Tetrahedron Letters No.22, pp. 1685-1692, 1965. Pergamon Press Ltd.
Printed in Great Britain.

PROTON MAGNETIC RESONANCE SPECTRAL LINE WIDTHS AND SPLITTINGS FOR TERTIARY METHYL GROUPS

M. J. T. Robinson

The Robert Robinson Laboratories, University of Liverpool,

and the Dyson Perrins Laboratory, Oxford.*

(Received 12 April 1965)

The recent communications (1, 2) about proton magnetic resonance (PMR) spectral line widths (width at half-height, $w_{\frac{1}{2}}$) and splittings in several steroids prompts me to report and comment on measurements on simpler compounds with tertiary methyl groups. Because the resolution of spectrometers vary from time to time the observed line widths are not constant for any given compound but the difference, $\Delta w_{\frac{1}{2}}$, between the line widths for a methyl group and for tetramethylsilane ($w_{\frac{1}{2}}$ varied from 0.4 to 0.7 cps in the measurements described here) in the same solution should be more nearly constant: this was tested explicitly for 10-methyl-cis-2-decalone and $\Delta w_{\frac{1}{2}}$ for the methyl group in this compound was found to be constant to within 0.1 cps when $w_{\frac{1}{2}}$ for tetramethylsilane varied from 0.4 to 1.0 cps.

In comparable pairs of derivatives of cis- and trans-9-methyldecalin $\Delta w_{\frac{1}{2}}$ for the angular methyl groups is regularly greater for the trans than for the cis isomers (Table 1), and similar differences are found in the pairs of octahydrophenanthrenes IV and benzhydrindanes V. The difference in $\Delta w_{\frac{1}{2}}$ for each pair of stereoisomers agrees

---

* Present address

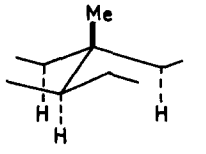
qualitatively with the "M" or "W" rule (1,3) for maximum coupling through four bonds in saturated systems since the trans isomers, containing part structure A (or A'), always allow more antiparallel relationships between vicinal carbon-hydrogen and carbon-methyl bonds than do the cis isomers, containing part structure B (or B') (Table 1). Such easily measured and regular differences provide a simple, reliable means of distinguishing pairs of stereoisomers differing in ring fusion.

An analogous difference in line width was expected for axial and equatorial methyl groups in geminal pairs as in part structure C (Table 2). The assignment of lines to the axial and equatorial methyl groups in each geminal pair is based unambiguously on chemical shifts for the compounds VIII and X to XII (Table 2) and in each instance the axial methyl group has the broader resonance line. No independent evidence is available for assigning the methyl resonances in compounds VII and IX. Presumably differences in line width will provide a useful criterion for distinguishing stereoisomers differing in the configuration of a single tertiary methyl group, subject to limitations imposed by virtual coupling effects (4, and below).

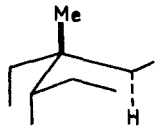
The number of 1,2-diaxial or antiparallel relationships between a given carbon-methyl bond and vicinal carbon-hydrogen bonds satisfying the "M" or "W" rule is a sufficient basis for qualitative comparisons of values of $\Delta w_{\frac{1}{2}}$ for the pairs of stereoisomers given in Table 1 but the data for cis-decalin derivatives (Table 3) show that line widths and, where observed, splittings for isolated methyl groups can be influenced by other factors. For example, 9-methyl-cis-2-decalone (XIII), which undergoes rapid ring inversion between two conformations, D and E, of approximately equal energy, and its 8a-methyl and 6a-t-butyl derivatives XIV and XV, which are presumably locked in the conformation D, show resolved splittings of 0.59 cps for XIII and of $\sim$0.9 cps for XIV and XV for the 9β-methyl groups. The difference in

TABLE 1

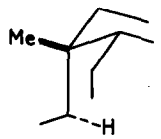
Line Width Differences Relative to Tetramethylsilane ($\Delta w_{\frac{1}{2}}$, cps), and Chemical Shifts ($\nu_o \delta$, cps) Downfield from Tetramethylsilane as Internal Standard for Angular Methyl Groups in cis- and trans-fused Ring Systems.

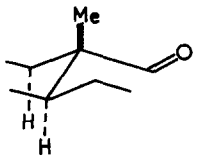


A

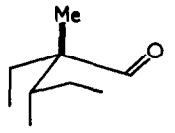


B

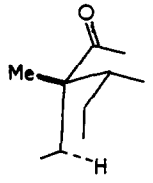




A'



B'



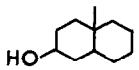
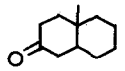
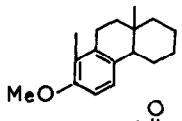
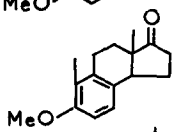
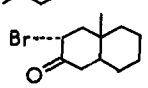
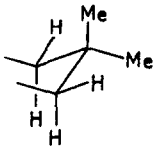
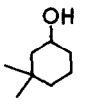
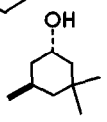
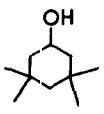
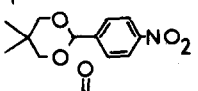
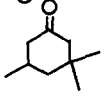
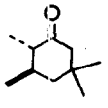
Compound		cis		trans	
		$\nu_o \delta$	$\Delta w_{\frac{1}{2}}$	$\nu_o \delta$	$\Delta w_{\frac{1}{2}}$
I:		57.7	0.1_5	49.7	0.6_5
II:		57.5	0.5_0	50.6	0.8_5
III:		71.6	0.3_5	62.9	1.0_5
IV:		58.7	0.6_0	55.6	1.0_0
V:		64.9	0.4_5	43.3	0.8_0
VI:		79.6	0.6_0	67.4	1.0_5

TABLE 2

Line Width Differences Relative to Tetramethylsilane ($\Delta w_{\frac{1}{2}}$, cps) and Chemical Shifts ($\nu_o \delta$, cps) Downfield from Tetramethylsilane as Internal Standard for Geminal Methyl Groups using 10% (w/v) Solutions in Chloroform.



C

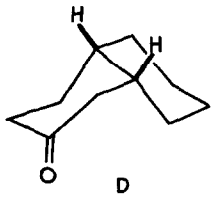
Compound		Ax. methyl		Eq. methyl	
		$\nu_o \delta$	$\Delta w_{\frac{1}{2}}$	$\nu_o \delta$	$\Delta w_{\frac{1}{2}}$
VII:		53.7	1.0_5	56.9	0.6_5
VIII:		65.0	0.9_5	51.7	0.6_0
IX:		56.1	1.0_0	60.9	0.7_0
X:		76.8	1.1_5	49.1	0.7_0
XI:		41.6[a]	1.5_0[a]	46.0[a]	0.8_0[a]
XII:		51.5	1.0_0	63.0	0.6_0

[a] Benzene, not chloroform, as solvent

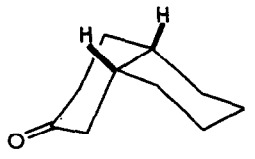
splittings is accounted for if the principle coupling is with the 1 α-proton, as seems certain by analogy with results for 5α-cholestan-2-one (I). A similar splitting is found for 1,3-dibenzylidene-10-methyl-cis-2-decalone, for which the conformation E will be preferred in order to avoid interactions between the 1-benzylidene and C-8 methylene groups. These relatively large couplings in XIII - XVI may be caused by

TABLE 3

Line Width Differences Relative to Tetramethylsilane ($\Delta w_{\frac{1}{2}}$, cps), Splittings ("J", cps) and Chemical Shifts ($\nu_o \delta$, cps) Downfield from Tetramethylsilane as Internal Standard for Angular Methyl Groups in Derivatives of cis-2-Decalone, using 10% (w/v) Solutions in Chloroform



D



E

	Substituents (R)	$\nu_o \delta$	$\Delta w_{\frac{1}{2}}$	"J"	Preferred Conformation
XIII:	9β-Me	58.1	0.7_0	0.5_9	a
XIV:	8α,9β-Me_2	58.2	1.1_5	0.8_8	D
XV:	6α-t-Bu, 9β-Me	46.2[b]	1.1_0[b]	0.9_4	D
XVI:	1,3-dibenzylidene, 10β-Me	52.3	1.2_5	0.6_4	E
XVII:	10β-Me	71.6	0.4_0	-	c
XVIII:	1α,3,3,8,8-d_5, 10β-Me	71.5	0.6_0	0.3_8	c
XIX:	3α,10β-Me_2	75.9[d]	0.7_0[d]	0.4_2[d]	E
XX:	3β,10β-Me_2	61.0[d]	0.5_0[d]	-	D
XXI:	3α-Br,10β-Me	79.6	0.7_5	0.4_5	E
XXII:	3β-Br,10β-Me	68.5	0.4_0	-	D
XXIII:	1α-Br,10β-Me	81.3	0.7_5	-	E
XXIV:	6β-t-Bu,10β-Me	75.1	0.6_0	-	E

[a] D and E in approximately equal amounts. [b] Benzene as solvent.

[c] D and E present in a ratio of c 1:2 (7) [d] Acetonitrile as solvent.

the trigonal carbon atom C-2 or C-3 modifying the axial 1a- or 4a-carbon-hydrogen orbital by a hyperconjugative type of effect (5).

10-Methyl-cis-2-decalone XVII and its derivatives (Table 3) present a superficially more complex variation in line width and splittings for the angular methyl group and provide cautionary examples of the variable effects of virtual couplings. Those derivatives of 10-methyl-cis-2-decalone expected to be predominantly in the conformation E show relatively broad methyl resonance lines for which a resolvable splitting (c 0.4 cps) is observed only when there is a 3-substituent (including two deuterium atoms). This is understandable if the principle methyl group coupling is with the axial 4a-proton (at 8.01 τ in XVII) in agreement with the "M" or "W" rule. Because the 4a-proton is strongly coupled with the 3a- and 3β-protons (at c 7.6 - 7.8 τ in XVII) with similar chemical shifts the methyl group resonance is also split by smaller 'virtual' couplings and so gives a single peak. Substitution at C-3 either removes both 3a- and 3β-protons (as in XVIII) or increases the difference in chemical shift between the 3β- and 4a-protons (as in XXI and, very probably, XIX) and so reduces the virtual couplings. The equatorial* 4β-proton (at $\not<$8.6 τ in XVII) absorbs at considerably higher fields than the axial* 4a-proton so that the strong geminal coupling does not lead to such large virtual couplings. Those derivatives, XX and XXII, of 10-methyl-cis-2-decalone which would be expected to exist mainly in the conformation D have relatively narrow unsplit methyl resonances ($\Delta w_{\frac{1}{2}}$ = 0.4 - 0.5 cps). If the principle methyl-hydrogen coupling is with the 5a-proton there should also be a considerable number of virtual couplings, since the chemical shifts for the C-5 and C-6 protons should be similar, with the result that no resolvable splitting should be observed. Paradoxically the effect of these additional virtual couplings is to

* In the more abundant conformation E

make the methyl group resonances narrower. It may readily be shown for model ABX (6) systems in which protons B and X are not directly coupled that when $J_{AX} \ll J_{AB}$ the two detectable virtual lines (transitions 10 and 11) in the X region of the spectrum come between, and are essentially equal in intensity to, the 'first order' lines (transitions 9 and 12): two other transitions (14 and 15) have an insignificant intensity. When J_{AX} is so small that the resulting splitting is only just resolvable the additional virtual couplings not only reduce the X-proton spectrum to a single peak but make it narrower if transitions 10 and 11 are more or less superimposed, as happens when J_{AB} is considerably greater than $\nu_A - \nu_B$. When 9β-methyl-cis-decalin or one of its derivatives, e.g. XVII, exists to a substantial extentin both two-chair conformations a further narrowing of the methyl group resonance is caused by having two relatively small time averaged couplings with the 1α- and 8α-protons instead of the single principle coupling when one conformation or the other is strongly preferred. The result is to increase the difference between cis and trans isomers and is thus unimportant for the assignment of configuration.

Virtual couplings and a multiplicity of direct couplings rather than conformational differences probably explain the variations in line width and splittings of C-18 protons in steroids recently described by Bhacca, Gurst and Williams (2), although the rather large change of shape which might be expected to result from a 16, 17-double bond may be important in two examples.

The compounds studied have either been described previously in the literature or have given satisfactory analyses and will be included later in full papers, with the following exceptions. Ketones XIX and XX have been obtained as a mixture only (7). The bromoketones XXI-XXIII are formed as a mixture from which the individual isomers may be concentrated by silica gel chromatography sufficiently well to allow

unambiguous identification of the position and configuration of the bromine substituents (8). The spectra were measured on a Varian A60 spectrometer (60 Mcps) in the Robert Robinson Laboratories, the University of Liverpool, using side band calibrations and scanning speeds of 0.1 or 0.2 cycles/sec^2. The solutions were 10% (w/v) in chloroform unless another solvent was used to get better spaced bands, or the amount of the solute available was inadequate.

I thank Mr. D. R. Elliott and Mr. F.G. Riddell for preparing some of the compounds.

REFERENCES

1. C. W. Shoppee, F. P. Johnson, R. Lack and S. Sternhell, Tetrahedron Letters, 2319 (1964).

2. N. S. Bhacca, J. E. Gurst and D. H. Williams, J. Amer. Chem. Soc , 87, 302 (1965).

3. A. Rassat, C. W. Jefford, J. M. Lehn and B. Waegell, Tetrahedron Letters, 233 (1964).

4. J. I. Musher and E. J. Corey, Tetrahedron, 18, 791 (1962).

5. A. S. Kende, Tetrahedron Letters No. 14, 13 (1959); K. M. Wellman and F. G. Bordwell, loc. cit. 1703 (1963); W. D. Cotterill and M. J. T. Robinson, loc. cit. 1833 (1963).

6. J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill, New York, 1959, pp. 132-138.

7. W. D. Cotterill and M. J. T. Robinson, Tetrahedron, 20, 777 (1964).

8. D. R. Elliott, F. G. Riddell and M. J. T. Robinson, unpublished results.