graphic analysis, a small amount of the reaction product was isolated by this technique for confirmatory identification by refractive index and infrared spectrum.

The yields were measured by comparing the peak area of the reaction product with the peak area of a standard solution of the same material. Thus all yields reported are actual, rather than normalized values. There were two exceptions to this procedure. Triphenylmethane was isolated and weighed to establish the yield, and the products from *t*-amyl chloride, because of their high volatility, were analyzed utilizing an internal standard.

Checks of the analytical procedure, utilizing synthetic mixtures, indicated that the actual compositions could be reproduced with an uncertainty of ±2% for each component. Since the values are as likely to be high or low, it is not surprising that in some cases the actual yields total slightly more than 100%.

Rate Measurements. The rate of solvolysis of benzhydryl chloride in the presence of borohydride was measured by following the rate of formation of diphenylmethane, determined by gas chromatographic examination of aliquots. The rate in the absence of borohydride was measured by the usual titrimetric technique.

7,12-Dihydropleiadenes. I. Free-Energy Barriers to Conformational Inversion[1]

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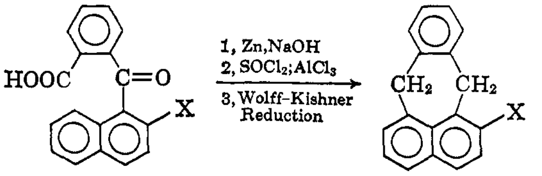
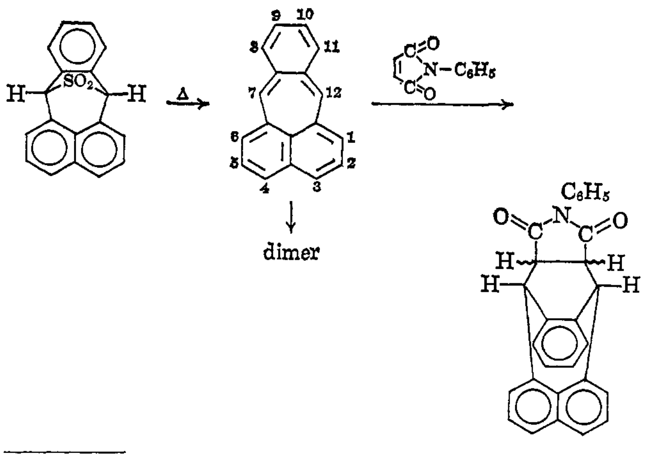
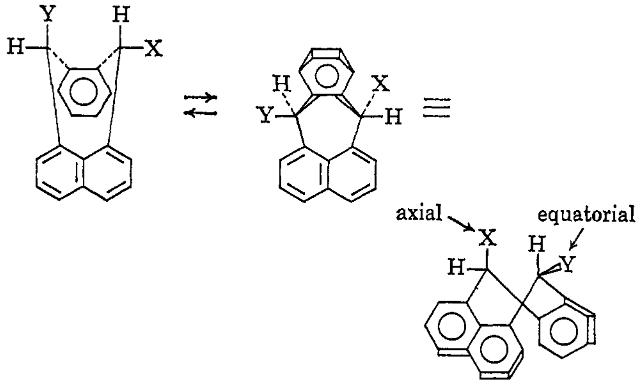
Received October 25, 1965

Abstract: A variety of 7,12-dihydropleiadenes has been prepared by multistep syntheses from 1,8-naphthalic anhydride and aryl Grignard reagents. These nonplanar molecules, whose seven-membered rings are "boat shaped," undergo conformational inversion at rates too fast to permit isolation of enantiomeric or diastereomeric atropisomers. From variable temperature nmr measurements, free energies of interconversion of 13.2–15.6 kcal/mole were calculated for the ring "flip" of several dihydropleiadenes. The transition state for the inversion is deduced to be planar.

Some time ago, Fieser and co-workers prepared a variety of polycyclic cyclohepta[*d*,*e*]naphthalenes from the condensation of phthalic anhydride and 2-substituted naphthalenes.[3] Reduction of the keto acids, followed by intramolecular acylation and further reduction of the resultant ketones, gave polynuclear products containing a central cycloheptane ring, whose parent structure was given the trivial name "pleiadene."[3] Actually Fieser's compounds were 7,12-dihydro analogs of the fully conjugated system that resisted synthesis until Cava and Schlessinger's successful generation and "trapping" experiments (above).[4] The parent pleiadene molecule proved to be a highly reactive "*o*-xylylene," which dimerizes or polymerizes unless trapped by dienophiles. Unlike planar pleiadenes, 7,12-dihydropleiadenes (hereafter abbreviated DHP) are stable molecules which exist in folded conformations with geometry not unlike the more common 9,10-dihydroanthracenes.[5]







Several consequences of conformational interconversion in dihydropleiadenes can be distinguished. In the first case (X = Y), a degenerate process occurs in which the conformer flips into *itself* (*cf.* compounds I, IV, VII, VIII, and IX in Tables I and II). A second group of compounds, exemplified by 8-methyl-7,12-

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(1) Partially reported in preliminary form: P. T. Lansbury and J. F. Bieron, *J. Am. Chem. Soc.*, **86**, 2524 (1964).

(2) (a) Alfred P. Sloan Foundation Fellow, 1963–1967; (b) National Science Foundation Predoctoral Fellow, 1962–1964.

(3) L. F. Fieser and M. A. Fieser, *J. Am. Chem. Soc.*, **55**, 3010, 4963 (1933).

(4) M. P. Cava and R. H. Schlessinger, *ibid.*, **85**, 835 (1963); *Tetrahedron*, **21**, 3073 (1965).

(5) A. H. Beckett and B. A. Mulley, *Chem. Ind.* (London), 146 (1955).

Table I. Properties of 7,12-Dihydropleiadenes

Compound	Mp, °C	Anal, %[a]			
		Carbon		Hydrogen	
		Calcd	Found	Calcd	Found
7,12-Dihydropleiadene (I)	114.5–115	...	...	...	...
7,12-Dihydropleiadene-7,7-d_2 (II)[b]	114.5	...	...	...	...
8-Methyl-7,12-dihydropleiadene-12,12-d_2 (III)	140–141	92.64	92.62	7.26	7.12
8,11-Dimethyl-7,12-dihydropleiadene (IV)	190–191	92.97	93.05	7.03	6.90
7-Methylene-7,12-dihydropleiadene (V)	58–59	94.18	94.07	5.82	5.78
7-Isopropylidene-7,12-dihydropleiadene (VI)	103–104	93.29	93.21	6.71	6.82
trans-7,12-Dihydroxy-7,12-dihydropleiadene (VII)	204–205	...	...	...	...
trans-7,12-Diacetoxy-7,12-dihydropleiadene (VIII)	170–170.5	76.29	76.20	5.24	5.14
trans-7,12-Dimethoxy-7,12-dihydropleiadene (IX)	111–112	82.73	82.56	6.25	6.25

[a] Data for new compounds only. [b] Deuterium anal. Calcd: excess D, 14.28. Found: excess D, 14.03.

Table II. Barriers to Ring Inversion of 7,12-Dihydropleiadene

Compound	Solvent	δ_ω,[a] cps	T_c, °C	k_{T_c}, sec^{-1}	$\Delta F^*_{T_c}$, kcal/mole
7,12-Dihydropleiadene (I)	$CDCl_3$	71	+8	158	13.6
7,12-Dihydropleiadene-7,7-d_2 (II)	$CDCl_3$	71	+8	158	13.6
	C_6H_5Cl	66.3	+6	147.4	13.2
8-Methyl-7,12-dihydropleiadene-12,12-d_2 (III)	$CDCl_3$	40.3	+20	89.5	14.5
	C_6H_5Cl	38.2	+19	84.8	14.5
8,11-Dimethyl-7,12-dihydropleiadene (IV)	$CDCl_3$	40.9	+42	90.8	15.6
	C_6H_5Cl	38.5	+39	85.6	15.5
7-Methylene-7,12-dihydropleiadene (V)	$CDCl_3$	72.0	+40	160.0	15.2
	C_6H_5Cl	72.0	+45	160.0	15.4
7-Isopropylidene-7,12-dihydropleiadene (VI)	$CDCl_3$	74.0	>200	...	>20
trans-7,12-Dimethoxy-7,12-dihydropleiadene (VIII)	$CDCl_3$	16.0	+7	36.0	14.3
trans-7,12-Dimethoxy-7,12-dihydropleiadene (IX)	$CDCl_3$	18.5	+23	41	15.2
	C_6H_5Cl	15.7	+28	35	15.5
3,4-Ethano-7,12-dihydropleiadene (X)	$CDCl_3$	72.6	+5	161.3	13.4

[a] Calculated from the expression (1–3) = $\sqrt{\delta_{AB}^2 + J_{AB}^2}$ for compounds where the methylene protons were AB quartets (all except VIII and IX).

dihydropleiadene (III), undergoes conformational inversion into their *enantiomers*. In the third case ($X \neq Y$), a conformer flips into its *diastereomer*, as discussed further in the following paper. Compounds of the first class for which $X = Y \neq H$ are not racemizable if optically active, whereas those of the second class (*e.g.*, II, III, V, and VI) can maintain optical activity only if the free energy of inversion is sufficiently high (*i.e.*, $\Delta F^* \approx 20$ kcal/mole) to prevent facile ring flipping. Finally optically active compounds of class three can exist as isolable diastereomers or undergo mutarotation, depending on ΔF^* inversion.[6a] From examination of models it is clear that substituents on C_7 and C_{12} can occupy either "axial" or "equatorial" positions[6b] and that the reactivity of groups may vary depending on their position. Clearly the dihydropleiadene system poses many interesting problems in organic stereochemistry dealing with structural effects on inversion barriers, isolation of diastereomeric conformers, and/or determination of conformational preferences for readily interconvertible DHP derivatives, as well as related physical–organic studies, such as steric deuterium isotope effects. This paper is the first in a series concerning such investigations and deals with the important question of the magnitude of the energy barrier separating the enantiomorphic conformers in simple DHP's. Such information is needed to predict the possibility of isolating atropisomers.

Recently we prepared 7-phenyl-7,12-dihydropleiadene and found that the C_{12} protons exhibited magnetic nonequivalence, showing an AB spectrum with $\delta_{AB} = 0.87$ ppm and $J_{AB} \sim 15$ cps that was temperature invariant from +40 to −50°.[7] Since two AB spectra could be expected from the presence of two diastereomeric pairs of atropisomers,[8] it was felt that only one isomer was present or that rotation was fast over the entire temperature range, resulting in a time-average quartet with nonequivalence stemming from the asymmetric center at C_7. To resolve this problem, the synthesis of a variety of DHP derivatives and measurement of their free energies of inversion was begun.

Results and Discussion

The general synthetic approach to the dihydropleiadenes of interest to us is outlined in Chart I. In order to ensure the formation of the seven-membered ring in the intramolecular acylation step (C) we proceeded *via* 8-aroyl-1-naphthoic acids,[9] in spite of their

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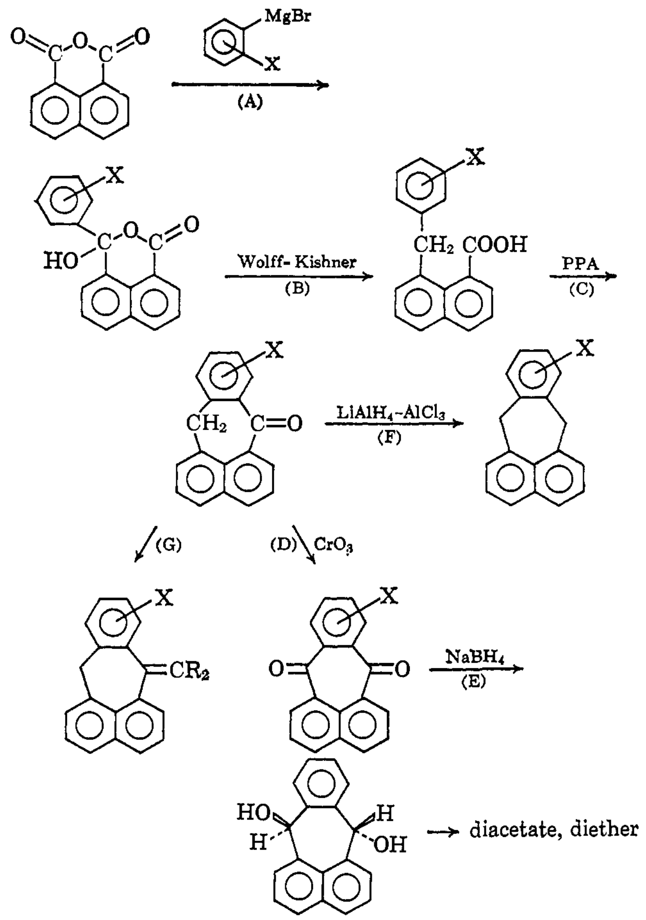
(6) (a) For an example, see K. Mislow and H. Joshua, *J. Am. Chem. Soc.*, **87**, 666 (1965). (b) This nomenclature is not to be confused with cyclohexane stereochemical terminology. However, the terms seem appropriate and we have chosen to use them, rather than coin new ones.

(7) P. T. Lansbury, *J. Am. Chem. Soc.*, **81**, 4325 (1959).

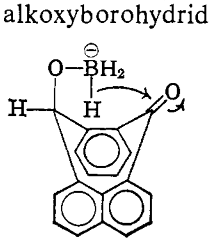
(8) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 379.

(9) W. S. Wagner, Ph.D. Dissertation, University of Missouri, 1952.

Chart I

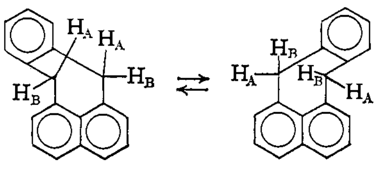


ψ-acid structures[10] which were indicated by infrared and nmr spectroscopy. This tautomeric preference of the keto acids caused some difficulty in the reduction to methylene acids and, of numerous methods tried, we finally settled on the Huang–Minlon procedure as the best alternative. The 7(12H)-pleiadenones obtained in step C[11] were readily reduced to dihydropleiadenes by mixed hydride reduction[12] or oxidized to 7,12-pleiadiones, from which the *trans* diol and its derivatives were prepared by standard reactions (see the Experimental Section). The *trans* stereochemistry of the diol was inferred from its mode of synthesis, on the assumption that the second carbonyl group was reduced *intramolecularly* by the alkoxyborohydride initially formed.



This assumption proved correct on the basis of infrared spectroscopy (no intramolecular O—H ... O bonding) and from nmr studies of ring inversion in the derived diacetate and diether (*vide infra*). Finally, 7-pleiadenone could be allowed to react with alkyllithium reagents and the tertiary alcohols dehydrated to 7-alkylidene derivatives. Table I gives physical properties and analytical data for all pertinent compounds used in determination of inversion barriers.

The inversion barriers for the above dihydropleiadenes were determined by variable-temperature nmr spectroscopy.[13] In compounds I–VI, the methylene protons at C_7 and C_{12} occupy different positions relative to the aromatic rings (one "axial" and one "equatorial") and ring inversion produces an enantiomeric conformer of equal free energy, or is a degenerate interconversion. Thus a single signal is observed for H_A and H_B when inversion is fast ($k >> \delta_{AB}$) whereas H_A and H_B give a pair of doublets with separation δ_{AB} when the rate of inversion is slow, due to magnetic nonequivalence and geminal coupling ($J_{gem} \approx 14$–15 cps). At the coalescence temperature, the rate of inversion is calculated from the expression[14] $k = \pi\delta_{AB}/\sqrt{2}$, and from the rate constant one obtains the free energy of activation for inversion from the Eyring equation, using a transmission coefficient of 1. Actually Gutowsky's equation applies rigorously only to exchanges where the nuclei are not spin coupled; however, when $\delta_{AB} > J_{AB}$ (as in the present cases) the relationship is considered to be satisfactory.[15] In compounds VIII and IX, the methyl signals of the methoxy and acetoxy groups were observed as a function of temperature; in these cases, cooling produced a pair of equally intense single peaks, one due to the axial group and one to the equatorial one. The rate and ΔF^* for the inversion process were calculated as above. In Table II we have listed the significant nmr data and derived rate constants for the dihydropleiadenes studied. The ΔF^* values are considered to be accurate to within ±0.1 kcal/mole. Thus far, only chloroform-*d* and chlorobenzene have been used as solvent, but further studies of solvent effects are in progress.



Although we calculated several Arrhenius activation energies from the temperature dependence of line width above T_c,[16] we have refrained from placing much reliance on these data because of several sources of error involved.[17] These would cause especially serious errors when entropies of activation are calculated.[18] Our values of ΔS^*, which were usually close to 0 as

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(10) P. T. Lansbury and J. F. Bieron, *J. Org. Chem.*, **28**, 3564 (1963).

(11) Had we used *o*-(α-naphthoyl)benzoic acids, which exist in the open-chain form and are easily reduced to methylene acids, cyclization would have proceeded entirely to benzanthrones instead of the desired pleiadenones. We did, however, use this route for some compounds (accompanying paper) when a 2 substituent was present on the α-naphthoyl group to prevent cyclization to a benzanthrone.

(12) (a) R. F. Nystrom and C. R. A. Berger, *J. Am. Chem. Soc.*, **80**, 2896 (1958); (b) E. L. Eliel, *Record Chem. Progr.*, **22**, 129 (1961).

(13) *Cf.* (a) F. A. L. Anet and M. Ahmad, *J. Am. Chem. Soc.*, **86**, 119 (1964); (b) A. T. Bottini and J. D. Roberts, *ibid.*, **80**, 5203 (1958); (c) K. G. Untch and R. J. Kurland, *ibid.*, **85**, 346 (1963); (d) G. Claeson, G. Androes, and M. Calvin, *ibid.*, **83**, 4357 (1961); (e) F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *ibid.*, **84**, 386 (1962); (f) F. A. L. Anet and J. S. Hartman, *ibid.*, **85**, 1204 (1963); (g) F. A. L. Anet and M. Z. Haq, *ibid.*, **87**, 3147 (1965); (h) F. A. Bovey, E. W. Anderson, F. P. Hood, and R. L. Kornegay, *J. Chem. Phys.*, **40**, 3099 (1964).

(14) H. S. Gutowsky and C. H. Holm, *ibid.*, **25**, 1228 (1956).

(15) F. A. L. Anet, *J. Am. Chem. Soc.*, **86**, 458 (1964).

(16) (a) F. A. L. Anet, *ibid.*, **86**, 458 (1964); (b) J. B. Lambert, *Tetrahedron Letters*, 1901 (1963); (c) L. H. Piette and W. A. Anderson, *J. Chem. Phys.*, **30**, 899 (1959).

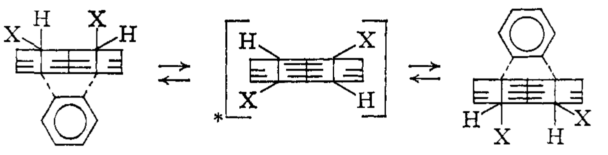
(17) A. Allerhand and H. S. Gutowsky, *ibid.*, **41**, 2115 (1964).

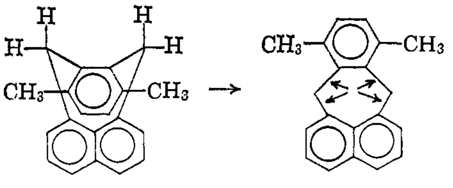
(18) L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 7 (1963).

expected,[19] could appear to be either positive or negative depending on the error and are therefore of little use for interpretation.

The most obvious conclusion from the ΔF^* values reported in Table II is that the inversion barriers for simple dihydropleiadene derivatives are too low to allow isolation of atropisomers. Thus, rather than isolating diastereomeric conformers of 7-substituted DHP's (see the introductory material), we are instead confronted with the problem of determining conformational preferences for these rapidly equilibrating molecules.[20] It should be noted, however, that among several 7-alkylidene derivatives studied, 7-isopropylidene DHP (VI) is resolvable into atropisomers. The magnetic nonequivalence of the C_{12}-methylene protons in VI is still apparent at 200° (spectrum run in molten naphthalene) meaning that inversion of the seven-membered ring in VI is very slow ($<<74$ sec^{-1}) even at that elevated temperature.[21]

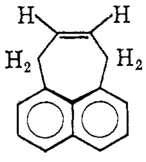
A second conclusion derivable from the free energies of inversion of I, III, and IV is that the transition state for the interconversion is planar, with both C_7 and C_{12} inverting simultaneously. This hypothesis is based on the observation that 8-methyl DHP[22] has $\Delta F^* = 14.5$ kcal/mole for inversion which is approximately halfway between the values for DHP (13.6) and 8,11-dimethyl DHP (15.6). The increased energy barriers resulting from introduction of methyl groups *ortho* to the inverting methylene carbons are apparently due to a "buttressing" effect[23] which leads to more steric compression in the transition state (when bond angles in the seven-membered ring spread out) than in the ground state. Such buttressing effects are well documented in studies of optically active biphenyls.[24] If the transition state for inversion of III were asymmetric, with one methylene group inverting before the other, ΔF^* would have been close to I, since the lower energy pathway avoiding compression of C_7 and the C_8–CH_3 would be preferred.



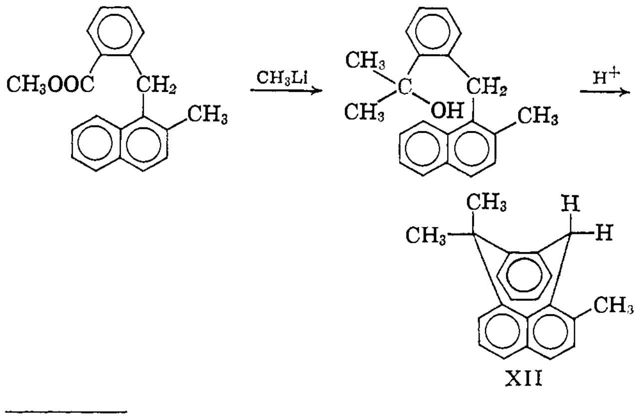


Finally, we felt that comparison of the inversion barriers for 7,12-dihydropleiadene (I) and 7,12-dihydropleiadene-7,7-d_2 (II) might reveal a steric deuterium isotope effect since simple conformational changes, uncomplicated by bond making and breaking, are ideal for studying such effects.[25] Ground-state steric compression might be less severe in II, thus lowering its inversion rate relative to I. Although the nmr method did not reveal any rate differences (*i.e.*, apparently identical T_c and δ_ω values for I and II), it is possible that $k_H/k_D \leq 1.2$ would have been undetected and this is the usual magnitude of previously reported steric deuterium isotope effects.[25] Thus, the nmr technique does not seem to be sensitive enough to demonstrate such small rate differences.

The *trans*-7,12-diol derivatives VIII and IX gave inversion barriers somewhat higher than DHP although the nonplanar ground-state conformations appear to have greater nonbonded interactions. However, it is possible that restricted rotation within the methoxy or acetoxy groups in the transition state ($-\Delta S^*$) may be responsible for the enhanced free energies of activation. We also synthesized an analog of DHP in which the *o*-phenylene group is replaced by a double bond, XI. This compound, prepared by lead tetracetate oxidation of *trans*-2,3-pleiadanedicarboxylic acid,[26] underwent ring inversion much more rapidly than the DHP's used in this study, there being no evidence of hindered inversion of the nmr spectra down to −60°.[27] Apparently XI is considerably more flexible than I. An additional compound of interest was 7,12-dihydro-1,7,7-trimethylpleiadene (XII), which was synthesized by a route different from that described above.[28] In



XI



XII

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(19) Solvent effects on ΔS^* are considered negligible since both solute and solvents are nonpolar. Furthermore, compounds of group 1 (undergoing degenerate interconversion) have ΔS^* of only R ln 2 due to symmetry contributions (assuming a planar transition state); ΔS^* is also R ln 2 for group 2 DHP's (undergoing enantiomeric inversion), due, in this case, to the entropy of mixing.

(20) This aspect of the work is discussed in the following paper.

(21) The resolvability of VI is indicated by the isolation of optically active (−)-VI from partial dehydration of (±)-7-isopropyl-7-hydroxy-7,12-dihydropleiadene with (+)-camphorsulfonic acid. It is hoped that the complete resolution of VI and the isolation of diastereomeric conformers of 12-substituted 7-isopropylidene DHP's will be realized in the near future: M. Klein, unpublished results.

(22) The compound actually used was 7,12-dihydro-8-methylpleiadene-12,12-d_2, so that only one AB spectrum (C_7-methylenes) could be observed without interference from the other quartet (which had different T_c and δ_{AB}).

(23) G. W. Wheland, "Advanced Organic Chemistry," 3rd ed, John Wiley and Sons, Inc., New York, N. Y., 1960, pp 272–288.

(24) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 163.

(25) (a) K. Mislow, R. Graeve, A. J. Gordon, and G. H. Wahl, *J. Am. Chem. Soc.*, **86**, 3497 (1964); (b) L. Melander and R. E. Carter, *ibid.*, **86**, 295 (1964).

(26) V. Boekelheide and G. Vick, *ibid.*, **78**, 653 (1956).

(27) P. T. Lansbury and A. J. Lacher, unpublished results.

(28) The reaction of alkyllithium reagents with 8-substituted 1-naphthoate esters, containing a bulky group *peri* to the ester function, proceeds only to the ketone stage and then enolizes: R. L. Letsinger

addition to assessing the effect of the bulky *gem*-dimethyl group on the inversion barrier, which should be substantially lowered by the enhanced CH_3–H steric repulsions produced by *both* methyls in the enantiomeric "folded" conformations, XII presented the opportunity to study inversion rates using both the C_7-*gem*-dimethyl signal (no spin coupling) and the C_{12} protons (geminal coupling). Unfortunately, the latter effort failed, probably because the above-mentioned ground-state steric strains did in fact lower ΔF^* for inversion of XII drastically. At any rate no peak broadening of the methyl or methylene signals was shown from +40 to −60°. The degree of folding in XII is probably less than in I, somewhat like 9,10-dihydroanthracene, which also undergoes "boat–boat" inversion too fast to observe under our conditions. In fact, Curtin, *et al.*,[29] have shown that hindered inversion of some 9,10-dihydro-9,9-dimethyl-10-methylene-anthracenes is detectable only when the 10-methylene group contains two large substituents, *e.g.*, $>{=}CBr_2$. This may be compared with 7-methylene DHP (V) in the present investigation which has a substantial inversion barrier and 7-isopropylidene DHP (VI) which exhibits atropisomerism.

One point not yet discussed is the assignment of the two doublet signals arising from the C_7 and C_{12} methylene groups in the nmr spectra of "frozen" 7,12-dihydropleiadenes to the axial and equatorial protons. The high-field doublet can be attributed to the equatorial proton and the low-field signal to axial. These conclusions are based on long-range coupling studies and conformational analysis of 7-substituted DHP's, which are discussed in detail in the following paper.

We are continuing our investigations of ring inversion in the 7,12-dihydropleiadene system and hope to enhance our understanding of the factors affecting the energy barrier for this conformational change.

Experimental Section[30]

8-Benzyl-1-naphthoic Acid. Thirty-five grams (0.12 mole) of 8-benzoyl-1-naphthoic acid,[31] 40 g (0.72 mole) of potassium hydroxide, 40 ml (0.68 mole) of 85% hydrazine hydrate, and 250 ml of diethylene glycol were combined and refluxed at 90–100° for 9 hr. The condenser was then removed and the reddish violet solution heated until the pot temperature reached 170°, during which nitrogen evolution began (*ca.* 130°). After 3 hr reflux at 170–185°, nitrogen evolution ceased; the cooled reaction mixture was diluted with water, extracted with ether, and filtered through a mixture of Norit and Celite. Acidification with cold hydrochloric acid precipitated the product as a red, amorphous mass, which was redissolved in sodium carbonate, retreated with Norit, and again precipitated with acid. After several such treatments, the acid was recrystallized several times from methanol–water, affording cream-colored crystals, mp 137–137.5°, in 52% yield (17 g). The infrared spectrum (Nujol) showed carbonyl absorption at *ca.* 1690 cm^{-1}.

Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.5; H, 5.37. Found: C, 82.64; H, 5.32.

7(12H)-Pleiadenone. A solution of 4.1 g of 8-benzyl-1-naphthoic acid in 60 g of polyphosphoric acid was heated at 85–95° (steam bath) for 45 min. The dark red mixture was then poured into ice water. The product was taken up in ether and washed with 10% sodium hydroxide solution and water. After drying over sodium sulfate, the ether solution was concentrated to give light yellow crystals which were recrystallized from methanol–water. There was obtained 2.9 g (77%) of colorless crystals, mp 118–119°, whose infrared spectrum showed carbonyl absorption at 1655 cm^{-1}.

Anal. Calcd for $C_{18}H_{20}O$: C, 88.5; H, 4.92. Found: C, 88.39; H, 4.84.

7,12-Dihydropleiadene (I). An ether solution containing equimolar portions (*ca.* 11 mmoles) of lithium aluminum hydride and aluminum chloride was added to 1.85 g (7.6 mmoles) of 7(12H)-pleiadenone dissolved in ether. After 0.5 hr at room temperature, the reaction mixture was hydrolyzed with dilute hydrochloric acid and worked up as usual to yield 1.70 g (essentially quantitative yield) of 7,12-dihydropleiadene, mp 114.5–115° (lit[32] mp 114°), as colorless needles (from methanol–water).

7,12-Dihydropleiadene-7,7-*d*$_2$. Lithium aluminum deuteride (Metal Hydrides) was substituted for lithium aluminum hydride in the above reduction procedure, giving the dideuterated analog II in 94% yield, mp 114.5–115°.

Anal. Calcd for $C_{18}H_2D_2$: excess D, 14.28. Found: excess D, 14.03.

trans-**7,12-Dihydro-7,12-dihydroxypleiadene** (VII). 7,12-Pleiadione, prepared by chromic acid oxidation of 7(12H)-pleiadenone or I, was reduced by excess sodium borohydride in methanol for 5 hr at room temperature. Dilution with water led to precipitation of the diol, which was recrystallized from benzene–ligroin, mp 204–205° (lit[4] mp 198–200°). A high-dilution infrared spectrum showed no evidence for intramolecular hydrogen-bonded O—H. . .O stretching.

trans-**7,12-Dihydro-7,12-diacetoxypleiadene** (VIII). To a solution of 1 ml of acetic anhydride in 10 ml of pyridine was added 0.94 g of 7,12-dihydro-7,12-dihydroxypleiadene and the mixture was kept overnight. The reaction mixture was then poured onto ice–water and extracted with ether. The ether extract was washed with 10% hydrochloric acid and water, dried over sodium sulfate, and finally concentrated to give a light brown solid. Chromatography over alumina with benzene as eluent resulted in initial elution of the *trans*-diacetate VIII (0.44 g) as a waxy solid. Recrystallization from chloroform–ligroin gave white crystals, mp 170–170.5°, whose infrared spectrum showed acetate carbonyl absorption at *ca.* 1735 cm^{-1}.

Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.29; H, 5.24. Found: C, 76.20; H, 5.14.

trans-**7,12-Dihydro-7,12-dimethoxypleiadene** (IX). One-half gram (10.3 mmoles) of sodium hydride was added to 0.924 g (3.55 mmoles) of *trans*-7,12-dihydro-7,12-dihydroxypleiadene dissolved in 25 ml of 1,2-dimethoxyethane. The mixture was heated under nitrogen for 4 hr, then treated with 2.28 g (16 mmoles) of methyl iodide and stirred overnight at room temperature. The reaction mixture was poured into ice water and extracted with ether and benzene. The organic extracts were washed with water, dried over sodium sulfate, and concentrated to give an oil. Chromatography of the latter on alumina gave 0.25 g of the diether IX by elution with 1:1 benzene–petroleum ether (bp 30–60°). Recrystallization from ligroin gave fine white crystals of IX, mp 111–112°, whose infrared spectrum showed no O–H absorption and whose nmr spectrum was consistent with the expected structure.

Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.56; H, 6.25.

7-Methylene-7,12-dihydropleiadene (V). To a solution of 3.19 g (13.5 mmoles) of 7(12H)-pleiadenone in 50 ml of tetrahydrofuran was added 50 ml of 0.422 *N* methyllithium in ether solution. The deep purple solution was stirred for 2 hr, then poured into ice water and worked up in the conventional manner. The crude, oily alcohol (hydroxyl absorption in the infrared) was dissolved in 25 ml of methanol containing 1 drop of concentrated hydrochloric acid and refluxed for 12 hr. The reaction mixture was then diluted and worked up to give an oil which was chromatographed over

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and P. T. Lansbury, *J. Am. Chem. Soc.*, **81**, 953 (1959). Thus we were compelled to use the above *o*-alkyl *benzoate* ester to ensure formation of the tertiary alcohol, as the precursor to the *gem*-dimethyl compound (XII). The C_1–CH_3 group was present merely to prevent cyclization at C_2, which would give an unwanted dihydrobenzanthracene.

(29) D. Y. Curtin, C. G. Carlson, and C. G. McCarty, *Can. J. Chem.*, **42**, 565 (1964).

(30) Melting points and boiling points are uncorrected. Infrared spectra were obtained on a Beckmann IR-5A spectrometer, using Nujol mulls or neat films between sodium chloride plates. Ultraviolet spectra were obtained on a Beckman DK-2 spectrometer. Nuclear magnetic resonance spectra were obtained on a Varian Associates A-60 spectrometer equipped with a variable-temperature probe and a Model A-6040 temperature controller. Carbon–hydrogen analyses were by Dr. A. Bernhardt, Mulheim, Germany, and deuterium analyses were by Mr. Josef Nemeth, Urbana, Ill.

(31) D. V. Nightingale, W. S. Wagner, and R. H. Wise, *J. Am. Chem. Soc.*, **75**, 4701 (1953).

(32) A. Rieche, H. Southoff, and O. Muller, *Ber.*, **65**, 1380 (1932).

alumina. Petroleum ether eluted 1.2 g of olefin V, mp 58–59° after recrystallization from methanol. The infrared spectrum was free of carbonyl absorption and the nmr spectrum consistent with structure V, showing the nonequivalent vinyl protons at 313 and 337 cps ($J \sim 2.5$ cps) and the C_{12}-methylene protons centered at *ca.* 260 cps (above the coalescence temperature).

Anal. Calcd for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.07; H, 5.78.

7-Isopropylidene-7,12-dihydropleiadene (VI). Following the above procedure for preparation of V, excess isopropyllithium was treated with 7(12H)-pleiadenone in ether–tetrahydrofuran. The crude product still contained some unidentified ketone (possibly from conjugate addition) but chromatography on alumina successfully separated the hydrocarbon VI from more polar materials by elution with petroleum ether. Recrystallization from methanol gave the analytical sample, mp 103–104°.

Anal. Calcd for $C_{21}H_{18}$: C, 93.29; H, 6.71. Found: C, 93.21; H, 6.82.

The nmr spectrum showed two methyl singlets at 103 and 113 cps and the nonequivalent C_{12} protons as an AB spectrum centered at 266 cps with $\delta_{AB} = 74$ cps and $J_{AB} \sim 14$ cps.

7,12-Dihydro-8,11-dimethylpleiadene (IV). The same sequence of steps were used as in the preparation of I from 8-benzoyl-1-naphthoic acid.

8-(2,5-Dimethylbenzoyl)-1-naphthoic acid[33] was subjected to Huang–Minlon reduction, as above, giving only *ca.* 5% of the reduced acid (confirmed by infrared spectra). The latter was not characterized further but cyclized directly in hot polyphosphoric acid to 8,11-dimethyl-7(12H)-pleiadenone, $\nu_{\max}^{>=O}$ 1670 cm⁻¹. The ketone was subjected to mixed hydride reduction (as in preparation of I and II), giving IV as white needles (from methanol–benzene), mp 190–191°.

Anal. Calcd for $C_{10}H_{18}$: C, 93.0; H, 7.03. Found: C, 93.05; H, 6.90.

The nmr spectrum at 30° showed the methyl signal at 143 cps and the C_7 and C_{12} methylene protons as a broad hump centered at 265 cps, which sharpened into an AB quartet, $\delta_{AB} \sim 41$ cps and $J_{AB} \sim 15$ cps, on cooling to −20°.

7,12-Dihydro-8-methylpleiadene-12,12-d_2 (III). As in the above-described preparations of Ia nd IV, 1-*o*-toluoyl-8-naphthoic acid was prepared by addition of *o*-tolylmagnesium bromide to 1,8-naphthalic anhydride in ether–toluene, in 70% yield, mp 195–197°. Huang–Minlon reduction of this keto acid proceeded in 41% yield to 8-(*o*-methyl)benzyl-1-naphthoic acid, mp 165–168°, whose infrared and nmr spectra were consistent with the proposed structure. Cyclization of the methylene acid with PPA produced 11-methyl-7(12H)-pleiadenone in 58% yield, mp 143–148°; mixed hydride reduction of the ketone with lithium aluminum hydride (or deuteride) and aluminum chloride in ether afforded III or the undeuterated analog in 75% yield, mp 140–141° (from methanol).

Anal. Calcd for $C_{19}H_{14}D_2$: C, 92.64; H, 7.36. Found: C, 92.62; H, 7.12.

Nuclear Magnetic Resonance Experiments. Variable-temperature nmr measurements were performed on an A-60 spectrometer equipped with a calibrated A-6040 temperature controller. Determinations of coalescence temperatures and maximum peak separations in the absence of exchange were done at least four times for each compound and usually by different operators (J. F. B. and M. K.) at widely separated times. Coalescence temperatures were determined to ±1° by numerous readings immediately above and below the apparent coalescence temperature.

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[33] F. A. Mason, *J. Chem. Soc.*, 125, 2119 (1924).

7,12-Dihydropleiadenes. II. Conformational Analysis of Some 7-Substituted 7,12-Dihydropleiadenes[1]

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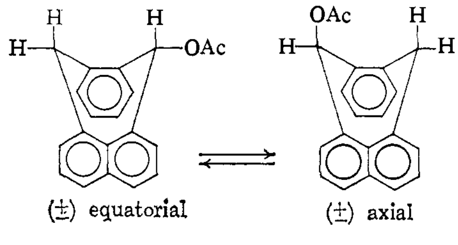
Abstract: The syntheses of 7-chloro-, 7-methoxy-, and 7-acetoxy-7,12-dihydropleiadenes have been accomplished and the conformational preferences of these groups, as well as a 7-phenyl group, established as axial. Evidence for these conclusions is obtained from nmr spectroscopy, using conformationally homogeneous model 7,12-dihydropleiadenes of known stereochemistry, and evaluation of long-range coupling between C_7 and C_{12} protons and aromatic protons. When ring inversion is slow, the diastereomeric C_{12}-methylene protons show AB quartets with $\Delta\nu_{AB}$ *ca.* 1–2 ppm, the equatorial protons appearing at higher field than the axial ones.

In the first paper of this series,[3] it was established that simple 7,12-dihydropleiadenes (DHP) undergo boat-to-boat ring inversion at rates too fast to permit isolation of atropisomers (unless 7-alkylidene groups were used to restrict inversion). Thus 7-substituted dihydropleiadenes will exist as a mobile equilibrium mixture containing two diastereomeric conformers, as illustrated for 7-acetoxy-7,12-dihydropleiadene. In this paper we discuss the evaluation of the conformational equilibrium constants of four 7-substituted DHP's and



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[3] P. T. Lansbury, J. F. Bieron, and M. Klein, *J. Am. Chem. Soc.*, 88, 1477 (1966).