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THE ADDITIVITY OF SUBSTITUENT EFFECTS APPLIED TO ANGULAR METHYL CHEMICAL SHIFTS IN THE DECALIN RING SYSTEM: THE CONFORMATION OF 10-METHYL-CIS-2-DECALONE

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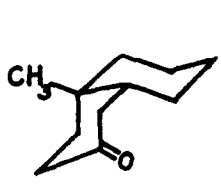
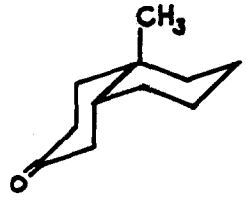
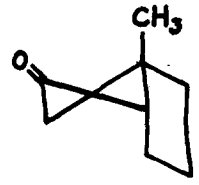
Analysis of chemical shifts and coupling constants of protons adjacent to the carbonyl group has recently led Elliott, Robinson, and Riddell (1) to conclude that 3α-methyl and 3α- and 1α-bromo derivatives of 10-methyl-cis-2-decalone exist predominantly in the "nonsteroid" form A, and not in the alternative "steroid" chair form B or the A-ring twist conformation C. By an unspecified method those authors calculate that the parent 10-methyl-cis-2-decalone (II) exists as an equilibrium mixture in which conformations A:B ≃ 2:1.



A
Nonsteroid



B
Steroid



C
Twist

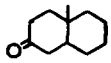
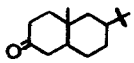
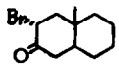
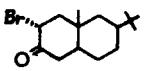
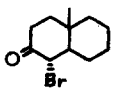
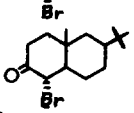
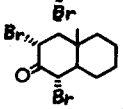
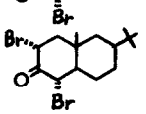
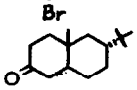
Previously, optical rotatory dispersion and circular dichroism measurements led Djerassi, et al. (2) "to the inescapable conclusion that the anticipated 'nonsteroid' form A does not play an important role in the conformational equilibrium in 10-methyl-cis-2-decalone."

We have shown (3) that a quantitative additivity effect of substituents on the chemical shift of the angular methyl group applies in the decalin ring system, just as it has been shown to apply to hundreds of steroids (4, 5). In this communication we will show that the conclusions of Elliott, Robinson, and Riddell (1) are confirmed by a reinterpretation of their data for compounds III-X (see Table I) by this substituent additivity method.

Inspection of Table I reveals that the effect of a 6β-t-butyl group on the angular methyl resonance can be obtained simply by subtracting the chemical shift of the t-butyl derivative from the chemical shift of the unbutylated compound. This should be equal to ν V - ν IV = -0.24 c.p.s., ν VII - ν VI = -0.12 c.p.s., ν IX - ν VIII = -0.42 c.p.s. or an average value of -0.26 c.p.s. Compounds III, V, VII, and IX must have the "nonsteroid" conformation because the bulky 6β-t-butyl group must be in the equatorial conformation. This means that the angular methyl group must be axial to ring A in compounds III, V, VII, and IX. Therefore the distance and angular relationships between carbonyl groups at C-2 and the (axial) 10-methyls in III, V, VII, and IX are exactly the same as they are in the trans-ketone II. Thus, to calculate the effect of a carbonyl at C-2 on an axial

TABLE I

CHEMICAL SHIFTS OF ANGULAR METHYL GROUPS
(c.p.s. downfield from TMS at 60 Mc. in $CDCl_3$)

	Compound	Conformation of cis-Fused Isomer	γ cis	γ trans
I[a]		-	57.7	49.7
II[a]		A	71.6	62.9
III[b]		A	75.18	
IV[b]		A	79.62	
V[b]		A	79.38	
VI[b]		A	81.30	
VII[b]		A	81.18	
VIII[b]		A	85.20	
IX[b]		A	84.78	
X[b]		B	61.92	

a. M. J. T. Robinson, Tetrahedron Letters, 1685 (1965).

b. Reference 1.

10-methyl we simply subtract γ trans-I from γ trans-II = 13.2 c.p.s. (This can be compared to the value of 14.5 c.p.s. for a 3-keto-5α-steroid (4).) To calculate the chemical shift of the angular methyl group in 10-methyl-cis-2-decalone (assuming it exists in the "nonsteroid" conformation A) we simply add 13.2 c.p.s. (the carbonyl contribution) to 57.7 c.p.s. (the chemical shift of cis-I) to give 70.9 c.p.s.

Since the contribution of equatorially disposed alkyl groups to the chemical shift of an axial angular methyl group is quite small, generally being on the order of 0.5 c.p.s. (4), one can assume that if 10-methyl-cis-2-decalone existed in the "steroid" conformation, it would have, like compound X, γ 10-methyl $\simeq$ 62 c.p.s. This means that the contribution of a C-2 carbonyl group to the chemical shift of the 10-methyl group (equatorial to ring-A) in a "steroid" conformation would be equal to 62 c.p.s. - γ cis-I = 4.3 c.p.s. (This can be compared to the value of 7.0 c.p.s. for a 3-keto-5β-steroid (4).) From the above we have seen that the assumption of a "nonsteroid" conformation for II gives a calculated angular methyl chemical shift of 70.9 c.p.s. and the assumption of a "steroid" conformation gives ca. 62 c.p.s. The observed value is 71.58 c.p.s., hence we conclude that 10-methyl-cis-2-decalone exists predominantly in the "nonsteroid" conformation A.

Another and probably more accurate way to reach this conclusion is as follows: We have shown that III exists in the "nonsteroid" conformation A and that the t-butyl group

contributes -0.26 c.p.s. to the methyl resonance. Thus we would calculate a chemical shift of γ III — (-0.26 c.p.s.) = 75.44 c.p.s. for compound II. The observed value is 71.58 c.p.s., a discrepancy of 3.86 c.p.s. This is consistent with the observation of Elliott, Robinson, and Riddell (1) that the methyl resonance of 10-methyl-cis-2-decalone moves to lower field as the temperature is lowered from +30 to -50°. In fact it should approach 75.44 c.p.s. as a limit. If a linear relationship exists between the chemical shifts of II in conformations A and B, then we can calculate that II exists as ca. 70% A and 30% B, in complete agreement with Elliott, et al. (1), again assuming that A and B are the only conformations contributing to the equilibrium. Conformation C can be completely disregarded because it decreases the distance between the carbonyl and the methyl groups and it puts the angular methyl group into the shielding cone of the carbonyl group (7).

To illustrate further the additivity effect of substituents one can calculate the contributions to the angular methyl chemical shifts made by a 3α bromine atom, γ V - γ III = 4.20 c.p.s., and a 1α bromine atom, γ VII - γ III = 6.0 c.p.s. These values are comparable to the effect (both 4.5 c.p.s.) of equatorial 2α-(5) and 4α-(8) bromine atoms in the A ring of 5α-steroids.

Further examples of additivity effects of substituents in the decalin ring system, again indicating that these effects are very similar to those observed in steroids, and an illustration of the usefulness of this additivity principle in deducing stereochemistry will be published elsewhere (3).

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