(5), γ = 87.055(6)°, V = 956.19(16) Å^3, T = 173 K, Z = 2, μ(Mo-$K\alpha$) = 0.085 mm^{-1}. 3522 unique reflections (R_{int} = 0.092) were used. The final $wR(F^2)$ was 0.187 (all data) and $R[F^2 > 2\sigma(F^2)]$ = 0.089.

Crystal Data for 12

$C_{23}H_{27}N_3O_2$, Mr = 377.48, triclinic, space group *P*-1 (no. 2), a = 9.5222(15), b = 9.9649(14), c = 10.7224(16) Å, α = 80.681(8), β = 72.874(7), γ = 86.028(8)°, V = 961.0(2) Å^3, T = 173, Z = 2, μ(Mo-$K\alpha$) = 0.085 mm^{-1}. 3719 unique reflections (R_{int} = 0.076) were used. The final $wR(F^2)$ was 0.177 (all data) and $R[F^2 > 2\sigma(F^2)]$ = 0.102.

The structures were solved by a direct method, applying the SHELXS-97 program [31]. Full matrix, least squares refinements on *F2* were performed [31]. In all cases, the CH hydrogen atoms were included at fixed distances with fixed displacement parameters from their host atoms. The OH hydrogen atoms were refined isotropically with fixed displacement factors. The Figures were drawn with ORTEP-3 for Windows [32]. The deposition numbers CCDC 682347-682350 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat) + 44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk].

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