Stereochemical Studies. Part 89. Saturated Heterocycles. Part 84.[1] Preparation and Nuclear Magnetic Resonance Study of Norbornane–Norbornene-fused 2-Phenylimino-1,3-oxazines and -thiazines

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diexo- and *diendo*-3-hydroxymethylbicyclo[2.2.1]hept-2-yl- and hept-5-en-2-yl-amines (**1**)—(**4**) and their *N*-methyl and *N*-benzyl derivatives with phenyl isothiocyanate furnished *via* thioureas (**5**)—(**8**) the condensed skeleton tricyclic 2-phenylimino-1,3-thiazines (**9**)—(**12**) and 1,3-oxazine-2-thiones (**13**) and (**14**) as by-products in acidic medium. By base-catalysed cyclization of the isothiuronium salts of (**5**)—(**8**), the 2-phenylimino-1,3-oxazines (**15**)—(**18**) were obtained. The complete series of structural and annelation isomers of the norbornanes–norbornenes and oxazines–thiazines permitted a systematic ^1H and ^{13}C n.m.r. spectroscopic study of the correlation between the spectral parameters and the structural features in this family of compounds.

In the course of our research on fused saturated 1,3-oxazine derivatives,[2–6] numerous 1,3-oxazine analogues containing a methylene-bridged cyclohexane ring have recently been synthesized by the ring closure of stereohomogeneous 1,3-aminoalcohols obtained in the reduction of the corresponding norbornane and norbornene 1,2-amino acids.[7,8] These compounds were converted into linearly and angularly fused azetidinones by cycloaddition.[9,10] A systematic spectroscopic study of these compounds provided confirmatory evidence of the stereochemistry of the annelation of the alicyclic and heterocyclic rings, and the *cis*- or *trans*-annelation of the oxazine and azetidinone rings, the steric position of the substituents (the configurations of the substituted skeletal carbon atoms), and the preferred conformations.[9–13]

In this paper we report the synthesis and a systematic spectroscopic study of the 2-arylimino-1,3-oxazines and -thiazines obtained from the stereoisomeric norbornene or norbornane 1,3-aminoalcohols.

Results and Discussion

3-*endo*-Hydroxymethylbicyclo[2.2.1]hept-5-en-2-*endo*-ylamine (**1a**) was obtained by LAH reduction of the 3-*endo*-aminobicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid.[7a] The amino acid obtained by catalytic hydrogenation and hydrolysis of the ethyl ester of the latter amino acid was reduced with LAH to 3-*endo*-hydroxymethylbicyclo[2.2.1]hept-2-*endo*-ylamine[7b] (**3a**).

The isomeric *diexo*-aminoalcohols (**2a**) and (**4a**) were prepared by reduction of the 3-*exo*-aminobicyclo[2.2.1]heptane-2-*exo*-carboxylic acid and its 5-unsaturated analogue, obtained by reduction[14,15] and hydrolysis of the chlorosulphonyl isocyanate adducts[16] of the norbornadiene or norbornene, respectively.

The *N*-methyl (**1b**)—(**4b**) and *N*-benzyl derivatives (**1c**)—(**4c**) of the aminoalcohols (**1a**)—(**4a**) were obtained from the corresponding amino acids by our earlier methods.[7b,17]

With phenyl isothiocyanate the aminoalcohols (**1**)—(**4**) were converted into thioureas (**5**)—(**8**) in nearly quantitative yields (Scheme).

On refluxing in ethanol containing 20% HCl,[18,19] the thioureas (**5**)—(**8**) were cyclized to the saturated and 6-unsaturated *diendo*- and *diexo*-2-phenylimino-5,8-methano-3,1-benzothiazines (**9a—c**)—(**12a—c**).

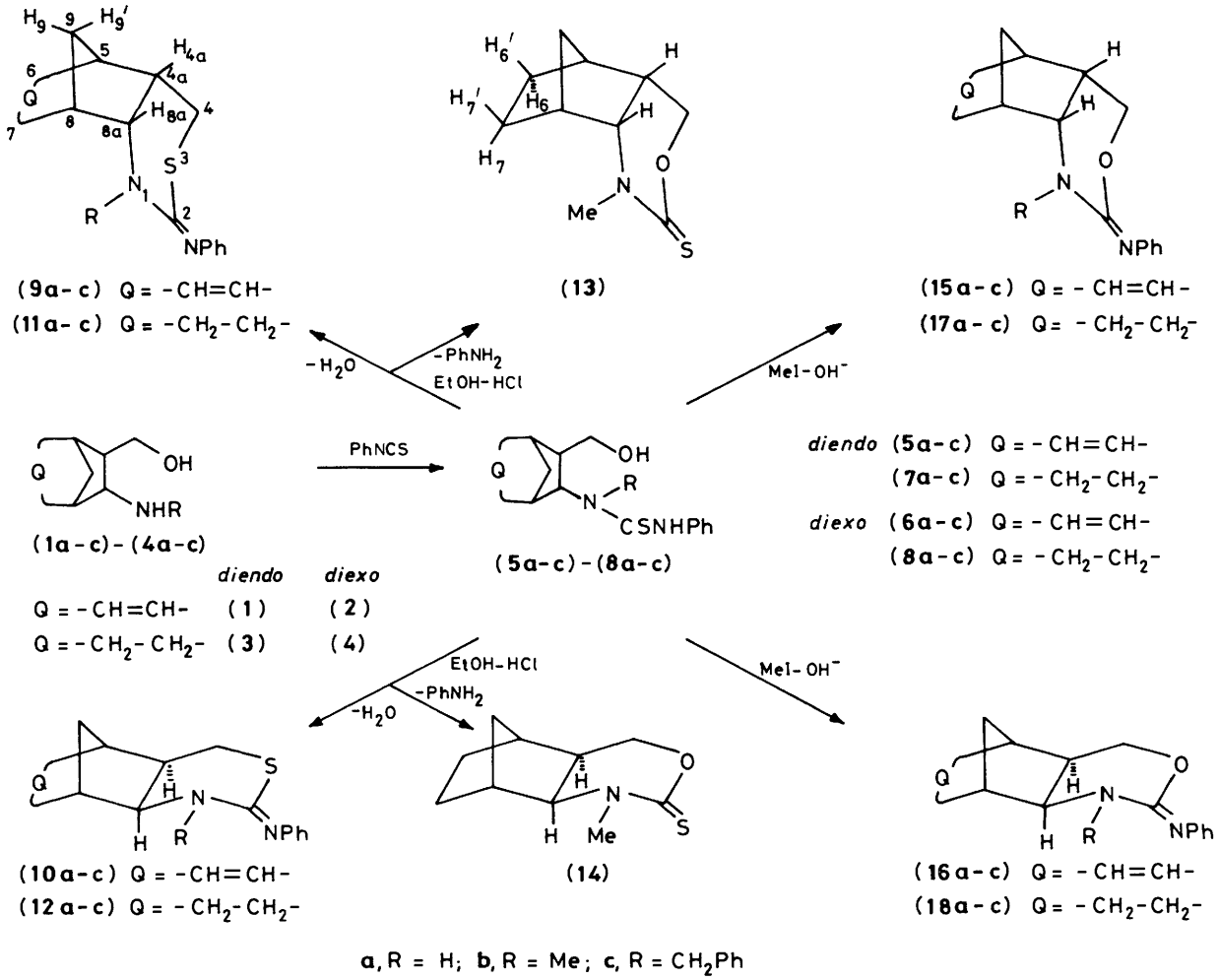
It was found that the acid-catalysed cyclization can follow two reaction paths, since the nucleophilic attack of the sulphur on the non-cyclic methylene carbon atom results in the formation of 1,3-thiazines (**9**)—(**12**), whereas the attack of the oxygen of the hydroxyurea intermediate on the thiocarbonyl carbon gives rise to the formation of tricyclic 1,3-oxazine-2-thiones. Two of the latter compounds, (**13**) and (**14**), could be isolated besides (**11b**) and (**12b**). These 1,3-oxazine-2-thiones were synthesized earlier.[7a,b] Analogous monocyclic 1,3-oxazine-2-thiones were prepared in 87% yield by refluxing aliphatic hydroxythioureas in toluene.[20] They assumed amine elimination and the formation of an isothiocyanate intermediate.

From the thioureas (**5**)—(**8**) with methyl iodide, we prepared isothiuronium salts, which were cyclized to the 1,3-oxazines (**15a—c**)—(**18a—c**) with base.[21] In the case of (**15b**), the isothiuronium salt intermediate was also isolated.

I.r., ^1H, and ^{13}C N.m.r. Spectroscopic Study.—The characteristic i.r. data are collected in Table 1. The intense diffuse ν(NH) bands of the *N*-unsubstituted compounds (series **a**) appear in the range 3 250—2 750 cm^{-1}. In every spectrum the $\gamma(C_{Ar}H)$ and $\gamma(C_{Ar}C_{Ar})$ bands appear at *ca.* 770 and 700 cm^{-1}, respectively, frequencies characteristic of the monosubstituted benzene ring;[22] in series **c**, which contain a benzyl moiety too, they are split, or more intense. The γ(=CH) bands of the olefinic ring in the norbornenes appear at 705—741 cm^{-1}. The highest group frequency of the heteroring functional group [cyclic –NR–C(=NPh)X, where X = O or S] occurs between 1 616 and 1 684 cm^{-1} in the oxazines, and between 1 600 and 1 622 cm^{-1} in the thiazines. These groups display intense bands between 1 570 and 1 600 cm^{-1}, and between 1 200 and 1 260 cm^{-1}, and in the *N*-substituted series **b** and **c** in the region of 1 050—1 150 cm^{-1}.

The series **a**—**c** can also be distinguished through the ^1H and ^{13}C n.m.r. signals of the NR groups. In series **a** the NH signals between δ 5 and 8 could easily be recognized, partly on the basis of their broad contours, and partly because they disappear upon addition of D_2O. The *N*-methyl singlet of 3 H intensity appears between δ 2.9 and 3.1, and the corresponding ^{13}C line at δ 35.5—36.1 p.p.m. in the case of analogues **b**. The methylene proton and carbon signals of the benzyl group in derivatives **c** appear at δ 4.0—4.8 and 5.15—5.5 [the two protons are not equivalent, $J(A,B)$ 15—16 Hz] and δ 50.8—52.0 p.p.m., respectively, and the multiplets of the second benzene ring and the four carbon lines are also seen in the ^1H and ^{13}C n.m.r. spectra.

The norbornenes and norbornanes can easily be recognized



Scheme.

from the n.m.r. signals of H-6, -7 and C-6, -7 in the ^1H and ^{13}C n.m.r. spectra, respectively. The two double doublets of the olefinic protons in the unsaturated compounds, each of 1 H intensity, appear between δ 5.90 and 6.30 [merged into a singlet of 2 H intensity in the case of (**9a** and **b**)], whereas the signals of the methylene protons in the saturated analogues, overlapping those of the group in position 9, appear in the region δ 0.9—1.9 (6 H). In the norbornenes the C-6, -7 lines lie between δ 134.6 and 140.6 p.p.m., whereas the signals of the saturated carbon atoms of the norbornane compounds appear between δ 20 and 30 p.p.m. (Tables 2 and 3).

The thiazine and oxazine derivatives can be identified through the chemical shifts of H-4 and C-4. In the ^1H n.m.r. spectra of the former compounds the signals of the non-equivalent methylene protons appear between δ 2.4 and 2.95, whereas in the case of the latter compounds they appear in the region δ 3.65—4.30, as anticipated.[23a] The regions of the corresponding carbon chemical shifts for the two types of compounds, also as expected,[23b] are δ 26.7—31.1 and 65.5—69.8 p.p.m., respectively.

A considerable difference is found for the shift of C-2. In the thiazines compared with the oxazines, the adjacent sulphur atom causes a marked downfield shift of the C-2 signal. The C-2 signal in the thiazines appears between δ 156.7 and 160.0 p.p.m., whereas in the oxazines (**15**)—(**18**) it falls between δ 144.5 and 148.6 p.p.m. The chemical shift of C-1′ (2-phenyl group), however, though to a lesser extent, reveals an opposite effect: it is found in the interval δ 147.1—151.6 for the thiazines and 151.5—153.4 p.p.m. for the oxazines.

The *diendo*- or *diexo*-annelation of the hetero- and carbobicyclic rings is indicated by the multiplicity of the H-8a signal in the region δ 3.0—4.0.[9] For the *diexo*-compounds this signal is a doublet (J 7—10 Hz), corresponding to 4a,8a coupling, whereas in the spectra of the *diendo* compounds it appears as a double doublet: besides the splitting originating from the 4a,8a spin–spin interaction (the magnitude of which varies in the range 6.5—12.5 Hz in this series), another significant splitting is observed due to the 8,8a coupling (3—4 Hz). The H-8–C-8–C-8a–H-8a dihedral angle is *ca.* 50°, whereas that in the *diexo*-compounds is *ca.* 90°, and therefore no splitting can be anticipated[24] [J(H-8,H-8a) < 1 Hz].[9]

The H-8a chemical shift depends mainly on the annelation: it is δ 3.01—3.36 for the *endo*-H-8a atom of the *diexo*-series and δ 3.30—3.95 for the *exo*-H-8a atoms of the *diendo*-compounds in accord with the literature data for norbornane and norbornene. Values of δ 1.18 and 1.46 have been measured for the protons of the former and δ 0.96 and 1.59 for those of the latter in the *endo*- and *exo*-configurations, respectively.[25–27]

This holds for the H-4a signal as well (Table 2): for (**10**) and (**16**) the shielding is stronger (δ 1.98—2.23) than for the isomers (**9**) and (**15**) (δ 2.5—2.8) and similarly is stronger for (**12**) and (**18**) (δ 1.98—2.2) than for (**11**) and (**17**) (δ 2.3—2.4).

Similarly, as expected, we have found that the position of the H-8a signal is also slightly dependent on the saturation of the

Table 1. Characteristic i.r. frequencies of compounds (**9a**—**c**)—(**12a**—**d**) and (**15a**—**c**)—(**18a**—**c**) in KBr (cm^{-1})

Compound	ν(NH)	Cyclic	–NR–C(=NPh)X (X = O or S)[a]		γ(=CH)	$\gamma(C_{Ar}H)$	$\gamma(C_{Ar}C_{Ar})$
(**9a**)	3 250—2 750	1 622, 1 587	1 207		727	773	700
(**9b**)		1 585	1 217	1 065	731	770	698
(**9c**)		1 601, 1 580	1 211	1 124	741[b]	771[c]	696[c]
(**10a**)	3 250—2 750	1 614, 1 589	1 198		714	766	696
(**10b**)		1 582	1 215	1 061	717	773	700
(**10c**)		1 574	1 211	1 109	719	773, 743[d]	698[c]
(**11a**)	3 250—2 750	1 614, 1 587	1 209			771	698
(**11b**)		1 580	1 227	1 069		771	698
(**11c**)		1 603, 1 582	1 219	1 142		771, 735[d]	696[c]
(**12a**)	3 250—2 750	1 618, 1 587	1 209			773	700
(**12b**)		1 600, 1 582	1 221	1 067		777	698
(**12c**)		1 560	1 225	1 155		765, 735[b]	690[c]
(**15a**)	3 250—2 750	1 684, 1 591	1 223		735	764	698
(**15b**)		1 643, 1 595	1 261	1 101	725	746	698
(**15c**)		1 616, 1 578	1 252,[e] 1 246[e]	1 134,[e] 1 124[e]	729[b]	760[c]	694[c]
(**16a**)	3 250—2 750	1 674, 1 595	1 220		708	764	694
(**16b**)		1 670, 1 595	1 258	1 084	714	773	694
(**16c**)		1 624, 1 582	1 252	1 123	735[b]	754[c]	692[c]
(**17a**)	3 250—2 750	1 678, 1 591	1 221			771,[e] 758[e]	698
(**17b**)		1 643, 1 593	1 265	1 053		746	700
(**17c**)		1 639, 1 585	1 256	1 124		781, 774[d]	704, 690[d]
(**18a**)	3 250—2 750	1 666, 1 589	1 236			770,[e] 750[e]	702,[e] 690[e]
(**18b**)		1 651, 1 593	1 259	1 097		775,[e] 756[e]	712,[e] 694[e]
(**18c**)		1 636, 1 591	1 252	1 125		758[c]	694[c]

[a] The two higher frequencies are due to group frequencies of ν(C=N) and $\nu(C_{Ar}=C_{Ar})$ character, and the two lower ones to bands of ν(C–N) type vibrations of the ring and the N–C(R) group, respectively. [b] Overlapped by the $\gamma(C_{Ar}H)$ band of the *N*-benzyl (NR) group. [c] Coalesced bands of the two benzene rings. [d] *N*-benzyl (NR) group. [e] Split bands.

carbocycle. The H-8a atom of norbornenes is more shielded in the *diexo*-isomers with chemical shifts of δ 3.01—3.30, while for norbornanes the shifts between δ 3.10 and 3.36 were observed. For the *diendo*-compounds these intervals of chemical shifts are δ 3.3—3.6 for norbornanes, whereas for the norbornene analogues it is δ 3.61—3.95.

There are significant differences in the H-5, -8 chemical shifts of the saturated and unsaturated compounds. In the latter group of compounds the $-I$ effect of the olefinic group causes downfield shift: the H-5 signal is in the region δ 2.5—2.9, while that of H-8 lies at δ 2.54—3.25. In the norbornanes, however, the two shift intervals are δ 2.05—2.25, and 2.05—2.7, respectively.

In the ^{13}C n.m.r. spectra of the norbornenes the C-5, -8, signals undergo a downfield shift due to the greater α-effect[23c] of the olefinic bond (δ 45.2—48.3 and 46.2—49.5, respectively, compared with the observed values of δ 39.5—42.1 and 39.6—44.1, respectively, for the norbornanes; Table 3).

In the spectra of the norbornanes, the C-4a and C-8a lines are shifted upfield due to the steric hindrance between H-6, -7 (*endo*) and the NR moiety or H-4 (steric-compression shift: carbons bearing sterically hindered groups are more shielded[28]).

In compounds (**11**) and (**17**) the mean shift of the C-4a signal is δ 42.2 and 38.3 p.p.m., respectively; this means a field effect of 5.2 p.p.m. compared with those in the analogues (**12**) and (**18**) (δ 47.4 and 43.5 p.p.m., respectively). For the C-8a signal the mean field effect is 4.1 and 3.9 p.p.m. In the norbornenes, due to the greater distance of the olefinic protons from H-4 and the NR group, the field effect disappears; furthermore, for the H-4a signal an opposite, albeit lower (average of 1.9 and 1.3 p.p.m.), shift can be observed.

Steric hindrance is also present in the *diexo*-compounds, but instead of H-6, -7 (*endo*), H-9′ (*endo*) is involved with 4-CH_2 or the NR group. This is indicated by the large field effect on the C-9 signals, which can be observed for both the norbornanes and the norbornenes. The average field effects for the pairs (**10**)—(**9**), (**12**)—(**11**), (**16**)—(**15**) and (**18**)—(**17**) are 5.1, 4.4, 4.5, and 4.2 p.p.m.

In the norbornene derivatives annelation also affects the chemical shift of the 9-methylene protons: in the *diexo*-compounds the heteroatoms in close proximity give rise to a downfield shift of *ca.* 0.4 p.p.m. in the H-9′ (*endo*) signal, and a similar, but smaller shift (*ca.* 0.1 p.p.m.) in the H-9 (*exo*) signal. This is in agreement with the assignment of the two signals, which is also proved by differential nuclear Overhauser effect experiments on the analogues.[9] The difference in the chemical shifts can be attributed to the anisotropic effect of the olefinic bond,[23d] which gives rise to an increased shielding at the H-9 (*exo*) atom over the plane of the double bond. In the norbornanes only one doublet of the AB spectrum is separated (the other overlaps the H-6, -6′, -7, -7′ signals) and this is hardly altered by annelation [in compounds (**11**), (**12**), (**17**), and (**18**) the average shifts are δ 1.80, 1.70, 1.84, and 1.80, respectively.]

All these data are in good agreement with our findings[9,29] from the systematic spectroscopic study of norbornane-condensed 2-aryldihydro-oxazines, and lend further support to the probable, but not unambiguous, assignments (especially concerning the C-4a, -5, -8 and C-4, -9 lines for certain compounds).

It is noteworthy that a potential *endo* ⇌ *exo* C=N bond tautomeric equilibrium is possible in the *N*-unsubstituted compounds (**9a**)—(**12a**) and (**15a**)—(**18a**). The synthesis route means that the corresponding *N*-substituted series **b** and **c** are exclusively isomers substituted on the ring nitrogen, containing an exocyclic C=N bond (Scheme). The fact that neither the chemical shifts of the aromatic protons of the 2-phenylimino group, nor those of the carbon atoms in this ring (with the exception of C-1′), are altered significantly compared with those in the *N*-substituted analogues is unambiguous evidence of the predominance of the tautomeric form containing an exocyclic C=N bond (*i.e.* an NH group in the ring) in $CDCl_3$ solution.

Table 2. ^{1}H N.m.r. data of compounds (**9a**—**c**)—(**12a**—**c**) and (**15a**—**c**)—(**18a**—**c**)[a]

	Chemical shifts (δ)															
Compound	H-4 2m (2 × 1 H)[b]		H-4a m (1 H)[c]	H-5 ~s (1 H)	H-8 ~s (1 H)	H-8a d or dd (1 H)[d]	H-6 m (2 H or 4 H)[e]	H-7	H-9 2d (2 H)[f]		NH/NMe/NCH$_2$[g]		ArH[o] dd (2 H)	ArH[m] dt (2 H)	ArH[p] ~t (1 H)	ArH (NCH$_2$Ph) m (5 H)
(**9a**)	2.49	2.64	2.70	2.83	2.92	3.95	6.15[h]		1.42	1.55	~6.0		6.95	7.28	7.05	
(**9b**)	2.45—2.55		2.70	2.81	3.21	3.61	6.22[h]		1.40	1.62	2.98		6.80	7.25	7.00	
(**9c**)	2.44	~2.8	~2.8[j]	~2.8[j]	3.15	3.78	6.15	6.25	1.32	1.42	4.34	5.31	6.68	7.25	6.95	7.3—7.5
(**10a**)	2.65—2.75		2.12	2.50	2.54	3.26	6.21	5.90	1.42	1.94	~6.1		6.95	7.30	7.05	
(**10b**)	2.65—2.70		2.15	2.55	3.25	3.01[m]	6.30	6.02	1.48	1.94	3.08		6.85	7.25	7.00	
(**10c**)[i]	2.75—2.85		2.23	2.61	3.24	3.30	6.30	6.24	1.45	2.00	4.78	5.28	6.84	~7.3[j]	7.04	~7.25—7.55[j]
(**11a**)	2.52	2.92	~2.4	2.25	2.32	3.60	1.3—1.6 m (5 H), ~1.8 m (1 H)				~5.35		7.00	7.30	7.10	
(**11b**)	~2.4[j]	2.89	~2.4[j]	2.25	2.55	3.30	1.4—1.7 m (6 H)				2.93		6.84	7.28	7.02	
(**11c**)	~2.4	2.93	~2.4	2.25	~2.4	3.50	~1.37 m (4 H), ~1.7 m (2 H)				4.19	5.47	6.80	~7.3[j]	7.00	7.2—7.4[j]
(**12a**)	2.6—2.8		2.15	~2.05[j]	~2.05[j]	3.36	1.1—1.3 m (3 H), 1.5—1.6 m (2 H) 1.88 d (1 H)				~5.2		6.90	7.30	7.05	
(**12b**)	2.65—2.8 m (3 H)[j]		2.15	2.05	~2.7[j]	3.10	1.1—1.3 m (3 H), 1.4—1.6 m (1 H) 1.6—1.75 m (1 H), 1.87 d (1 H)				3.05		6.82	7.25	7.00	
(**12c**)	2.7—2.85		2.20	2.05	2.62	3.32	0.9—1.3 m (3 H), 1.4—1.6 m (2 H) 1.85 d (1 H)				4.61	5.25	6.80	~7.3[j]	7.00	7.2—7.4[j]
(**15a**)	3.76	4.25	2.65	2.87	2.96	3.90	6.18	6.21	1.38	1.55	~5.5		7.04	7.26	6.96	
(**15b**)	~3.71[j]	4.14	2.70	2.90	3.24	~3.71[j]	6.18	6.21	1.40	1.62	2.93		~6.95[k]	7.25	~6.95[k]	
(**15c**)	3.65	~4.05[j]	2.50	2.72	3.01	3.65	6.14	6.04	1.13	1.42	~4.07[j]	5.16	6.90		7.15—7.45 m (8 H)	
(**16a**)[i]	3.70	4.30	1.98	2.63	2.82	3.18	6.26	6.14	1.34	1.81	~7.7		7.15—7.30 m (4 H)		6.90	
(**16b**)	3.94	4.19	2.10	2.68	3.18	3.12[m]	6.30	6.09	1.48	1.90	3.04		~6.95[j]	7.22	~6.95[j]	
(**16c**)	4.00	4.22	2.06	2.69	3.12	3.19	6.24	6.00	1.47	1.97	4.34	5.25	6.95		7.2—7.45 m (8 H)	
(**17a**)	4.03	4.19	2.30	2.25	2.25	3.60	1.35—1.50 m (4 H), 1.7—1.8 m (2 H)				~5.85		7.10	7.28	7.00	
(**17b**)	3.98	4.07	2.37	2.27	2.59	3.38	1.4—1.8 m (6 H)				2.90		~6.95[j]	7.22	~6.95[j]	
(**17c**)	~4.03[j]	4.10	2.30	2.25	2.44	3.46	1.4—1.5 m (4 H), ~1.70 t (1 H) ~1.86 t (1 H)				~4.02[j]	5.34	~7.0[k]	~7.3[l]	~7.0[k]	7.2—7.4[l]
(**18a**)	3.80	4.19	2.0—2.15 m (3 H)			3.28	1.05—1.25 m (3 H), 1.45—1.55 m (2 H) 1.86 d (1 H)				~5.9		~7.0[j]	~7.3	~7.0[j]	
(**18b**)	3.89	4.08	2.05	2.10	2.57	3.12	1.05—1.25 m (3 H), 1.4—1.7 m (2 H) 1.75 d (1 H)				2.97		~6.95[j]	7.20	~6.95[j]	
(**18c**)	3.92	4.08	1.98	2.10	2.54	3.16	0.9—1.6 m (5 H), 1.80 d (1 H)				4.22	5.20	~6.95[j]	~7.3[l]	~6.95[j]	7.2—7.4[l]

[a] In $CDCl_3$ solution at 250 MHz (reference Me_4Si). [b] A and B parts (2dd) of an ABX multiplet. In the case of (**9a**—**c**) and (**10a**—**c**) in a rudimentary form as d + s. The upfield or downfield dd appears as a triplet, J(A,B) ≈ J(A,X) ≈ 12.5 Hz in the spectrum of (**9a**—**c**) and (**11a**—**c**), respectively. For compounds (**12a**—**c**) δA ≈ δB and the A and B lines partly overlap. J(A,B) 10.8—11.2 Hz. (**15**)—(**18**), J(A,X) 7.3 (**15a,b**), 8.4 (**16a**), 5.8 (**16b**), 4.8 (**16c**), 6.3 (**17a,b**), 9.1 (**18a**) 5.4 (**18b**), and 4.4 Hz (**18c**), J(B,X) 6.4 (**15a**), 5.9 (**15b**), 7.0 (**16a**) and (**18a**), 5.7 (**16b**), 5.4 (**16c**) and (**18b**), 6.0 (**17a,b**), 5.5 (**17c**), and 5.1 Hz (**18c**). [c] Symmetric complex multiplet, for the *diendo*-compounds dq. [d] d for *diexo*-compounds, J(4a,8a) 7.3 (**10a**), 7.5 (**10b,c**) and (**14b**), 7.1 (**12a**), 7.8 (**12c**), (**16a**), and (**18a**), 8.8 (**16b,c**), 8.4 (**18b**) and 10.0 Hz (**18c**). For the *diendo*-compounds dd, J(4a,8a) 8.4 (**9a,c**), 8.6 (**9b**), 10.2 (**11a**), and (**17a**), 10.0 (**11b,c**), 9.4 (**15a**), 6.6 (**15b**), 11.6 (**17b**), and 12.1 Hz (**17c**), J(8,8a) 3—4 Hz. [e] Complex multiplets, overlapping with one d or both d of H-9,9′ with a total intensity of 5 H or 6 H, respectively, for the norbornanes. 2dd (2 × 1 H) for norbornenes, J(6,7) 5.6—5.7 Hz, J(5,6) ≈ J(7,8) 2.6—3.2 Hz. [f] AB spectrum, J(A,B) 8.8—10.0 Hz. The downfield d has a further triplet splitting of *ca.* 1 Hz for (**9a,b**), (**15a,b**), and (**18b**). [g] Broad signal of 1 H intensity for compounds **a**, s (3 H) in series **b** and AB spectrum for compounds **c**, J(A,B) 15.0—15.8 Hz. [h] s (2 H). [i] In [$^2H_6$]DMSO solution. [j–l] Overlapping signals. [m] Further d splitting by *ca.* 1 Hz.

Table 3. ^{13}C N.m.r. data of compounds (**9a**—**c**)—(**12a**—**c**) and (**15a**—**c**)—(**18a**—**c**)[a,b]

	Chemical shifts (δ)													
Compound	C-2	C-4	C-4a[c]	C-5[c]	C-6	C-7	C-8[c]	C-8a	C-9	NCH_3 NCH_2	C-1′	C-2′,6′	C-3′,5′	C-4′
(**9a**)	159.9	29.9	44.7	46.3	135.9	135.3	47.4	56.7	46.9		147.1	122.4	128.8	123.4
(**9b**)	159.1	28.7	45.8	47.2[d]	136.6	134.0	47.2[d]	63.2	47.8	36.0	150.5	122.2	128.6	122.8
(**9c**)	158.3	29.3	46.4	48.3	138.3	135.5	48.2	61.9	48.6	52.0	151.6 140.0[e]	123.2 130.0[f]	129.1[f] 129.6[f]	123.7 128.0[e]
(**10a**)	159.5	31.1	43.5	46.8	134.4	139.5	49.5	56.6	43.0		148.4	122.2	128.9	123.3
(**10b**)	159.3	29.4	44.0	46.8	134.6	140.6	46.2	62.7	42.2	35.9	150.2	121.9	128.4	122.5
(**10c**)	158.2	29.7	43.7	47.0	135.2	140.6	47.2	61.3	43.0	51.4	150.2 139.1[e]	122.1 127.8[f]	128.7[f] 128.3[f]	122.8 126.6[e]
(**11a**)	160.0	27.8	42.2	40.6	23.0	20.8	41.8	56.6	37.7		148.0	122.3	128.9	123.3
(**11b**)	160.0	26.7	42.6	41.7	23.8	20.0	41.3	63.0	37.6	36.1	150.8	122.2	128.7	122.7
(**11c**)	157.9	26.7	41.9	41.3	24.0	20.2	41.1	60.2	37.4	50.8	150.5 138.2[e]	121.9 128.0[d,f]	128.0[d,f] 128.6[f]	122.5 126.5[e]
(**12a**)	158.6	29.9	47.7	41.9	25.8	29.4	44.1	60.0	33.0		148.6	122.3	128.7	123.0
(**12b**)	158.9	28.7	47.5	42.1	26.3	29.5	40.4	67.0	33.1	35.9	150.2	122.2	128.6	122.7
(**12c**)	156.7	28.4	46.9	42.1	26.2	29.4	41.9	65.0	33.6	51.0	149.9 139.0[e]	121.9 127.5[f]	127.9[f] 128.3[f]	122.2 126.3[e]
(**15a**)	144.5	67.9	39.6	45.6	135.9	134.8	48.0	54.0	48.5		152.4	121.8	128.8	122.2
(**15b**)	148.6	66.8	40.7	45.4	136.8	132.7	46.8	60.4	47.9	35.5	152.4	123.5	128.2	121.5
(**15c**)	148.3	66.3	40.3	45.4	136.6	132.6	46.6	57.4	47.8	50.9	151.5 138.2[e]	123.2 128.0[f]	128.2[f] 128.1[f]	121.1 126.8[e]
(**16a**)	146.4	69.8	38.7	45.8	137.0	140.4	48.5	54.6	44.3		153.1	122.3	129.7	122.3
(**16b**)	148.5	67.6	39.1	45.2	135.3	140.3	47.2	60.7	43.1	36.1	152.5	121.4	128.3	123.4
(**16c**)	148.3	67.6	39.0	45.4	135.4	140.3	47.8	58.1	43.3	51.3	152.0 138.5[e]	121.4 128.0[f]	128.3[f] 128.2[f]	121.4 129.9[e]
(**17a**)	145.5	66.8	38.7	40.3	24.1	21.0	43.0	53.8	37.3		153.3	122.1	128.8	122.0
(**17b**)	148.3	65.5	37.9[d]	40.7	23.9	20.2	39.6	60.1	37.9[d]	35.5	152.7	123.2	127.8	120.9
(**17c**)	148.4	65.9	38.3	41.0	24.4	21.1	40.4	57.3	38.1	51.0	152.5 138.1[e]	123.4 128.1[f]	128.2[f] 128.3[f]	121.2 126.9[e]
(**18a**)	146.0	67.6	44.1	39.5	25.8	29.2	42.5	57.1	33.2		153.4	122.6	128.7	122.1
(**18b**)	148.3	66.6	42.9	39.9	25.5	29.1	40.0	64.2	33.4	35.7	152.5	123.2	127.9	121.0
(**18c**)	148.4	67.1	43.4	40.6[d]	25.8	29.4	40.6[d]	61.7	34.1	51.0	152.4 138.6[e]	123.4 128.3[f]	128.1[f] 128.2[f]	121.4 127.0[e]

[a] In $CDCl_3$; in the cases of (**9c**) and (**16a**) in $[^2H_6]$DMSO solution. [b] At 20.14 MHz; in the cases of (**9a**—**c**), (**10b**), and (**15c**) at 62.89 MHz. [c-f] Assignments may be interchanged. [d] Overlapping lines. [e] Lines of the benzene carbons in the *N*-benzyl (NR) group.

Since this is also valid for compound (**16a**) a detectable change in the tautomeric equilibrium cannot be observed in $[^2H_6]$DMSO solution either.

By comparison of the spectra of *exo*- and *endo*-*N*-substituted 2-arylaminothiazolines of fixed structure, we have shown that the conjugation of the C=N double bond and the phenyl ring gives rise to a considerable upfield shift in the signals of the *ortho* and *para* protons and carbon atoms.[30,31] Accordingly, the ^1H and ^{13}C shifts observed [δ(H-2′,6′) 6.90—7.15, δ(H-4′) 6.90—7.10, δ(C-2′,6′) 121.8—122.6 p.p.m., δ(C-4′) 122.0—123.4 p.p.m.] indicate that the non-conjugated tautomeric form does not make a significant contribution to the tautomeric equilibrium. For comparison, for the thiazolines in question δ(C-4′) was 122.0—123.6 and 127.8—129.6 p.p.m. for the conjugated *N*-methyl isomers and the non-conjugated isomers, respectively.

Experimental

General Methods.—I.r. spectra were run in KBr discs on a Bruker IFS-113v Fourier transform spectrometer equipped with an ASPECT 2000 computer. ^1H and ^{13}C n.m.r. spectra were recorded in $CDCl_3$ or $[^2H_6]$DMSO solution in 5 and 10 mm tubes, at room temperature on Bruker WM-250 and WP-80-SY Fourier transform spectrometers, controlled by an ASPECT 2000 computer at 250.13 MHz (^1H) and 62.89 or 20.14 MHz (^{13}C), respectively, using the deuterium signal of the solvent as the lock and $SiMe_4$ as internal standard. The most important measurement parameters were: sweep width 5 and 5 or 15 kHz, pulse width 1 and 7 or 3.5 μs (*ca.* 20°) and *ca.* 30° flip angle), acquisition time 1.64 and 1.02 or 1.64 s, number of scans 32 and 1K—4K, computer memory 16K. Complete proton-noise decoupling (*ca.* 3 or *ca.* 1.5 W) for the ^{13}C spectra and Lorentzian exponential multiplication for signal-to-noise enhancement were used (line width 0.7 and 1.0 Hz).

Preparation of Thioureas (**5a**—**c**)—(**8a**—**c**).—To a solution of an aminoalcohol (**1**)—(**4**) (0.01 mol) in dry ether (25 ml), phenyl isothiocyanate (1.35 g, 0.01 mol) was added dropwise under stirring. After stirring for 1 h, the separated solid was filtered off and crystallized. Data for the thioureas (**5**)—(**8**) are in Table 4.

Preparation of 5,8-*Methano*-2-*phenylimino*-*tetrahydro*-(**9a**—**c**) *and* (**10a**—**c**) *and* -*hexahydro*-4H-3,1-*benzothiazines* (**11a**—**c**) *and* (**12a**—**c**).—A thiourea derivative (**5**)—(**8**) (0.01 mol) was boiled in ethanol (20 ml) containing 20% dry HCl. The reaction was monitored by t.l.c. [silica gel, benzene–ethanol–light petroleum (4:1:3), detection with iodine vapour]. After evaporation of the mixture, the residue was neutralized with 10% sodium carbonate solution and extracted with chloroform (3 × 15 ml). After washing with water and drying (Na_2SO_4), the solvent-free residue was recrystallized. Data on the thiazines (**9a**—**c**)—(**12a**—**c**) are in Table 4.

Isolation of 5,8-*Methano*-1-*methyl*-1,4,r-4a,t-5,6,7,t-8,c-8a-*octahydro*-3,1-*benzoxazine*-2-*thione* (**13**) *and* 5,8-*Methano*-1-

Table 4. Physical and analytical data of compounds (**5a**—**c**)—(**12a**—**c**) and (**15a**—**c**)—(**18a**—**c**)

Compound	M.p. (°C)	Yield %	Found (%) C	H	N	Formula	Required (%) C	H	N
(**5a**)	143—145[a]	94	65.8	6.5	10.2	$C_{15}H_{18}N_2OS$	65.7	6.6	10.2
(**5b**)	153—154[c]	92	66.75	7.3	9.65	$C_{16}H_{20}N_2OS$	66.6	7.0	9.7
(**5c**)	119—120[d]	84	72.35	6.7	7.5	$C_{22}H_{24}N_2OS$	72.5	6.6	7.7
(**6a**)	156—157[b]	95	65.75	6.6	10.0	$C_{15}H_{18}N_2OS$	65.7	6.6	10.2
(**6b**)	154—156[a]	96	66.5	7.1	9.9	$C_{16}H_{20}N_2OS$	66.6	7.0	9.7
(**6c**)	121—123[d]	94	72.4	6.85	7.8	$C_{22}H_{24}N_2OS$	72.5	6.6	7.7
(**7a**)	112—114[b]	90	65.3	7.2	10.1	$C_{15}H_{20}N_2OS$	65.2	7.3	10.1
(**7b**)	120—122[a]	95	65.9	7.7	9.7	$C_{16}H_{22}N_2OS$	66.2	7.6	9.65
(**7c**)	71—72[b]	85	72.1	7.05	7.6	$C_{22}H_{26}N_2OS$	72.1	7.15	7.6
(**8a**)	156—158[b]	96	65.1	7.4	10.2	$C_{15}H_{20}N_2OS$	65.2	7.3	10.1
(**8b**)	158—160[b]	97	66.3	7.9	9.4	$C_{16}H_{22}N_2OS$	66.2	7.6	9.65
(**8c**)	130—132[b]	97	71.9	7.2	7.7	$C_{22}H_{26}N_2OS$	72.1	7.15	7.6
(**9a**)	235—236[d]	61	70.6	6.4	11.2	$C_{15}H_{16}N_2S$	70.3	6.3	10.9
(**9b**)	128—130[g]	45	71.25	6.6	10.3	$C_{16}H_{18}N_2S$	71.1	6.7	10.4
(**9c**)	92—94[g]	71	76.4	6.3	7.9	$C_{22}H_{22}N_2S$	76.3	6.4	8.1
(**10a**)	181—183[d]	63	70.2	6.3	11.05	$C_{15}H_{16}N_2S$	70.3	6.3	10.9
(**10b**)	95—97[g]	77	71.05	6.9	10.4	$C_{16}H_{18}N_2S$	71.1	6.7	10.4
(**10c**)	119—121[d]	62	76.4	6.3	7.9	$C_{22}H_{22}N_2S$	76.3	6.4	8.1
(**11a**)	237—238[e]	67	69.8	7.0	10.9	$C_{15}H_{18}N_2S$	69.75	7.0	10.8
(**11b**)	139—140[d]	54	70.4	7.6	10.3	$C_{16}H_{20}N_2S$	70.55	7.4	10.3
(**11c**)	89—91[g]	85	76.0	6.9	7.9	$C_{22}H_{24}N_2S$	75.8	6.9	8.0
(**12a**)	189—191[f]	77	69.85	7.1	10.55	$C_{15}H_{18}N_2S$	69.75	7.0	10.8
(**12b**)	70—72[g]	59	70.6	7.3	10.0	$C_{16}H_{20}N_2S$	70.55	7.4	10.3
(**12c**)	90—92[h]	77	76.1	6.9	7.9	$C_{22}H_{24}N_2S$	75.8	6.9	8.0
(**15a**)	194—195[b]	98	75.1	6.8	12.1	$C_{15}H_{16}N_2O$	75.0	6.7	11.7
(**15b**)	116—118[d]	98	76.0	7.1	11.0	$C_{16}H_{18}N_2O$	75.6	7.1	11.0
(**15c**)	65—67[g]	60	79.85	6.85	8.4	$C_{22}H_{22}N_2O$	80.0	6.7	8.5
(**16a**)	167—169[d]	85	75.1	6.9	11.3	$C_{15}H_{16}N_2O$	75.0	6.7	11.7
(**16b**)	88—90[d]	81	75.8	7.3	11.2	$C_{16}H_{18}N_2O$	75.6	7.1	11.0
(**16c**)	94—96[d]	51	79.9	6.6	8.6	$C_{22}H_{22}N_2O$	80.0	6.7	8.5
(**17a**)	176—177[c]	82	74.2	7.2	11.6	$C_{15}H_{18}N_2O$	74.35	7.5	11.6
(**17b**)	79—81[d]	71	74.8	7.9	10.65	$C_{16}H_{20}N_2O$	75.0	7.9	10.9
(**17c**)	143—145[a,i]	61	59.7	4.8	12.3	$C_{28}H_{27}N_5O_8$	59.9	4.85	12.5
(**18a**)	176—177[a]	86	74.5	7.1	11.7	$C_{15}H_{18}N_2O$	74.35	7.5	11.6
(**18b**)	84—86[d]	85	74.8	7.9	11.0	$C_{16}H_{20}N_2O$	75.0	7.9	10.9
(**18c**)	147—149[a,i]	72	59.6	4.7	12.4	$C_{28}H_{27}N_5O_8$	59.9	4.85	12.5

Crystallization solvents. [a] Ethanol. [b] Chloroform. [c] Nitromethane. [d] Benzene. [e] Ethyl acetate. [f] Benzene–chloroform (3:1) mixture. [g] Ether. [h] Chloroform–light petroleum (1:3) mixture. [i] Picrates. For i.r. and n.m.r. spectroscopy the bases liberated from the salt with KOH were applied.

methyl-1,4,r-4a,c-5,6,7,c-8,c-8a-*octahydro*-3,1-*benzoxazine*-2-*thione* (**14**).—A mixture of (**11b**) and (**12b**) was evaporated and transferred to an aluminium oxide column (Woelm neutral; activity grade I). The column was eluted with benzene, and then with ethyl acetate. The ethyl acetate eluate was evaporated and the residue (*ca.* 30%) was recrystallized from benzene and identified from the m.p. and i.r. spectrum.[7a,b]

Preparation of 5,8-*Methano*-2-*phenylimino*-*tetrahydro*-(**15a**—**c**) *and* (**16a**—**c**) *and* -*hexahydro*-4H-3,1-*benzoxazines* (**17a**—**c**) *and* (**18a**—**c**).—A thiourea derivative (**5**)—(**8**) (0.01 mol) and methyl iodide (7.10 g, 0.05 mol) were stirred together for 1—2 h. The mixture was evaporated and the residue was stirred with methanol (40 ml) containing 3N-KOH for 4 h. After evaporation and the addition of water (5 ml), the product was extracted with chloroform (3 × 15 ml). The extract was washed with water and dried (Na_2SO_4). Data on the compounds obtained after evaporation and recrystallization are in Table 4.

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