Stereochemistry and Transannular Reactions of 7,12-Dihydropleiadenes

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Cycloalkanes of seven or more atoms have lower inversion barriers[1] and more strain-free conformations of lower symmetry than cyclohexane,[2] thus compounding the problems of conformational analysis of such flexible molecules.[2] In addition to these challenging problems, the medium-ring cycloalkanes have attracted the attention of organic chemists because of their propensity to undergo transannular reactions.[3] We have accumulated a good deal of data dealing with ring inversion rates, conformational preferences, and transannular rearrangements in 7,12-dihydropleiadenes,[4] a particularly rigid cycloheptane system which has only a single low-energy conformation.
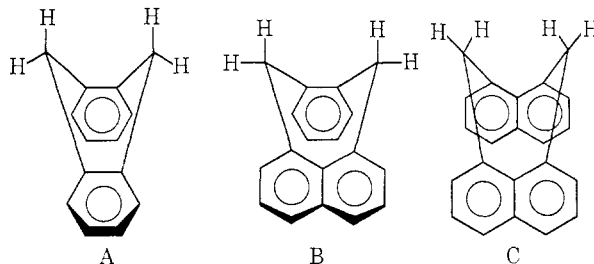
By virtue of its fused aryl rings, the seven-membered ring in DHP is confined to a "half-boat" conformation. The inversion of this ring can produce an identical species, as in *trans*-7,12-dimethoxy-DHP (**1**), an enantiomeric conformer, as in 1-methoxy-DHP (**2**), or a diastereomeric conformer, as in 7-methoxy-DHP (**3**).

1, R = R′ = OCH₃; R″ = H
2, R = R′ = H; R″ = OCH₃
3, R = OCH₃; R′ = R″ = H
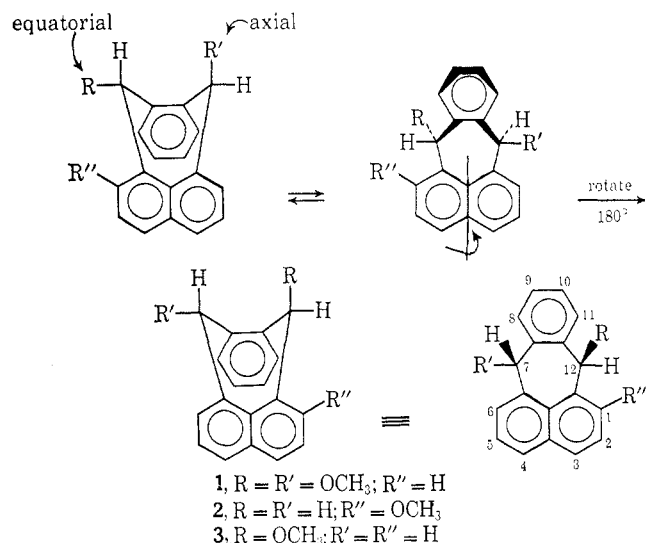
If the free energy barriers for inversion in **1–3** and relatives are suitably high (*ca.* $\gtrsim$ 20 kcal/mol), the individual conformers could be isolable. On the other hand, lower barriers (*i.e.*, 10–20 kcal/mol) would still permit facile detection of the conformers by nmr

spectroscopy,[1] which turned out to be the case[5] with DHP's whose seven-membered rings are not altered by large holding groups (*vide infra*).

The stage was thus set to consider such questions as (1) the effect of various buttressing substituents next to the central ring (at positions 1, 6, 8, and 11) on ΔF^* and the magnetic nonequivalence of the diastereomeric methylene groups at carbons 7 and 12; (2) how replacement of tetrahedral carbons on the ring by one or more trigonal carbons (*e.g.*, $>C=O$, $>C=CR_2$ would alter conformational stability, and (3) which conformation 7-substituted DHP's prefer; that is, would the substituent reside in an equatorial or axial position,[6] as in **3a** and **3e**, respectively. Some of these points can in turn be extended to the related 9,10-dihydroanthracenes (A)   and   1,8-(1′,8′-naphthyldi-

methyl)naphthalenes (C), whose six- and eight-membered central rings are respectively less and more folded than those of DHP. Examining models of these three ring systems permits one to predict interesting similarities and contrasts, several of which are enumerated below and discussed again later.   (1) The relative rates of ring inversion for similar derivatives will decrease in the order A > B > C, if a major factor

ground state   transition state
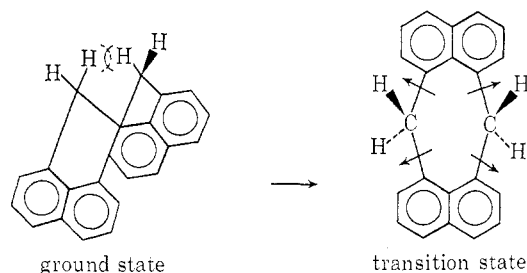
(1) Recent reviews: J. E. Anderson, *Quart. Rev.* (London), **19**, 426 (1966); L. W. Reeves, *Advan. Phys. Org. Chem.*, **3**, 187 (1965).

(2) (a) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1964; (b) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962.

(3) For a recent review, see A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev.* (London), **20**, 119 (1966).

(4) For brevity, 7,12-dihydropleiadene = DHP.

(5) P. T. Lansbury, J. F. Bieron, and M. Klein, *J. Am. Chem. Soc.*, **88**, 1477 (1966), and portions of the Ph.D. dissertations of M. Klein and F. D. Saeva, State University of New York at Buffalo, 1968.

(6) Although axial and equatorial terminology in DHP's may be confused with cyclohexane stereo nomenclature we prefer not to introduce yet another pair of terms (*e.g.*, the two positions on carbons 9 and 10 in 9,10-dihydroanthracenes have been described as *lin* and *perp*.[2a]).
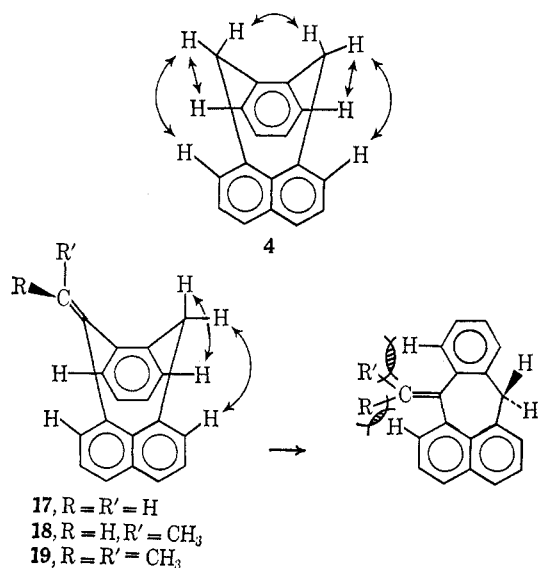
raising ΔF^* is bond angle strain in the transition state (arrows).[7] (2) Spatial proximity of the "hinge" carbons increases in going from A to B to C; thus transannular phenomena are most likely in C. (3) The degree of "folding" in the hydrocarbons as well as in the corresponding diketones is A < B < C. (4) Conformational preferences of a given substituent will become increasingly equatorial in going from A to B to C.[7]

Some of these predictions have been experimentally verified, and these findings constitute the major theme of this Account, while a good deal of additional work on other points remains to be completed.

Ring-Inversion Barriers

The major purpose for determining $\Delta F^*_{inversion}$ was to assess the possibility of isolating DHP invertomers. From variable-temperature nmr spectra for a number of DHP's containing "buttressing" substituents on the aryl rings, free energies of activation for the ring-flipping process (which is presumed to have a planar transition state) of 12.5–15.5 kcal/mol (at the coalescence temperature) were calculated.[8] The data[5] are summarized in Table I, which also records the dramatic effect of neighboring substituents on $\Delta\nu_{AB}$ for geminal diastereomeric protons on the "hinge" carbons (e.g., note 1-fluoro-DHP (14) compared with other 1 (substituents). It should be noted, in contrast, that these substituents had no marked influence on the barrier height in most cases (assuming $\Delta S^* \simeq 0$ in most cases,[8b] so that ΔF^* values calculated at different temperature could be compared).

Not surprisingly, 7-methylene-DHP (17) has a higher ΔF^* than DHP itself, since replacement of one sp³ methylene group in 4 relieves some ground-state

4

⟶

17, R = R' = H
18, R = H, R' = CH₃
19, R = R' = CH₃

steric compression (see arrows) and increases it in the transition state (ecliped arcs). The barrier height increases as methyls are introduced into the terminal methylene positions, so that **19** is "frozen" (on the nmr time scale) even at 200°, since the AB quartet due to the 12-methylene protons fails to collapse at that temperature.[5] Using conventional kinetic techniques with the *axially* C₁₂-monodeuterated **19** (preparation described below), the free energy of activation was found[9] to be *ca.* 31 kcal/mol at 130°.

Similar large alkylidene groups have been used to slow down the normally fast "boat-to-boat" inversion of 9,10-dihydroanthracenes. For example, Curtin, *et al.*,[10] observed that 9,9-dimethyl-10-dibromomethylene-9,10-dihydroanthracene (**21**) has $\Delta F^*_{22°} = 18$ kcal/mol. The two Br–H interactions in the transition state are similar to the situation in racemization of optically active 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid (**22**) which has $\Delta F^* = 19.5$ kcal/mol, thus suggesting that little additional hindrance to "flipping" is provided by the dihydroanthracene ring itself.

21   **22**
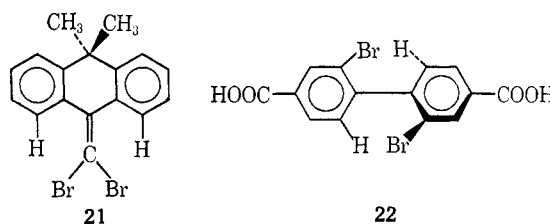
Conformational Preferences of 7-Substituted DHP's

Since the low inversion barrier in simple DHP's ruled out isolation of diastereomeric invertomers (e.g., **3e** and **3a**), we set about to measure conformational preferences in a selected group of 7-substituted DHP's so as to compare the relative steric requirements in DHP's with those in cyclohexanes (where the steric order is alkyl > OH ~ OR > halogen).[2] The detection of both conformers of a 7-substituted DHP seemed assured, so that our major problem became the unambiguous assignments of the chemical shifts of the 7- and 12-protons in each species, particularly H_A and H_E in the conformers shown. This was solved by four independent approaches, as illustrated below,
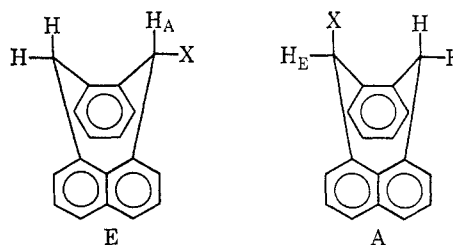

E   A

(7) Ground-state strain involving "bow–stern" (inside or axial) hydrogen repulsion is least serious in A but is a problem in C, where one trigonal "hinge" carbon would be a relief.

(8) (a) *Cf.* F. A. L. Anet and A. J. Bourn, *J. Am. Chem. Soc.*, **89**, 760 (1967); M. Oki and H. Iwamura, *Tetrahedron*, **24**, 2377 (1967). (b) A complete line-shape analysis of the variable-temperature nmr spectra of several DHP's gave ΔF^* values similar to our results and $\Delta S^* \approx 0$ eu (M. E. C. Biffin, L. Crombie, T. M. Connor, and J. A. Elvidge, *J. Chem. Soc., B*, 841 (1967)).

(9) P. T. Lansbury and M. Klein, unpublished results. In the case of 19-d₁, repeated ring inversion produces equal amounts of both diastereomers from *each* specifically deuterated conformer. The lack of an observable equilibrium deuterium isotope effect (same situation in DHP-7,7,12-d₃) justifies consideration of this process as analogous to racemization of enantiomers.

(10) D. Y. Curtin, C. G. Carlson, and C. G. McCarty, *Can. J. Chem.*, **42**, 565 (1964). A more recent study of several related dihydroanthracenes has been reported by Z. M. Holubec and J. Jonas, *J. Am. Chem. Soc.*, **90**, 5986 (1968).

Table I
### Free Energy Barriers for Ring Inversion of 7,12-Dihydropleiadenes[a]

Substituent	Fast exchange, δ		T_c, deg		Slow exchange, $\Delta\nu_{AB}$		$\Delta F^*_{T_c}$	
	C7	C12	C7	C12	C7	C12	C7	C12
None (4)	260		8		71	71	13.5	
1-CH₃-7,7-d₂ (6)		265		-10		19		13.1
1,5-DiCH₃ (7)	259	259	5	-10	73	19	13.3	13.0
1,6-DiCH₃ (8)		256		-14		17		12.7
8-CH₃-12,12-d₂ (9)	260		20		40		14.3	
8,11-DiCH₃ (10)		260		42		40		15.5
1-Cl (5)	265	283	8	-6	67	17	13.5	13.2
1-OAc (11)	259	259	10	0	69	20	13.6	13.5
1-OCH₃[b] (2)	267	282	10	0	69	32	13.6	13.4
1-C₂H₅ (12)	258	258	-2	-10	73	21	13.0	13.0
1-i-C₃H₇-12,12-d₂ (13)	266		3		76		13.2	
1-F (14)	266	269	4		71	0	13.2	
8-Cl (15)	275		2		13		13.6	
8-OCH₃[c] (16)	266	274	-7[c]	10	17[c]	74	13.1[c]	13.6
7-Methylene (17)		265		42		72		15.4
7-Ethylidene[d] (18)		267		188		64		22.1
7-Isopropylidene (19)		265		>200[e]		74		31.0[f]
trans-7,12-DiOCH₃[g] (1)			23		19		15.2	
trans-7,12-DiOCOCH₃[g] (20)			7		16		14.3	

[a] ΔF^* values are calculated at the coalescence temperature in $CDCl_3$ solvent, unless otherwise specified. Time-average chemical shifts and $\Delta\nu_{AB}$ values for "frozen" DHP's are given in Hz downfield from internal TMS at 60 MHz. Estimated errors in ΔF^* are ±0.3 kcal/mol. [b] Pyridine solvent. [c] Toluene was solvent for the C₇ data. [d] In nitrobenzene solvent. [e] In molten naphthalene where no AB collapse occurred at the high-temperature limit of the A-6040 temperature controller. [f] By conventional kinetics. [g] Data for these compounds were obtained from the methyl signals.

$$K_{eq} = \frac{[\text{area of } H_E]}{[\text{area of } H_A]} = \frac{\% \, A}{\% \, E}$$

from which the general trend of axial C₇ or C₁₂ protons to resonate downfield from their equatorial counterparts was established.

(1) The Model Compound Approach. At low temperatures, trans-7,12-dimethoxy-DHP (1) showed two equally intense OCH₃ signals, whose assignments follow from the two model compounds shown[11] (23 and 24, in their only available conformation). Inversion

1

23   24
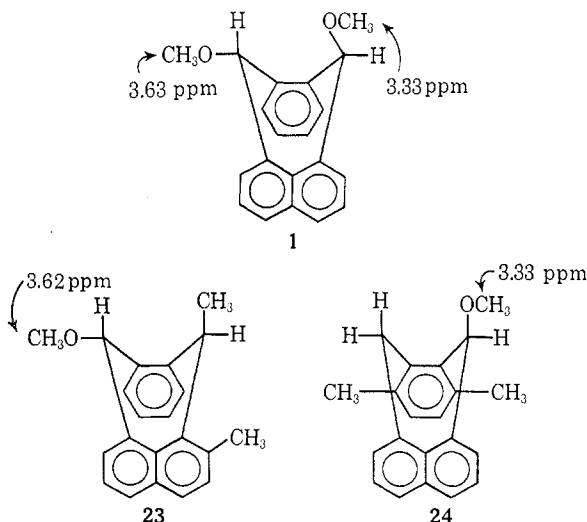
of 7-methoxy-DHP (3) is sufficiently slow at -20° to

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

detect both conformers (Figure 1); integration of the appropriate OCH₃ signals gives $K = [3a]/[3e] = 2.2$. It is also clear from Figure 1 that the more intense C₇-methine must now correspond to the equatorial proton in 3a, and this is 0.97 ppm upfield from its axial counterpart in 3e. Furthermore, upon inspecting the two C₁₂ AB quartets, we see that the upfield equatorial protons in each are relatively unaffected by the 7-OCH₃, but that the axial proton transannularly opposed by the axial OCH₃ in 3a is strongly deshielded (by 0.75 ppm) relative to the one in 3e. It should also be mentioned that irradiation of the axial 12-proton
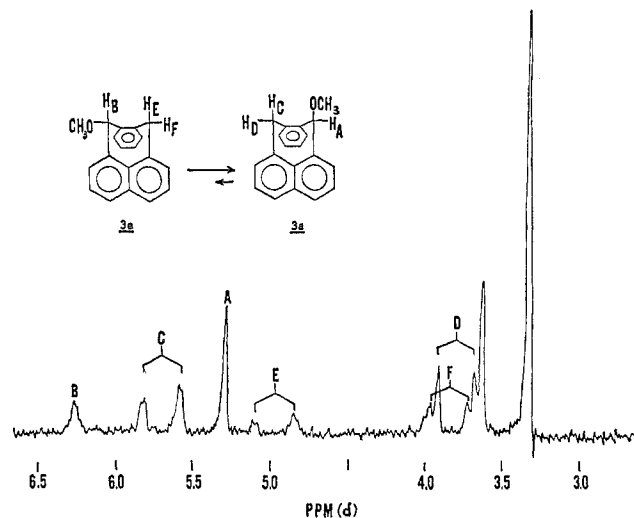

Figure 1. Partial 60-MHz nmr spectrum of 7-methoxy-DHP (3) at -20° in $CDCl_3$, showing the nonaromatic protons of both "frozen" conformers.

in **3e** produced a nuclear Overhauser effect[12] at the axial C_7-methine proton, but not in **3a** (see below for discussion of this technique). Such a set of data rigorously confirms the assignments of 7- and 12-protons in both conformers of **3**; similar approaches were used with 7-acetoxy-[11] and 7-alkyl-DHP's.[13] Equilibration studies with diastereomeric disubstituted DHP's provided even further proof of conformational preferences.[13]

(2) **Stereospecific Long-Range Benzylic Coupling.** In 7-chloro-DHP (**25**) one observes a temperature-invariant spectrum ($+60$ to $-60°$) consistent with the overwhelming existence of a single conformer. Careful examination[11] of the aliphatic proton signals shows that the axial 12-proton peaks (downfield doublet in the AB spectrum) are *ca.* two times wider at half-height than the equatorial C_{12} and the C_7-methine peaks. This finding appeared to be a case of benzylic long-range coupling[14] with *ortho* and *para* aromatic protons, which is expected to be maximum (<1 Hz) for axial protons perpendicular to the ring plane, as was confirmed by decoupling experiments. The identical line widths (before aryl decoupling) of the C_7 and C_{12} equatorial proton signals thus established the axial position of the chlorine[11] in **25**; this technique applies to other DHP's as well.

(3) **Stereospecific Chemical Reactions.** Potassium *t*-butoxide and DMSO-d_6 react with **19** at room temperature within minutes to introduce one and only one deuterium. This results in collapse of the original AB spectrum, leaving only a broad singlet (due to equatorial C_{12}-H in place of the upfield doublet).[5] The stereospecific axial exchange (which is possible only in a relatively rigid DHP such as **19** (Table I) and not in the ethylidene analog **18**) is readily understandable because the inert equatorial proton is labilized only by the aryl inductive effect and not by incipient aryl resonance in the transition state for proton transfer. Thus, the latter resembles triptycene in kinetic acidity, whereas the axial proton resembles triphenylmethane.[15]

(4) **Nuclear Overhauser Effect (NOE).** The identification of protons which are not on adjacently bound atoms in a molecule but are nevertheless close in space and coupled by dipole–dipole interaction can be achieved using nmr spectroscopy by saturation of one proton signal so that the populations of energy levels of the other proton change. The resulting enhanced signal intensity arising from the latter proton is referred to as the NOE.[12] We have used transannular NOE's to detect axial C_7-protons and NOE's involving aryl substituents *ortho* to the seven-membered ring to identify equatorial C_7 protons,[12] as illustrated in Chart I.

Chart I[a]

[a] The asterisk indicates the nucleus showing nmr signal enhancement. The brackets indicate the nucleus undergoing saturation by a second radiofrequency field.

It had now been firmly established that, in diastereomeric C_7 or C_{12} CH_2 groups with $\Delta\nu_{AB} \geq 1$ ppm, the equatorial protons generally resonate at higher field than the axial ones.[16] Therefore, it was somewhat disconcerting to find that methyl groups on C_7 (as in 7-methyl-DHP) have virtually identical chemical shifts.[17] Even more surprising was the finding that methyl groups one or more atoms further removed from the ring (*e.g.*, C_7 methoxy, acetoxy, ethyl) had reversed chemical shifts; that is, the axial signal was now at higher field[11,13] ($\delta_{ax} - \delta_{eq} \simeq 0.3$ ppm). These observations reinforce the notion that chemical shift assignments made "by analogy with similar compounds" can be risky practice!

The conformational equilibrium constants of a variety of 7-substituted DHP's are summarized in Table II.

One immediately notes that there is no similarity between these group preferences and the analogous cyclohexyl derivatives,[18] not that any should be expected. What is noteworthy, however, is the importance of "β atoms" in the substituent on conformational preference. The "A values" of groups on cyclohexanes depend mostly on the atom directly attached to the ring;[19] thus OH, OCH_3, and $OCOCH_3$ all have $A \simeq 0.7$–0.8 kcal/mol and CH_3, CH_2CH_3, $CH(CH_3)_2$ have $A \simeq 1.8$–2.1 kcal/mol. The same series of substituted DHP's,[20] however, show equatorial preferences for OH (**27**) and CH_3 (**29**) and increasingly greater axial demands when the "β portion" of the substituent enlarges (*e.g.*, $CH(CH_3)_2$ (**31**) is $\gg95\%$ axial). Apparently steric compression of the outer part of the group with neighboring aromatic protons causes the axial shift. The clear lesson arising from these steric size fluctuations is the potential error
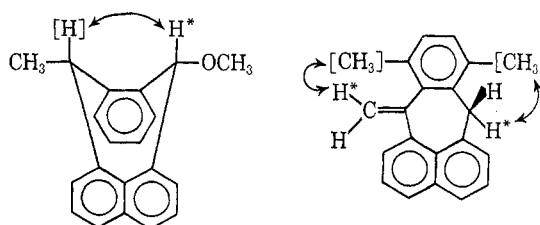
(12) J. G. Colson, P. T. Lansbury, and F. D. Saeva, *J. Am. Chem. Soc.*, **89**, 4987 (1967), and references cited therein.

(13) P. T. Lansbury, A. J. Lacher, and F. D. Saeva, *ibid.*, **89**, 4361 (1967).

(14) S. Sternhell, *Pure Appl. Chem.*, **14**, 15 (1964).

(15) A. Streitwieser, *et al.* (*J. Am. Chem. Soc.*, **86**, 3578 (1964)), have noted that $(C_6H_5)_3CT$ exchanges its tritium with lithium cyclohexylamide in cyclohexylamine *ca.* 10^6 more rapidly than triptycene-1-*t*.

(16) However, when $\Delta\nu_{AB} \lesssim 0.3$ ppm as in the 12-CH_2 group of some 1-substituted DHP's (see Table I), the peak assignments are then by no means clear-cut.

(17) Conformer populations in 7-methyl-DHP could only be determined from the C_7-methine peaks.[20]

(18) Reference 1a, p 44.

(19) E. L. Eliel, *Angew. Chem. Intern. Ed. Engl.*, **4**, 761 (1965).

(20) Several of the conformational equilibria summarized in Table II were compared with chemical equilibration of diastereomeric 7,12-disubstituted DHP's. Thus, diequatorial *cis*-7,12-dimethyl-DHP predominates over the *trans* isomer[13] and *trans*-7,12-dimethoxy-DHP predominates over the *cis* isomer after treatment with *t*-butoxide–DMSO and acidic methanol, respectively (P. T. Lansbury and A. J. Lacher, unpublished results).

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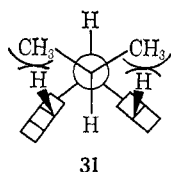
from unwarranted extrapolation between different molecular arrays.

A related system for stereochemical study presented itself with the finding that certain 7-aryl-7-hydroxy-DHP's (**33**) as well as 1-phenyl-12-hydroxy-DHP's (**34**) readily cyclize to benzfluorenes in acid.[11,21]

33

34   *cis* and *trans*
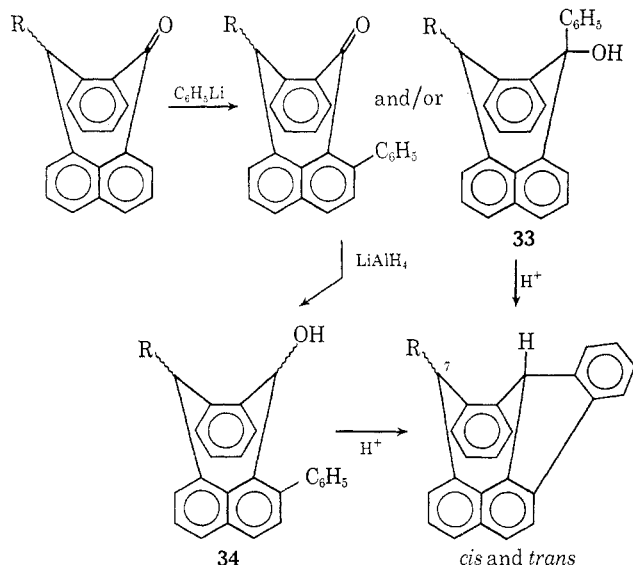
As shown, two rigid diastereomeric 1,12-(*o*-phenylene)-7,12-dihydropleiadenes can be formed if a **7** substituent is present. These possess a conformation of the seven-membered ring which is not dissimilar from that of DHP's. In addition, being fluorene derivatives, such compounds can be interconverted by base. Beginning with 12-methyl-7(12H)-pleiadenone, only the *cis* isomer of 7-methyl-1,12-(*o*-phenylene)-DHP (**35**) was obtained in pure form from either of the above reaction sequences.[21] However, butyllithium metalation of **35**, followed by kinetic protonation, produced a *cis–trans* mixture (identified by nmr); subsequent equilibration[21] afforded only **35**, a result consistent with the conformer preference in 7-methyl-DHP[13] (**29**).

35
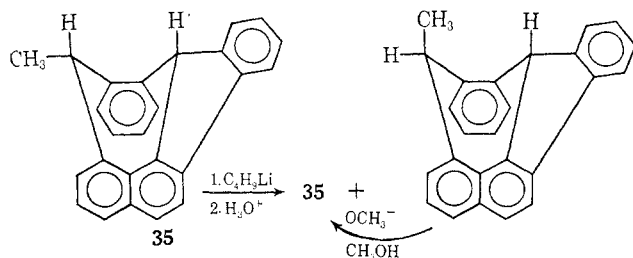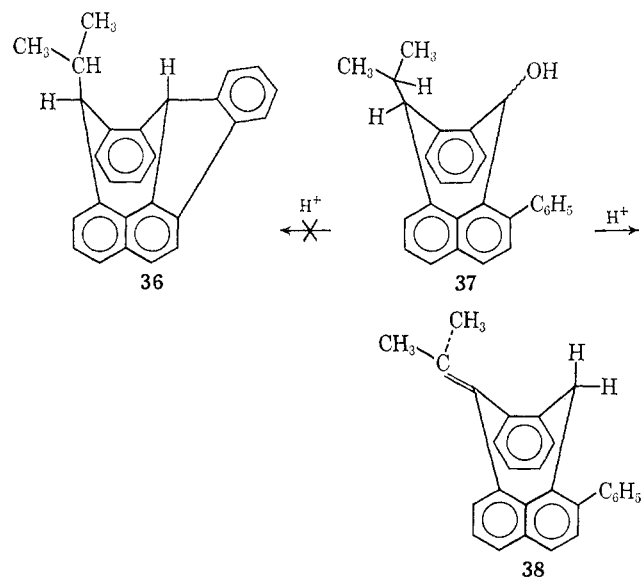
Transannular Hydrogen Shifts

When we attempted to prepare 7-isopropyl-1,12-(*o*-phenylene)-DHP (**36**) by cyclodehydration of car-

(21) P. T. Lansbury, J. B. Bieber, F. D. Saeva, and K. R. Fountain, *J. Am. Chem. Soc.*, **91**, 399 (1969).

binol **37**, an entirely different reaction, leading to **38**, took precedence. A more detailed look at this

36   **37**

38

transformation, using deuterium as tracer and 7-isopropyl-12-hydroxy-DHP as substrate, revealed that the isopropyl α-hydrogen migrates by a 1,5 shift rather than the more labile benzylic one, producing 25% **40** and 75% **19** under kinetic control. 7-Methyl-12-

stable conformer   **39**

**40**   **19**
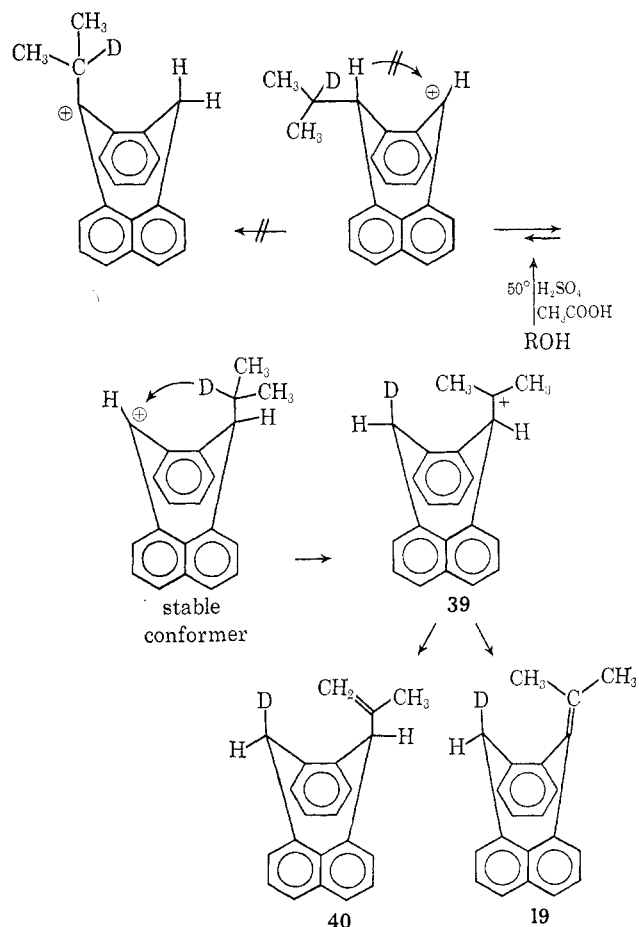
hydroxy-DHP (**41**) gave no analogous rearranged product when subjected to rearrangement conditions, although a 1,4 shift is conformationally feasible and

Table II

**Conformational Energies for 7-Substituted 7,12-Dihydropleiadenes**

7 substituent	T, °K	K_{eq}[e]	$\Delta F°$, kcal/mol	Method and comments	Ref
OH[a] (27)	213	0.3	+0.5	Integration of aliphatic C–H	a
	223	0.4	+0.4	signals	
OCH₃ (3)	242	2.2	−0.4	Integration of OCH₃ peaks	11
OCOCH₃ (28)	243	3.3	−0.6	Integration of OCOCH₃ peaks	11
CH₃[b] (29)	243	0.14	+1.0	Integration of C₇–H quartets	13
	233	0.09	+1.2		
C₂H₅[c] (30)	253	1.1	−0.1	Integration of C₇–H and CD₂CH₃	13
	223	0.6	+0.3	singlets	
CH(CH₃)₂ (31)	243–313	>20	<−1.6[d]	Only axial conformer detected by C₇–H at position for equatorial proton	13
Cl (25)	213–313	>20	<−1.6[d]	Only axial conformer detected from line-width measurements	11
C₆H₅ (32)	213–313	>20	<−1.6[d]	Only axial conformer detected; C₁₂-Hs shielded by transannular phenyl ring in axial position	
COOCH₃ (26)	233–313	>20	<−1.6[d]	As with 25	

[a] Unpublished experiments with Dwight Chasar, using the 7-d molecule.   [b] Using the 12,12-d_2 molecule to clarify the nmr spectrum. [c] Using the 12,12-(ethyl-α,α-d_2)-d_4 molecule to clarify the nmr spectrum.   [d] For T = 273°K.   [e] [Axial]/[equatorial].

41
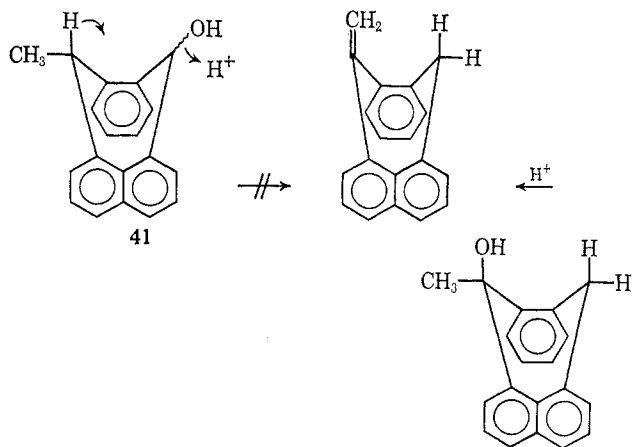
1,5-hydride transfer from a primary carbon appears unlikely.

The absence of a 1,4 shift in **41** is especially surprising since just such a process did occur readily with the potassium salt **42** (X = Cl), which rearranged to **43** in DMSO at ∼50° with $t_{1/2} \simeq$ 45 min ($\Delta F^* \simeq$ 24 kcal/mol).[22] The expected rate enhancement with


42   **43**

X = Cl, CH₃
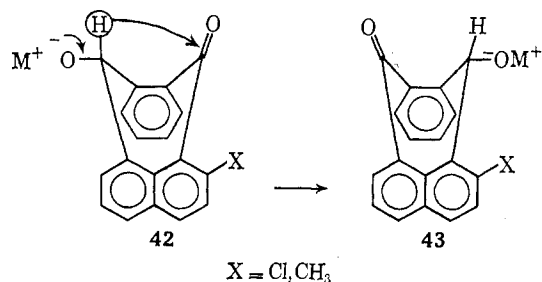
increased ionic character of the alkali metal–oxygen bond in **42** was observed (Cs > K > Na > Li).[22] These hydroxypleiadenone rearrangements constitute the first kinetic studies of transannular hydrogen shifts.

Comparisons of Dihydropleiadenes with Related Ring Systems

Some comment is now in order regarding comparisons of DHP chemistry with 9,10-dihydroanthracenes (A) and 1,8-(1′,8′-naphthyldimethyl)naphthalenes (C), as noted in the introductory paragraphs.

(1) Conformational inversion barriers do, in fact, increase in the order predicted. Thus, simple 9,10-dihydroanthracenes invert too rapidly to "freeze out" (on the nmr time scale), suggesting an inversion barrier of <5 kcal/mol, whereas analogous DHP's show $\Delta F^* \sim$ 13–15 kcal/mol. Yet another 8–10-kcal increase in barrier height results on going to the eight-membered ring analogs, three of which are shown (**44–46**). The optically active diketone **44** racemizes with $t_{1/2}$ = 102 min at 26° (ΔF^* = 22.9 kcal/mol).[23] Since the diastereomeric methylene protons in **45** and **46** exhibit temperature-invariant AB spectra up to

44   **45**

46

(22) P. T. Lansbury and F. D. Saeva, *J. Am. Chem. Soc.*, **89**, 1890 (1967).
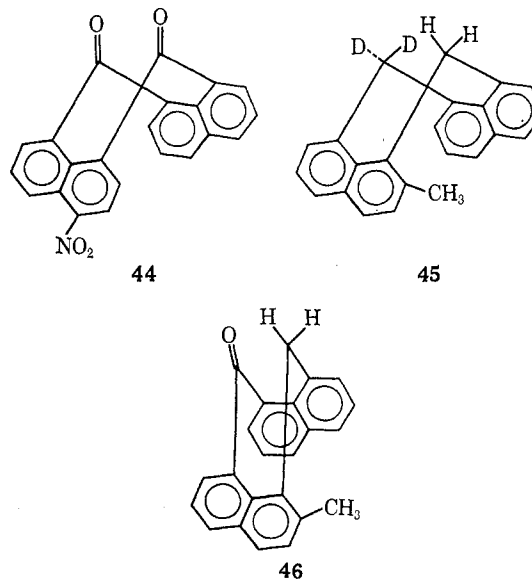
(23) W. C. Agosta, *ibid.*, **89**, 3926 (1967).

$200°$, only minimum values of ΔF^* could be calculated;[24] both barriers exceed 23 kcal/mol.

(2) That spatial proximity of the "hinge" carbons increases on going to the eight-membered ring compounds is evident from Agosta's report[25] that diketone **47** forms very stable transannular bridged compounds which exist only in the cyclic form, upon nucleophilic attack at one (and only one) carbonyl group. On the
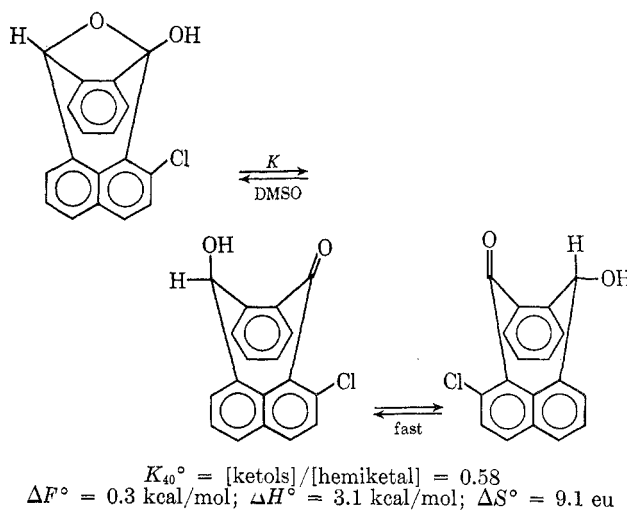

47

Nu = H, CH₃, OH, NHNH₂
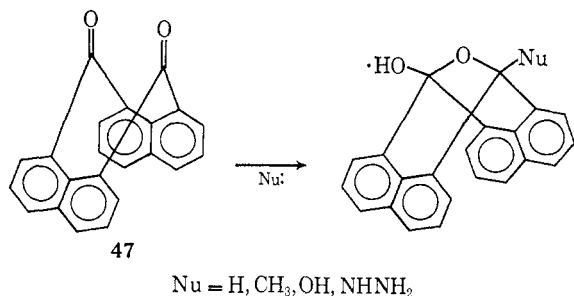
other hand, 7,12-pleiadiones can undergo organometallic additions and hydride reductions at both carbonyl functions, although it is possible to achieve monoaddition selectively.[22] Moreover, hydroxypleiadenones exist as ring-chain tautomeric pairs of approximately equal free energy[22] (e.g., as shown in Chart II). At higher temperatures, the freely inverting ketol tautomers are favored ($K_{160°} = 2.34$) on entropy grounds.

(3) Increased proximity of hinge atoms goes hand in hand with greater molecular nonplanarity. Thus anthraquinone is planar, whereas **47** is highly folded, based on infrared and ultraviolet spectral properties.[26] 1-Chloro-7,12-pleiadione (**48**) is also nonplanar (the average angle between the two nuclear planes is 138°), as revealed by X-ray crystallographic studies.[27] The specific deformation of the 12-carbonyl group by C_1–Cl, which is detectable by infrared spectroscopy[28] as well, undoubtedly contributes to the driving force of the above-mentioned rearrangement of 1-chloro- (or 1-methyl) 7-hydroxy-12(7H)-pleiadenone (**42**).[22]

(4) As intramolecular folding increases, so does the steric compression between axial groups at tetravalent hinge carbons. Based on models, without deforming bond angles, the axial bonds diverge in dihydroanthracenes, converge slightly in DHP's, and converge acutely in 1,8-(1′,8′-naphthyldimethyl)naphthalenes. The actual structures will, of course, be different, but the expectation of greater equatorial preferences in going from A to B to C is nevertheless reasonable. There are

(24) P. T. Lansbury and M. Klein, *Tetrahedron Letters*, 1981 (1968).

(25) W. C. Agosta, *J. Am. Chem. Soc.*, **89**, 3505 (1967).

(26) R. L. Letsinger and J. A. Gilpin, *J. Org. Chem.*, **29**, 243 (1967).

(27) K. M. S. Islam and G. Ferguson, *J. Chem. Soc., B*, 1135 (1967). An independent crystal structure study of **48** was also carried out in our laboratory in collaboration with Professor Eli Shefter and Dr. K. R. Fountain.

(28) G. Eglington, G. Ferguson, and K. M. S. Islam, *J. Chem. Soc., B*, 1141 (1967). We have also noted differences of 13–32 cm⁻¹ in the two carbonyl stretching frequencies of several 1-substituted 7,12-pleiadiones (F. D. Saeva, Ph.D. Dissertation, State University of New York at Buffalo, 1968).

Chart II

$$K_{40°} = [\text{ketols}]/[\text{hemiketal}] = 0.58$$
$$\Delta F° = 0.3 \text{ kcal/mol}; \quad \Delta H° = 3.1 \text{ kcal/mol}; \quad \Delta S° = 9.1 \text{ eu}$$

some data on 9,10-dihydroanthracenes[29] which indicate that the axial position is less crowded and that *cis*-(diaxial) 9,10-disubstituted-9,10-dihydroanthracenes (e.g., the dimethyl compound) are more stable than the *trans* isomers. On the other hand, Nicholls and Szwarc[30] concluded that several 9-alkyl-9,10-dihydroanthracenes prefer the conformation with an equatorial alkyl group. Their conclusions, while possibly correct, must be regarded as open to serious question because they naively assumed that the upfield aliphatic C_{10}-proton doublet in the AB spectrum of the methylene group (whose chemical shift was similar to the C_9 methine) was the axial one, by analogy with simple cyclohexanes. This assumption is clearly not justifiable, since the opposite assignments have been unambiguously confirmed in the more similar DHP's. Obviously, some additional conformational studies are necessary to clear up discrepancies in dihydroanthracene stereochemistry.

In 7-substituted DHP's we have already seen that methyl and hydroxyl have equatorial preferences, although β-methyl substitution reverses the trend, as in methoxyl and isopropyl. Any possible generalizations based on such oxygen and alkyl substituents are inappropriate for explaining the axial preference of chlorine whose van der Waals radius (1.8 Å) is slightly smaller than that of methyl (2.0 Å). Perhaps London forces[19,31] need to be considered here.

No conformational studies have yet been completed with 1,8-(1′,8′-naphthyldimethyl)naphthalenes, in part because of synthetic difficulties. It seems reasonable at present to guess that no substituent will dare to venture toward the axial position.

(29) Reference 1a, pp 242–243.

(30) D. Nicholls and M. Szwarc, *J. Am. Chem. Soc.*, **88**, 5757 (1966); *Proc. Roy. Soc.* (London), **A301**, 231 (1967).

(31) Reference 1a, pp 13–19, discusses the role of London attractive forces in *n*-propyl chloride and related acyclic molecules, where conformations with *gauche* CH₃–Cl interactions are highly populated.