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Substituent Chemical Shifts in NMR

Part 4*—^{1}H SCS in Some 2-Substituted Norbornanes and Bornanes

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The ^{1}H chemical shifts and substituent chemical shifts (SCS) were recorded for several monosubstituted norbornanes and bornanes. The observed substituent effects are generally similar for the two ring systems, but differ considerably from those observed for the cyclohexanoid systems in steroids. A consistent trend for the eclipsed C-2—C-3 fragment in this ring system is that all the substituents produce the largest SCS on the *trans* oriented proton, rather than the spatially nearer *cis* oriented proton. Indeed, for the OH substituent these SCS are opposite in sign, that for the *cis* oriented proton being negative (i.e. to high field). This trend is not observed in the cyclohexane system, in which the distance dependence of the vicinal SCS is as expected. The major cross-ring SCS are of the 2-*endo* substituents with the C-6 protons, giving a large positive SCS at the 6n proton and a small negative SCS at the 6x proton. This trend is very similar to that observed in the cyclohexane ring (axial–axial SCS), and suggests a similar electric field mechanism.

KEY WORDS Norbornanes Bornanes ^{1}H NMR Substituent chemical shifts

INTRODUCTION

Previous parts of this series[1–3] have been concerned with the analysis and assignment of the proton spectrum of some rigid molecules with one substituent, in order to obtain the substituent chemical shifts (SCS) of all the protons in these molecules. These data might be of interest in the quantitative evaluation and calculation of proton SCS.

The proton spectra and geometries of the parent molecules norbornene, norbornane and adamantane were obtained[1] and subsequently the full analysis of the proton spectra of some bromo[2] and cyano[3] derivatives of these molecules was presented. This led to the deduction of the SCS of these groups at every proton in the molecule, and mere inspection of these data showed that present theories of proton SCS[4,5] failed to explain these effects.

It was felt that comparative data for a wider range of substituent groups may be of value in identifying the major factors responsible for proton SCS in these molecules, and we report here the analysis and assignments of the proton spectra of some monosubstituted chloro-, iodo-, hydroxy- and keto-norbornanes and also the corresponding bornanes, together with the analysis of the parent compound bornane. These results, taken together with the previous results in this series, allow the deduction of the proton SCS for a variety of substituent groups in the norbornane and bornane series in both the *exo* and *endo* positions. These SCS are compared both within the bicycloheptane series and also with analogous data for the cyclohexane[6,7] and steroid[8,9] ring systems.

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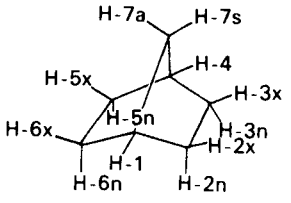
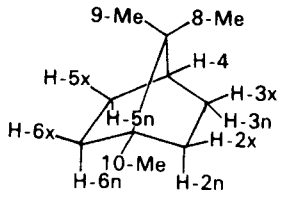
ASSIGNMENT OF THE SPECTRA



Norbornane



Bornane

Bornane

The proton spectrum of bornane has been reported previously[10] together with the spectra of a number of substituted bornanes, but these studies were at 60 MHz and thus could not resolve the majority of the ring proton resonances. Indeed, the studies were concentrated on the methyl proton chemical shifts, all of which coalesce in the parent compound at δ 0.83. The spectrum of this molecule at 250 MHz is not first order (Fig. 1), and the methyl resonances are still unresolved. The remainder of the spectrum consists of two large multiplets at *ca.* 1.20 ppm (with an integration of four protons) and a large downfield multiplet at 1.70 ppm which, on closer examination, consists of two complex multiplets (integration of two protons for each multiplet) separated by a triplet at 1.60 ppm. With the aid of a ^{1}H–^{13}C 2D correlated spectrum and the ^{13}C NMR assignment of Grutzner *et al.*,[11] a full analysis was completed. Analysis of this 2D spectrum reveals a correlation between C-4 and the triplet at 1.60 ppm. This triplet can thus be assigned to the bridgehead proton H-4 which couples to H-3x and H-5x [J(4, 3x)

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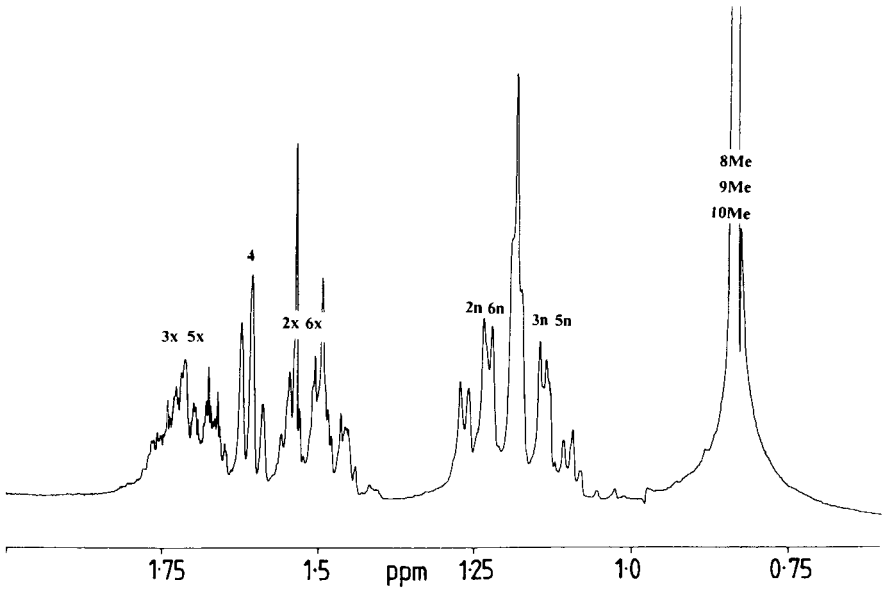

Figure 1. 250-MHz ^{1}H NMR spectrum of bornane.

= J(4, 5x) = 4.4 Hz]; this is in agreement with previously observed couplings for bridgehead protons.[2] Correlation can also be seen between C-2, C-6 and the multiplet at *ca.* 1.50 ppm and also to the downfield half of the multiplet at *ca.* 1.18 ppm. The C-3 and C-5 carbons couple to the multiplet at *ca.* 1.70 ppm and also to the upfield part of the multiplet at *ca.* 1.18 ppm. The two correlations observed for each carbon are to their respective *endo* and *exo* protons. By comparison with norbornane,[1] where the signals of the *exo* protons are downfield of those of the *endo* protons, the upfield multiplet at *ca.* 1.18 ppm can be assigned to the *endo* resonances H-2n, H-6n (1.23 ppm) and H-3n, H-5n (1.13 ppm). The multiplet at 1.71 ppm can be attributed to H-3x, H-5x and the multiplet at 1.49 ppm to H-2x, H-6x, showing the large shielding effect of the bridgehead methyl.

Exo derivatives

2-*exo*-Norbornyl chloride. The spectrum at 250 MHz (Fig. 2(A)), despite not being first order, is relatively easy to assign owing to the similarities with the 2-*exo*-bromo derivative.[2] The assignments of H-2, H-1 and H-4 follow from the bromo assignment. The large multiplet at 1.70–2.00 ppm is due to three protons (by integration), which by comparison with previous assignments can be assumed to be due to H-3n, H-3x and H-7s. The quartet of doublets clearly visible on the downfield side of the multiplet can be assigned to H-3n [J(3n, 3x) = 13.9 Hz, J(3n, 2n) = 7.1 Hz, J(3n, 7a) = 2.1 Hz]. This splitting pattern is characteristic of the H-3n resonance in monosubstituted *exo* derivatives.[3,12] The remainder of the multiplet, consisting of the two resonances H-7s and H-3x, on closer examination reveals a doublet of quintets on the upfield side which can be assigned to H-7s, with a large coupling to H-7a [J(7s, 7a) = −10.0 Hz] and smaller couplings to H-1, H-4 and H-6n, H-5n giving this characteristic splitting pattern. The H-3x resonance can hence be assigned to the centre of the multiplet at 1.80 ppm and H-6x and H-5x to 1.61 and 1.47 ppm, respectively, by comparison with the bromo derivative. The doublet of quintets at 1.24 ppm is characteristic of an H-7 resonance in *exo* derivatives and hence can be assigned to H-7a, coupling to H-7s, H-1 and H-4 [J(7a, 4) = 1.4 Hz]. The final multiplet at *ca.* 1.10 ppm (with an integration of 2) is due to the overlap of the two remaining unassigned resonances, H-6n and H-5n. The splitting pattern of this multiplet suggests, by comparison with that of the individual resonances of H-6n and H-5n, that one resonance can be assigned to the upfield part of the multiplet (1.07 ppm) and one to the downfield part (1.14 ppm). Comparison with previous assignments in the bromo derivative indicates that the upfield resonance is that of H-5n and the downfield resonance H-6n.

2-*exo*-Norbornyl iodide. At 250 MHz, like that of the chloro derivative, the spectrum is not completely first order (Fig. 2(B). The low-field complex doublet at 3.98 ppm is the H-2n resonance, with a large coupling to H-3n [J(2n, 3n) = 7.7 Hz]. The large doublet at 2.60 ppm is from the bridgehead H-1 proton, which is deshielded rather more by the C-2 iodo substituent than by the chloro substituent. The multiplet at 2.24 ppm (with an integration of 2) arises from the overlap of the signals of the bridgehead proton H-4 and of H-3x which, like H-1, has been deshielded by the C-2 iodo substituent.

The protons H-3n, H-7s which formed the large multiplet at *ca.* 1.80 ppm in the chloro derivative are now clearly resolved upfield of the H-3x signal. The quartet of triplets at 2.11 ppm can be attributed to H-3n, coupling to H-3x [J(3n, 3x) = 15.7 Hz], H-2n, H-7a and unlike the chloro and bromo derivative (where the splitting pattern was a quartet of doublets) to another resonance, probably that of H-4. This is

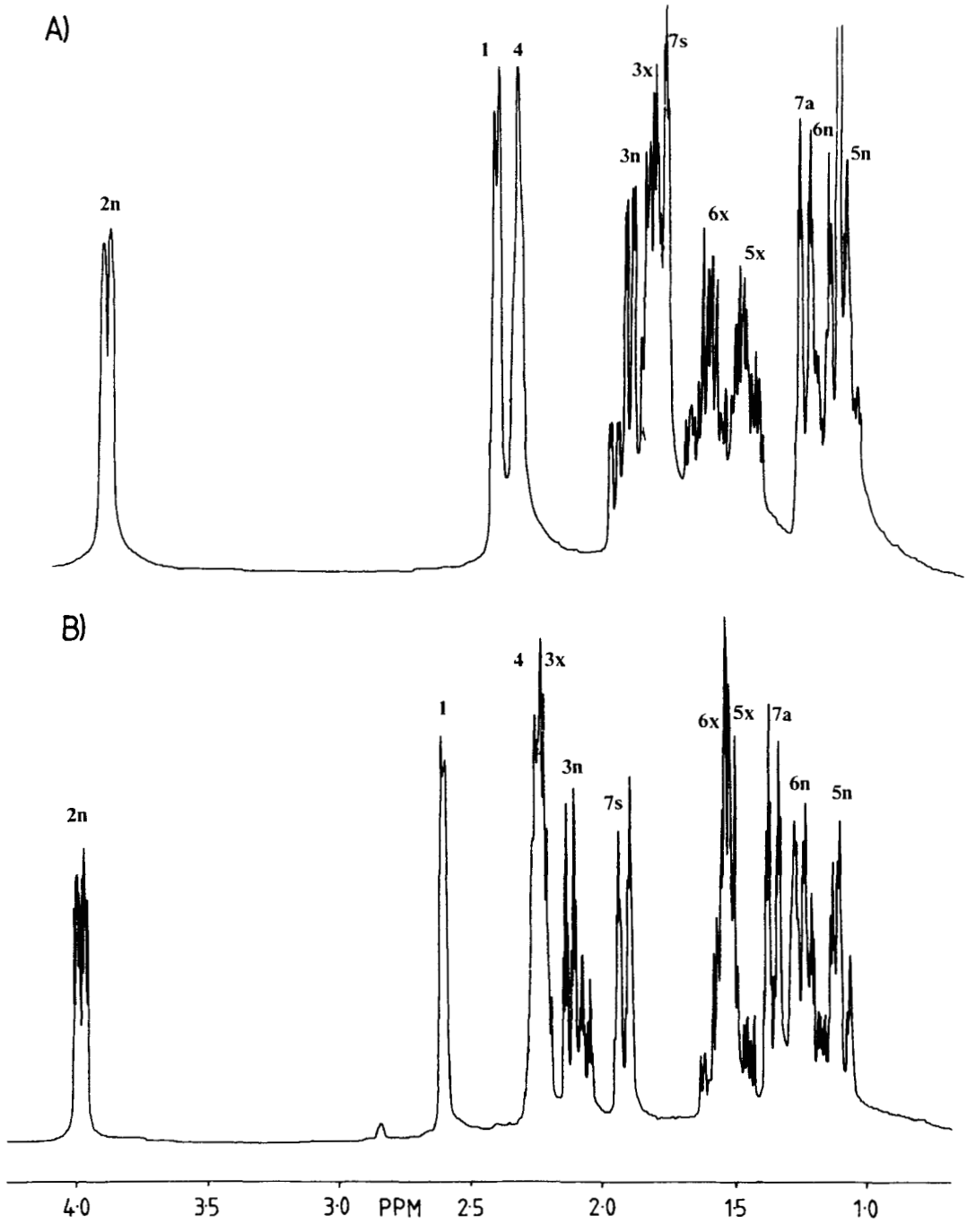

Figure 2. 250-MHz ^{1}H NMR spectra of (A) 2-*exo*-norbornyl chloride and (B) 2-*exo*-norbornyl iodide.

probably due to virtual coupling, as H-3x and H-4 are very strong coupled. The doublet of quintets (1.92 ppm) can be easily assigned to H-7s, the large coupling being to H-7a [J(7s, 7a) = −10.0 Hz]. The multiplet at *ca.* 1.50 ppm from two protons can be attributed to the merger of the H-6x and H-5x signals, the former being assigned to low field of the latter (1.57 and 1.49 ppm) from the splitting pattern and by comparison of the relative shifts in the analogous chloro and bromo derivatives. The remaining three resonances are first order and can be attributed to H-7a 1.35 ppm, H-6n 1.23 ppm and H-5n 1.10 ppm.

2-*exo*-Bornyl alcohol (isoborneol). The spectrum at 500 MHz (Fig. 3) of the *exo* alcohol is very complex. The downfield resonance at 3.60 ppm can be assigned to H-2n. On removal of the CH–OH coupling (D_2O shake), the H-2n resonance becomes a quartet, coupling to H-3n and H-3x only [J(2n, 3n) = 7.4 Hz, J(2n, 3x) = 4.0 Hz]. The multiplet at *ca.* 1.75 ppm has an integration of four. Using the observed SCS values for *exo*-norborneol[12] and the chemical shifts for bornane, the resonances constituting this large multiplet are assigned as H-3n, H-3x, H-4 and H-5x; this is in agreement with the chemical shifts obtained using lanthanide shift techniques.[13] On decoupling H-2n, the upfield part of the multiplet remains unaffected and hence, owing to its complexity, can be assigned to H-5x (1.66 ppm). The H-4 resonance is also unaffected by decoupling H-2n but has the characteristic triplet at 1.72 ppm. The

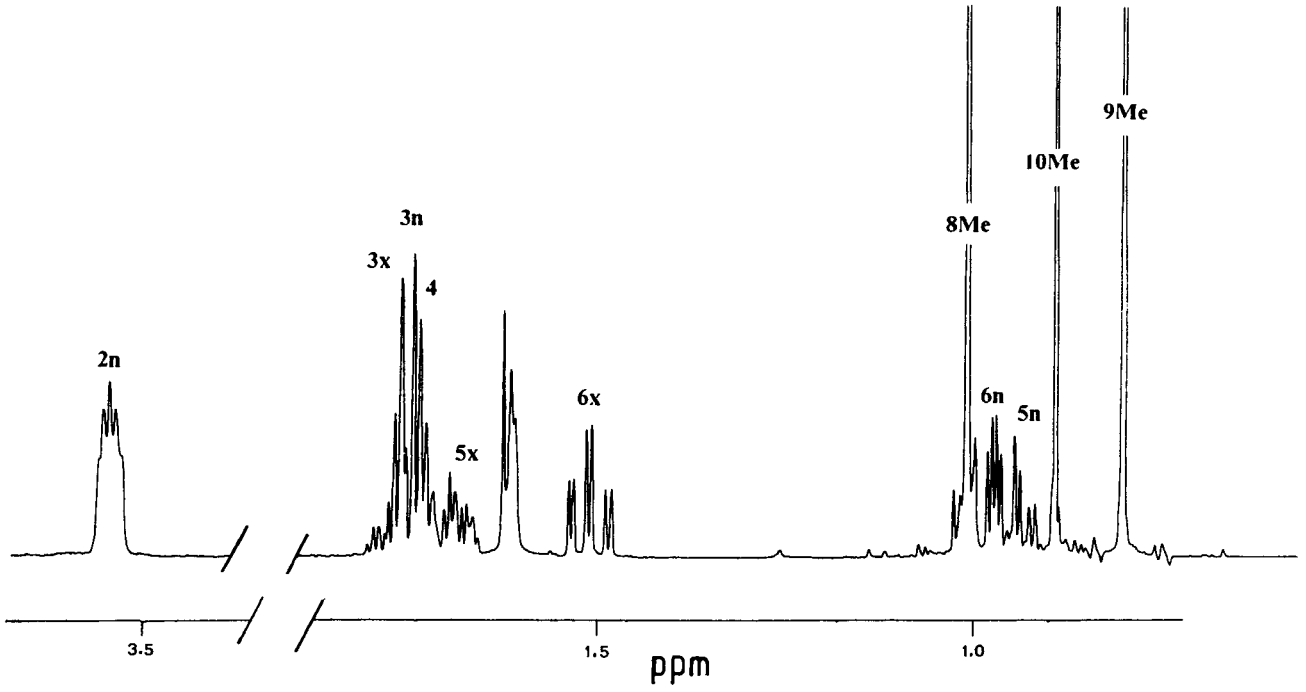

Figure 3. 500-MHz ^{1}H NMR spectrum of isoborneol.

remainder of the multiplet is significantly altered by decoupling H-2n, confirming the presence of H-3n and H-3x (no other resonance is affected by decoupling H-2n). Liu,[13] from the extrapolation of the lanthanide-shifted spectrum back to zero concentration of lanthanide, predicted these chemical shifts as 1.74 (H-3x) and 1.69 (H-3n). Using this assignment together with the observed splitting pattern (Fig. 3) gives an estimate of the observed shifts as 1.75 (H-3x) and 1.739 (H-3n), in good agreement with Liu's extrapolated figures. The triplet of doublets at 1.50 ppm can be assigned to H-6x using the SCS value. This is verified by the splitting pattern, which consists of the two virtually identical couplings to H-5x and H-6n giving the deceptively simple triplet structure, and a smaller coupling to H-5n [J_{av}(6x, 6n) = 12.0 Hz, J_{av}(6x, 5x) = 12.0 Hz and J(6x, 5n) = 3.5 Hz]. The remaining multiplet at *ca.* 1.0 ppm is due to H-6n and H-5n (SCS predicted values are 1.10 and 0.97 ppm, respectively), and on this basis and the observed splitting pattern we assign the signal of H-6n (1.01) to low field of that of H-5n (0.96).

Endo substituents

2-*endo*-Norbornyl alcohol. The analysis of this spectrum (Fig. 4) was aided considerably by the previous assignment of the *endo*-cyano derivative.[3] The complex pattern at 4.23 ppm is due to H-2x [J(2x, 3x) = 10.2 Hz, J(2x, 3n) = 3.4 Hz], and the two triplets at 2.25 and 2.17 ppm are due to the two bridgehead protons H-1 and H-4. By comparison with the cyano derivative the downfield signal can be assigned to H-1. Analysis of the COSY plot confirms, by the correlation to H-2x, that the assignment is correct. The H-2x proton couples to two other protons (Fig. 4), which give a large multiplet at *ca.* 1.9 ppm (integration of 2) and a doublet of triplets at 0.84 ppm. Comparison with *endo*-cyanonorbornane suggests that the large multiplet comprises H-3x and H-6n; correlation of the downfield part of this multiplet to H-4 and to H-2n assigns H-3x at 1.95 ppm, and hence H-6n absorbs as the upfield half at 1.87 ppm. The upfield doublet of triplets at 0.84 ppm (H-3n) couples to H-2x, H-3x and H-7a [J(3n, 3x) = 12.9 Hz, J(3n, 2x) = J(3n, 7a) = 3.4 Hz]. The multiplet at 1.57 ppm can be assigned to H-5x by the large correlation to H-4 and small correlations to H-6n and H-3x. The remaining large multiplet at *ca.* 1.34 ppm has an integration of 4 and can be attributed to H-7a, H-7s, H-6x and H-5n. Expansion of this multiplet reveals a doublet of quintets on the upfield side involving coupling to H-3n, indicating that the resonance is due to H-7a (a 'w' coupling). The downfield part of the multiplet has a large coupling to H-5x and can be assigned to either 6x or 5n.

Unfortunately, no correlation is seen to H-2x (expected 'w' coupling) and the small correlation to H-1 is not conclusive. The H-7s resonance can be assigned to the large central peaks in the multiplet (1.34 ppm) and the two remaining protons, H-6x and H-5n, are assigned at 1.36 and 1.34 ppm, respectively, by comparison with other *endo* derivatives (see later).

2-*endo*-Bornyl alcohol (1-borneol). Despite much interest in this molecule in connection with the LIS technique,[12,13] no complete proton assignment has been given. The spectrum at 250 MHz (Fig. 5) is almost first order except for the resonance at *ca.* 1.25 ppm (integration of two protons). The methyl resonances at 0.87, 0.86 and 0.85 ppm can be assigned following Liu[13] to 9-Me, 8-Me and 10-Me, respectively. The doublet at 4.00 ppm can be immediately assigned to H-2x [J(2x, 3x) = 9.5 Hz, J(2x, 3n) = 3.5 Hz]. From COSY DQF one can see three correlations to H-2x, two large couplings to resonances at *ca.* 2.25 and 0.95 ppm and a small coupling to

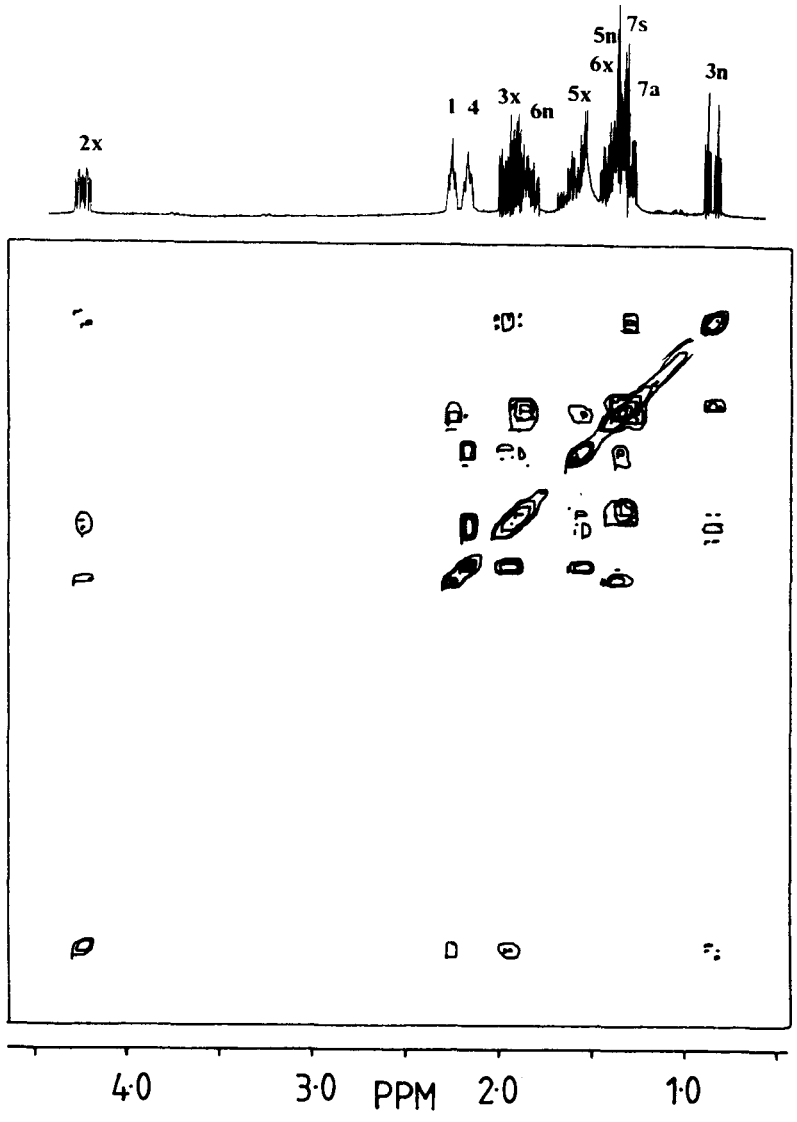

Figure 4. 250-MHz $^1H/^1H$ COSY for 2-*endo*-norborneol.

a resonance at 1.23 ppm. The small coupling is a 'w' coupling to H-6x and the two large couplings are to H-3n and H-3x. Comparison with the *endo*-norborneol chemical shifts confirms the doublet of doublets as the H-3n resonance (a characteristic pattern for H-3n in *endo*-bornane derivatives), coupling to H-3x and H-2x [J(3n, 2x) = 3.45 Hz and J(3n, 3x) = 13.35 Hz], which also assigns H-3x at 2.3 ppm. H-3x is involved in coupling with the characteristic H-4 triplet at 1.60 ppm [J(4, 5x), J(4, 3x) = 4.50 Hz), confirming the assignment for H-3x. This resonance in turn couples to a multiplet at 1.73 ppm which can be assigned as H-5x. The remaining large multiplet (integration of 2) at 1.23 ppm is due to the H-6x and H-5n resonances, confirmed by correlations to H-2x, H-6n and H-5x. The small width of this multiplet suggests that both resonances have the same chemical shift, 1.24 ppm.

2-*endo*-Bornyl chloride. This spectrum was obtained at 250 and 500 MHz. The spectrum of bornyl chloride at 250 MHz (Fig. 6(A)), like that of the alcohol, is not completely resolved but at 500 MHz the proton resonances are separated. The methyl resonances at 0.93 and 0.88 ppm (integration of 6) can be assigned as to 10-Me and 8-Me and 9-Me, respectively, and the doublet of quartets at 4.17 ppm to H-2x. Here, all the couplings for H-2x can be obtained, J(2x, 3n) = 4.3 Hz, J(2x, 5x) = 2.5 Hz, J(2x, 3x) = 10.5 Hz. The multiplet at 2.45 ppm is from H-3x which couples to four other protons H-4, H-2x, H-3n and H-5x [J(3x, 3n) = 13.8 Hz, J(3x, 4) = 4.6 Hz and J(3x, 5x) = 3.4 Hz], and those at 2.07 and 1.75 ppm can be assigned to H-6n and H-5x, respectively. The characteristic triplet of the H-4 proton can clearly be seen, just upfield of the H-5x resonance, at 1.68 ppm. On decoupling this triplet, a loss of coupling is observed for H-3x and H-5x, confirming their assignments. The remaining multiplet at 1.30 ppm has an integration of three protons. The large doublet of doublets clearly visible on the downfield side of the resonance can be instantly assigned to H-3n. The remaining part of the multiplet can be assigned to the two resonances H-6x and H-5n, which can be fully resolved at higher fields. Analysis of the couplings of the two resonances confirms H-5n to absorb upfield of H-6x at 1.27 and 1.34 ppm, respectively [J(5n, 5x) = 11.8 Hz, J(5n, 6x) = 9.2 Hz, J(5n, 6n) = 4.2 Hz].

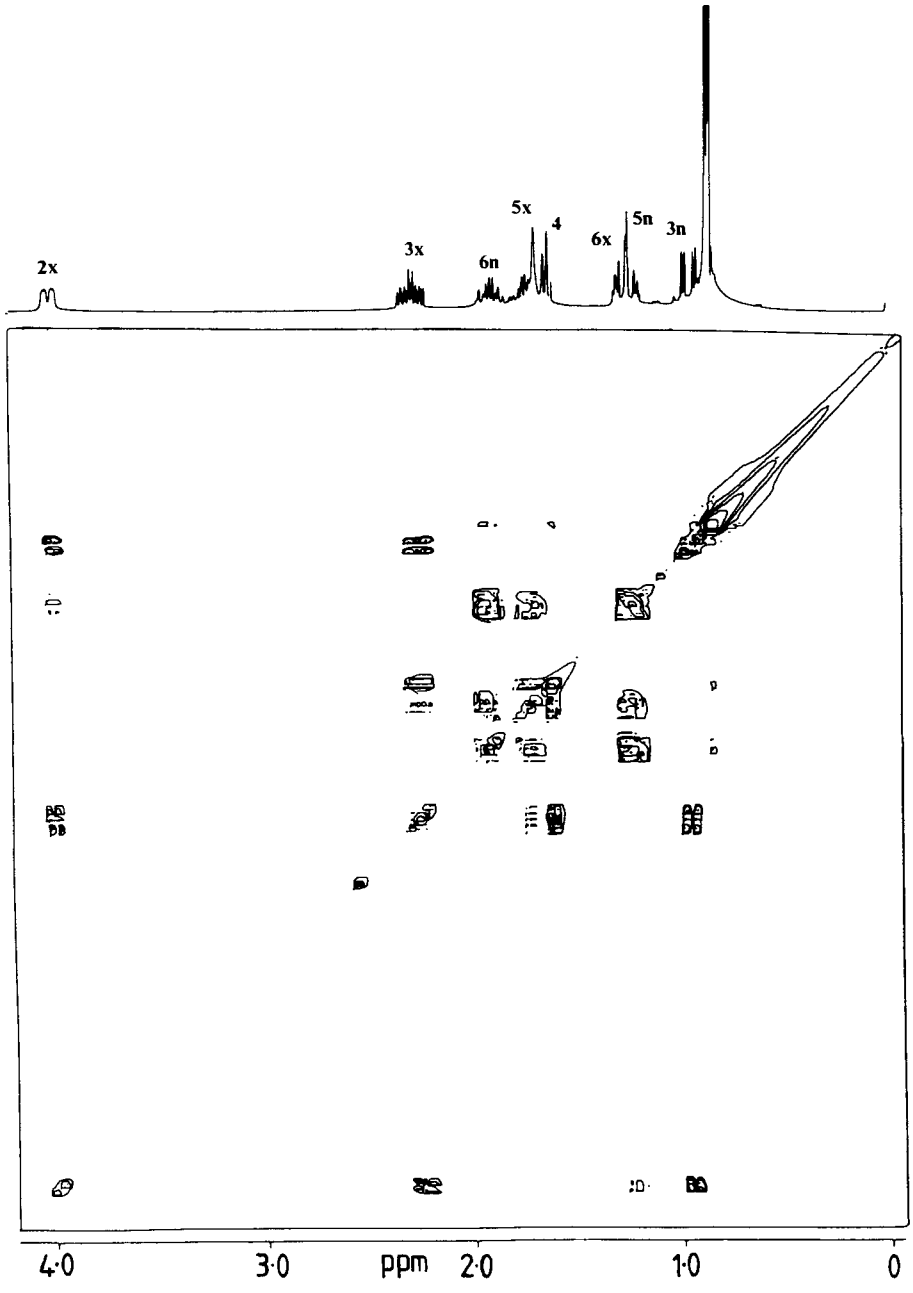

Figure 5. 250-MHz ^{1}H/^{1}H DQF COSY for 1-borneol.

2-*endo*-Bornyl bromide. The spectrum of the bromo derivative (Fig. 6(B)) is very similar to that of the chloro derivative except that at 250 MHz it is virtually completely first order. The assignment follows by direct comparison with the chloro derivative. The H-2x resonance at 4.32 ppm is involved in coupling with H-3n, H-3x and H-6x [J(2x, 6x) = 2.7 Hz, J(2x, 3n) = 4.5 Hz, J(2x, 3x) = 10.6 Hz]. The quartet of quartets at 2.46 ppm is the H-3x resonance [J(3x, 3n) = 14.0 Hz, J(3x, 5x) = 3.8 Hz]. H-6n can be assigned to the multiplet at 2.07 ppm, H-5x to the multiplet at 1.75 ppm, and H-4 to the triplet at 1.66 ppm [J(4, 5x) = J(4, 3x) = 4.5 Hz]. The remaining three resonances are easily assignable since the bromo substituent has deshielded H-3n and H-6x, separating these resonances from that of the H-5n resonance, 1.53 ppm, 1.42 ppm and 1.27 ppm, respectively. The additional fine structure in the H-6x resonance (coupling to H-2x) compared with that of H-5n is clearly visible.

2-Norbornanone (norcamphor)

The full analysis of the ketone has been previously performed at low field (100 MHz) in a polydeuteration study by Marshall and Walter.[14] In order to obtain chemical shifts under standard conditions, the ^{1}H NMR spectrum was recorded at 500 MHz (Fig. 7). Even at this high field the spectrum is not completely first order. The bridgehead protons are assigned as H-1, H-4 at 2.59 and 2.67 ppm, respectively, the quartet at 2.06 ppm to H-3x and the quartet at 1.83 ppm to H-3n. The multiplet upfield of this resonance is due to the H-6x and H-5x signals overlapping at 1.77 ppm. The doublet of quintets at 1.73 is the H-7s resonance, and the remaining resonances for H-7a, H-6n, H-5n are not fully resolved. On decoupling either of the bridgehead resonances the H-7a resonance becomes more visible and has a chemical shift at 1.56 ppm. The H-6n resonance (1.53 ppm) can be seen slightly overlapping with that of H-7a,

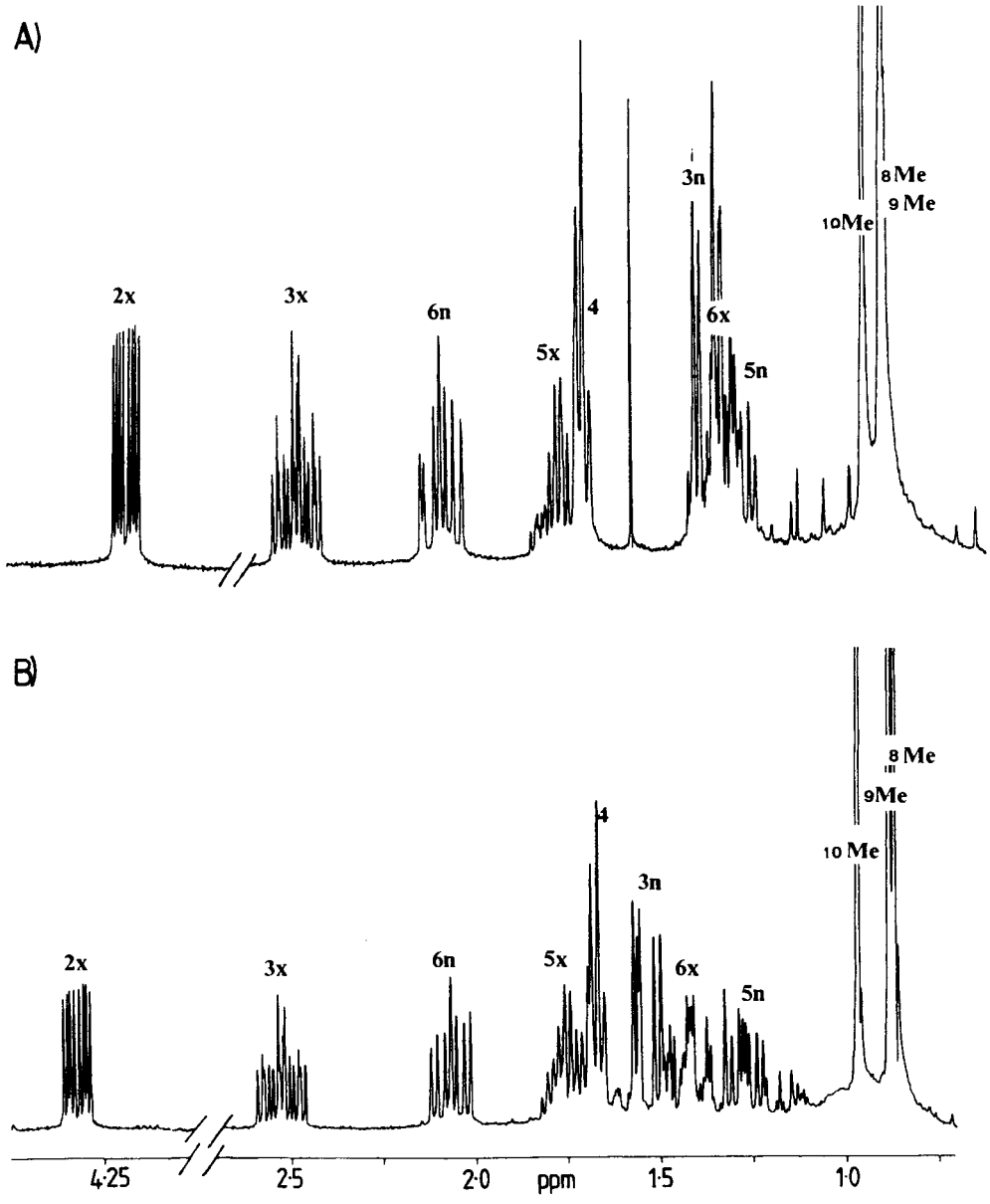

Figure 6. 250-MHz ^{1}H NMR spectra of (A) 2-*endo*-bornyl chloride and (B) 2-*endo*-bornyl bromide.

with the H-5n resonance further upfield at 1.45 ppm. The above assignments were verified with the aid of a COSY at 360 MHz and by decoupling experiments. The assignments are in agreement with those of Marshall and Walter[14] but the actual chemical shifts are considerably different, presumably owing to the concentrated solutions used in reference 14.

2-Bornanone (camphor)

The assignment of the proton chemical shifts for 2-bornanone (camphor) has been given recently at high field, with the aid of multipulse techniques.[15] In order to record the chemical shifts in similar conditions to the previous derivatives the spectra of the ketone was recorded at 360 MHz. The chemical shifts obtained are again significantly different from those of reference 15, who used concentrated (100 mgm/ml) solutions in CD_3OD. However they are identical to those of Demarco *et al.*,[16] who also used dilute $CDCl_3$ solutions at 220 MHz, but did not provide any evidence for their assignments.

DISCUSSION

The results of the spectral analyses are collected in Tables 1–4, which also include pertinent data from Refs 1–3 for comparison. The first-order coupling constants obtained from these spectra are in accord with previous measurements for these ring systems[1–3] and are not tabulated here, as no complete analysis has been performed on these spectra.

However, the analyses do enable the SCS for both *endo* and *exo* substituents in the norbornane and bornane system to be derived for a range of substituents, and these are given in Tables 3 and 4. Analogous

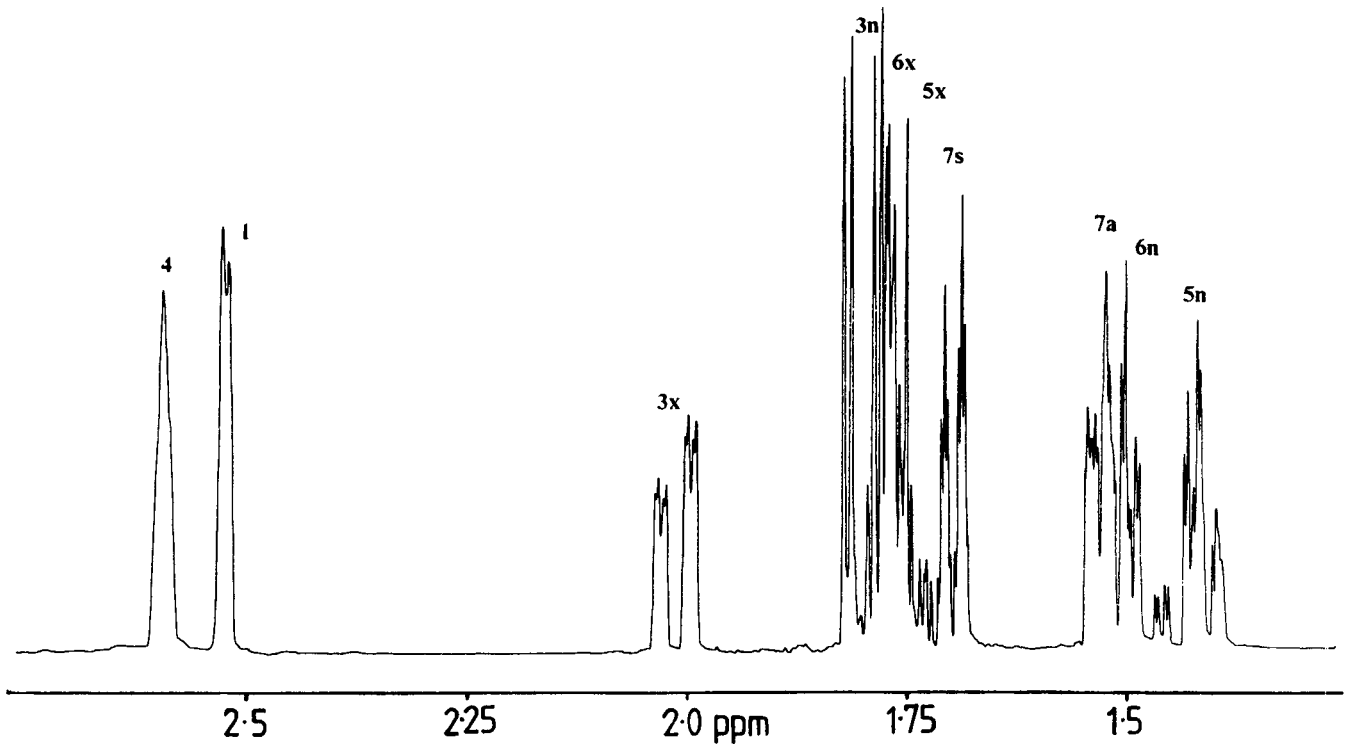

Figure 7. 500-MHz ^{1}H NMR spectrum of 2-norcamphor.

Table 1. ^{1}H chemical shifts (δ) for 2-substituted norbornanes

	Substituent						
		Endo				*Exo*	
Proton	H[a]	=O	OH	Cl	Br[b]	I	OH
H-1	2.191	2.599	2.248	2.396	2.516	2.601	2.144
H-2n(H-2x)	1.162	—	(4.226)	3.875	3.989	3.977	3.765
H-3x	1.471	2.062	1.957	1.802	2.070	2.231	1.285
H-3n	1.162	1.842	0.841	1.910	2.030	2.106	1.667
H-4	2.192	2.673	2.168	2.316	2.313	2.252	2.255
H-5x	1.471	1.790	1.570	1.467	1.480	1.487	1.425
H-5n	1.162	1.450	1.34	1.074	1.083	1.100	1.015
H-6x	1.471	1.814	1.36	1.613	1.645	1.566	1.459
H-6n	1.162	1.532	1.878	1.144	1.179	1.231	1.015
H-7s	1.181	1.734	1.34	1.774	1.857	1.916	1.570
H-7a	1.181	1.560	1.29	1.237	1.289	1.353	1.123

[a] Ref. 1.
[b] Ref. 2.

Table 2. ^{1}H chemical shifts (δ) for 2-substituted bornanes

	Substituent					
		Endo			*Exo*	
Proton	H	=O	OH	Cl	Br	OH
H-2x(H-2n)	1.489	—	4.006	4.172	4.319	(3.632)
H-3x	1.709	2.351	2.274	2.457	2.524	1.753
H-3n	1.130	1.842	0.943	1.348	1.533	1.739
H-4	1.602	2.090	1.623	1.682	1.665	1.721
H-5x	1.709	1.948	1.734	1.746	1.747	1.675
H-5n	1.130	1.404	1.243	1.271	1.272	0.958
H-6x	1.489	1.684	1.243	1.339	1.421	1.505
H-6n	1.230	1.338	1.888	2.071	2.067	1.008
8-Me	0.830	0.960	0.858	0.877	0.878	1.018
9-Me	0.830	0.838	0.869	0.877	0.865	0.828
10-Me	0.830	0.915	0.848	0.929	0.965	0.906

Table 3. Proton SCS (ppm) for 2-*exo* substituents in bicycloheptanes

	Substituent							
Proton	=O[a]	=O[b]	OH[a]	OH[b]	CN[a,c]	Cl[a]	Br[a,d]	I[a]
H-1	0.41	(0.13)[e]	−0.05	(0.08)	0.41	0.20	0.32	0.41
H-2n	—	—	2.60	2.50	1.20	2.71	2.83	2.82
H-3x	0.59	0.64	−0.19	0.04	0.40	0.33	0.60	0.76
H-3n	0.68	0.71	0.51	0.61	0.54	0.75	0.87	0.94
H-4	0.48	0.49	0.06	0.12	0.21	0.12	0.12	0.06
H-5x	0.32	0.24	−0.05	−0.03	0.06	0.00	0.01	0.02
H-5n	0.29	0.21	−0.15	−0.17	0.01	−0.09	−0.08	−0.06
H-6x	0.34	0.20	−0.01	0.02	0.10	0.14	0.17	0.10
H-6n	0.37	0.11	−0.15	−0.22	0.66	−0.02	0.02	0.07
H-7s	0.55	(0.13)	0.39	(0.19)	0.44	0.59	0.68	0.74
H-7a	0.38	(0.01)	−0.06	(−0.00)	0.20	0.06	0.11	0.17

[a] Norbornanes.
[b] Bornanes.
[c] Ref. 3.
[d] Ref. 2.
[e] Methyl substituents in parentheses.

Table 4. Proton SCS (ppm) for 2-*endo* substituents in bicycloheptanes

	Substituent				
Proton	OH[a]	OH[b]	CN[a,c]	Cl[b]	Br[b]
H-1	0.06	(0.02)[e]	0.33	(0.10)	(0.14)
H-2x	2.76	2.52	1.22	2.68	2.83
H-3x	0.49	0.57	0.51	0.75	0.82
H-3n	−0.32	−0.19	0.30	0.22	0.40
H-4	−0.02	0.02	0.16	0.08	0.06
H-5x	0.10	0.03	0.15	0.04	0.04
H-5n	0.18	0.11	0.19	0.14	0.14
H-6x	−0.11	−0.25	0.09	−0.15	−0.07
H-6n	0.72	0.66	0.65	0.84	0.84
H-7s	0.16	(0.03)	0.13	(0.05)	(0.05)
H-7a	0.11	(0.04)	0.24	(0.05)	(0.04)

[a] Norbornanes.
[b] Bornanes.
[c] Ref. 3.
[d] Methyl substituents in parentheses.

Table 5. SCS for substituted cyclohexanes (from Ref. 8)

	Substituent				
Proton	Cl	Br	I	OH	=O
Equatorial substituents					
H-1a	2.63	2.80	2.93	2.34	—
H-2e	0.53	0.65	0.70	0.29	0.80
H-2a	0.33	0.63	0.70	0.00	0.98
H-3e	0.10	0.06	−0.09	0.07	0.35
H-3a	0.12	0.14	0.15	0.05	0.45
Axial substituents					
H-1e	2.83	3.05	3.26	2.38	
H-2e	0.40	0.45	0.47	0.14	
H-2a	0.45	0.46	0.23	0.28	
H-3e	−0.18	−0.13	−0.14	−0.18	
H-3a	0.65	0.68	0.66	0.47	

data for the cyclohexanoid ring A in steroids from Ref. 8 are given in Table 5.

Inspection of these data shows generally good consistency between the norbornane and bornane ring systems, as may have been expected, but there are some intriguing differences.

The carbonyl SCS for norbornane and bornane for the C-3 and C-4 protons are essentially identical; however, those at the C-5 and C-6 protons differ considerably (Table 3). The corresponding ^{13}C SCS at C-5 and C-6 are the same for the two ring systems,[11] so the possibility that the different proton SCS are due to slightly different ring geometries does not appear to be tenable. However, the positions of the hydrogen atoms on C-5,6 could be affected by steric repulsions with the C-9 methyl group in bornane, which would tip the CH_2 groups slightly compared with those in the norbornane ring. Any change in the CO anisotropy or dipole moment would be expected to influence the nearer C-3 and C-4 protons more than the more distant C-5 and C-6 protons. Reaction field effects in the ketones would be expected to be larger in norbornanone (the smaller molecule) than bornanone, and they do not have a simple distance dependence. However, reaction field effects in 2-bromonorbornanone were shown to be very small for all but the 2-*endo* and 7-*cis* protons.[1]

The only other substituent that is common to the bornane and norbornane system is the hydroxy group, but in this case the SCS are generally similar in the two ring systems, particularly for the more distant protons, as may be expected. A 2-*exo* hydroxy group has a considerable affect on the vicinal protons, but this is very orientation dependent. A large positive SCS is observed for the 3-*endo* protons, a small negative SCS for H-1 and small SCS of either sign for H-3 *exo*. Exactly analogous behaviour is observed for the 2-*endo*-hydroxy substituent. Again, a large positive SCS is observed for the C-3 *trans* proton (which is now the *exo* proton) whereas the SCS for H-1 is very small and that for the C-3 *cis* oriented proton (H-3n) is now considerable but negative, i.e. to high field.

The SCS of the C-2 *exo*-hydroxy at the C-5 and C-6 protons are surprisingly mostly negative, although these SCS are only significant for the *endo* protons. In contrast, the C-2 *endo* hydroxy has a large positive SCS at the 6-*endo* proton, a smaller positive SCS at the 5-*endo*

proton, but a negative SCS at the 6-*exo* proton. The large positive SCS at the 6-*endo* proton is undoubtedly due to the close proximity of the 2-*endo* substituent to this proton.

The same general behaviour is observed for the other substituents studied, although there are considerable variations between the substituents. The *trans*-oriented vicinal proton (H-3n for the 2-*exo* substituents, H-3x for the 2-*endo* substituents) always experiences the largest shift, which is invariably positive, the *cis*-oriented vicinal proton also has large SCS, which are positive except for the OH substituent. A possible explanation of this intriguing observation is that the OH group has the opposite polarity compared with the other substituents considered, i.e. the positive centre (the hydrogen) may be closest to the eclipsed proton. This implies a sizeable electric field mechanism at this proton, but this is certainly not the only mechanism operating. This negative SCS is not observed for the corresponding protons in the cyclohexane ring (Table 5), presumably because the dihedral angles involved are the standard *gauche* and *trans* orientations, not the eclipsed fragment observed here.

The major mechanisms invoked for proton SCS are the electric field, van der Waals and magnetic anisotropy mechanisms,[4,5,8] and the effects of an almost constant electric field contribution with varying van der Waals and anisotropy contributions are clearly evident in the SCS for the halogens. The C—X dipole moment is very similar for Cl, Br and I, yet the SCS increase, particularly for the nearer protons, in the order Cl < Br < I. This suggests a short-range mechanism increasing in this order and this would be consistent with either anisotropy or van der Waals mechanisms.

These substituents do produce small but significant high-field shifts, i.e. negative SCS at some more distant protons (e.g. H-5n for the 2-*exo* and H-6x for the 2-*endo*). The latter could simply be a polarization mechanism. The 2-*endo* substituents produce a large low-field shift at the 6-*endo* proton, and by the electric field mechanism this is due to polarization of the electrons in the C-6—H-n bond towards the carbon atom. This could be further transmitted into a small high-field shift of the 6-*exo* proton. Whatever the precise mechanism, an exactly analogous effect is observed in the cyclohexane ring system (Table 5), where the 1-axial halogen substituent produces a large positive SCS on the adjoining C-3 axial proton which is reflected in a small negative SCS on the C-3 equatorial proton. Schneider *et al.*[8] analysed the observed SCS in the cyclohexane ring in terms of electric field and anisotropy effects for the ketone substituent, and of only the electric field mechanism for the chloro substituent, with generally good agreement. However, the vicinal protons were omitted from these correlations. It would be of interest to pursue these calculations on the present molecules. One cautionary note is that methyl SCS, in which neither electric field nor anisotropy contributions are present, are considerable and of either sign for near protons. This can be observed by comparison of the chemical shifts of the parent hydrocarbons norbornane and bornane (Tables 1 and 2). The SCS of the C-10 Me are −0.22 (H-2, 6x) and 0.10 (H-2, 6n), whereas the SCS of the two bridging methyls C-8 and C-9 are 0.59 (H-4), 0.23 (H-3, 5x) and −0.03 (H-3, 5n). Similar SCS for methyl substitution have been recorded in several investigations[7,17] and clearly no theory of SCS which does not explain these large effects can be wholly accepted.

EXPERIMENTAL

Spectra

All proton spectra were recorded in 5-mm tubes in deuteriochloroform at concentrations less than 0.2 mol l^{-1} (*ca.* 10 mg in 0.3 ml) with all shifts referenced to TMS. Most spectra were recorded on a Bruker WM250 spectrometer. All FIDs at 250 MHz were recorded over 64 transients, with a spectral width of *ca.* 1200 Hz (*ca.* 900 Hz for camphor and bornane) in 16K memory space, giving a digital resolution of 0.15 Hz per point, and with the aid of resolution enhancement factors (*ca.* LB = −0.5, GB = 0.2). The spectra recorded at 500 MHz had a resolution of less than 0.3 Hz. The automation microprograms for the 2D experiments are provided with the Bruker Aspect 2000 data system. Conditions for the COSYs were a spectral width of 1300 Hz in the F_2 domain. The spectra were acquired with 1K data points in F_2 (one order of zero filling in the F_1 domain) with 32 transients (four dummy scans) and 128 experiments. A sine-bell multiplication was applied in order to avoid truncation artifacts. The correlated 2D spectra were acquired with a spectral width of 3500 Hz in the F_2 domain and 1200 Hz in F_1. The spectra were acquired with 1K data points in F_2 and 512W in F_1 with 16 transients (two dummy scans) over 256 experiments.

Compounds

Norbornyl chloride was prepared by adaptation of work by Brown and Liu.[18] Hydrogen chloride gas was bubbled through norbornene (Aldrich) in dichloromethane at −78 °C whilst stirring. Purification was carried out by distillation (130 °C).

Norbornyl iodide was prepared by an analogous route. To a solution of norbornene in diethyl ether, hydriodic acid was added dropwise whilst stirring. After neutralization and removal of free iodine, the product was purified by column chromatography. Unfortunately, the compound readily decomposes, liberating free iodine.

Bornyl chloride was prepared by the addition of hydrogen chloride gas to a solution of α-pinene in dichloromethane at 0 °C. The resulting product was extracted and purified by sublimation. Bornyl bromide was prepared in a similar manner.

Bornane was prepared by the Huang–Minlon modification to the Wolff–Kischner reduction of a carbonyl group. To 20 g of camphor, concentrated KOH was added together with 130 cm^3 of diethylene glycol and 13.3 cm^3 of hydrazine hydrate and refluxed for 4 h. The resulting product was purified by flash column chromatography.

All other compounds mentioned were purchased from Aldrich and were used without further purification, except for isoborneol, which was purified by preparative gas chromatography.

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