

## Long Range Proton-Proton Coupling in *endo*-3,4-Disubstituted Bornanones

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### Abstract

The coupling constant  ${}^4J_{\text{exo-H } 3, \text{exo-H } 5}$  of 3,4-disubstituted bornanones increases or decreases depending on the point of attachment of substituents.

Proton-proton coupling between nuclei separated by four bonds is well documented<sup>1</sup> and it has been shown<sup>2,3</sup> that an electron-withdrawing substituent located at the central carbon of a propanic fragment causes an increase in  ${}^4J_{\text{H,H}}$ . Since the greatest differences were observed<sup>3</sup> in the essentially conformationally rigid<sup>4</sup> 4-substituted bornanones (Y = H; see Table 1), where a linear dependence was noted between the magnitude of  ${}^4J_{\text{H,H}}$  and the linear free energy parameter  $\sigma_1$ , we felt that it would be instructive to examine the effect of electron-withdrawing substituents at the terminal carbon of the propane fragment. To this end we have prepared a series of *endo*-3,4-disubstituted bornanones (1)–(9). The relevant coupling constant and the corresponding chemical shift are presented in Table 1.

It is seen that introduction of an electron-withdrawing substituent Y at C 3 causes a reduction in the value of the coupling constant  ${}^4J_{\text{exo-H } 3, \text{exo-H } 5}$ , determined as described previously, with respect to the corresponding 4-substituted bornanones (10)–(12) where Y = H. Data for these ketones are included in Table 1 also.

Two factors may be responsible for this decrease. Firstly, introduction of the *endo*-3 substituent may bring about some distortion of the bicyclic skeleton,<sup>4</sup> with a resultant change in the angle between the planes *exo*-H 3–C 3–C 4 and C 4–C 5–*exo*-H 5. However, since the dihedral angle between the substituents X and Y approximates to 90° it is unlikely that the ring conformation differs as a result of substituent interaction.

Secondly, the effect may be purely electronic in character and in accord with this viewpoint we note that in compounds (1)–(3) introduction of an *endo*-3-bromo substituent causes an essentially constant reduction in  ${}^4J_{\text{exo-H } 3, \text{exo-H } 5}$  so that its magnitude is now 0.65 that of the corresponding compound (10)–(12) where Y = H.

<sup>1</sup> Sternhell, S., *Q. Rev., Chem. Soc.*, 1969, **23**, 236; Barfield, M., and Chakrabarti, B., *Chem. Rev.*, 1969, 757.

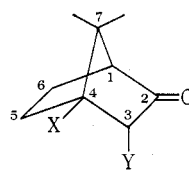
<sup>2</sup> Sardella, D. J., *J. Mol. Spectrosc.*, 1969, **31**, 70; Abraham, R. J., and Oliver, W. L., *Org. Magn. Reson.*, 1971, **3**, 725.

<sup>3</sup> Morris, D. G., and Murray, A. M., *Org. Magn. Reson.*, 1974, **6**, 510.

<sup>4</sup> Altona, C., and Sundaralingam, M., *J. Am. Chem. Soc.*, 1970, **92**, 1995.

For the carboxylic acids (5) and (9) a slightly greater but again common reduction is observed. In the case of the 4-substituted bornanones (Table) the reduction in the magnitude of  $^4J_{exo-H\ 3,exo-H\ 5}$  with respect to (11) generally increases with the electron-withdrawing character of Y, although no correlation is exhibited with either  $\sigma_1$  or the electronegativity parameter,  $E_R$ .

Table 1. Proton-proton coupling constants and chemical shifts of *exo*-H 3 in bornanones



Cpd	X	Y	$^4J_{exo-H\ 3,exo-H\ 5}$ (Hz)	<i>exo</i> -H 3 ( $\delta$ )
(1)	Me	Br	1.52	4.28
(2)	Cl	Br	2.24	4.61
(3)	NO <sub>2</sub>	Br	2.43	5.37
(4)	Cl	OH	1.35	4.25
(5)	Cl	CO <sub>2</sub> H	1.93	3.56
(6)	Cl	SC <sub>6</sub> H <sub>4</sub> Cl- <i>p</i>	2.31	3.75
(7)	Cl	SePh	2.47	3.97
(8)	NO <sub>2</sub>	I	2.64	5.78
(9)	NO <sub>2</sub>	CO <sub>2</sub> H	2.21	4.37
(10)	Me	H	2.33	—
(11)	Cl	H	3.50	—
(12)	NO <sub>2</sub>	H	3.85	—

The present results indicate conclusively that  $^4J_{H,H}$  increases or decreases depending on the point of attachment of substituents, and find support in the much smaller values observed previously.<sup>5</sup> The substituent influence is almost certainly directed through the  $\sigma$  bonding framework<sup>6</sup> and no unusual effects are noted for the more polarizable heavy atom substituents.

## Experimental

The n.m.r. measurements were carried out as previously described except for (6) and (7) where a Perkin-Elmer R32 spectrometer was used. Microanalyses were carried out by the Microanalytical Department, University of Glasgow.

### The Bromobornanones (1)–(3)

4-Substituted *endo*-3-bromobornanones were prepared from the 4-substituted bornanone by the method of Ingersoll and Babcock.<sup>7</sup> The products were purified by thin-layer chromatography and recrystallization from ethyl acetate to give for (1) m.p. 112–114° (Found: C, 53.8; H, 6.7. C<sub>11</sub>H<sub>17</sub>BrO requires C, 53.9; H, 7.0%), for (2) m.p. 127–128° (Found C, 45.5; H, 5.3. C<sub>10</sub>H<sub>14</sub>BrClO requires C, 45.2; H, 5.3%), for (3) m.p. 148–149° (Found: C, 43.8; H, 5.2; N, 4.9. C<sub>10</sub>H<sub>14</sub>BrNO<sub>3</sub> requires C, 43.5; H, 5.1; N, 5.1%).

### 4-Chloro-2-oxobornan-endo-3-carboxylic Acid (5)

To a stirred solution of 4-chlorobornanone (11) (2.0 g, 1.1 mmol) in dry tetrahydrofuran under dry nitrogen was added a solution of butyllithium in hexane (5 ml, 1.3 mmol),<sup>8</sup> and a further quantity of tetrahydrofuran to restore homogeneity. After 30 min at room temperature a stream of dry CO<sub>2</sub> was passed into the solution of enolate. Water was then added and the solution extracted into ether. The aqueous layer was acidified and extracted twice with ether; these combined extracts

<sup>5</sup> Sardella, D. J., *J. Am. Chem. Soc.*, 1972, **94**, 5206.

<sup>6</sup> Bubb, W. A., Fallick, C. J., and Sternhell, S., *Org. Magn. Reson.*, 1977, **9**, 167.

<sup>7</sup> Ingersoll, A. W., and Babcock, S. H., *J. Am. Chem. Soc.*, 1933, **55**, 341.

<sup>8</sup> Joshi, G. C., and Warnhoff, E. W., *J. Org. Chem.*, 1972, **37**, 2383.

were dried ( $\text{Na}_2\text{SO}_4$ ) and after removal of ether the solid was recrystallized from EtOAc to give the acid (5) (730 mg, 32%), m.p. 142–144° (Found: C, 57.4; H, 6.5; Cl, 15.5.  $\text{C}_{11}\text{H}_{15}\text{ClO}_3$  requires C, 57.3; H, 6.6; Cl, 15.4%).

*4-Nitro-2-oxobornane-endo-3-carboxylic Acid (9)*

The nitro acid was prepared analogously, m.p. 128–130° (Found: C, 55.0; H, 6.5; N, 6.0.  $\text{C}_{11}\text{H}_{13}\text{NO}_5$  requires C, 54.8; H, 6.3; N, 5.8%).

*endo-3-Iodo-4-nitrobornanone (8)*

The same procedure was followed as for (5) above, except that iodine was added to the enolate of (12). T.l.c. analysis (silica with 30% EtOAc/light petroleum) showed the presence of three bands of which that with lowest  $R_F$  was the iodo nitro ketone (8), m.p. 132–134° (Found: C, 37.4; H, 4.4.  $\text{C}_{10}\text{H}_{14}\text{INO}_3$  requires C, 37.2; H, 4.4%).

*4-Chloro-endo-3-p-chlorophenylthiobornanone (6)*

To 4-chlorocamphor (1.2 g, 6.3 mmol) in dry tetrahydrofuran under dry nitrogen was added a solution of butyllithium in hexane (c. 7 mmol). After stirring for 1 h a solution of *p*-chlorophenyl *p*-chlorobenzenethiosulfonate<sup>9</sup> (2.05 g, 6.4 mmol) in dry tetrahydrofuran was added dropwise over 30 min and stirring was continued overnight. The reaction mixture was poured into water and extracted twice with ether. The combined ether layers were dried ( $\text{Na}_2\text{SO}_4$ ); removal of ether after filtration gave an oily solid (2.2 g) which after recrystallization from light petroleum 60–80° gave the ketone (6) (1.2 g, 58%), m.p. 91–92° (Found: C, 58.7; H, 5.8; Cl, 21.1.  $\text{C}_{16}\text{H}_{18}\text{Cl}_2\text{OS}$  requires C, 58.4; H, 5.5; Cl, 21.5%).

*4-Chloro-endo-3-phenylselenobornanone (7)*

This was prepared analogously; the enolate of (11) was treated with phenylselenenyl bromide and (7) was separated from some diphenyl diselenide by column chromatography on alumina, a petroleum spirit/ethyl acetate solvent gradient being used as eluent. Recrystallization from petroleum spirit (b.p. 60–80°) gave the seleno compound (7), m.p. 61–62° (Found: C, 56.4; H, 5.9; Cl, 10.5.  $\text{C}_{16}\text{H}_{19}\text{ClOSe}$  requires C, 56.2; H, 5.6; Cl, 10.4%).

*4-Chloro-endo-3-hydroxybornanone (4)*

A solution of 4-chlorobornane-2,3-dione (0.23 g, 1.1 mmol) and triethyl phosphite (0.20 g, 1.1 mmol) in AnalaR, but not dried, benzene (5 ml) was set aside at room temperature for 7 days, during which time the yellow colour was discharged. Evaporation of the solvent followed by preparative t.l.c. (silica with 10% EtOAc/light petroleum) gave, after recrystallization from EtOAc, the hydroxy ketone (4) (0.11 g, 49%), m.p. 166–168° (Found: C, 59.5; H, 7.7.  $\text{C}_{10}\text{H}_{15}\text{ClO}_2$  requires C, 59.2; H, 7.5%).  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 3600, 1761  $\text{cm}^{-1}$ . The structure of (4) is also confirmed by the  $^{13}\text{C}$  n.m.r. spectrum (c. 0.2 M in  $\text{CDCl}_3$ , chemical shifts in ppm from internal  $\text{SiMe}_4$ ): C1, 58.14 (s); C2, 213.71 (s); C3, 78.90 (d); C4, 74.87 (s); C5, 27.35 (t); C6, 30.69 (t); C7, 47.39 (s); C8, 17.39 (q); C9, 15.81 (q); C10, 10.28 (q). The letters in brackets denote off-resonance multiplicities. This reaction was not always reproducible, however, and work is in hand both to systematize this reaction and also to elucidate its mechanism.

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<sup>9</sup> Leandri, G., Mangini, A., and Tundo, A., *J. Chem. Soc.*, 1957, 52.