9-Isopropylidene-9,10-dihydroanthracene. Synthesis, Stereochemistry, and the Effect of 10-Alkyl Group Size on the Equilibrium with 9-Isopropyl-10-alkylanthracene

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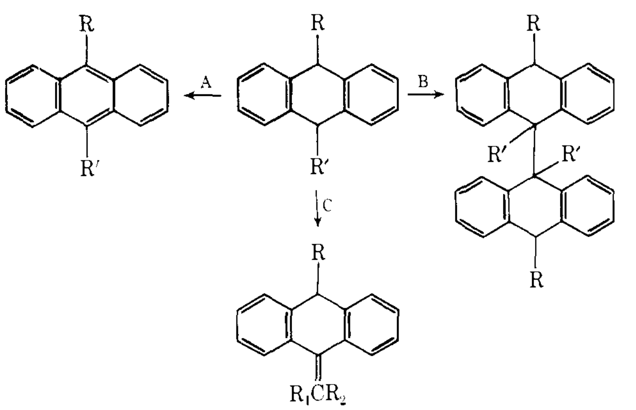
Abstract: 9-Isopropylidene-10-alkyl-9,10-dihydroanthracene (**3**) is synthesized *via* reaction of the 10-alkyl-9,10-dihydro-9-anthryl carbanion with acetone and dehydration of the resulting alcohols with *p*-toluenesulfonic acid in refluxing benzene. The *cis*-9-(1-hydroxyisopropyl)-10-alkyl-9,10-dihydroanthracene intermediates afford directly **3**, while the trans isomers proceed through the related 9-isopropenyl intermediates. The tautomeric equilibrium between **3** and 9-isopropyl-10-alkylanthracene (**4**) is shown to be dependent upon group size. In particular, 9-isopropylidene-10-isopropyl-9,10-dihydroanthracene is stable with respect to 9,10-diisopropylanthracene, the first example of a 9-alkylanthracene unsubstituted in the 1,4,5,8 positions in which the methylene form is the more stable tautomer. Variable-temperature nmr spectroscopic investigation of **3** provides evidence for a preferred cis "boat" or "butterfly" conformation of this unusual ring system and the effect of group size on the conformational interconversion.

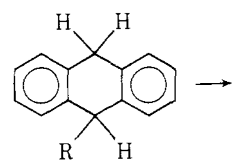
In preceding papers,[2,3] we reported a new general method of dehydrogenation of polycyclic hydrocarbons utilizing the alkyllithium-*N,N,N',N'*-tetramethylethylenediamine (TMEDA) complex. This reagent was shown to effectively deprotonate hydroaromatic molecules to dianionic intermediates which upon treatment with a metal salt, such as cadmium(II) chloride, gave dehydrogenated products in high yield (path A). However, the presence of a secondary or tertiary alkyl group in the 9 position of 9,10-dihydroanthracene (DHA) altered the course of reaction to favor either oxidative dimerization (path B) or methylene formation (path C), dependent upon whether a second alkyl group was present in the 10 position (R′ = H or alkyl).



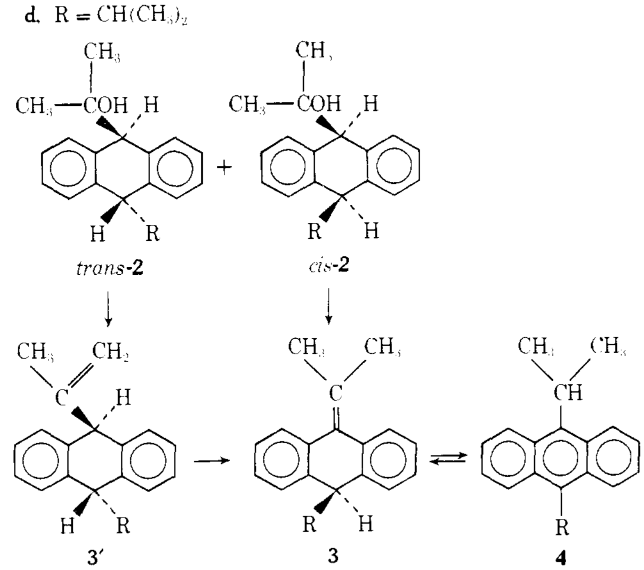
This paper reports a convenient synthesis of compounds, such as 9-isopropylanthracene and 9-isopropylidene-10-alkyl-DHA (**3**) not available *via* the foregoing route due to the limitations cited. In addition, the tautomeric equilibrium between **3** and 9-isopropyl-10-alkylanthracene is investigated and shown to be dependent upon group size. In particular, 9-isopropylidene-10-isopropyl-DHA (**3d**) is shown to be stable with respect to 9,10-diisopropylanthracene (**4d**) and appears to be the first example of a 9-alkylanthracene unsubstituted in the 1,4,5,8 positions in which the methylene form is the more stable isomer. Finally, the stereochemistry of **3** is investigated by variable-temperature nmr spectroscopy providing evidence for a preferred cis "boat" or "butterfly" conformation and the effect of group size on the conformational interconversion of this unusual ring system.

Results

Reaction of the 10-alkyl-9,10-dihydro-9-anthryl carbanion, generated through treatment of the parent hydrocarbons (**1a–d**) with *n*-butyllithium in tetrahydrofuran at −33°, with acetone at −78° afforded *cis*- and *trans*-9-(1-hydroxyisopropyl)-10-alkyl-DHA (**2a–d**).[4] The cis isomers

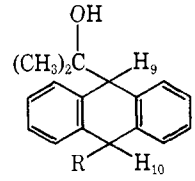


1a. R = H
b. R = CH_3
c. R = CH_2CH_3
d. R = $CH(CH_3)_2$



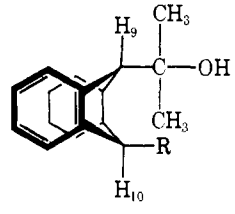
crystallized in relatively pure state from solutions of the mixture in petroleum ether after preliminary chromatography. The cis–trans assignments of these alcohols are based upon nmr spectral data (Table I). As demonstrated earlier,[6] the 9-alkyl-DHA's exist in a flattened boat conformation with the substituent group preferentially in the pseudo-axial (a′) orientation. It would be anticipated, therefore, that the bulky 9-(1-hydroxyisopropyl) group of **2a–d** would be

Table I. Proton Nmr Data for 9-(1-Hydroxyisopropyl)-10-alkyl-DHA (**2b–d**)



Compd	R	Chemical shifts in ppm H_{10}	H_9	$(CH_3)_2COH$	OH
cis-**2b**	CH_3	4.10	3.93	1.17	0.93
trans-**2b**	CH_3	4.20	3.87	1.14	1.22
cis-**2c**	CH_3CH_2	3.73	3.94	1.22	0.81
trans-**2c**	CH_3CH_2	4.22	3.86	1.00	
cis-**2d**	$(CH_3)_2CH$	3.32	3.97	1.33	0.79
trans-**2d**	$(CH_3)_2CH$	4.19	3.85	1.04	1.14

locked into the pseudo-axial position in both cis and trans isomers, directing the 10-alkyl group into the pseudo-axial position in the cis isomers and into the pseudo-equatorial (e′) position in the trans isomers. As a consequence, the H_{10}



cis-**2**

proton may be expected to be e′ for the cis isomers and a′ for the trans isomers (neglecting for the moment possible flattening of the ring system due to transannular steric interaction). Since in the 9-alkyl-DHA's the pseudo-equatorial protons were found to absorb at higher field than their pseudo-axial counterparts, the cis configuration may be assigned to the isomers of **2b–d** in which the H_{10} proton appears at higher field.

This assignment was confirmed unambiguously for **2d** by nuclear Overhauser experiments. As demonstrated earlier,[6,7] irradiation of the peri aryl hydrogens of 9-alkyl- and 9,10-dialkyl-DHA's produces an enhancement of the equatorial meso hydrogen signal intensities. In agreement with this expectation, double irradiation of the aromatic protons of *cis*-**2d** produced a nuclear Overhauser enhancement (NOE) of 13.4% at H_9 and 12.9% at H_{10} in the normal range.[8] For *trans*-**2d**, the NOE measurements were 9% to H_9 and essentially zero to H_{10}, consistent with this assignment. Further confirmatory evidence was provided by the long-range homoallylic coupling constants. It is known[6,7,9] that these interactions depend upon the relative orientation of the coupled protons and follow the order $J_{a,a} > J_{a,e} > J_{e,e}$. The observed couplings for *cis*- and *trans*-**2d** were <0.5 and 0.9 Hz, respectively, with the trans isomer exhibiting the expected larger value. An additional transannular NOE of 14% from the 1-hydroxyisopropyl methyl protons of *trans*-**2d** to H_{10} was also noted.

The cis–trans ratio of products **2b–d** was observed to decrease with increasing size of the 10-alkyl group in the series Me > Et > *i*-Pr; the observed ratios were 4:1, 3:1, and 1.25:1, respectively. This trend is consistent with the previous observations[5,7,10,11] that methylation of the 9-isopropyl-9,10-dihydro-10-anthryl carbanion with methyl halide afforded stereoselectively *cis*-9-isopropyl-10-methyl-DHA, whereas analogous reaction with isopropyl halide led to formation of predominantly *trans*-9,10-diisopropyl-DHA.[12,13]

Dehydration of the cis alcohols **2b–d** under mild conditions (30 min in refluxing benzene) catalyzed by *p*-toluenesulfonic acid furnished the corresponding 9-isopropylidene-10-alkyl-DHA compounds (**3b–d**) in good yield. The nmr spectra were consistent with the assigned structures and are quite informative regarding the structure and conformational properties of these interesting molecules (*cf.* Discussion section). Minor amounts (6–12%) of the alkylanthracenes **4b,c** were detected among the products of mild dehydration of the alcohols *cis*-**2b,c.** Under more vigorous conditions (2 hr or more in refluxing toluene), **3b,c** underwent smooth isomerization to afford the corresponding isomeric 9-isopropyl-10-alkylanthracenes (**4b,c**). However, **3d** failed to isomerize to 9,10-diisopropylanthracene (**4d**) under normal or forcing conditions. On the other hand, **4d** underwent isomerization to **3d** smoothly in refluxing toluene in the presence of *p*-toluenesulfonic acid, indicating the thermodynamic equilibrium to strongly favor the isopropylidene derivative. Although several examples of stable ring-substituted methylene-DHA's have been reported,[3,16-18] **3d** is apparently the first example lacking bulky groups in the adjacent peri 1,4,5,8 positions.[19]

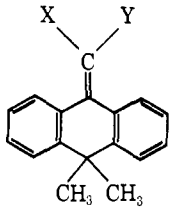
More remarkably, **2a** and the trans alcohols **2b–d** underwent facile dehydration under mild conditions to afford as the major products isomeric compounds in which proton loss occurred from the methyl rather than the benzylic position, namely 9-isopropenyl-DHA (**3a′**) and *trans*-9-isopropenyl-10-alkyl-DHA (**3b′–d′**). Accompanying **3b′** (60%) was **3b** (40%) and a trace of **4b,** while **3c′** (80%) was found with **3c** (20%), and **3d′** was obtained as the sole product. The nmr spectra of **3a′–d′** were consistent with the assigned structures; thus, the nmr spectrum of **3d′** exhibited a pair of vinylic protons as an apparent singlet at δ 5.28 and benzylic protons H_9 and H_{10} at δ 4.67 (singlet) and 3.71 ppm (doublet, J = 6 Hz), respectively, among other features. The product mixtures from **2a** and *trans*-**2b** on treatment with tosic acid for more prolonged periods (or in greater excess) underwent smooth isomerization to the corresponding isopropylidene derivatives **3a** and **3b,** accompanied by lesser amounts of **4a** and **4b,** respectively. Somewhat more drastic conditions, 10 hr in refluxing toluene, were required for conversion of **3d′** to **3d.** It is conceivable that dehydration of the cis alcohols proceeds *via* isopropenyl intermediates less stable than the *trans*-isopropenyl compounds **3a′–c′.** However, this seems unlikely since attempts to detect such intermediates in reactions of *cis*-**2b** at shorter time periods or lower temperatures were uniformly unsuccessful.

For synthetic purposes, direct transformation of the alcohols to the fully aromatic compounds is most convenient. However, pure isopropylanthracene (**4a**) is more conveniently obtained *via* the two stage procedure since 9-isopropylidene-DHA is more easily freed of unreacted DHA by simple crystallization than anthracene can be removed from **4a.**

Discussion

The stability of 9-isopropylidene-10-isopropyl-DHA with respect to its tautomer 9,10-diisopropylanthracene provides striking contrast to the usual pattern of thermodynamic stability observed even with the 10-ethyl homolog. The loss in delocalization energy in **3d** must be more than compensated for by the relief in steric compression in **4d.** However, this observation raises an interesting problem concerning the structure of the isopropylidene compounds **3a–d.**

Variable-temperature nmr studies of 10,10-dimethyl-9-methylene-DHA (**5,** X = Y = H) by Curtin and coworkers[20] have demonstrated rapid interconversion between "boat" conformers down to −27°. Relatively large substitu-



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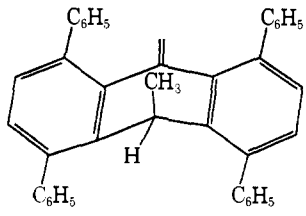

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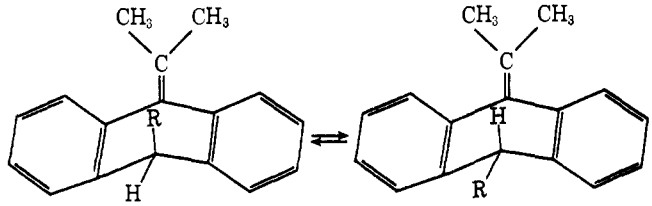
ents on methylene[20] (*e.g.*, X = Y = Br) or in the adjacent 1,8 positions[21] were found necessary to "freeze out" a single conformation. The highly crowded molecule 1,4,5,8-tetraphenyl-10-methyl-9-methylene-DHA (**6**) was assigned a boat structure having the methyl group in the axial position on the basis of the nmr spectrum and chemical shift data,[16]

On the basis of these considerations, **3a–d** would be expected to exist in related boat structures, Cis and trans conformers in which (i) the group is a′ and on the same side of the ring as the isopropylidene (*cis*-**3**), or (ii) the group is e′ and on the periphery (*trans*-**3**) are conceivable. Interconversion of the conformers through ring inversion may be expected to be facile and favor *cis*-**3** as a consequence of the steric interaction between the 10-alkyl group and the adjacent peri hydrogens[22] of *trans*-**3.** Variable-temperature nmr experiments were conducted to examine the validity of these concepts.



cis-**3** *trans*-**3**

The nmr spectrum (CS_2) of 9-isopropylidene-DHA showed an aromatic multiplet at 6,9 ppm, a single broadened signal at 3.55 for the benzylic protons, and a singlet at 2,0 for the methyl groups, Lowering the temperature resulted in continued broadening of the benzylic protons, followed by the emergence of an AB quartet representing the a′ and e′ benzylic protons, with $\Delta\nu$ = 11.7 Hz and J_{AB} = 15.5 Hz (parameters measured from spectrum taken at −20°), The coalescence temperature was determined to be 31,5°, with ΔG = 15,1 kcal/mol determined by the relationships[23] $K = [\pi/(2)^{1/2}](\Delta\nu^2 + 6J^2)^{1/2}$ and $\Delta G^* = 2.303RT(10.319 + \log T - \log K)$.

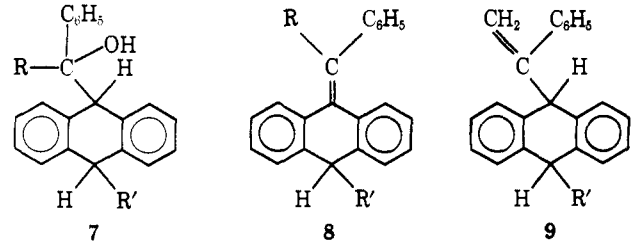
The nmr spectrum (CS_2) of 10-methyl-9-isopropylidene-DHA showed a multiplet at 6,9 ppm for the aromatic protons, a broadened multiplet at 3,6 for the benzylic proton, a sharp singlet at 2.0 for the isopropylidene methyls, and a broadened, poorly resolved doublet at 1,3 for the 10-methyl group, Lowering the temperature resulted in the gradual sharpening of this doublet, together with the emergence of a second smaller doublet[24] at 1.7 ppm. In addition, the multiplet representing the benzylic proton at C_{10} developed into a sharp quartet, which was superimposed upon a second much smaller signal (presumably the expected second quartet). Hence, at −20° the population of the two conformational isomers is 85% for the 10-methyl pseudo-axial and 15% for the 10-methyl pseudo-equatorial.[25]

The nmr spectra (CS_2) of 10-ethyl-9-isopropylidene-DHA (δ 6.8, m; 3.35, t, J = 5 Hz; 2.0, s; 1,5, m; 0.85, t, J = 5.5 Hz) and 10-isopropyl-9-isopropylidene-DHA (δ 6.9, m; 3.12, d, J = 6 Hz; 2.0, s; 1.6, m; 0.8, d, J = 4.5 Hz) both showed temperature independence down to −100° when crystallization took place. This observation, taken with the fact that the 10-methyl derivative shows only 15% of the *trans*-**3** conformation, indicates that both the ethyl and isopropyl derivatives exist preferentially in the *cis*-**3** conformation with the substituent in the a′ position. This is quite consistent with the stereochemical properties of the 9-alkyl-DHA and 9,10-dialkyl-DHA systems.

In general, it is concluded that the 9-isopropylidene-10-alkyl-DHA ring system exists in a flattened "boat" or "butterfly" conformation. Although cis and trans conformers bearing the 10-alkyl group in the a′ and e′ position, respectively, are interconvertible through ring inversion, the former exists preferentially (in the case of methyl) or exclusively (with larger groups) at ambient temperature.

The remarkable influence of the stereochemistry of the alcohols **2a–d** on the direction of dehydration to afford either isopropenyl or isopropylidene compounds requires explanation, The unsubstituted alcohol **2a** undergoes preferential dehydration to the isopropenyl isomer which on equilibration is transformed to the thermodynamically favored isopropylidene compound. Tentatively, we suggest that initial proton loss from a methyl position is kinetically favored due to the greater energy barrier to be overcome in partial flattening of the ring to form the isopropylidene structure,[26] In the cis isomers the barrier is diminished by the transannular steric compression which leads to flattening of the ring system which is expected to increase as the 10-alkyl group becomes larger. The increase in the magnitude of the transannular proton coupling for larger groups provides direct evidence for this effect which has also been observed with other 9,10-dialkyl-DHA compounds.[8] In the trans isomers, the transannular steric compression is essentially zero.

A similar explanation would also appear to hold for the earlier observation by Rigaudy and Kha-Vang-Thang[27a,b] that dehydration of the alcohol **7a** with sulfuric acid or formic acid gave the expected isopropylidene compound **8** while similar reaction of **7b** furnished instead the isopropenyl isomer **9b.** However, 9-isopropenyl-DHA was not detected as the primary product of dehydration of **2a** by these authors who did not employ nmr spectroscopy and identified (by ultraviolet spectrum and ozonolysis) only 9-isopropylidene-DHA. Their conclusion that conjugation with the phenyl ring is the primary factor directing formation of **9** (R′ = H) appears untenable since **2a** lacking a phenyl substituent is now found to also afford the unconjugated primary product, 9-isopropenyl-DHA. The further observation of these authors[27c] that dehydration of the related 10-carboxylic acids, *cis*- and *trans*-**7c,** gave **8c** and **9c,** respectively, is also explicable on the basis of the concepts outlined in the preceding paragraph.



7 **8** **9**

a, R = C_6H_5, R′ = H; b, R = CH_3, R′ = H; c, R = CH_3, R′ = CO_2H

Experimental Section

Physical Data. Proton nmr spectra were obtained on Varian T-60 and HA 100 and Brucker 270 MHz spectrometers; chemical shifts are reported relative to TMS in CCl_4 unless specified otherwise; integration was consistent with all assignments. Variable temperature nmr measurements were taken on a JEOL C60HL spectrometer equipped with a JNM-VT-3B temperature controller. Accurate temperatures, where necessary, were obtained using

the chemical shift dependence of propane-1,3-diol or methyl alcohol. Gas chromatographic analyses were performed on an F & M Model 500 chromatograph employing a 6 ft × 0.25 in. 10% SE 30 60–80 mesh Chromosorb W column at 180°. Microanalyses were performed by Atlantic Microlab, Inc., Atlanta, Ga.

Materials. Tetrahydrofuran (THF) was dried over lithium aluminum hydride and redistilled. Acetone was distilled from $KMnO_4$ and stored over molecular sieves (4A, 10–16 mesh). *n*-Butyllithium (15% in hexane) was purchased from Apache Chemicals. 9-Alkyl-9,10-dihydroanthracenes (**1b–d**) were synthesized through alkylation of 9,10-dihydroanthracene according to the procedure described.[3] Alumina employed in chromatography was neutral alumina, AG 7, or basic alumina, AG 10, Brockmann Activity Grade I as supplied by Bio-Rad Laboratories.

9,10-Diisopropylanthracene (4d). A solution of *trans*-9,10-diisopropyl-9,10-DHA (2.6 g, 10 mmol) in benzene (50 ml) was heated under reflux with 2,3-dichloro-5,6-dicyanobenzoquinone (4.5 g, 20 mmol) for about 24 hr. The completion of reaction was indicated by the complete disappearance in the nmr spectrum of the doublet (σ 0.94, J = 7 Hz) of the isopropyl methyl groups of the starting material. Chromatography on basic alumina (50 g) with benzene–hexane (1:1) twice, evaporation, and crystallization from petroleum ether gave greenish crystals of **4d**[28] (~85%): nmr δ 1.75 (d, 12, J = 7 Hz, $(CH_3)_2CH$), 4.52 (heptet, 2, J = 7 Hz, $(CH_3)_2CH$), 7.15–7.50 (m, 4, aromatic), and 8.20–8.57 ppm (m, 4, aromatic).

9-(1-Hydroxyisopropyl)-9,10-dihydroanthracene (2a). To a stirred solution of **1a** (3.6 g, 20 mmol) in THF (75 ml) at −33° was added 14 ml of a 1.6 *M* solution of *n*-butyllithium (22 mmol) in hexane. A red-brown color developed immediately, and a yellow crystalline solid appeared on the wall of the flask within 5 min. The resulting greenish-yellow suspension was stirred at −33° for 30 min and at −78° for an additional 30 min, then decolorized by the addition of acetone (5 ml), followed by aqueous NH_4Cl solution (10%, 200 ml). The mixture was extracted with ether, washed with water, dried over $MgSO_4$, and evaporated to give a colorless oil (4.54 g). Glpc analysis indicated a 64% yield of **2a** along with 6% anthracene. The latter partially crystallized from a solution of the crude product in petroleum ether. Chromatography of the remainder on a column of Florisil (50 g) in petroleum ether and elution with 10% ether in petroleum ether afforded **2a** (2.5 g). Rechromatography gave pure **2a**; mp 71–73° (lit.[27a,b] 70.5–71°); nmr δ 1.07 (s, 6, $(CH_3)_2COH$), 1.30 (s, 1, OH), 3.86 (s, 1, H_9), 3.96 (q, 2, J = 19 Hz, H_{10}), and 7.00–7.40 ppm (split s, 8, aromatic).

9-(1-Hydroxyisopropyl)-10-methyl-9,10-dihydroanthracene (2b). Analogous reaction of 9-methyl-9,10-dihydroanthracene **1b** (3.9 g, 20 mmol) afforded a colorless oil (5.1 g), glpc analysis of which showed 72% conversion to the alcohols *cis*- and *trans*-**2b**. Chromatography on a column of Florisil (50 g) in petroleum ether and elution with 10% ether in petroleum ether afforded a crystalline product. Recrystallization of the initial fractions rich in the cis isomer (by nmr) from petroleum ether yielded *cis*-**2b** (1.2 g) as white crystals: mp 101.5–102°; nmr δ 0.93 (s, 1, OH), 1.17 (s, 6, $(CH_3)_2COH$), 1.75 (d, 3, J = 7.5 Hz, CH_3), 3.93 (s, 1, H_9), 4.10 (q, 1, J = 7.5 Hz, H_{10}), and 7.0–7.4 ppm (apparent s, 8, aromatic).

Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.63; H, 8.04.

A second chromatography on Florisil (30 g) of the later fractions (1 g) rich in the trans isomer with elution by petroleum ether and benzene (5–10%) gave *trans*-**2b** (0.5 g) in the later fractions. An additional chromatographic separation afforded the pure *trans*-**2b** (0.3 g) as a colorless oil: nmr δ 1.14 (s, 6, $(CH_3)_2COH$), 1.22 (s, 1, OH), 1.77 (d, 3, J = 7.5 Hz, CH_3), 3.87 (s, 1, H_9), 4.20 (q, 1, J = 7.5 Hz, H_{10}), and 7.0–7.6 ppm (m, 8, aromatic).

Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.57; H, 8.05.

9-(1-Hydroxyisopropyl)-10-ethyl-9,10-dihydroanthracene (2c). Analogous reaction of 9-ethyl-9,10-dihydroanthracene **1c** (4.16 g, 20 mmol) gave a pale yellow oil (5.3 g), glpc analysis of which indicated 73% conversion to *cis*- and *trans*-**2c**. Chromatography on Florisil (50 g) afforded colorless crystals. Recrystallization from petroleum ether provided *cis*-**2c** (1.3 g) as white crystals: mp 63–64°; nmr δ 0.81 (s, 1, OH), 1.22 (s, 6, $(CH_3)_2COH$), 1.17 (t, 3, J = 7.5 Hz, CH_3CH_2), 2.03 (quintet, 2, J = 7.5 Hz, CH_3CH_2), 3.73 (t, 1, J = 7.5 Hz, H_{10}), 3.94 (s, 1, H_9), and 7.2 ppm (apparent s, 8, aromatic).

Table II. Concentration Dependence of the Hydroxyl Chemical Shift of *cis*- and *trans*-**2d** at 25° in CCl_4

Concn, g/100 ml	*cis*-**2d**, δ	*trans*-**2d**, δ
10	0.82	1.21[a]
5	0.79	1.14
2	0.77	1.07[a]
1	0.76	1.00[a]
0.5	0.75	1.00[a]

[a] The hydroxyl absorption band overlaps other peaks.

Anal. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.73; H, 8.38.

trans-**2c** was an oil which could not be freed of trace quantities of the cis isomer by further chromatography; the essential nmr data are listed in Table I.

9-(1-Hydroxyisopropyl)-10-isopropyl-9,10-dihydroanthracene (2d). Analogous reaction of 9-isopropyl-9,10-dihydroanthracene **1d** (4.44 g, 20 mmol) gave a pale yellow oil (5.6 g), glpc analysis of which showed 82% conversion to *cis*- and *trans*-**2d**. Chromatography on Florisil (50 g) in the usual manner gave *cis*-**2d** eluted with petroleum ether. Recrystallization from petroleum ether provided pure *cis*-**2d** (1.15 g) as colorless plates: mp 115–117°; nmr δ 0.79 (s, 1, OH), 1.03 (d, 6, J = 7 Hz, $(CH_3)_2CH$), 1.33 (s, 6, $(CH_3)_2COH$), 1.80–2.70 (m, 1, $(CH_3)_2CH$), 3.32 (d, 1, J = 9.5 Hz, H_{10}), 3.97 (s, 1, H_9), and 7.11 ppm (apparent s, 8, aromatic). The hydroxyl protons of *cis*- and *trans*-**2d** exhibited a marked concentration dependence (Table II).

Anal. Calcd for $C_{20}H_{24}O$: C, 85.67; H, 8.67. Found: C, 85.66; H, 8.72.

trans-**2d** was eluted with ether–petroleum ether and recrystallized from petroleum ether to afford pure *trans*-**2d** (1.26 g) as white crystals: mp 85–86°; nmr δ 1.04 (s, 6, $(CH_3)_2COH$), 1.14 (s, 1, OH), 3.13 (d, 6, J = 7.5 Hz $(CH_3)_2CH$), 2.83 (heptet (J = 7.5 Hz) of doublets (J = 3 Hz), 1 $(CH_3)_2CH$), 3.85 (s, 1, H_9), 4.19 (d, 1, J = 3 Hz, H_{10}), and 7.0–7.6 ppm (m, 8, aromatic).

Anal. Calcd for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 85.75; H, 8.70.

9-Isopropylidene-9,10-dihydroanthracene (3a). A solution of **2a** (0.6 g, 2.5 mmol) in benzene (50 ml) was heated at reflux with *p*-toluenesulfonic acid monohydrate (0.5 g) for 30 min, washed with water, dried over $MgSO_4$, and evaporated to dryness. Glpc analysis showed **3a** (82%), 9-isopropenyl-DHA (6%) (confirmed by nmr), and 9-isopropylanthracene **4a** (12%). Recrystallization from petroleum ether gave colorless plates of **3a** (0.35 g): mp 99° (lit.[27a,b] 101°); nmr δ 2.07 (s, 6, CH_3), 3.72 (s, 2, H_{10}), and 6.9–7.4 ppm (m, 8, aromatic).

Anal. Calcd for $C_{17}H_{16}$: C, 92.68; H, 7.32. Found: C, 92.50; H, 7.47.

Similar reaction with 0.25 g of tosic acid afforded a crude product which contained **3a** (21%), 9-isopropenyl-DHA (69%), and **2a** (10%).

9-Isopropylidene-10-methyl-9,10-dihydroanthracene (3b). *cis*-**2b** (0.63 g, 2.5 mmol) underwent dehydration under similar conditions in the presence of 0.25 g of tosic acid to provide **3b** quantitatively (by glpc). Chromatography on neutral alumina (5 g) with petroleum ether (200 ml) furnished a white solid (0.55 g). Recrystallization from petroleum ether gave colorless crystals of pure **3b** (0.44 g): mp 93–93.5°; nmr δ 1.33 (broad d, 3, J = 7 Hz, CH_3), 2.10 (s, 6, isopropylidene), 3.81 (broad q, 1, J = 7 Hz, H_{10}), and 6.9–7.4 ppm (m, 8, aromatic).

Anal. Calcd for $C_{18}H_{18}$: C, 92.26; H, 7.74. Found: C, 92.13; H, 7.84.

Dehydration of *trans*-**2b** under similar conditions afforded a product consisting of *trans*-9-isopropenyl-10-methyl-DHA (**3'b**) and **3b** in a 3:2 molar ratio along with a trace of **4b**. The nmr spectrum of **3b'** exhibited peaks at δ 1.45 (d, 3, J = 7 Hz, CH_3), 1.47 (apparent s, 3, $CH_3C{=}CH_2$), 4.04 (q, 1, J = 7 Hz, H_{10}), 4.67 (s, 1, H_9), 4.95–5.25 (m, 2, vinylic) and 6.9–7.5 ppm (m, 8, aromatic).

The product mixture (100 mg) from the preceding experiment on treatment with tosic acid (100 mg) in refluxing benzene (10 ml) for an additional 30 min underwent isomerization to **3b** (85%) and **4b** (15%).

9-Isopropylidene-10-ethyl-9,10-dihydroanthracene (3c). Dehydration of *cis*-**2c** (0.67 g, 2.5 mmol) in refluxing benzene under the usual conditions provided **3c** (94%) and **4c** (6%) by glpc analysis. Chromatography on neutral alumina (5 g) eluted with petroleum ether (200 ml) followed by recrystallization from petroleum ether gave pure **3c** (0.41 g): mp 93–93.5°; nmr δ 0.88 (t, 3, J = 7 Hz, CH_3CH_2), 1.60 (quintet, 2, J = 7 Hz, CH_3CH_2), 2.10 (s, 6, isopropylidene), 3.53 (t, 1, J = 7 Hz, H_{10}), and 6.90–7.40 ppm (m, 8, aromatic).

Anal. Calcd for $C_{19}H_{20}$: C, 91.88; H, 8.12. Found: C, 91.79; H, 8.22.

9-Isopropylidene-10-isopropyl-9,10-dihydroanthracene (3d). Dehydration of *cis*-**2d** (0.70 g, 2.5 mmol) in refluxing benzene under the usual conditions furnished **3d** (100%) by nmr and glpc analysis. Passage through a column of neutral alumina and recrystallization from petroleum ether furnished the analytical sample of **3d**: mp 70–71°; nmr δ 0.83 (d, 6, J = 6.5 Hz, $(CH_3)_2CH$), 1.3–2.1 (m, 1, $(CH_3)_2CH$), 2.08 (s, 6, isopropylidene), 3.27 (d, 1, J = 8 Hz, H_{10}), and 6.9–7.4 ppm (m, 8, aromatic).

Anal. Calcd for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.56; H, 8.35.

When reaction time was shortened from 30 to 10 min conversion of *cis*-**2d** to **3d** dropped to 15%, and *cis*-9-isopropenyl-10-isopropyl-DHA was not detected by nmr. When the reaction mixture was stirred at room temperature for 30 min, no conversion was observed.

***trans*-9-Isopropenyl-10-isopropyl-9,10-dihydroanthracene (3d′).** Dehydration of *trans*-**2d** (0.70 g, 2.5 mmol) in refluxing benzene under the usual conditions gave **3d′** (97%) with a trace of **3d** (3%) by nmr. Recrystallization from petroleum ether provided colorless crystals of **3d′** (0.49 g): mp 80–80.5°; nmr δ 0.76 (d, 6, J = 6.5 Hz, $(CH_3)_2CH$), 1.34 (apparent s, 3, $CH_3C{=}CH_2$), 1.87 (apparent heptet, 1, methine), 3.71 (apparent d, 1, J = 6 Hz, H_{10}), 4.67 (s, 1, H_9), 5.28 (apparent s, 2, vinylic), and 7.20 ppm (apparent s, 8, aromatic).

Anal. Calcd for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.61; H, 8.37.

9-Isopropylanthracene (4a). Rearrangement of **3a** (0.55 g, 2.5 mmol) took place under more vigorous conditions in refluxing toluene (100 ml) in the presence of tosic acid (2 g) for 2 hr. The crude product, a brown solid, was shown by nmr and glpc to be **4a** (100%). Passage through a column of neutral alumina (10 g) eluted with petroleum ether (300 ml) furnished shining white crystals of **4a** (0.52). Recrystallization from petroleum ether provided pure **4a** (0.48 g): mp 75.5–76° (lit.[31] 75–76°); nmr δ 1.75 (d, 6, J = 7.5 Hz, $(CH_3)_2CH$), 4.53 (heptet, 1, J = 7.5 Hz, $(CH_3)_2CH$), 7.1–7.5 (m, 4, aromatic), 7.7–8.0 (m, 2, aromatic), and 8.1–8.5 ppm (m, 2, aromatic).

Similar reaction in the presence of 1 g of tosic acid afforded a 58% yield of **4a**.

Treatment of the alcohol **2a** (0.3 g, 1.25 mmol) with tosic acid (1 g) in refluxing toluene (50 ml) for 2 hr furnished crude **4a** (100% by glpc). Chromatography on neutral alumina (5 g) eluted with petroleum ether (200 ml) followed by recrystallization from petroleum ether afforded pure **4a** (0.22 g), identical with authentic **4a** by nmr and other properties.

9-Isopropyl-10-methylanthracene (4b). Rearrangement of **3b** (0.59 g, 2.5 mmol) was conducted in refluxing toluene (100 ml) in the presence of tosic acid (1 g) for 2 hr. The resulting crude **4b** (85% yield by glpc) was passed through a column of neutral alumina (10 g) eluted with petroleum ether (300 ml) and recrystallized from petroleum ether to provide a pale yellow crystal of pure **4b** (0.413 g): mp 98–99°; nmr δ 1.74 (d, 6, J = 7.5 Hz, $(CH_3)_2CH$), 3.03 (s, 3, CH_3), 4.54 (heptet, 1, J = 7.5 Hz, methine), 7.2–7.5 (m, 4, aromatic), and 8.1–8.5 ppm (m, 4, aromatic).

Anal. Calcd for $C_{18}H_{18}$: C, 92.26; H, 7.74. Found: C, 92.30; H, 7.60.

One-step dehydration and aromatization of the alcohol *cis*-**2b** (0.315 g, 1.25 mmol) took place in refluxing toluene under similar conditions to furnish **4b** (85% by glpc). Chromatography and recrystallization gave pure **4b** (0.22 g) identical (by nmr) with the authentic compound.

A crude mixture of *cis*- and *trans*-**2b** (0.4 g) underwent similar one-step dehydration and aromatization in refluxing toluene (50 ml) in the presence of tosic acid (0.64 g) for 2 hr. Chromatography and recrystallization of the crude product (0.34 g) gave pure **4b** (0.2 g).

9-Isopropyl-10-ethylanthracene (4c). Analogous reaction of **3c** (0.62 g, 2.5 mmol) in refluxing toluene with tosic acid (1 g) furnished crude **4c** (74% by glpc). Chromatography on neutral alumina (10 g) eluted with petroleum ether (300 ml) followed by recrystallization from the same solvent provided pale greenish-yellow crystals of **4c** (0.45 g): mp 110–111°; nmr δ 1.45 (t, 3, J = 7.5 Hz, CH_3CH_2), 1.75 (d, 6, J = 7.5 Hz, $(CH_3)_2CH$), 3.59 (q, 2, J = 7.5 Hz, CH_3CH_2), 4.53 (heptet, 1, J = 7.5 Hz, $(CH_3)_2CH$), 7.1–7.5 (m, 4, aromatic), and 8.1–8.5 ppm (m, 4, aromatic).

Anal. Calcd for $C_{19}H_{20}$: C, 91.88; H, 8.12. Found: C, 91.81; H, 8.23.

Direct transformation of the alcohol *cis*-**2c** (0.33 g, 1.25 mmol) to **4c** was carried out in refluxing toluene under similar conditions. The crude product (68% **4c** by glpc) was purified by chromatography and recrystallization to provide pure **4c** (0.17 g) identical with the authentic compound by nmr.

Isomerization of Isopropenyl to Isopropylidene (3d′ → 3d). A solution **3d′** (0.33 g, 1.25 mmol) in toluene (50 ml) was heated under reflux with tosic acid (1 g) for 10 hr. The reaction mixture was washed with water, dried over $MgSO_4$, and evaporated to dryness. The nmr spectrum indicated >96% conversion to **3d** and no detectable **4d**.

Isomerization of 9,10-Diisopropylanthracene (4d) to 3d. A solution of **4d** (0.33 g, 1.25 mmol) in toluene (50 ml) was heated under reflux with tosic acid (0.5 g) for 2 hr. The reaction mixture was washed with water, dried over $MgSO_4$, and evaporated to dryness. The nmr spectrum indicated essentially quantitative conversion to **3d**.

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Stereochemistry of 9,10-Dialkyl-9,10-dihydroanthracene and 9-Alkyl-10-lithio-9,10-dihydroanthracene

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Abstract: The stereochemistry of alkylation of 9-alkyl-10-lithio-9,10-dihydroanthracene (**2**) by alkyl halides is shown to be primarily dependent upon the steric requirements of the alkyl groups, with large groups in either reactant favoring trans stereoselectivity. Other factors (temperature, halide, solvent) influence more the yield than the stereochemistry. The steric assignments are based principally upon nmr analysis including measurement of nuclear Overhauser enhancement and homoallylic coupling constants. The latter techniques demonstrate existence of the 9,10-dialkyl-9,10-dihydroanthracene (**3**) ring system in a flattened boat structure with bulky groups such as *tert*-butyl and isopropyl preferentially occupying the pseudoaxial position. Evidence is presented for ring flattening as a consequence of transannular steric interaction and for preferred conformations due to restricted rotation of alkyl groups. A unified mechanistic scheme is proposed to explain the stereochemistry of the anions of **2** and **3**. Both are postulated to exist as an equilibrium mixture of ions and ion pairs (contact and solvent separated) with the dihydro ring in a flattened boat conformation and the 9-alkyl groups in a preferred axial orientation. The stereochemistry of the following reaction types is accounted for by this general mechanistic concept: (1) reduction of 9,10-dialkylanthracene and reductive alkylation of anthracene in liquid ammonia; (2) alkylation and protonation of **2** in organic solvents; and (3) epimerization of **3** with the alkyllithium–TMEDA reagent.

Previous studies have established rather remarkable steric preference in the alkylation and protonation of the monoanions and dianions of 9,10-dihydroanthracene (DHA). Thus, reduction of a series of 9,10-dialkylanthracenes[2a] and 7,12-dimethylbenz[*a*]anthracenes[2b] with lithium in liquid ammonia proceeded stereospecifically to provide the corresponding *trans*-9,10-dialkyl-DHA and *trans*-7,12-dialkyl-7,12-dihydrobenz[*a*]anthracenes, respectively. Alkylation of the anthracene dianion generated in analogous manner was initially demonstrated to exhibit cis stereoselectivity;[3,4] subsequently, however, diisopropylation was shown to provide *trans*-9,10-diisopropyl-DHA.[5] Alkylation of 9-alkyl-10-lithio-DHA in organic solvents has led to conflicting stereochemical results[6,8,9] which are difficult to interpret due to differences (halide, temperature, method of generation of anion, solvent, etc.) in the experimental procedures employed. The more fundamental problems underlying these observations concern the stereochemical properties of the 9-alkyl-9,10-dihydro-10-anthryl anion and the 9,10-dialkyl-DHA ring system, concerning which very little is known. Also the intimate details of the mechanism of these alkylations, particularly the role of ion-pair complexes and the possible importance of alternative mechanisms involving electron transfer[6c] or halogen–metal exchange[6b,10] are unexplored.

We now report a systematic study of the alkylation of 9-alkyl-10-lithio-DHA. Objectives of this investigation are: (1) to determine the role of steric and other experimental factors on the stereochemistry of product structure; and (2) to analyze by nmr spectroscopy the conformational properties of the 9,10-dialkyl-DHA ring system.

Results

Alkylation of the 9-alkyl-10-lithio-DHA (**2**) was selected for study since this is the product-determining step for both dianion and monoanion reactions. In initial experiments, the monoanions were generated through addition of the appropriate alkyllithium reagent to anthracene.[8] Although this procedure proved satisfactory for the primary alkyl groups,[11] conversions were somewhat lower, and product mixtures were more complex with the isopropyl- and *tert*-butyllithium compounds. The most efficient and general route to **2** proved to be metalation of 9-alkyl-DHA with *n*-butyllithium in THF at −30°; the pure 9-alkyl-DHA precursors (except 9-*tert*-butyl-DHA)[12] were themselves obtained *via* similar metalation and alkylation of DHA.[8,14]

Alkylations of 9-isopropyl- and 9-*tert*-butyl-10-lithio-DHA (**2a,b**) were conducted with a series of alkyl halides R′X (R′ = Me, Et, *i*-Pr, *t*-Bu; X = Cl, Br, I) under standard conditions in THF at −78 and 0°. The results are summarized in Tables I and II.

The stereochemical assignments of the *cis*- and *trans*-9,10-dialkyl-DHA (**3**) products were approached with considerable caution in view of the unreliability of previous chemical and physical criteria (*cf.* Discussion). Thus, *cis*- and *trans*-9,10-dimethyl-,[16] *cis*-9-ethyl-10-methyl-,[17,2] and