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THE EFFECT OF C$_1$-SUBSTITUTION ON CONFORMATION AND RING INVERSION OF 7,12-DIHYDROPLEIADENES[1]

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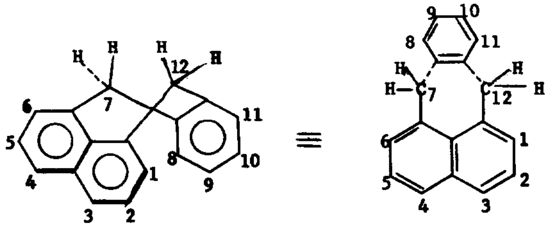
In our earlier study[2] of ring inversion of 7,12-dihydropleiadene (DHP) and derivatives, we observed that methyl substitution on the 8- and 11-positions of DHP raised the conformational inversion barrier, supposedly by producing greater steric congestion in the transition state than in the ground state. We have now found that 1-substituents, regardless of their polar character, have essentially no effect on ΔF^* for inversion of DHPs. The evidence presented below suggests that the steric "buttressing" effect of 1-substituents is similar in <u>both</u> ground and transition



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states, thus resulting in an inversion barrier comparable to the parent DHP.

A variety of 1-substituted-7,12-dihydropleiadenes were prepared in straight-forward fashion from 1-hydroxy-7,12-pleiadione[3]; their physical properties will be described in the full paper.[4] In the table below, the chemical shifts of the C_7- and C_{12}-methylene protons (geminal protons are equivalent under fast exchange conditions) in a variety of 1-substituted DHPs are given, together with the maximum chemical shift difference ($\Delta \nu_{AB}$) and coupling constants for the non-equivalent geminal protons (under very slow exchange conditions) when they appear as individual AB spectra. The free energies of inversion were calculated from the variable temperature data[1] for both 7- and 12-methylene groups in each DHP, using the relation[5] $k_{Tc} = \pi\Delta \nu_{AB}/\sqrt{2}$ and the Eyring equation with unit transmission coefficient. The two determinations of $\Delta F^{*}_{inv.}$ for each compound are equal within experimental error.

Table I

Inversion Barriers and Magnetically Non-equivalent Methylene Groups in Substituted-7,12-Dihydropleiadenes

Substituents	Fast Exchange cps from TMS		Coalescence Temperature °C		Slow Exchange[c] $\Delta\nu_{AB}$, cps at 60 mc		$\Delta F^{\ddagger}_{Tc}$ [a] Kcal/mole	
	νC_7-CH_2	νC_{12}-CH_2	C_7-CH_2	C_{12}-CH_2	C_7	C_{12}	C_7	C_{12}
1-Chloro[b]	265	283	8	-6	67	17	13.6	13.6
1,5-Dimethyl	259	259	5	-10	73	20	13.4	13.4
1-Methyl[b]	265	265	8	-10	73	19	13.5	13.5
1-Acetoxy	259	259	10	0	69	20	13.7	13.8
1-Methoxy	267	282	10	0	69	32	13.5	13.6
Hydrogen (none)	260		8		71	71	13.6	
11-Methyl[b]	260	260	--	20	71	40	--	14.5
8,11-Dimethyl	260		42		40	40	15.6	

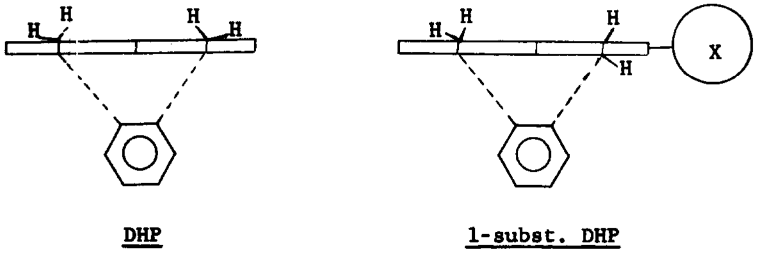
Probable error in $\Delta F^{\ddagger}$ is ± 0.2 Kcal/mole

[a] $CDCl_3$ was used in every case except with 1-methoxy DHP where pyridine was employed as the n.m.r. solvent.

[b] The temperature dependence of the individual methylene groups was also checked by studying the isomeric dideuterated DHP's in which each CH_2 group had been selectively deuterated, thus allowing unhampered observation of a single CH_2 group (P.T. Lansbury, J.F. Bieron and M. Klein, unpublished observations).

[c] All geminal coupling constants are ca. 15 c.p.s.

The important point to note is that ΔF^* is essentially unaffected by 1-substituents, regardless of their nature. Also, it can be seen that $\Delta \nu_{AB}$ for the C_{12}-methylene quartet is greatly reduced, compared with $\Delta \nu_{AB}$ for the C_7-CH_2 groups, which remains similar in magnitude to DHP. These data suggest that C_1-substituents deform the seven-membered central ring in DHPs toward a more planar conformation in which the C_{12}-protons are more equivalent (see drawing).



In 8-methyl and 8,11-dimethyl DHP, $\Delta\nu_{AB}$ for the adjacent methylene group(s) was reduced much less than in 1-methyl DHP indicating less deformation due to steric compression in the ground state, hence higher $\Delta F^*_{inv.}$ (vide supra). Another related observation suggesting that a C_1-substituent exerts more steric hindrance than at C_8 is the appearance of *two* $>C=O$ stretching bands in 1-methyl-7,12-pleiadione (at 1657 and 1673 cm^{-1}) whereas both 8-methyl-7,12-pleiadione and 7,12-pleiadione show a single $>C=O$ band at 1667 cm^{-1} (all measured in $CHCl_3$ solution, using a Perkin Elmer model 521 spectrometer). In fact, 1-chloro, 1-acetoxy and 1-methoxy-7,12-pleiadiones all show two carbonyl stretching bands ($\Delta\nu$ = 13 to 32 cm^{-1}), indicative of a steric compression induced shift of the 12-carbonyl group to higher frequency.

In summary, then, C_8- and C_1-substituents appear to exert steric compression in the transition state for inversion of dihydropleiadenes but only the latter substituents have substantial steric effects in the ground state.

Acknowledgement:

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References:

1. 7,12-Dihydropleiadenes, Part IV.

2. P.T. Lansbury, J.F. Bieron and M. Klein, J. Am. Chem. Soc., 88, 1477 (1966).

3. L.F. Fieser, J. Am. Chem. Soc., 53, 3546 (1931).

4. All compounds discussed in this paper gave satisfactory elemental analysis and were further characterized by spectroscopy.

5. H.S. Gutowsky and C.H. Holm, J. Chem. Phys., 25, 1228 (1956).

6. E.L. Eliel, "Stereochemistry of Carbon Compounds", McGraw-Hill Book Company, Inc., 1962, p. 163.

7. P.T. Lansbury, J.F. Bieron and A.J. Lacher, J. Am. Chem. Soc., 88, 1482 (1966).