procedure[7] or several others, failed to afford crystalline VII, which has been reported to have m.p. 89–90°[7] and m.p. 96–97°.[19] Chromatographically purified oil (3.3 g.) from a benzoylation [λ_{max}^{film} 5.83, 5.99, 6.20 (w), and 6.28 (w) μ] was epoxidized with 30% hydrogen peroxide according to Westen's procedure,[7] and the product solidified to afford, after recrystallization from ether, 1.2 g. of VI, m.p. 154–156°. Further recrystallization produced material with m.p. 156–158° (lit. m.p. 158°,[7] 158–158.5°[8]); λ_{max}^{KBr} 5.79 (sh), 5.83, 6.22 (w), and 6.31 μ (w).

Reduction of VI to X with Lithium Aluminum Hydride.—The crude triol X was prepared by a procedure based on that of Plattner.[20] To a magnetically stirred suspension of 0.59 g. (1.6×10^{-2} mole) of lithium aluminum hydride in 25 ml. of anhydrous ether was added dropwise a solution of 0.361 g. (1.20×10^{-3} mole) of VI, m.p. 156–158°, in 30 ml. of ether. The mixture was refluxed for 30 min. and cooled to room temperature. Excess lithium aluminum hydride was decomposed by dropwise addition of 2 ml. of wet ether and 1 ml. of 10% sodium hydroxide solution. The mixture was stirred for 10 min. more and 20 ml. of ether was added. The ether layer was carefully decanted and evaporated to yield 0.310 g. of oily residue (theoretical yield of X plus benzyl alcohol = 0.370 g.): λ_{max}^{film} 2.9–3.0 (vs) and 6.05 (vw) μ.

Conversion of X to III.—The crude triol product (0.310 g.) was dissolved in 50 ml. of acetone, which had been purified by distillation from potassium permanganate, and placed in an ice bath. Jones reagent[9] was added dropwise to the magnetically stirred solution until the red-orange color of the reagent persisted; this required 0.8 ml. of oxidant. After an additional 2 min. of stirring the reaction mixture was poured into 300 ml. of 5% aqueous potassium carbonate solution, which was then extracted with four 50-ml. portions of ether. The combined ether extracts were washed with four 20-ml. portions of water and two 20-ml. portions of saturated sodium chloride solution and were dried over magnesium sulfate. Evaporation of the ether gave a light yellow oil which was quickly dissolved in 20 ml. of acetone and poured through a column of Florisil. Failure to filter products from earlier runs through an adsorbent resulted in their turning dark, and no III was obtained upon subsequent chromatography. Evaporation of the eluted acetone afforded 0.079 g. (33% of III from VI) of an oil which solidified upon trituration with ether and had m.p. 138–141°. Further elution of the column gave only 0.024 g. of unidentified oil. Recrystallization of the solid from ether afforded pure III, m.p. 141–142°, which was compared with the compound prepared by cyclization of I and found to have an identical infrared spectrum and an undepressed mixture melting point.

(18) C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 2680 (1960). We have found the rather tedious purification of the sodium borohydride used for this selective reduction by Boyce and Whitehurst to be unnecessary with the sodium borohydride we had in hand (Metal Hydrides, Inc., 98+%, as supplied). We recommend that other investigators try unpurified reagent on a small scale when attempting a selective reduction of this type.

(19) F. Sondheimer and D. Elad, *J. Am. Chem. Soc.*, **79**, 5542 (1957).

(20) A. Fürst and Pl. A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949).

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Additivity of Chemical Shifts in the Decalin Ring System. Determination of Configuration of *cis*-9-Hydroxy-10-methyldecalin-2,5-dione

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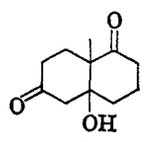
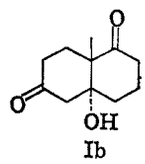
The principle of additivity of substituent effects on the n.m.r. chemical shift of the angular methyl group applies to the relatively flexible decalin ring system just as it does to steroids. This additivity principle has been used to determine as *cis* the configuration of the 9-hydroxy-10-methyldecalin-2,5-dione prepared by the cyclization of the adduct of methyldihydroresorcinol with methyl vinyl ketone, by consideration of the contributions of the hydroxyl and the two carbonyl substituents and the presence of a *cis* or *trans* ring juncture to the angular methyl resonance.

In their classical study of the n.m.r. spectra of steroids, Shoolery and Rogers[2] showed that the chemical shift of angular methyl protons is dependent on the nature and location of the various functional groups on the steroid skeleton and that the effects of these substituents are additive. These initial proposals have been extended by a number of workers, notably Zürcher.[3] He showed, in an extremely thorough analysis of the chemical shifts of some 260 steroids, that, with few exceptions, it is possible to calculate the chemical shifts for C-18 and C-19 protons to within 1 or 2 c.p.s. in a polysubstituted steroid, taking advantage of the additivity effect of each substituent on the angular methyl resonance.

Recently we have shown[4] that the additivity principle is applicable to angularly methylated decalins, by a consideration of chemical shift data for some *cis*-10-methyl-2-decalones published by Elliott, Robinson, and Riddell.[5] In the present work we sought to establish the generality of this additivity principle by an analysis of carefully measured chemical shifts for the angular methyl groups of *cis*- and *trans*-10-methyldecalin and certain of their derivatives. In particular we wished to use the additivity principle to determine whether the 9-hydroxy-10-methyldecalin-2,5-dione,[6] m.p. 141–142°, prepared by cyclization of the Michael adduct of methyldihydroresorcinol with methyl vinyl ketone,[7] had a *cis* (Ia) or *trans* (Ib) ring juncture.



Ia



Ib

(1) Petroleum Research Fund Scholar, summer 1964.

(2) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958).

(3) (a) R. F. Zürcher, *Helv. Chim. Acta*, **44**, 1380 (1961); (b) *ibid.*, **46**, 2054 (1963).

(4) K. L. Williamson and T. A. Spencer, *Tetrahedron Letters*, 3267 (1965).

(5) D. R. Elliott, M. J. T. Robinson, and F. G. Riddell, *ibid.*, 1693 (1965).

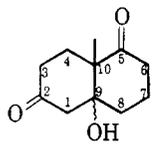
(6) All decalins in this paper are numbered as shown in structure I, Table I.

(7) T. A. Spencer, H. S. Neel, D. C. Ward, and K. L. Williamson, *J. Org. Chem.*, **31**, 434 (1966).

The solution to this problem necessitates a knowledge of the chemical shift contribution of carbonyl groups at C-2 and C-5 and hydroxyl groups at C-9 in both the *cis* and *trans* series, as well as knowledge of the chemical shift of the angular methyl group of the parent *cis*- and *trans*-10-methyldecalin. The data for the eight requisite compounds are given in Table I. In Table II the contribution of each substituent to the methyl group chemical shift is given. The calculation of these values is straightforward. For example, the contribution of the C-2 carbonyl in the *cis* series (+13.3 c.p.s.) is obtained by subtracting the shift of the parent hydrocarbon III (57.6 c.p.s.) from the shift of the ketone V (70.9 c.p.s.). Similarly, the contribution of a C-9 hydroxyl in the *cis* series (−3.3 c.p.s.) is obtained by subtracting the contribution of the C-2 carbonyl (+13.3 c.p.s.) plus the shift of the parent hydrocarbon III (57.6 c.p.s.) from the shift of the ketol IX (67.6 c.p.s.).

TABLE I

ANGULAR METHYL CHEMICAL SHIFTS FOR DECALINS AND DERIVATIVES AT 60 MC.



79.0 c.p.s.

I

Compd.	C.p.s.	Compd.	C.p.s.
II[a]	47.4	III[a]	57.6
IV[b]	61.4	V[b]	70.9
VI[c]	80.0	VII[d]	81.9
VIII[b]	73.5	IX[b]	67.6

[a] Sample kindly supplied by Professor W. G. Dauben. [b] Sample kindly supplied by Professor J. A. Marshall. [c] Prepared by the method of A. J. Birch, E. Pride, and H. Smith, *J. Chem. Soc.*, 4688 (1958). [d] Prepared by the method of S. Swaminathan and M. S. Newman, *Tetrahedron*, **2**, 88 (1958).

TABLE II

SHIELDING EFFECTS OF SUBSTITUENTS ON ANGULAR METHYL PROTONS OF DECALINS AT 60 MC.[a]

Decalin	C.p.s. *trans*	C.p.s. *cis*
5-Keto-	+18.6	+11.0
2-Keto-	+14.0	+13.3
9-Hydroxy-	+12.1	−3.3

[a] A positive value denotes a downfield shift caused by a substituent.

From the data in Table II it is possible to calculate the chemical shifts that would be expected for both the *cis* and *trans* isomers of 9-hydroxy-10-methyldecalin-2,5-dione, as shown in Table III.

TABLE III

	trans	*cis*
10-Methyldecalin	47.4	57.6
5-Keto-	+18.6	+11.0
2-Keto-	+14.0	+13.3
9-Hydroxy-	+12.1	−3.3
	92.1 c.p.s.	78.6 c.p.s.

The chemical shift of the 9-hydroxy-10-methyldecalin-2,5-dione (I) isolated from the Robinson annelation sequence[7] is 79.0 c.p.s. This is within 0.4 c.p.s. of the value calculated for the *cis* isomer Ia, but 13.1 c.p.s. from the value calculated for the *trans* isomer Ib.[8] We regard this as conclusive evidence that this compound possesses a *cis* ring juncture. This conclusion is in agreement with chemical evidence cited in the preceding paper.[7]

Although our sampling of compounds is limited to just nine examples, we feel that the internal agreement in chemical shifts is good enough to assert that the decalins show an additivity of chemical shifts of the same degree of precision as that found in steroids.

It is interesting to compare the chemical shift data from the decalins with the corresponding data for steroids (see Table IV). The chemical shifts for the methyl peaks of the parent decalin ring skeletons (II and III) are surprisingly[9] similar to the values for the isomeric 5α- and 5α,14α-androstanes (47.4 *vs.* 47.5 c.p.s. for the *trans* compounds and 57.6 *vs.* 55.5 c.p.s. for the *cis* compounds). The contributions made to

TABLE IV

A COMPARISON OF THE EFFECT OF SUBSTITUENTS ON THE CHEMICAL SHIFTS OF ANGULAR METHYL PROTONS IN DECALINS AND C-19 PROTONS IN STEROIDS[a]

trans Ring Juncture			
10-Methyldecalin	47.4 c.p.s.	47.5 c.p.s.	5α,14α-Androstane
5-Keto-	+18.6	+22.5	1-Keto-
2-Keto-	+14.0	+14.5	3-Keto-
9-Hydroxy-	+12.1	+10.8	5-Hydroxy-[b]
cis Ring Juncture			
10-Methyldecalin	57.6	55.5	5β,14α-Androstane
5-Keto-	+11.0	+13.0	1-Keto-
2-Keto-	+13.3	+7.0	3-Keto-
9-Hydroxy-	−3.3	−1.0	5-Hydroxy-[c]

[a] Except as noted, the steroid chemical shift effects are taken from the work of Zürcher.[3] A positive value denotes a downfield shift (in cycles per second) at 60 Mc. caused by the substituent. [b] J. C. Jacquesy, J. M. Lehn, and J. Levisalles, *Bull. soc. chim. France*, 2444 (1961). This value is derived from the comparison of the C-19 shift for 5α-cholestan-3-one with that of 5α-hydroxycholestan-3-one. Because of a dipole–dipole repulsion between the 3-keto and 5α-hydroxyl groups this value is larger than that quoted by Zürcher[3] (3.5 c.p.s.), based on a 3-acetoxy-5α-hydroxy-6-keto steroid. [c] Unpublished observation by K. L. Williamson on 5β-hydroxycholestan-3-one in carbon disulfide solution.

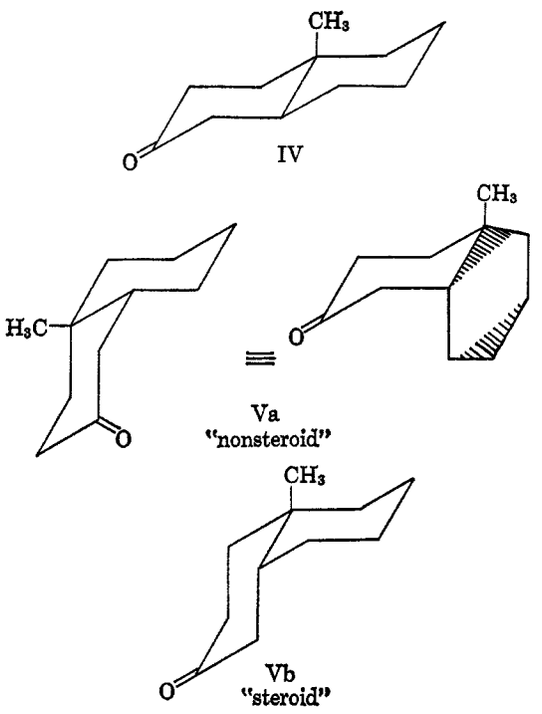
(8) Agreement within 2 c.p.s. of calculated and observed values in steroids is regarded as satisfactory: N. S. Bhacca and D. H. Williams, "Applications of N.M.R. Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, p. 25.

(9) See the discussion of the effect of rings C and D on the chemical shift of the C-19 methyl group in steroids by N. S. Bhacca and D. H. Williams, ref. 8, p. 16.

this basic shift by the various functional groups in the decalin system are very similar to the contributions made by the same substituents in steroids with one notable exception: the contribution made by a carbonyl group at C-2 in the *cis*-fused decalin ring system.

It will be noted from Table IV that in the *cis*-decalin ring system a carbonyl group at C-2 causes the methyl resonance to be shifted downfield by 13.3 c.p.s. This value is very similar to the shift caused by a C-2 carbonyl group in *trans*-10-methyldecalin (14.0 c.p.s.) and by a C-3 carbonyl in A/B-*trans* steroids (14.5 c.p.s.). It is quite different from the shielding effect of a C-3 carbonyl group in A/B-*cis* steroids (7.0 c.p.s.). One would immediately conclude that the carbonyl group is the same distance from and has the same orientation to the angular methyl group in the *cis*- and *trans*-decalins and *trans* steroids, but not in *cis* steroids.

This distinction leads again to the conclusion reached by Elliott, Robinson, and Riddell[5] and by us[4] that *cis*-10-methyl-2-decalone has the "nonsteroid" conformation.[9a] The geometric relationship of the carbonyl group to the angular methyl group in the "nonsteroid" form (Va) and in the *trans* compound (IV) is the same. That is, in both compounds Va and IV the methyl group is axial to the ring containing the carbonyl group. In the "steroid" form of the *cis*-fused decalin (Vb) the methyl group is farther away and at a different angle from the carbonyl group. As noted by Cross,[10] the C-3 carbonyl is more distant from the C-19 protons in 5β steroids (which cannot adopt the alternate nonsteroid conformation) than in 5α steroids, and consequently the long-range deshielding by carbonyl is weaker. This explains the rather small (7.0 c.p.s.) deshielding effect for a C-3 carbonyl group in A/B-*cis* steroids. The observed deshielding effect of 13.3 c.p.s. for *cis*-10-methyl-2-decalone (V) is thus consistent with predominance of the "nonsteroid" conformer Va, which has the same geometric relationship between carbonyl and methyl as do IV and 3-keto-*trans* steroids.



As we have shown, the additivity effects of substituents on the angular methyl resonances in decalins have a high degree of internal consistency, and, once it is accepted that *cis*-10-methyl-2-decalone has the "nonsteroid" conformation, it can be seen that a given substituent makes very nearly the same contribution to the angular methyl chemical shift in the decalin ring system as it does in the corresponding steroid.[11] To a first approximation it should be possible to use the wealth of data[3] already accumulated for steroids to calculate rough values for the angular methyl chemical shifts in decalins.

Experimental Section

The chemical shifts were measured on a Varian A-60 n.m.r. spectrometer employing 10% w./v. solutions in deuteriochloroform using 2% tetramethylsilane as an internal standard. From a number of measurements made at different times on freshly prepared solutions using different sample tubes we conclude that our values are accurate to ±0.5 c.p.s. To check on relative chemical shifts of certain of these samples, we have recorded a number of them at one time on one spectrum using a 50-c.p.s. sweep width and a 0.1-c.p.s. sweep time. Nevertheless, discrepancies outside the limits of experimental error exist between three of the values reported here and those recently reported by Robinson.[12]

Acknowledgments.—This research was supported by grants from the Public Health Service (GM 10224-03 and AM 05014-04) and the Petroleum Research Fund of the American Chemical Society. We wish to thank Professors W. G. Dauben and J. A. Marshall for generous gifts of compounds. The n.m.r. spectra were run through the courtesy of the University of Massachusetts on a Varian A-60 spectrometer located at that institution.

(9a) NOTE ADDED IN PROOF.—W. G. Dauben, R. M. Coates, N. D. Vietmeyer, L. J. Durham, and C. Djerassi [*Experentia*, **21**, 565 (1965)] have recently reported the use of essentially the same n.m.r. method as used in this paper to arrive at the same conclusion concerning the conformation of *cis*-10-methyl-2-decalone. The earlier conclusion that the "nonsteroid" conformation was unimportant, based on O.R.D. studies, was in error apparently because "the sign of the Cotton curve must be controlled by a conformer present in minor amounts and which has a large rotational value."

(10) A. D. Cross, *J. Am. Chem. Soc.*, **85**, 3226 (1963).

(11) For additional examples, see ref. 4.

(12) M. J. T. Robinson [*Tetrahedron Letters*, 1685 (1965)] reported 49.7 c.p.s. for *trans*-10-methyldecalin (II), 71.6 c.p.s. for *cis*-10-methyl-2-decalone (V), and 62.9 c.p.s. for the corresponding *trans* isomer IV.