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Preparation and Stereostructure of Norbornane/ene-Condensed Phenyl-Substituted *O,N*-Heterocycles*

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Norbornane/ene di-*exo*-condensed isoxazolines were reduced to amino alcohols and then cyclized to 1,3-oxazines. The phenylimino analogues, 1,3-oxazin-2(3*H*)-ones, the corresponding 2(3*H*)-thiones and 1,4-oxazepin-3(4*H*)-ones were also prepared. The structures, configurations and conformations of the new compounds were proved via ^{1}H and ^{13}C NMR studies, using DR, DNOE, DEPT and 2D-HSC measurements in addition to the routine spectra.

KEY WORDS Norbornane/ene-fused 4/5-phenyl-*O*(1),*N*(3/4)-heterocycles Synthesis Stereostructure ^{1}H and ^{13}C NMR (DEPT) DNOE 2D-HSC

INTRODUCTION

A number of norbornane- and norbornene-condensed 1,3- and 1,4-heterocycles have previously been prepared for pharmacological purposes and stereochemical studies[2–6] and their conformational analyses were achieved via NMR spectroscopy. We now report the synthesis and stereostructures of phenyl-substituted analogues, with the phenyl group vicinal to the ring annelation. The aim of this work was to study the influence of the aryl substituent on the conformations of the tricyclic compounds obtained.

SYNTHESIS

The cycloadducts **1** and **2** of norbornene or norbornadiene with benzonitrile oxide[7] (BNO) were reduced with lithium aluminium hydride (LAH) to amino alcohols **3** and **4** (Scheme 1). Similar reductions of other isoxazolines are known.[8] These amino alcohols were used for the preparation of saturated 1,3- and 1,4-heterocycles.

Although the addition of BNO to norbornene and to norbornadiene yields mixtures of di-*endo* and di-*exo* adducts,[9] we obtained **3** and **4** as stereohomogeneous products. From these, the partly saturated methylene-bridged 1,3-benzoxazines **5** and **6** were prepared by reaction with arylimidate. The thioureas obtained with phenyl isothiocyanate yielded tricyclic 2-phenylimino-1,3-oxazines **7** and **8** by elimination of MeSH. On cyclization with ethyl chloroformate, **3** and **4** gave 1,3-oxazin-2(3*H*)-ones **9** and **10**, while the corresponding thiones were formed with CS_2–KOH and subsequent cyclization of the dithiocarbamate with lead(II) nitrate. By acylation with ethyl chloroacetate or 2-chloropropionate and cyclization with NaH, **3** was transformed to the 1,4-oxazepin-3(4*H*)-ones **13** and **14**.

STEREOSTRUCTURE

The spectral data of the new compounds (Tables 1 and 2) prove their presumed structures unambiguously.

The unchanged di-*exo* annelation of the hetero ring follows from the doublet splitting of the H-8a signal by 7.5 Hz. This signal is a double doublet for a di-*endo* annelation, due to the H-8,H-8a coupling which, in addition to the H-4a,H-8a interaction (splitting of *ca.* 8.5 Hz), causes a further doublet splitting (by about 4.5 Hz) (the corresponding dihedral angle is about 90° for the di-*exo* analogues).[10]

Further points which must be clarified are the conformation of the hetero ring and the stereoposition of the 4-phenyl substituent (i.e. the C-4 configuration) and the methyl group in **14**.

Compounds **5–12** can exist in two relatively stable boat conformations (Fig. 1), in which O-1 and C-4 lie out of plane in the *endo* (**A**) or *exo* (**B**) direction to the plane of the other four atoms. In the **A** conformation the dihedral angles of the quasi-equatorial (*exo*) and quasi-axial (*endo*) C-H(4) with C-H(4a) are *ca.* 60–80° and *ca.* 60–40°, respectively, whereas in the **B** form these angles are *ca.* 30–40° and *ca.* 150–160°. As the ^3J(H-4, H-4a) value is 6.1 Hz, conformation **A** containing an *endo*-quasi-axial phenyl group is improbable for **5–12**. In this form the H-4,H-4a coupling would be smaller, corresponding to the dihedral angle of *ca.* 60–80°. Conformation **B** with an *exo*-axial 4-phenyl group is unfavourable for steric reasons, and no anisotropic shielding

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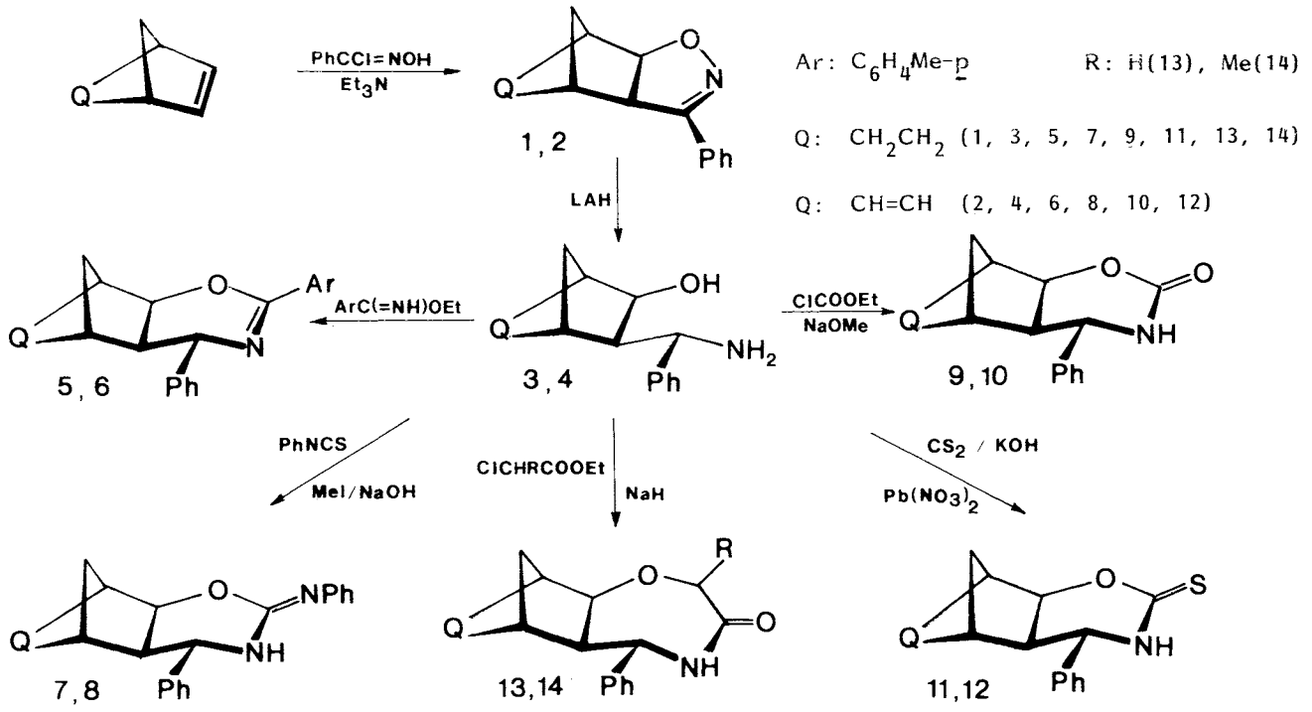

Scheme 1

Table 1. Characteristic IR bands and ^{1}H NMR data (chemical shifts in ppm, δ_{TMS} = 0 ppm, coupling constants in Hz)[a] for compounds 5–14 in $CDCl_3$ solution[b] at 250 MHz

Compound	νC=N νC=O[c]	γC$_{Ar}$H band[d]	γC$_{Ar}$C$_{Ar}$ band[d]	H-4 d (1H)[e]	H-4a t (1H)[f]	H-5 ~s (1H)	H-6	H-7 ms/dd (2/4H)[g]	H-8 (1H)[h]	H-8a (1H)[i]	H-9 2 × d[j]		ArH[d] 1–3 m (5H)
5	1646	752	704	~4.65	2.4[k]	1.85	0.9–1.5		2.62	4.56	0.9	1.55[l]	7.30,[m] 7.40,[n] 7.55[o]
6	1644	760	699	4.81	2.40	2.27	6.03	6.13	3.09	4.58	1.28	1.80	7.24,[m] 7.37,[n] 7.48[o]
7	1670	759	697	4.68	2.25	1.90	0.9–1.6[k]		2.54	4.44	~1.0[k]	1.82	6.95,[m] 7.2–7.6[p]
8	1653	760	699	~4.82	2.35[k]	~2.35[k]	6.05	6.18	3.07	4.50	1.40	2.10	6.96,[m] 7.2–7.5[p]
9	1715[q] 1689	768	697	4.75	2.12	1.97[r]	0.9–1.9[k]		2.62	4.55	1.08	1.81[k]	7.3–7.5
10	1722[q] 1694[q]	771[q] 759[q]	707[q] 695[q]	4.86	2.22	2.42	6.09	6.17	3.19	4.62	1.50[l]	2.08	7.25–7.45
11	1525	760	706	4.75	2.35	1.84	0.9–1.6[k]		2.48	4.52	0.97	1.4[k]	7.25–7.5
12	1546	758	697	4.83	2.35	2.48	6.11	6.20	3.31	4.69	1.55	1.98	7.25–7.5
13	1663	722	699	4.51	2.53	2.25	~1.1	~1.4	1.97	3.65	0.58		7.2–7.4
14	1658	753	708[q] 694[q]	4.59	2.57	2.17	~1.1	1.45	2.12	3.66	0.68	0.78	7.2–7.45

[a] Further data: IR: νNH 3410 (**7**), 3374 (**8**), 3223, 3108 (**9**), 3238, 3110 (**10**), 3175 (**11**), 3167 (**12**), 3194, 3060 (**13**), 3189, 3056 (**14**); γC$_{Ar}$H (*p*-disubst. ring) 826 (**5**), 822 (**6**). ^{1}H NMR: *AA'BB'*-type spectrum of the *p*-tolyl group, 2 × ~d(2 × 2*H*) for **5** and **6** 7.18 and 7.95 (J = 8.2); CH_3, s(3H) 2.38[k] (**5**), 2.34 (**6**); NH, broad signal (1H) 5.78 (**9**), 5.59 (**10**), 9.96 (**11**), 7.70 (**12**), 8.35 d(J = 7.5, **13**), 6.75 d(J = 7.5, **14**); OCH_2 (**13**), 2 × d(J = 17.4); CH_3 (**14**), d(J = 7.0) 1.70; OCHCO (**14**) *qa*. 4.30.

[b] In DMSO-d_6 solution for **11** and **13**.

[c] νC=N band for **5–8**, νC=O band for **9**, **10**, **13** and **14**, band of the thioamide group for **11** and **12**.

[d] 4-Phenyl group.

[e] J = 6.2 (**5**, **12**), 6.8 (**6**), 5.8 (**7**, **10**), 5.5 (**9**), 7.0 (**11**), t(J = 7.2) for **13**, **14** due to H-4, NH coupling.

[f] J = 6.5 (**5–10**), 7.3 (**11**), 6.8 (**12–14**).

[g] Overlapping ms(4H) for **5**, **7**, **9**, **11**, **13** and **14**, 2 × dd(2 × 1H), J = 5.7 and 3.0 for **6**, **8**, **10** and **12**.

[h] d(J = 5) for **5**, **7**, **9** and **11**, singlet-like signal for all other compounds.

[i] J(H-4a,H-8a) = 7.6 ± 0.2 (**5–12**), 6.6 for **13** and **14**.

[j] $J \approx 11$ (**5**, **9** and **14**), 9.6 (**6**, **8**, **10** and **12**), 10.5 (**7** and **11**).

[k] Overlapping signals.

[l] Further triplet split by <1 Hz.

[m] H-4′: ~t(1H).

[n] H-3′5′: ~t(2H).

[o] H-2,6′: ~d(2H).

[p] Overlapping ms of the 4-phenyl ring and of *ortho*- and *meta*-protons of the phenylimino group (9H).

[q] Split band pair.

[r] d($J \approx 3$).

Table 2. ^{13}C NMR chemical shifts (δ_{TMS} = 0 ppm)[a] for compounds 5–14 in $CDCl_3$ solution[b] at 20.14 MHz[c,d]

Compound	C-2	C-4	C-4a	C-5	C-6	C-7	C-8	C-8a	C-9	C-1′	C-2′,6′	C-3′,5′	C-4′
5	159.1	55.0	48.5	36.7	23.6	31.2	46.2	81.7	34.9	140.6	127.3[e,f]	128.3[e]	126.3
6	159.0	55.6	44.1[g]	42.6[g]	134.7	143.8	52.1	78.1	44.4[g]	140.6	127.1[e]	128.2[e]	126.3
7	151.6	54.9	48.7	36.5	23.7	30.6	45.3	83.1	34.9	141.3[e]	127.0	128.3[g]	126.5
8	151.7	55.2	44.0[e]	42.3[e]	134.7	143.9	51.0	79.8	44.3[e]	141.5[h]	126.9	128.3	126.6
9	157.2	55.7	48.6	37.8	24.7	31.3	45.7	85.0	35.9	141.3	129.9	128.5	128.9
10	156.4	55.4	43.4[e]	42.4[e]	135.2	143.3	50.8	81.6	44.5[e]	138.9	126.4	129.0	128.2
11	191.4	55.5	48.3	38.2	24.4	31.0	45.3	86.8	35.6	140.1	129.8	128.8	129.0
12	190.5	55.5	43.3[e]	42.2[e]	134.8	143.0	50.6	83.3	44.3[e]	137.1	126.4	128.8	128.2
13	175.1	58.6	56.0	39.2	25.2	29.1	41.7	87.7	33.7	140.6	128.0[e]	128.7[e]	127.3
14	177.6	59.7	55.1	39.3	25.1	29.1	42.2	88.0	33.5	140.5	127.7	129.0	127.1

[a] Further signals: 2-aryl ring, C-1′ 131.7 (**5** and **6**), 143.6[e] (**7**), 142.8[h] (**8**), C-2′,3′,5′,6′ 127.3[e,f], 128.8[e] (**5** and **6**), C-2′,6′ 119.2 (**7**), 119.5 (**8**), C-3′,5′ 128.7[g] (**7** and **8**), C-4′ 143.7 (**5**), 143.3 (**6**), 121.7 (**7**, **8**); CH_3 21.4 (**5**, **6**), 20.4 (**14**); CH_2O 72.8 (**13**); $\underline{C}H(CH_3)$ 80.0 (**14**).
[b] In DMSO-d_6 for **9** and **11**.
[c] At 62.99 MHz for **8** and **13**.
[d] The assignments were proved by DEPT (**13** and **14**) and/or 2D HSC measurements (**5**, **9** and **13**).
[e,g,h] Assignments may also be reversed.
[f] Two overlapping lines.

effect[11a] from the closely lying phenyl ring can be observed on the H-9(*endo*) atom expected for this stereostructure. This phenomenon was observed for homologues **13** and **14** (see later); accordingly, the above stereostructure can be neglected for **5**–**12**.

Thus, the *exo*-4-phenyl (4*R**) configuration with conformation **A** and the *endo*-4-phenyl (4*S**) configuration with conformation **B** must be considered. The 4-phenyl group is equatorial in both structures, and the H-4,4a coupling of *ca.* 6 Hz is compatible[12] with dihedral angles of both *ca.* 60–40° and *ca.* 150–160°.

For the final elucidation of the stereostructures we recorded the DNOE spectra of **5**–**9** (Table 3). These measurements made possible the firm assignment of the closely lying H-4,8a, H-5,8 and, for **6** and **8**, the H-6,7 signal pairs.

The strong NOE for the H-*ortho*(Ph) signal observed on irradiation of the H-5 singlet excludes the 4*S** (**A**) structure, in accordance with the H-4,H-4a coupling, as H-5 and the *ortho*-hydrogens in this structure are too far apart. Both of the **B** conformations can definitely be ruled out, owing to the absence of a NOE between H-9(*endo*) and the closely lying phenyl group or H-4 in

Table 3. Results of the DNOE experiments on compounds 5–9[a]

Irradiated signals	Signals showing enhanced intensity	No response
H-4	H-4a, H-*o*(Ph), NH[b]	H-9(*endo*)
H-4a	H-4, H-8a	
H-5	H-9, H-*o*(Ph)	
H-8a	H-4a, H-7,[c] H-8	
H-9(*endo*)	H-5, H-8, H-*o*(Ar)[d]	H-4, H-*o*(Ph)

[a] Only signals of importance for the distinction between the possible stereostructures are given. H-*o*(Ph) and H-*o*(Ar) are the *ortho*-hydorgens in the 4-phenyl and 2-aryl rings, respectively.
[b] For compounds **7**–**9**.
[c] For compounds **6** and **8**.
[d] For compound **6**.

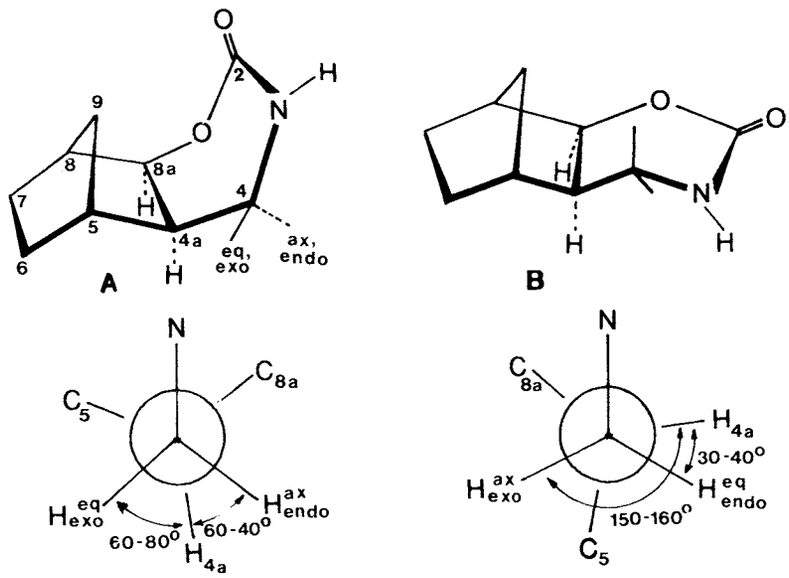

Figure 1. The relatively stable conformations **A** and **B** for compounds **5**–**12**, illustrated by the skeleton of compound **9**.

structures 4*R** (**B**) or 4*S** (**B**), respectively. For example, the distance between H-9(*endo*) and H-4 is *ca.* 2.1 Å in the 4*S** (**B**) conformations. Thus, the DNOE measurements confirmed the presence of the 4*R** (**A**) stereostructure, i.e. the *exo*-equatorial position of the 4-phenyl group in **5–12**. The 4*R** (**A**) form was confirmed directly for compound **6** from the strong NOE between H-9(*endo*) and the *ortho*-hydrogens of the 2-Ar ring.

This stereostructure explains the large difference in the shift of the H-5 and H-8 signals. For the 4-unsubstituted analogues of **5** and **6** the differences are 0.2 and 0.45 ppm, while the average measured for **5–12** was 0.73 ppm. For steric reasons the shielding of H-5, lying over the 4-phenyl group, is characteristically increased by the anisotropy[11a] of the phenyl ring. At the same time, the shielding around H-8 is significantly decreased as a consequence of the lone electron pair of the oxygen (i.e. of the anisotropy of the C—O bond[11b]).

The steric structure of the oxazepinone homologue **13** differs from those of **5–12**: the phenyl ring is in the *exo*-axial position (the phenyl-substituted carbon atom has the *R** configuration) and the hetero ring has conformation **B**: C-4,4a,8a and the O atoms are approximately coplanar, as are C-4, the O, the methylene carbon, the amide carbonyl carbon and the nitrogen (Fig. 2) (in order to facilitate comparison, the carbon numbering of **5–12** has also been used for **13** and **14**). This is proved by the following spectral data.

(i) The 9-methylene hydrogens are significantly more shielded (mainly the *endo*-hydrogen) than in **5–12**; the chemical shifts of the 9-*exo*- and 9-*endo*-hydrogens are 1.0 and 1.65 ppm, on average, in the norbornanes **5**, **7**, **9** and **11**, whereas their overlapping signal in **13** lies at about 0.58 ppm. This is a consequence of the anisotropy of the closely lying *axial* phenyl group, which of course affects H-9(*endo*) more strongly.

(ii) In **5–12** the shielding of the phenyl group is exerted around H-5, and this effect is absent in **13**. Hence, a downfield shift of 0.35 ppm was found for H-5 compared with the average shift of 1.9 ppm for **5**, **7**, **9** and **11**.

(iii) The shift difference $\Delta\delta$(H-5,H-8) is smaller than for the homologues **5–12** (0.28, and 0.05 ppm for **14**), because not only the shielding about H-5 but also the deshielding on H-8 (originating from the C—O bond in **5–12**) is weaker in the 4*R** (**B**) structure.

DNOE measurements supported the steric structure given in Fig. 2.

(a) On irradiation of the 9-methylene signal a multiplet from the aromatic hydrogens appeared in the DNOE spectrum; this proved that the 9-CH_2 and phenyl groups were close to each other. In accordance with the literature,[13] this experiment simultaneously showed that the downfield signal of the two multiplets of the 6,7-methylene hydrogens relates to H-6,7(*exo*). Hence, saturation of the H-4a signal resulted in an increase in the signal intensity of H-6, 7(*endo*).

(b) On saturation of the H-8a doublet the two signals of the heterocyclic *endo*-methylene hydrogen in the 1,3-diaxial position became more intense.

The NOE measurements also provided evidence in favour of the assignments. For example, the NOE between H-4 and NH, H-4a and H-5 and H-8 and H-8a allowed the assignments of the H-4, -5 and -8 signals.

On the basis of the very similar spectral data for the methyl-substituted derivative **14** and those for **13**, an analogous stereostructure is proposed for the seven-membered hetero ring and the *exo*-axial phenyl group: the 9-methylene hydrogens gave closely lying upfield signals, whereas an opposite shift of similar magnitude was observed for the H-5 singlet, as found for **13** relative to **5**, **7**, **9** and **11**.

From the stereostructure corresponding to that in Fig. 2 the methyl group should be *exo*-equatorial (*trans* to H-4a,8a), because in an *endo*-axial position there would be considerable steric hindrance between the methyl group and H-8a in the presumed conformation of the hetero ring (their distance apart would be *ca.* 1.0 Å). Therefore, the relative configuration of the methyl-substituted carbon atom is *R**.

The DNOE measurements provided the following direct evidence: (a) on saturation of the signal of H-8a and that of the hydrogen geminal to the methyl group, a mutual and significant intensity increase was observed, which proves their 1,3-*diaxal* positions; (b) saturation of the signal of the methyl group caused an Overhauser effect on the double doublet of the *ortho*-hydrogens of the phenyl group. The DNOE spectra also proved the assignments, for example for the closely lying H-5,8 singlets in this case.

The *ca.* 1.7 ppm upfield shift of the C-9 signal relative to the average shift of 35.3 ppm in **5**, **7**, **9** and **11** also indicates the *exo*-axial position of the phenyl group. This steric compression shift[14] is a result of the hindrance between the 9-methylene and phenyl groups. A similar field effect appears for the C-8 signal (3.5 ppm), presumably due to steric hindrance with the oxygen in conformation **B**. Owing to the more strained skeleton (a rigid six-membered hetero ring and the sterically unfavourable conformation **A**) and to the steric hindrance between the equatorial phenyl group and H-5 in the oxazines **5–12**, the field effect again appears for the C-4, 4a,5,8a absorptions.

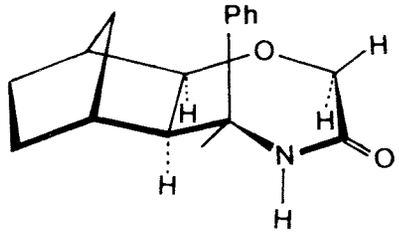

Figure 2. Stereostructure of compound **13**.

EXPERIMENTAL

The NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solution in 5- or 10-mm tubes at room temperature on Bruker WM-250 (^1H and ^{13}C) or WP-80-SY (^{13}C) Fourier transform spectrometers controlled by an Aspect 2000 computer at 250.13 MHz (^1H) and 62.89 or 20.14 MHz (^{13}C), with the deuterium signal of the solvent as the lock and TMS as internal standard. The

most important measuring parameters were as follows: sweep width, 5 and 16 or 5 kHz; pulse width, 1 μs (^{1}H) and 7.0 or 3.5 μs (^{13}C) (*ca.* 20° and *ca.* 90° flip angle, respectively); acquisition time, 1.64 and 0.40 or 1.64 s; number of scans, 16 (^{1}H) and 2–27K (^{13}C); computer memory, 16K. Lorentzian exponential multiplication was applied for signal-to-noise enhancement (line width 0.7 and 1.0 or 2.0 Hz), and complete proton noise decoupling (*ca.* 0.5 or 3.5 W) for the ^{13}C NMR spectra.

The DNOE MULT.AU standard Bruker microprogram to generate NOE was used with a selective pre-irradiation time of 5 s and a decoupling power (CW mode) of *ca.* 30–40 mW; number of scans, 32–512; relaxation delay, 0.15; dummy scans, 2.

DEPT[15] spectra were run in a standard manner,[16] using only the $\theta = 135°$ pulse to separate CH/CH_3 and CH_2 lines phased 'up and down,' respectively. Typical acquisition data were as follows: number of scans, 128–512; relaxation delay for protons, 3 s; 90° pulse widths, 17.5 and 43 μs for ^{13}C and ^{1}H, respectively. The estimated value for J(CH) resulted in a 3.7-ms delay for polarization.

The HETCOR 2D spectra were obtained using the standard Bruker pulse program XHCORRD.AU. The number of data points was 4K in the ^{13}C domain, and 64–256 increments were used, giving better than 5 Hz per point digital resolution in the ^{1}H domain; 256 transients were obtained with a relaxation delay of 5 s. All C–H correlations were established using a J(CH) value of 135 Hz for the calculation of the delay.

Preparation of 3-phenyl-3a,4,5,6,7,7a-hexahydro-4,7-methanobenzisoxazole[7] (1) and -3a,4,7,7a-tetrahydro-4,7-methanobenzisoxazole (2)

To a solution of benzhydroximic acid chloride (5.0 g, 32.0 mmol) and norbornene or norbornadiene (9.4 or 9.1 g, 10 mmol) in dry diethyl ether (10 ml), triethylamine (1.2 g, 12 mmol) in dry diethyl ether (30 ml) was added dropwise during stirring and cooling with ice–water. The mixture was washed with water (3 × 10 ml) and dried (Na_2SO_4), the solvent was removed by distillation, and the residue (**1**, 1.9 g, 89%; **2**, 1.8 g, 85%) was crystallized from benzene–light petroleum. Colourless crystals, m.p. 101–103 °C (**1**) (lit.[7] m.p., 99–100 °C). Data for compound **2** are listed in Table 4.

Preparation of *exo*-3-aminophenylmethyl-bicyclo[2.2.1]-hexan-*exo*-2-ol (3) and -hex-5-en-*exo*-2-ol (4)

To a mixture of LAH (14.0 g, 0.37 mol) in dry THF (600 ml), methanobenzisoxazole (**1**, 28.36 g; **2**, 28.1 g, 0.133 mol) was added in small portions over 1 h at 0 °C with stirring, and the mixture was then stirred and refluxed for 20 h. After cooling to 0 °C, water (3 ml) was added dropwise and the mixture was stirred at room temperature until it became white. The precipitate was filtered off by suction and the filtrate was evaporated. After crystallization from benzene–light petroleum, the residue gave colourless or beige crystals. Data for compounds **3** and **4** are listed in Table 4.

Preparation of 5,8-methano-*r*-4-phenyl-2-*p*-tolyl-*c*-4a,*c*-5,6,7,*c*-8,*c*-8a-hexahydro-4*H*-1,3-benzoxazine (5) and -*c*-4a,*c*-5,*c*-8,*c*-8a-tetrahydro-4*H*-1,3-benzoxazine (6)

A solution of amino alcohol **3** or **4** (2.17 or 2.15 g, 0.01 mol), EtOH (30 ml), 4-methyl benzimidate (1.6 g, 0.01 mol) and EtOH saturated with HCl (1 drop) was refluxed for 1 h. After evaporation, the residue was crystallized from EtOH–benzene. Data for compounds **5** and **6** are listed in Table 4.

Preparation of 5,8-methano-*r*-4-phenyl-2-phenylimino-*c*-4a,*c*-5,6,7,*c*-8,*c*-8a-hexahydro-(7) and -*c*-4a,*c*-5,*c*-8,*c*-8a-tetrahydro-4*H*-1,3-benzoxazine (8)

A mixture of amino alcohol **3** or **4** (4.35 or 4.30 g, 0.02 mol), diethyl ether (50 ml) and phenyl isothiocyanate (2.70 g, 0.01 mol) was left to stand at room temperature overnight. The solid formed was removed by suction and crystallized from EtOH; m.p. 169–171 and 187–189 °C, respectively.

The thiourea (3.5 g, 0.01 mol) and MeI (7.1 g, 0.05 mol) were stirred for 1 h at room temperature. The mixture was evaporated below 30 °C and the residue was stirred with MeOH–KOH (40 ml, 6.72 g) for 4 h. After removal of the solvent by distillation, ice–water (10 ml) was added and the mixture was extracted with

Table 4. Physical and analytical data for compounds 2–14

Compound	M.p. (°C)	Yield (%)	Formula	Mol. weight	Required/found (%) C	H	N
2	65–67	85	$C_{14}H_{13}NO$	211.27	79.59/79.68	6.20/6.22	6.63/6.60
3	139–141	80	$C_{14}H_{19}NO$	217.31	77.38/77.29	8.81/8.93	6.45/6.43
4	154–156	65	$C_{14}H_{17}NO$	215.30	78.10/78.21	7.96/7.87	6.51/6.60
5	116–118	72	$C_{22}H_{24}NO$	318.44	82.98/82.99	7.60/7.64	4.40/4.28
6	126–128	69	$C_{22}H_{22}NO$	316.43	83.51/83.45	7.01/7.19	4.43/4.55
7	108–110	42	$C_{21}H_{22}N_2O$	318.42	79.21/78.33	6.69/7.11	9.00/8.87
8	103–106	38	$C_{21}H_{20}N_2O$	316.41	79.72/79.67	6.37/6.41	8.85/8.90
9	223–225	45	$C_{15}H_{17}NO_2$	243.31	74.05/74.15	7.04/6.94	5.76/5.80
10	220–222	35	$C_{15}H_{15}NO_2$	241.29	74.67/74.57	6.27/6.21	5.80/5.78
11	248–250	48	$C_{15}H_{17}NOS$	259.37	69.46/68.39	6.61/6.54	5.40/5.53
12	225–228	42	$C_{15}H_{15}NOS$	257.35	70.00/70.15	5.88/5.64	5.44/5.40
13	218–220	38	$C_{16}H_{19}NO_2$	257.33	74.68/74.70	7.44/7.36	4.28/4.21
14	219–221	35	$C_{17}H_{21}NO_2$	271.36	75.25/75.15	7.80/7.67	5.16/5.03

$CHCl_3$ (3 × 20 ml). After washing with water and drying (Na_2SO_4), the solvent was evaporated off and the residue was crystallized from EtOH. Data for compounds **7** and **8** are listed in Table 4.

Preparation of 5,8-methano-*r*-4-phenyl-*c*-4a,*c*-5,6,7,*c*-8,*c*-8a-hexahydro- (9) and -*c*-4a,*c*-5,*c*-8,*c*-8a-tetrahydro-4*H*-1,3-benzoxazin-2(3*H*)-ones (10)

Ethyl chloroformate (0.54 g, 5 mmol) was added dropwise to a mixture of amino alcohol **3** or **4** (1.09 or 1.1 g, 5 mmol), $NaHCO_3$ (0.42 g, 5 mmol) and water (5 ml). The mixture was stirred and refluxed for 10 min, then evaporated. The residue was extracted with diethyl ether (3 × 10 ml) and the extract was washed with water, dried (Na_2SO_4) and evaporated. The residue was heated with EtONa (25 mg) in an oil-bath (120 °C, 5 min), then extracted with EtOAc (3 × 15 ml). The extracts were combined and the solvent was evaporated. The residue was transferred on to a silica gel column (Kieselgel 60; 0.063–0.2 mm) and eluted with EtOAc. After evaporation of the solvent the residue was crystallized. Data for compounds **9** and **10** are listed in Table 4.

Preparation of 5,8-methano-*r*-4-phenyl-*c*-4a,*c*-5,6,7,*c*-8,*c*-8a-hexahydro- (11) and -*c*-4a,*c*-5,*c*-8,*c*-8a-tetrahydro-4*H*-1,3-benzoxazine-2(3*H*)-thiones (12)

Amino alcohol **3** or **4** (2.2 g, 1.0165 moi) in an aqueous solution (10 ml) of KOH (1.1 g) was cooled to 0 °C and stirred with CS_2 (1.3 g) in dioxane (8 ml) for 5 min. KOH (0.55 g) in water (10 ml) and then an aqueous solution (30 ml) of lead(II) nitrate (5.5 g) were added, followed by stirring at 60 °C for 10 min. The PbS was filtered off, washed with hot water and extracted with hot EtOH. The filtrate and the ethanolic extract were combined and evaporated to dryness. The residue gave colourless crystals from EtOH. Data for compounds **11** and **12** are listed in Table 4.

Preparation of 6,9-methano-*r*-5-phenyl-*c*-5a,*c*-6,7,8,*c*-9,*c*-9a-hexahydro-1,4-benzoxazepin-3(4*H*)-one (13) and the 2-methyl derivative (14)

To a solution of amino alcohol **3** (2.2 g, 0.01 mol) in benzene (20 ml), ethyl chloroacetate (1.22 g, 0.01 mol) or ethyl chloropropionate (1.37 g, 0.01 mol) and an oily suspension of NaH in benzene (80%, 0.3 g, 12 mol) were added dropwise with stirring. After 10 min, the mixture was refluxed (1 h) and then cooled. Benzene (50 ml) was added and the mixture was washed with cold 5% HCl (30 ml) and water (30 ml). The benzene solution was dried (Na_2SO_4) and evaporated to dryness, and the residue was transferred on to a silica gel column, then eluted with benzene (**13**) or EtOAc (**14**). The residue of the eluate was crystallized from acetonitrile (**13**) or EtOAc (**14**). Data for compounds **13** and **14** are listed in Table 4.

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