Configuration and NMR Study of Tricyclic Oxazines Fused to a Norbornene or Norbornane Skeleton†

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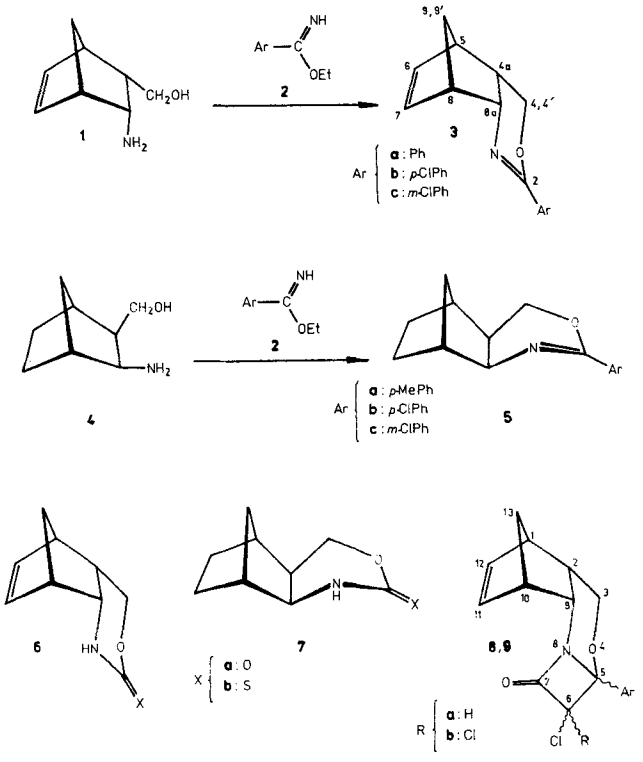
Tricyclic oxazines fused with norbornene or norbornane were synthesized for pharmacological and stereochemical purposes. Analogous oxazin-2-ones and -2-thiones were also obtained. The *diendo* or *diexo* anellation of the hetero ring to the norbornene or norbornane skeleton was confirmed by ^1H and ^{13}C spectral data. The assignment of the proton signals was proved and the proton–proton coupling values were determined by double resonance experiments. With mono- and dichloroacetyl chloride, the oxazines fused to norbornene gave azetidinones which are mixtures of two isomers. The mixtures were separated into homogeneous substances, the configuration and conformation of which were determined via differential NOE experiments.

INTRODUCTION

Numerous partly or fully saturated quinazolines and 1,3-benzoxazines have been previously synthesized and have proved to have anti-inflammatory and analgesic activity.[2–4] A norbornane derivative was recently found which had beta-adrenergic neuron-blocking activity;[5] the fusion of these two structures into tricyclic compounds, therefore, seemed to be very promising as a source of new pharmacologically active substances.

endo-2-Amino-*endo*-3-hydroxymethylbicyclo[2.2.1]-hept-5-ene (**1**) and *exo*-2-amino-*exo*-3-hydroxy-methylbicyclo[2.2.1]heptane (**4**) were reacted with arylimino ethers (**2**) to yield fused tricyclic *diendo*- and *diexo*-3,1-oxazines **3** and **5**, respectively (Scheme 1). Reaction of the amino alcohols **1** and **4** with ethyl chloroformate and sodium methylate, or with CS_2–KOH and $Pb(NO_3)_2$, leads to the analogous 3,1-oxazin-2-ones (**6a**, **7a**) and oxazine-2-thiones (**6b**, **7b**), respectively.[6a]

Azetidinones were produced on the reaction of **3b** with chloroacetyl chloride or dichloroacetyl chloride. Both products were mixtures of two isomers (**8** and **9**). The isomeric mixtures were separated into homogeneous substances.[6b]



Scheme 1

PROTON RESONANCE SPECTRA

The presumed *diendo* and *diexo* configurations of the tricyclic compounds **3** and **5**, respectively, were proved by ^1H NMR spectroscopy. As examples, the spectra of the *p*-chlorophenyl derivatives **3b** and **5b** are presented in Figs 1 and 2, respectively. In the 250 MHz spectrum of **3b**, in order of decreasing magnetic field (Table 1), the AB multiplet of the bridging methylene group appears first, slightly broadened by the 5,9, 5,9′, 8,9 and 8,9′ couplings, followed by the H-4a multiplet and the singlet-like signal of the anellated protons H-5

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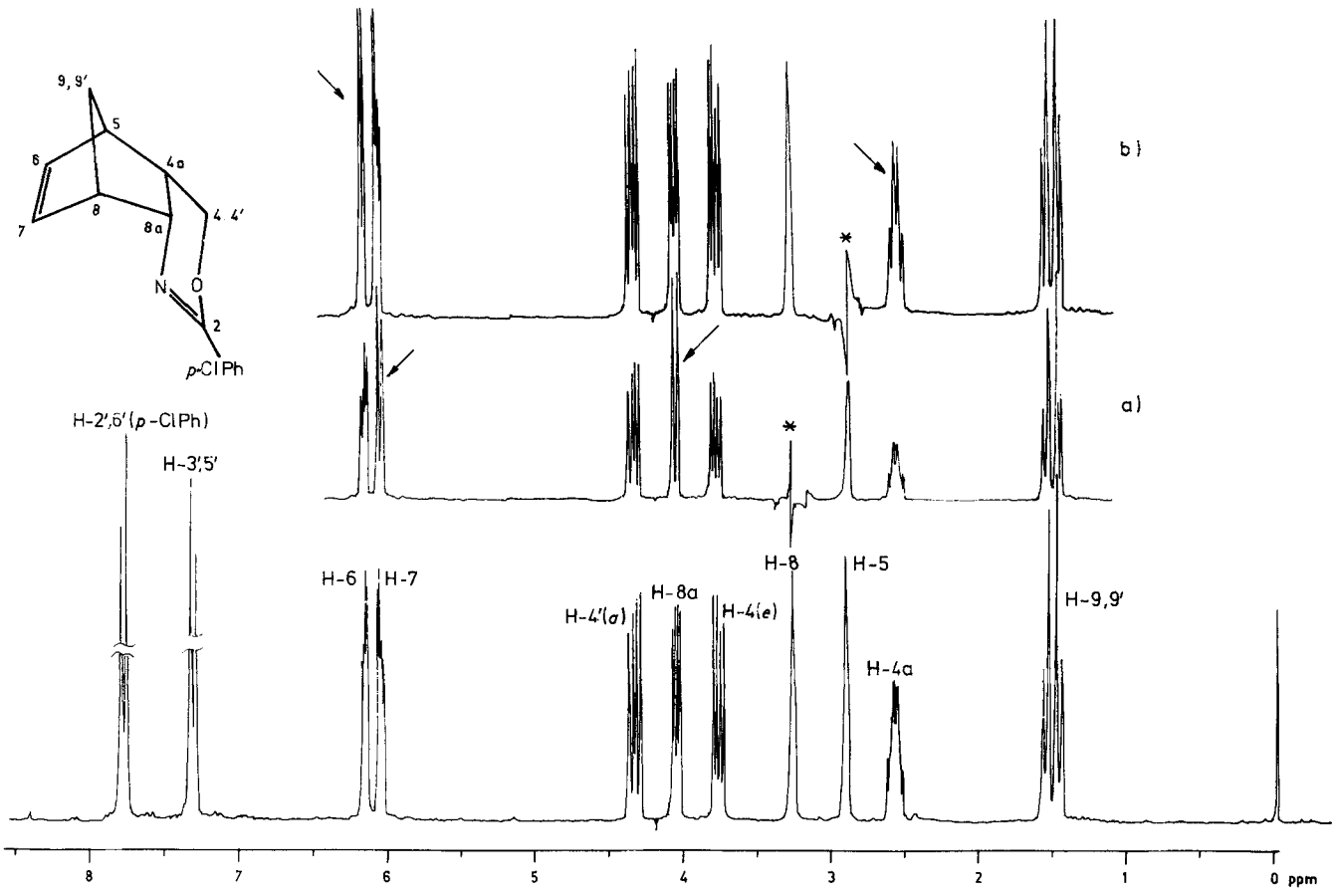


Figure 1. ^{1}H NMR spectrum of **3b** at 250 MHz. Double resonance spectra, saturating the H-8 (a) and H-5 (b) signals, respectively. * Saturated signal; ↘ signal changed by saturation.

and H-8. The next three double doublets can be assigned to H-4, H-8a and H-4'. The multiplets of the olefinic H-6 and H-7 and those of the aromatic protons appear at lowest fields.

The correct assignment of the 5,8, 4,4' and 6,7 signal pairs was helped by double-resonance experiments. On saturation of the anellated (5 or 8) proton at lower field the upfield olefinic signal and the H-8a signal were simplified (Fig. 1a). On the other hand, on saturation of the upfield signal the downfield olefinic multiplet and the H-4a signal became simpler (Fig. 1b), proving that δH-5 < δH-8 and δH-6 > δH-7.

The assignment of the double doublets corresponding to H-4 and H-4' poses a further problem, as the use of the relationships[7a] $\delta H_a < \delta H_e$ and $J_{a,a} > J_{a,e}$, which are generally valid for cyclohexanes and their hetero analogues, leads to opposite conclusions.

There are two stable conformations of **3b**, arising from the flexibility of the hetero ring (Scheme 2). In conformer **A** the dihedral angles of the C—H-4a and

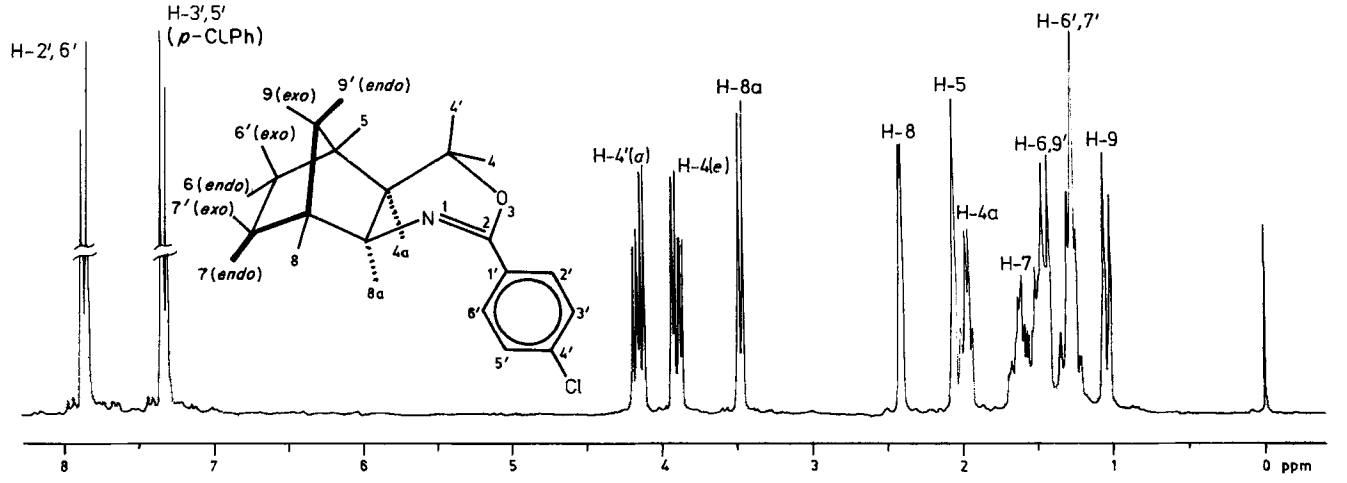


Figure 2. ^{1}H NMR spectrum of **5b** at 250 MHz.

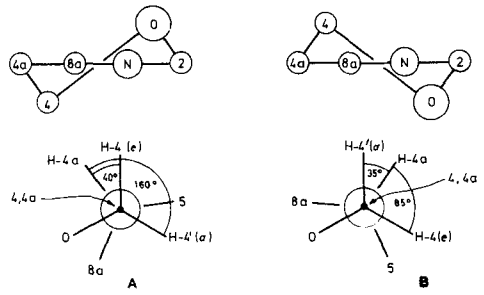
Table 1. ^{1}H NMR chemical shifts ($\delta_{TMS} = 0$ ppm) of compounds 3a–c, 5a–c, 6a,b–9a,b

Compound	δH-4(e) 2×d	δH-4′(a) 2×d	δH-4a m	δH-5 ~s	δH-6 m[a]	δH-7 m[a]	δH-8 ~s	δH-8a 2×d,d[b]	δH-9′ endo	δH-9 exo	δArH or δNH	
3a	3.76	4.32	2.55	2.88	6.13	6.05	3.27	4.05	1.54	1.64	7.35[c]	7.85[d]
3b	3.77	4.33	2.59	2.90	6.14	6.04	3.25	4.05	1.47	1.56	7.30[e]	7.77[e]
3c	3.72	4.26	2.53	2.85	6.11	6.03	3.24	4.03	1.43	1.53	H-5′: 7.21t,[f] H-6′: 7.71[d,f]	H-4′: 7.31d[f] H-2′: 7.84~s
5a[g]	3.86	4.11	1.93	2.02	~1.25,[h] ~1.5, 1.6[i]		2.42	3.46	~1.5	1.02	7.13[e]	7.80[e]
5b	3.89	4.15	1.97	2.05	~1.3,[h] ~1.5		2.40	3.47	1.45	1.04	7.31[e]	7.84[e]
5c	3.88	4.13	1.95	2.03	1.25[h] ~1.5, 1.6[i]		2.40	3.47	1.45	1.03	H-5′: 7.25t,[f] H-6′: 7.78d[f]	H-4′: 7.34d[f] H-2′: 7.92~s
6a	4.30	3.91	~2.65	2.91	6.27	6.15	3.05	3.98	1.41	1.57	~6.65s, broad	
6b	4.40	3.95	2.81	3.00	6.27	6.19	3.19	3.94	1.44	1.61	~8.9s, broad	
7a	4.27	3.90	~2.1	~2.10	~1.15,[h] ~1.55[j]		2.26	3.35	1.75	1.25	~6.85s, broad	
7b	4.34	4.00	2.25	2.18	~1.3,[h] ~1.6[j]		2.43	3.40	1.65	1.25	~9.0s, broad	
8a[k]	4.18	3.32	2.61	2.74	5.72	5.66	3.09	4.37	1.35	1.50	7.20–7.45m (4H)	
8b	4.37	3.47	2.64	2.78	5.75	5.52	3.07	4.48	1.36	1.50	7.20–7.40m (4H)	
9a[k]	3.88	3.64	2.10	2.88	~6.30s (2H)		3.69	3.95	1.27	1.60	7.30–7.50m (4H)	
9b	4.03	3.68	2.34	2.88	6.25	6.40	3.62	3.80	1.28	1.66	7.40s (4H)	

[a] ~2×d (A and B parts of an ABXY multiplet) of 2H intensity in the case of **3a–c**, **6a,b**, **8a,b** and **9a,b**; 2 or 3 multiplets (AB and CD or A, B and CD parts of an ABCDXY multiplet) of 4H intensity in the case of **5a–c** and **7a,b**.
[b] 2×d in the case of **3a–3c**, **6a**, **6b**, **8a**, **8b** and **9a**, **9b**; d in the case of **5a–5c** and **7a**, **7b**.
[c,d] A (*meta*), B (*para*) and X (*ortho*) parts of an AA′BXX′ multiplet: 2×m (3+2H).
[e] A(H-3′, 5′) and B(H-2′, 6′) parts of an AA′BB′ multiplet, *J*(AB): 8.6 Hz.
[f] $J(4', 5') \approx J(5', 6') \approx 8$ Hz.
[g] δCH_3: 2.34s (3H).
[h] *endo* H-6, 7 (see text).
[i] *exo* H-7 (see text).
[j] *exo* H-6, 7.
[k] δH-11 = 4.87 (**8a**) and 4.77 ppm (**9a**).

C—H-4 or C—H-4a and C—H-4′ bonds, which are ~40° and ~160° respectively, would suggest well split signals and $J(4a, 4') > J(4a, 4)$. On the other hand, in conformer **B**, the corresponding dihedral angles are ~35° and ~85°, and thus one of the couplings would be expected to be <1 Hz. Since the measured couplings are rather high (~6 Hz and ~7 Hz, see Table 2) conformation **A** is presumed to predominate, resulting in the unusual relationship $\delta H-4'(a) > \delta H-4(e)$. This anomaly may be caused by the anisotropy of the aromatic ring, which is coplanar with the C—H-4′ bond, and which considerably deshields the axial H-4′.

The *diendo* anellation of the hetero ring in **3a–c** is proved by the value of ~4 Hz for the 8,8a couplings, corresponding to a dihedral angle of ~50°. In the event of *diexo* anellation this angle would be ~90°. In accordance with the above, in the case of **5a–c** for which the *diexo* structure was predicted (see Fig. 2 and Table 2), the H-8a signal was a doublet, i.e. $J(8, 8a) < 1$ Hz.



Scheme 2

The partially saturated analogues **5** of **3a–c** exhibit characteristically different chemical shifts compared with those of **3a–c**. Thus, as a consequence of the absence of the neighbouring double bond, H-5,8 in **5a–c** are more shielded by approximately 0.85 ppm than in **3a–c**. For similar reasons, owing to the anisotropy of the saturated C—C bonds causing shielding and to the lack of the opposite effect of the C=C bond, the *exo* H-9 in **5a–c** is also more shielded (an upfield shift of the corresponding signal by 0.5–0.6 ppm was observed). In the case of the *endo* H-9′ the analogous shielding is compensated for by the anisotropy of the nearby C=N double bond, causing deshielding on the hydrogen above it. For the shifts of the methylene

Table 2. Vicinal proton–proton couplings (in Hz) of compounds 3a–c, 5a–c, 6a,b–9a,b

Compound	J(4, 4′)	J(4, 4a)	J(4′, 4a)	J(4a, 8a)	J(5, 6)	J(6, 7)	J(7, 8)	J(8, 8a)	J(9, 9′)
3a	11.2	5.8	7.0	8.9	3.0	5.6	3.0	4.0	8.6
3b	11.2	5.8	7.0	8.8	2.9	5.6	3.0	4.0	8.6
3c	11.1	5.8	7.1	8.8	3.0	5.5	3.0	3.9	8.5
5a	11.1	4.9	6.3	7.7				<1	10.3
5b	11.1	4.8	6.4	7.7				<1	10.4
5c	11.1	4.8	6.4	7.7				<1	10.4
6a	11.4	5.6	6.1	11	2.9	5.6	2.9	5.7	8.9
6b	11.5	6.0	6.5	10.0	2.8	5.6	2.8	4.2	9.1
7a	11.2	6.6	7.6	8.1				<1	10.6
7b	11.4	6.4	6.5	8.2				<1	10.9
8a	12.2	8.0	9.7	9.8	2.7	5.6	2.7	3.5	9.0
8b	12.4	7.2	7.3	9.9	3.0	5.7	3.0	3.6	9.0
9a	12.4	5.1	6.7	9.0				3.7	9.0
9b	12.0	6.2	9.3	8.8	3.0	5.7	2.9	3.6	9.0

protons in the hetero ring, the unusual relationship $\delta H_e < \delta H_a$ still holds, but the shift difference, $\Delta\delta_{e,a}$, is reduced from ~0.55 to ~0.25 ppm.

The H-6,6′,7,7′ complex multiplet separates into three groups: two hydrogens have a common multiplet at approximately 1.3 ppm, one of the other two has a signal at about 1.5 and the other at ~1.6 ppm. For norbornane[8a] the *endo* H-6,7 atoms are more shielded; consequently, the signal at ~1.3 ppm can be assigned to the *endo* H-6,7. This is supported by the downfield shift of one of the *exo* signals, due to the anisotropy of the C=N bond. The *exo* H-7′ is the nearest to the nitrogen and, thus, the downfield multiplet at ~1.6 ppm can be assigned to this proton.

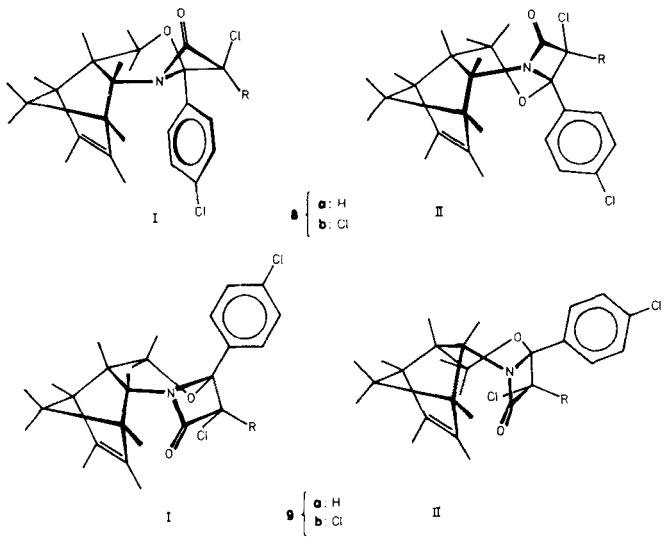
H-4a and H-8a are also more shielded, by about 0.55 ppm. This can be partly explained by the removal of the anisotropic olefinic bond present in **3a–c**, resulting in an upfield shift of the H-4a and H-8a signals and to a more significant extent, by the change in position of these hydrogens (from quasi-equatorial to quasi-axial) with respect to the cyclohexane ring.

The spectra of **6a,b** and **7a,b** are very similar to those of **3a–c** and **5a–c**, respectively, as they have analogous skeletons. The only essential difference is the restored normal relationship $\delta H_e > \delta H_a$ for the H-4,4′ methylene protons, as proved by the 4,4a and 4′,4a couplings. This supports our assumption concerning the origin of the irregularity (the anisotropy of the phenyl ring) in **3a–c** and **5a–c**, which disappears on replacement of the phenylimino group by an amide or thioamide group. A slight downfield shift of almost all signals is observed in the thiourethanes as compared with their urethane pairs (**6a,b** and **7a,b**), due to the stronger electron affinity of the thiooxo group (cf., e.g. Ref. 7b). This effect is overcompensated by the stronger anisotropic shielding of the thiooxo bond for H-8a in **6b** and H-9′ in **7b**.

The coupling constants are also similar to those measured for the phenylimino analogues with identical skeletons (i.e. **6a,b** and **3a–c**, and **7a,b** and **5a–c** display similar couplings). The higher electron density around H-8a (due to the neighbouring NH group instead of the imino nitrogen with its stronger $-I$ effect) is revealed in the higher values of the 4a,8a and 8,8a couplings. (This is not significant in **7a,b** of course, proving the *exo* anellation of the hetero ring.)

STEREOSTRUCTURE OF THE AZETIDINONES

For the dichloro derivative two isomers **8b** and **9b**, differing in the anellation of the oxazine and the azetidinone ring (i.e. differing in the configuration at C-2) can arise, while in the monochloro compounds two further isomers, differing in the mutual position of the chlorine and of the phenyl ring, are possible (Scheme 3). [Compound **8b** is *rel*-(2*R*, 5*S*, 9*R*)- and **9b** is *rel*-(2*R*, 5*R*, 9*R*)-8-aza-6,6-dichloro-5-(*p*-chlorophenyl)-4-oxatetracyclo[8.2.1.0.0]tridec-11-en-7-one. This numbering of the azetidinones according to IUPAC (Scheme 1) is not identical with that used in the text, figures, tables or Scheme 2, for ease of comparison of spectroscopically analogous atoms in **3**, **5–7**, and **8**, **9**,



Scheme 3

respectively. The relative configurations of the four monochloroazetidinones are 2*R*, 5*R*, 6*R*, 9*R*; 2*R*, 5*R*, 6*S*, 9*R* = **8a**; 2*R*, 5*S*, 6*R*, 9*R* = **9a** and 2*R*, 5*S*, 6*S*, 9*R*.] In addition to the configuration, the conformation of the flexible oxazine ring must also be considered.

Differentiation of structures **8** and **9** is based on the changes in the chemical shifts of the olefinic protons compared with **3b**. These shifts decrease significantly in compounds **8a** and **8b** (Table 1). This can be explained by the anisotropy of the phenyl ring near the olefinic protons (~3 Å) in structure **8a** and **8b**.

Regarding the conformation, the values of the 4,4a and 4′,4a couplings are the deciding factor. In conformation I the corresponding dihedral angles are ~35° and ~160°, while in II they are ~40° and ~90°, respectively. As the corresponding coupling constants of **8a** are 9.7 and 8.0 Hz (Table 2), the preferred conformation is I. It should be noted that, for the same reason, conformation II should be taken into account in isomer **9a**. Here H-7 and C=O, and H-4′(a) and the *endo* chlorine atoms are near each other, but no sign of such a situation is observed in the spectrum. The magnitudes of the 4,4a and 4′,4a couplings point to the fact that the anomalous δH-4(e) < δH-4′(a) chemical shift relationship in **3b** is normalized here: δH-4(e) = 4.18 ppm and δH-4′(a) = 3.32 ppm. Consequently, compared with **3b**, the H-4 signal of **8a** is shifted by 0.4 ppm downfield, and the H-4′ signal by 1 ppm in the opposite direction. This significant increase in the shielding of H-4′ is also caused by the anisotropic effect of the aromatic ring, giving additional proof of conformation I. In conformation II, the anisotropic effect would appear in the signal of H-7, but not for those of H-6 and H-4′.

In the spectra of the two isolated dichloro compounds (Figs 3a and 4a) the H-8a signal appears unchanged as a double doublet, as in the cases of **3b** and **8a**. Consequently, the *diendo* anellation of the norbornene skeleton and the hetero ring is unaltered, as predictable. Thus, only structures **8b** and **9b**, differing in the anellation of the azetidinone ring, need be taken into consideration. From analogous spectral

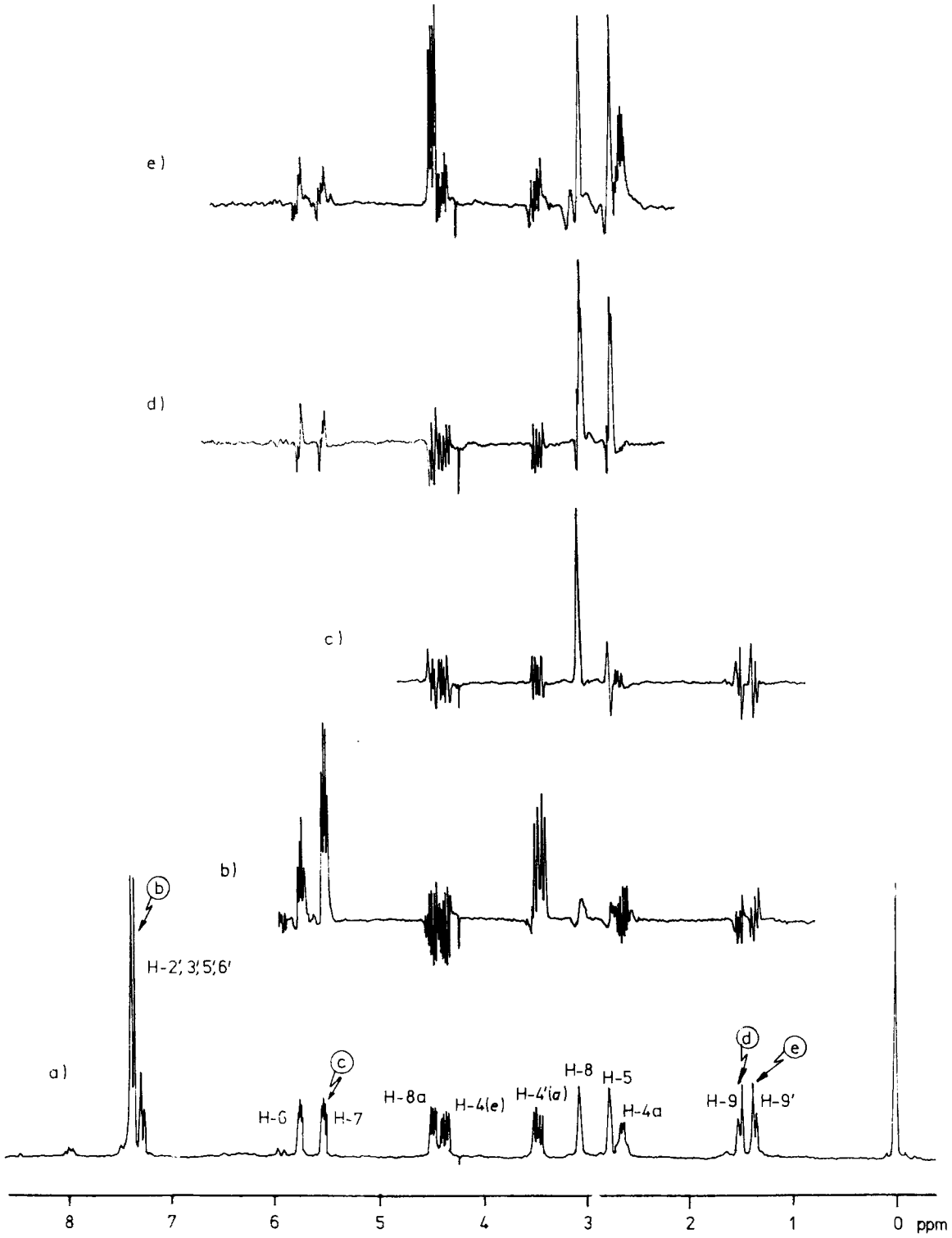


Figure 3. ^{1}H NMR spectrum of **8b** at 250 MHz (a). Differential NOE experiments, saturating the H-2',3',5',6' (b), H-7 (c), H-9 (d) and H-9' (e) signals, respectively.

data for the monochloro derivative **8a**, one isomer has an **8b**-type structure and the I-type conformation, while the other one has a **9b** structure similar to **9a** and conformation II. This is verified by the following facts:

1. The shielding of H-6,7 in **9b** does not increase, but decreases compared with that of **3b**. The 0.4 ppm downfield shift of the H-7 signals is caused by the proximity of the carbonyl oxygen.

2. Conformation II is proved by the values of the 4',4a and 4,4a couplings (9.3 and 6.2 Hz for **9b** and 7.3 and 7.2 Hz for **8b**).

3. H-8a in **9b** is shielded by 0.7 and 0.6 ppm compared with **8b** and **8a** having conformation I, where the anisotropy of the carbonyl group (which is much closer to H-8a) causes a downfield shift of the H-8a signal. Owing to the mutual positions of H-8a and the carbonyl group in conformation II of structure **9b**, this effect manifested itself as an opposite shift.

4. The 4,4'-methylene hydrogens of **9b** are shielded

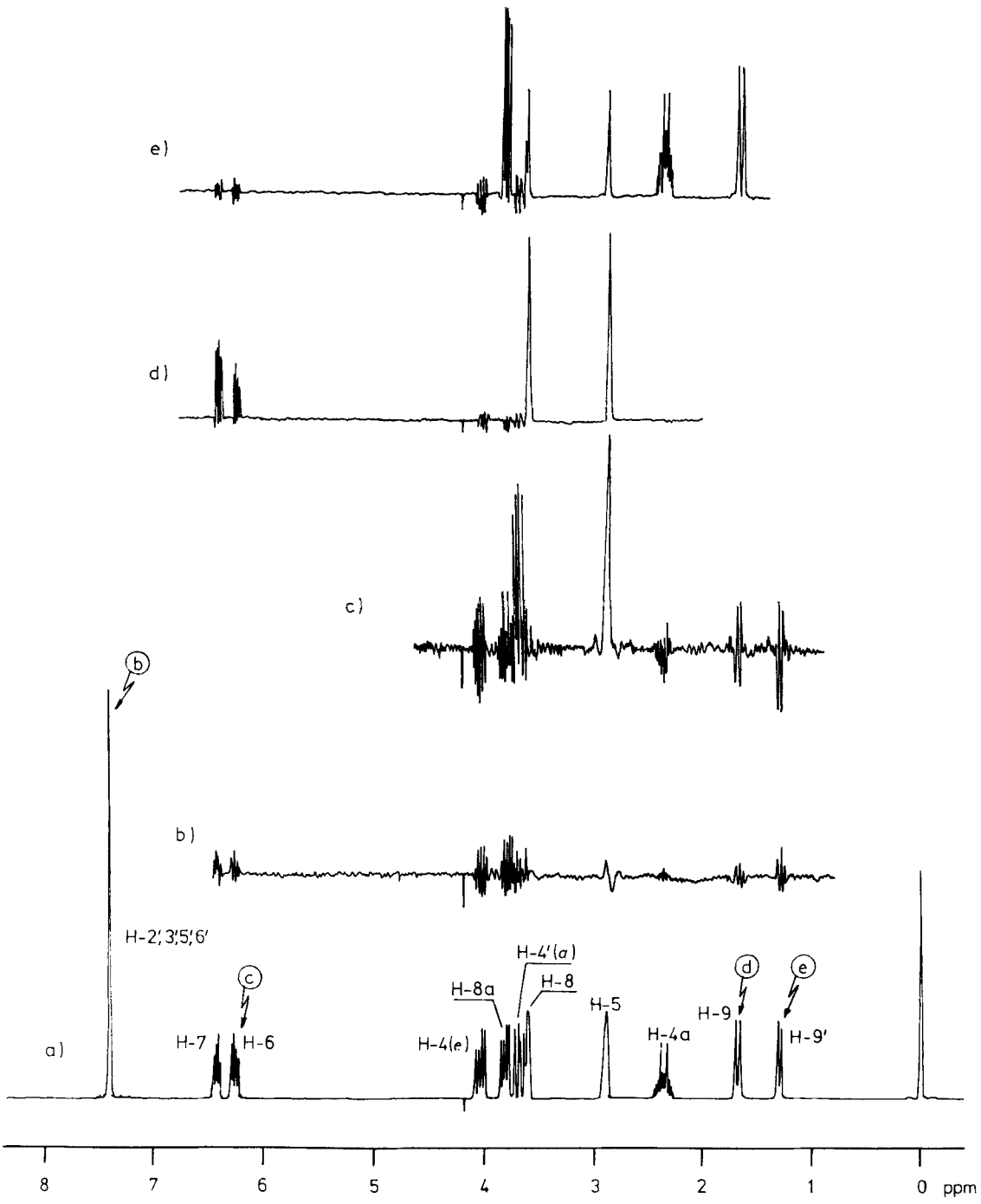


Figure 4. ^{1}H NMR spectrum of **9b** at 250 MHz (a). Differential NOE experiments, saturating the H-2',3',5',6' (b), H-6 (c), H-9 (d) and H-9' (e) signals, respectively.

by the anisotropy of the four-membered ring and that of the C—Cl bond. In the case of H-4' this does not compensate for the strong shielding effect of the phenyl ring operative in **8b**. Consequently, H-4 is more shielded while H-4' is deshielded compared with **8b**, but the H-4' signal in **9b** is more shielded than that of **3b**. Thus, in **9b**, the normal relationship δH-4(e) > δH-4'(a) is again observed, but the difference $\Delta\delta$H-4,4' decreases.

The postulated configuration and conformation of the azetidinones were unambiguously proved by differential NOE experiments. The same technique was used to confirm the assignment of the 4,4', 9,9', 5,8 and 6,7 signal pairs.

On saturation of the aromatic protons, no change in intensity of any signal was observed in **9b**, while the same experiment on **8b** led to increases in the intensities of the H-7 and H-4'(a) signals and, to a smaller degree, also in that of H-6 (Figs 4b and 3b). These results demonstrate that H-4',6,7 and the phenyl ring are sterically close in **8b**, while the opposite situation is valid for **9b**, corresponding to the hypothetical configurations and conformations mentioned above.

On irradiation of the upfield doublet of the H-9,9' signal, the H-4a,5,8,8a signals become stronger (Figs 3e and 4e), suggesting the assignment of this doublet to the *endo* H-9'. In accordance with this observation, the saturation of the downfield part of the AB signal

increased the intensities of the H-5,8 signals only (Figs 3d and 4d). Due to the anisotropy of the phenyl ring and the carbonyl bond in **8b** (conformation I) and in **9b** (II), the relationships δH-7 < δH-6 (**8b**) and δH-7 > δH-6 (**9b**) are plausible. When the upfield olefinic signal of **8b** (δH-7) and of **9b** (δH-6) was irradiated, the differential NOE showed increased intensities for H-8 and for H-5,4′, respectively, proving the proposed assignments and steric structures (Figs 3c and 4c).

The close similarity of the chemical shifts and coupling constants of the pairs **8a**, **8b** and **9a**, **9b** is evidence for their analogous structures, including the conformations.

^{13}C NMR SPECTRA (TABLE 3)

The *diendo* and *diexo* structures of the molecules are well manifested by the ^{13}C data of **3a–c** and **5a–c**. As compared with the *diendo* compounds **3a–c**, in the *diexo* forms of **5a–c** C-4a and C-9 are more shielded because of the steric hindrance between the hetero ring and the norbornane skeleton: the mean values of 46.7 and 39.0 ppm decrease by 5.5 and 5.0 ppm, respectively (γ-effect, steric compression shift).[9] Naturally, the shielding of C-5 and C-8 also increases (by ~5.3 and ~4.0 ppm) due to the different α-effect of the —CH_2—CH_2— group which has replaced the olefinic bond,[8b] and the C-6,7 signals also move from the region characteristic of olefins to that for saturated methylene carbons.

The C-8a shift changes in the opposite manner, downfield from the ~55.6 ppm value for **3a–c** to ~58.8 ppm in the analogues **5a–c**. This indicates that for the C-4a and C-9 signals the downfield shift caused by the β-effect[10] is overshadowed by the γ-effect, c.f. with the shifts of the anellated carbons in norbornane and norbornene, respectively.[8c] In the case of C-8a the γ-effect also operates in **3a–c**, due to the steric hindrance between H-8 and the lone pair of the nitrogen. Consequently, the isolated differences in the β-effect of the olefinic and saturated C-6,7 atoms in **3a–c** and **5a–c**, respectively, can be observed.

There is no significant difference between the C-2 and C-4 shifts of **3a–c** and **5a–c**, or in any of the other shifts of **6a,b** and **7a,b** compared with their **3a–c** and **5a–c** analogues (except, naturally, that for the C-2 signal and, to a smaller extent, that of the vicinal C-4 signal). The small downfield shift of the C-4 signal originates from the stronger $-I$ effect of the urethane or thiourethane group compared with that of the phenylimino ether group. C-2 of the thiocarbonyl group in **6b** and **7b** is extremely strongly deshielded, which is characteristic for this functional group (cf. e.g. Ref. 7c).

In the spectra of the azetidinones, the C-2 signal appears at approximately 92 ppm. Except for this signal, as expected, only the C-8a shift changes substantially compared with **3a–c** and **6a,b**. The spectra of the isomeric pairs **8a–9a** and **8b–9b** do not differ significantly: the steric hindrance caused by the phenyl ring in **8a,b** is substituted by the similar effect of the azetidinone ring in **9a,b**.

In **9b** the carbon signals of the C=O and C-7 (which are spatially very close) shift upfield from 166.2 to 159.8 ppm, and from 136.7 to 135.0 ppm, respectively, relative to **8b**. The more crowded structure **9b** compared with **8b** is manifested by the upfield shifts of the C-2, C-5, C-8 and C-8a signals.

The hindered rotation of the phenyl ring in **8b** is unambiguous proof of the assumed structure. As a consequence of the hindered rotation, the C-2′,6′ and

Table 3. ^{13}C NMR chemical shifts ($\delta_{TMS} = 0$ ppm) of compounds 3a–c, 5a–c, and 6a,b–9a,b

Compound	C-2	C-4	C-4a[a]	C-5[a]	C-6[b]	C-7[b]	C-8[a]	C-8a	C-9	Other signals
3a	156.4	66.1	46.6	47.8	135.5	134.7	48.5	55.4	38.9	C-1′ = 134.2, C-2′,6′ = 127.0,[c] C-3′,5′ = 127.7,[c] C-4′ = 129.9
3b	155.7	66.5	46.8	48.2	135.7	135.1	48.7	55.7	39.1	C-1′ = 136.5, C-2′,6′ = 128.2,[c] C-3′,5′ = 128.6,[c] C-4′ = 132.9
3c	155.3	66.4	46.8	48.1	135.7	135.0	48.6	55.8	39.1	C-1′ = 136.2, C-2′ = 130.1,[c] C-3′ = 134.2, C-4′ = 127.3, C-5′ = 125.3, C-6′ = 129.1[c]
5a	157.3	66.6	41.2	42.8	30.0	26.8	44.6	58.8	34.0	C-1′ = 131.7, C-2′,6′ = 127.2,[c] C-3′,5′ = 128.7,[c] C-4′ = 140.4, CH_3 = 21.3
5b	156.0	66.6	41.1	42.6	29.9	26.8	44.5	58.8	33.9	C-1′ = 136.5, C-2′,6′ = 128.1,[c], C-3′,5′ = 128.6,[c] C-4′ = 132.8
5c	156.3	66.8	41.2	42.7	30.0	26.9	44.6	58.9	34.0	C-1′ = 136.2, C-2′ = 130.4,[c] C-3′ = 134.4, C-4′ = 127.5, C-5′ = 125.3, C-6′ = 129.2[c]
6a	157.2	67.9	45.9	48.3	136.7	133.9	48.4	54.1	38.3	
6b	190.3	69.5	45.7	47.9	136.5	133.8	48.1	54.2	38.1	
7a	157.4	68.2	39.5	40.5	28.8	25.1	43.8	57.1	32.7	
7b	190.9	69.4	39.9	40.5	28.8	25.0	43.6	57.7	33.1	
8a	90.5	65.5	44.4	47.7	136.0	136.7	48.5	52.4	35.0	C-1′ = 139.1, C-2′,6′ = 128.3,[c] C-3′,5′ = 128.8,[c] C-4′ = 134.0, C-10 = 66.1, C=O = 168.2
8b	93.1	65.5	44.8	47.2	135.8	136.7	49.2	53.0	35.7	C-1′ = 135.6, C-2′,6′ = 127.5, 127.8,[c,d] C-3′,5′ = 128.8, 131.0,[c,d] C-4′ = 134.0, C-10 = 89.7, C=O = 166.2
9a	89.1	66.3	46.3	47.1	135.7[e]		47.7	53.6	36.3	C-1′ = 135.4, C-2′,6′ = 128.8,[c] C-3,′5′ = 128.9,[c] C-4′ = 133.8, C-10 = 64.9, C=O = 162.2
9b	92.0	66.4	45.7	45.9	135.8	135.0	48.0	52.7	39.3	C-1′ = ?, C-2′,6′ = 128.5,[c] C-3′,5′ = 128.8,[c] C-4′ = 134.0, C-10 = ?, C=O = 159.8

[a,b,c] An alternative assignment is also possible.
[d] The C-2′,6′ and C-3′,5′ signals are split owing to hindered rotation of the benzene ring in **8b**.
[e] Two overlapping signals.

C-3',5' pairs are chemically non-equivalent and their signals are split.

As this phenomenon does not appear in the monochloro compound **8a** formed as the main product, we presume that the phenyl ring and the chlorine atom are in the *trans* position.

EXPERIMENTAL

The syntheses and chemical study of the compounds investigated will be published elsewhere.[6a,b] The elemental analysis data are in good agreement (±0.1%) with the theoretical values. M.p.s (uncorrected) are as follows (°C): 104–105 (**3a**), 41–42 (**3b**), 61–63 (**3c**), 82–84 (**5a**), 49–51 (**5b**), 61–62 (**5c**), 62–64 (**6a**), 136–138, decomp. (**6b**), 89–91 (**7a**) 147–149, decomp. (**7b**), 180–182 (**8a**), 137–139 (**8b**), 146–148 (**9a**) and 194–195 (**9b**).

The ^{1}H and ^{13}C NMR spectra were recorded in 5 and in 5 or 10 mm tubes, respectively, at room temperature on a Bruker WM-250 FT spectrometer at 250.13 and 62.9 MHz, respectively, in $CDCl_3$ solution using the deuterium of the solvent as the lock and TMS as the internal standard. The most important measuring parameters of the ^{1}H and ^{13}C NMR spectra are as follows: sweep width, 5 and 15–16 kHz; pulse width, 1 and 15–19 μs (~20° and ~65–80° flip angle); acquisition time, 1.64 and 1.02–1.08 s; number of scans, 2–4 and 2^{10}–2^{14}; computer memory, 16 and 32K. Complete proton noise decoupling (~3 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). Conventional CW irradiation of approximately 0.15 W was used for the double resonance experiments. NOE-difference experiments were performed with the Bruker microprogramme 12.5 in the Aspect 2000 pulse programmer. Gated decoupling to generate NOE was used with a delay time of 30 s and a decoupling power of 40 mW: number of scans, 32; relaxation delay, 0.1 s; dummy scans, 2.

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