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THE STEREOCHEMISTRY OF ALKYLATION OF 7-ALKYL-7,12-DIHYDROPLEIADENE ANIONS

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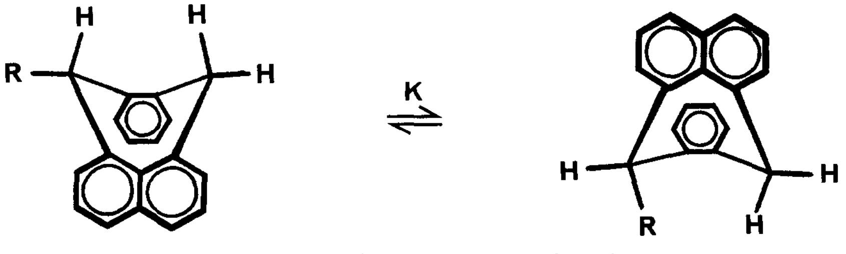
Summary: *Attempts to rationalize the stereochemistry resulting from the alkylation of 7-R-12-metallo-7,12-dihydropleiadene from the geometries of the neutral precursors were not successful. A new model is suggested.*

The alkylation of 9-alkyl-10-metallo-9,10-dihydroanthracene has received considerable attention.[1] Stereochemical models for these anions have included inverting boat conformations with an sp^3 anionic center preferentially in a pseudoaxial position. More recently, however, sp^2 hybridization has been suggested on the basis of direct proton and carbon NMR studies,[2] and a "flattened" geometry seems to be most consistent with carbon chemical shifts.[2a] Unfortunately, the question of whether or not the conformational characteristics of the neutral precursors serve as a useful model for the anions cannot be answered. This is due to the fact that the early concept of boat-to-boat ring inversion in 9,10-dihydroanthracenes (DHA's) has never been demonstrated by NMR (in solution).[3] Either the inversion barriers are quite low, or as recent molecular mechanics calculations suggest,[4] DHA's have broad potential wells with planar or near planar minima in many cases. In view of all the attention given to DHA anion alkylation,[1] we felt that it would be interesting to investigate a ring system that does have a well characterized geometry.

The 7,12-dihydropleiadene (DHP) ring system is particularly well suited since inversion barriers are relatively high ($\Delta G^\dagger$ = 13-16 kcal/mol).[5] This is important since if alkylation rates are faster than

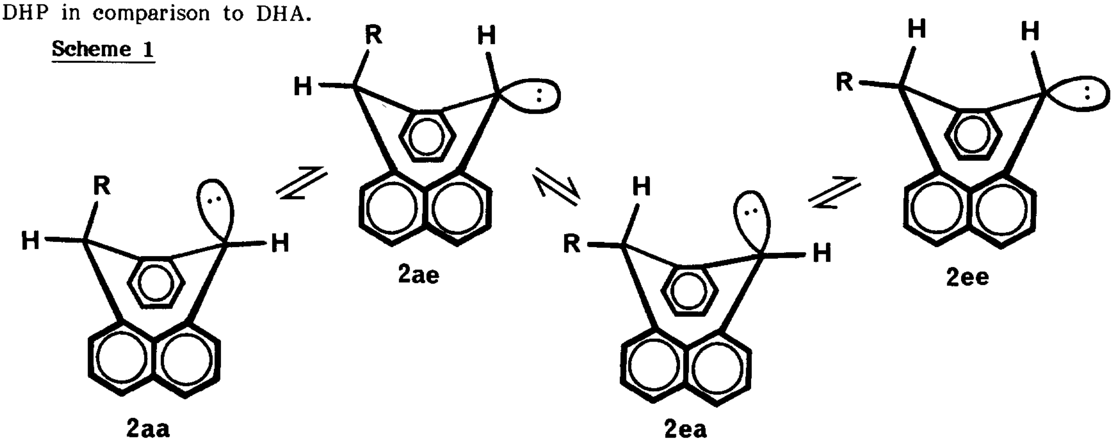


1a, R=Me (K=0.14); 1b, R=Et (K=1.1); 1c, R=iPr (K>20)

interconversion rates, this produces a Curtin-Hammett kinetic system expected to produce "kinetic quenching", and product ratios would reflect precursor geometries.[6] Another interesting feature of DHP's is substituent group preference.[5] Methyl occupies the pseudoequatorial position to the extent of 90%, whereas isopropyl is exclusively pseudoaxial. Ethyl, on the other hand, shows little preference. It appears then, that DHP provides an excellent system to determine if a prediction of anion geometries based on neutral precursors will lead to a rationalization of alkylation stereochemistry.

Analogy with the earlier proposed structures for dihydroanthracene anions would lead to the possibilities shown as scheme 1. Before evaluating these structures, several points should be noted about DHP in comparison to DHA.

Scheme 1



(1) The pseudoaxial bond (and hence H or R) is directed in towards the central ring to a much greater extent in DHP, and transannular effects are expected to be more important. (2) Ring flattening is more difficult to achieve with DHP due to the interior angles of the central ring. This is evidenced by the considerably higher (10-16 kcal/mol) barriers to ring inversion. (3) In DHP, a p-orbital (i.e., sp^2 hybridization of the anion) would not overlap with the adjacent aromatic rings as well as DHA due to consideration (1) above. Moreover, flattening of the central ring to accommodate p-orbital overlap would be more difficult with DHP as outlined in consideration (2). For these reasons, this type of model (i.e., puckered boats, sp^3 hybridization) is actually more appropriate for DHP than DHA.

We will consider iPrDHP first since the geometry of the hydrocarbon shows exclusive pseudoaxial substituent preference. For this reason, we would expect either 2aa or 2ae to be reasonable intermediates. However, due to a substantial transannular effect from the relatively large isopropyl group, product formation would appear more likely from 2ae.[7] This would, of course, produce trans products. Treatment of 7-iPrDHP with n-butyllithium in THF at 0°C[8] for 30 min. followed by addition of R'X produced high to exclusive amounts of trans products in the series R' = Me (92%), Et (95%) and iPr (100%)[9] (see Table 1). These results are, of course, consistent with 2ae as an intermediate.

In constrast to iPrDHP, the ethyl derivative shows almost equal amounts of pseudoaxial and pseudoequatorial conformers. With this in mind, it is surprising to find such a high degree of stereoselectivity with this system. Isopropylation produces 90% trans and methylation affords 78% cis (ethylation produced only a slight (59%) preference for trans). Application of scheme 1 to this case presents some problems. Since the ethyl substituent can easily adopt the pseudoequatorial position, one might expect 2ea as the important intermediate with an absence of substituent transannular effects as

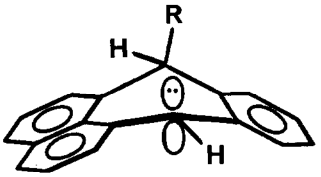
Table 1. Deprotonation/Alkylation Reactions of Alkyl-7,12-Dihydropleiadenes[a,b]

			cis/trans ratio	
Substrate	ax/eq[c]	CH_3I	CH_3CH_2Br	$(CH_3)_2CHBr$
7-MeDHP	10/90	57:43	40:60	10:90
7-EtDHP	50/50	78:22	41:59	10:90
7-iPrDHP	100/0	8:92	5:95	0:100

a. Ratios from glpc on an OV-1 column. b. Isomer assignment by NMR. c. Ratio of pseudoaxial to pseudoequatorial substituent preference in the substrates.

well as a pseudoaxial anionic center. This would lead to trans products, however, and is certainly not consistent with 78% cis methylation. With 7-MeDHP, intermediate 2ea would appear even more probable due to the strong (90%) pseudoequatorial preference of the methyl group. However, even though isopropylation does produce trans products (90%), ethylation gives only 60% trans, and methylation shows cis preference (57%). Hence, the results with both 7-MeDHP and 7-EtDHP raise serious questions about the use of neutral precursors to predict the geometries of the intermediate anions.

In view of this obviously poor correlation of hydrocarbon conformations with alkylation stereochemistry, some other interpretation is required. We propose a model similar to our suggestion for the DHA anion.[2a] That is, sp^2 hybridization with a somewhat flattened central ring (3). In this model, we feel that all substituent groups will occupy a pseudoaxial position. This can be rationalized by inspection



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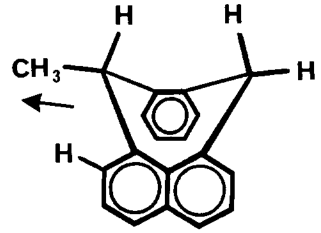

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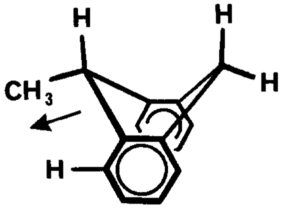

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of models. In 7-MeDHP, the relatively small methyl group is up past the peri interactions[10] (see 4) due to the angle of the pseudoequatorial bond. In 7-MeDHA (5), for comparison, the pseudoequatorial bond is angled towards the peri hydrogens. A slight flattening of the DHP ring, however, directs a pseudoequatorial substituent into the peri hydrogens, and, at the same time, the transannular interaction of the pseudoaxial position with the 11-H is being relieved. Hence a shift to pseudoaxial group preference.

With this model for the alkylation of 7-RDHP anions, we would expect DHP to resemble DHA except that transannular effects will still be more important for DHP. In fact, DHP does show more trans products, especially when R and/or R' are large, but shows the same tendency to favor cis products as the size of R and R' is reduced. Future work with molecular mechanics calculations as well as direct carbon NMR studies with DHP anions should provide further insight.

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6. a. J. I. Seeman, Chem. Rev., 1983, 83, 83. b. Although ring inversion may be slow, anion pyramidal inversion could be rapid so structures with pseudoequatorial electron pairs could be important for product formation even if present in small amounts.
7. Temperatures below 0°C produced poorer results perhaps due to solubility problems. We would have preferred lower temperatures since this results in greater dissociation of the metal counter ion.[8a,b,c] In anions where sufficient energy barriers exist between contact ion pairs and solvent separated ion pairs, reactions with electrophiles can be "metal directed". This appears more important for protonation than for alkylation,[8c] however, and such processes are not suggested by the data herein. Similarly, it is unclear as to what effect aggregation might have on our results, but we feel that aggregates are unlikely in this large, delocalized system.[8d]
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9. All new products gave satisfactory C,H analysis. Identification was made on the basis of characteristic proton NMR chemical shifts of pseudoequatorial and pseudoaxial hydrogens as well as temperature dependent NMR and nuclear Overhauser enhancements. A complete proton and carbon NMR study of these interesting compounds will be provided in the full paper.
10. A slight distortion of bond angles might "pull up" the methyl even more. We shall try to determine the feasibility of this with molecular mechanics calculations.

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