The Syntheses and Nuclear Magnetic Resonance Studies of Some Sterically Hindered Methylenedihydroanthracenes Bearing Methyl Groups in the 1,8-Aryl or Methylene Positions[1,2]

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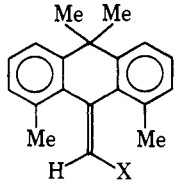
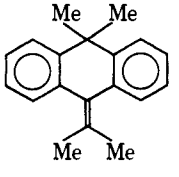
Abstract: A versatile synthetic route for the preparation of 9-methylene-1,8,10,10-tetramethyl-9,10-dihydroanthracene (**1a**) and several of its vinyl derivatives (**1b, 1c,** and **1d**) is described. The key step in the scheme involves the closing of the central ring of the dihydroanthracene system. The preferred axial conformation of 9-substituents in the 1,8,10,10-tetramethyl-9,10-dihydroanthracenes is confirmed by the observation of a nuclear Overhauser effect (NOE) on 9-(hydroxymethyl)-1,8,10,10-tetramethyl-9,10-dihydroanthracene (**11**) and its tosylate (**12**). The free energies for ring inversion for compounds **1a** and **2** [9-(isopropylidene)-10,10-dimethyl-9,10-dihydroanthracene] were found to be 15.8 and 16.0 kcal/mol at coalescence temperatures of 39.5 and 45.5°, respectively. The "cogwheel effect" of the methyl group is also indicated in the present study by comparison of barriers to ring inversion with those of other members of this class of compounds. Two empirical equations, $\delta_{ppm} = 0.99Z_{gem} + 5.56$ and $\delta_{ppm} = 0.75Z_{gem} + 5.65$, for the estimation of the vinyl proton chemical shifts in the monosubstituted 10,10-dimethyl- and 1,8,10,10-tetramethylmethylenedihydroanthracenes, respectively, have been derived and related to the additive shielding coefficient Z_{gem} of the polysubstituted ethylenic system. Methods for the transformation of hydroxyphthalans to the corresponding anthrones and dihydroanthracenes have been developed. This also provides an alternative synthetic route for the preparation of methylenedihydroanthracenes.

Previous studies[3-5] have shown the central ring of the methylenedihydroanthracene system to be constrained to the boat conformation by the two fused benzene rings; when 10,10-dimethyl groups are present, they occupy nonequivalent axial and equatorial positions.[3-5] Thus boat–boat ring inversion produces an enantiomeric conformer of equal free energy. The barrier to ring inversion, as suggested from previous studies, depends on the size[3,4] as well as the steric orientation of the substituents at the methylene and 1,8-aryl positions.[4] Since no compounds with methyl substituents at these positions have been studied, this paper reports the



1a, X = H
b, X = Br
c, X = Cl
d, X = SC_6H_5



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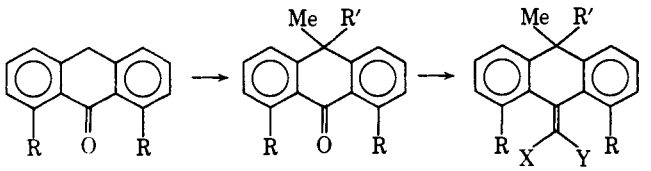
syntheses and NMR studies of some methylenedihydroanthracenes with such substituents at the 1,8-aryl positions (**1a–1d**) and on the methylene carbon (**2**).

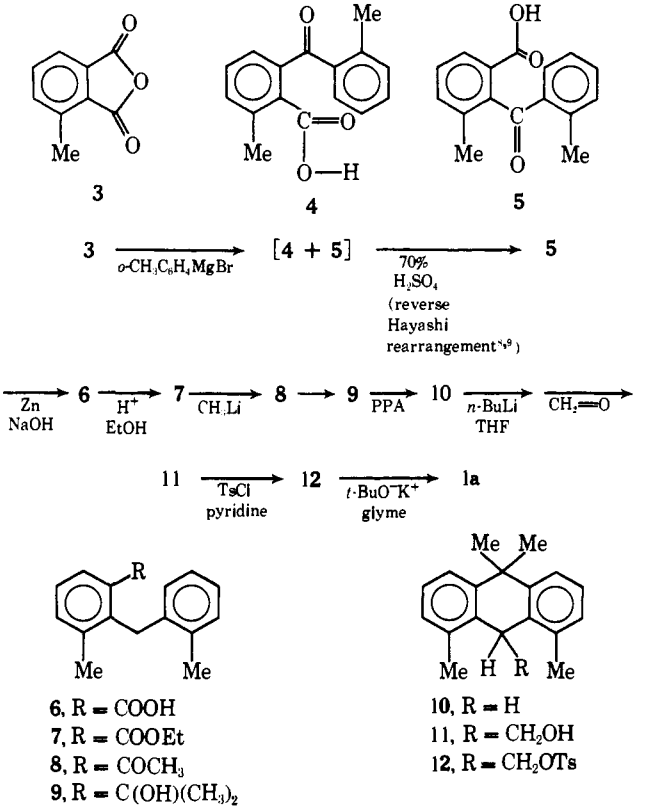
Result and Discussion

Syntheses. The preparation of methylenedihydroanthracenes, from the corresponding anthrones with subsequent introduction of the meso substituents and the methylene functionality, has been developed earlier.[5-7]



The synthetic pathway employed, although satisfactory for certain compounds of this type, has limitations to its general application. It is the purpose of this investigation to explore other synthetic routes involving the closure of the central ring of the anthracene system. The approach as shown in Scheme I involved: (a) discovery of a suitable transformation of 3-methylphthalic anhydride to give the alcohol desired for ring closure; (b) intramolecular cyclization to form the anthracene ring bearing desired meso substituents; and (c) the transformations necessary to attach the required substituted vinyl group.

Scheme I



6, R = COOH
7, R = COOEt
8, R = $COCH_3$
9, R = $C(OH)(CH_3)_2$

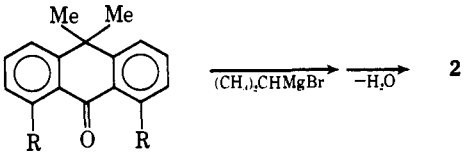
10, R = H
11, R = CH_2OH
12, R = CH_2OTs

During our synthetic venture, we have observed that reaction of ester **7** with excess methyllithium in ether gave a mixture of ketone **8** and alcohol **9** in almost equal amounts. Even when a great excess of methyllithium reagent and severe reaction conditions were employed, alcohol **9** was accompanied by ketone **8**. However, hydrolysis of the crude reaction mixture with an equivalent amount of absolute ethanol followed by further treatment with methyllithium reagent gave the desired alcohol **9** in 100% yield. If as generally assumed a free ketone is an intermediate in the Grignard preparation of tertiary alcohols from esters,[10] it might be expected that the yield of the tertiary alcohol from the ketone precursor **8** should be at least as high as that from the ester **7**. However, treatment of ketone **8** with excess methyllithium in ether gave little tertiary alcohol and much unreacted ketone. This indicates that addition of methyllithium to ketone **8** competes with an enolization reaction. Lower yields of tertiary alcohol from the ketone than from the ester have been reported elsewhere[11,12] and the question of whether a free ketone is indeed an intermediate in the Grignard preparation of tertiary alsohols from esters has been raised.[11,12]

The configurational assignments of the alcohol **11** and the tosylate **12** are of particular interest in view of the recent controversy on the question of whether the 9-substituent in 9,10-dihydroanthracenes occupies the axial[13,14] or the equatorial[15] position. In a conformer in which the R group occupies the axial position, the equatorial benzyl proton is appreciably closer to the peri aryl methyl groups than is the methylene group of the 9-substituent; in another conformer in which the R group occupies the equatorial position, of course, the situation is reversed. Thus a measurement of the nuclear Overhauser enhancement[16,17] of the benzylic proton and the methylene protons upon irradiation of the aryl methyl absorption should show which conformer predominates since it has been known that those protons in closest proximity will show the greater nucelar Overhauser effect.[16,17] When the aryl methyl signal was irradiated, the enhancement observed for the benzylic proton was at least 25% greater than that observed for the methylene protons in compound **12** and at least 18% in compound **11** (see Table I). Thus, the benzylic proton seems to be in closer proximity to the aryl methyl groups than are the methylenic protons. It is apparent that the 9-substituents in the 1,8,10,10-tetramethyl-9,10-dihydroanthracene system occupy the axial position of the central ring, presumably because of greater steric interaction in the equatorial position than the axial. This conclusion is also in harmony with NMR studies in the 9-alkyl-9,10-dihydroanthracene series.[14]

The vinyl bromide **1b** was prepared by bromination, followed by in situ thermal dehydrobromination of the parent olefin **1a**. The vinyl chloride **1c** was similarly prepared. Although the nucleophilic displacement reactions of the vinyl halides (**1b** and **1c**) have not yet been investigated extensively, it has been shown that replacement of the bromide **1b** can be accomplished with a "soft" base such as sodium thiophenoxide to give the desired substituted product **1d**.

To compare the effect of methyl substituents on the vinyl group on the barrier to ring inversion, 9-(isopropylidene)-10,10-dimethyl-9,10-dihydroanthracene (**2**) was also prepared by addition of isopropylmagnesium bromide to the known 10,10-dimethylanthrone **13a** followed by dehydration in an overall yield of 24%.



13a, R = H
b, R = CH_3

Table I. Nuclear Overhauser Effects in 9-Substituted 1,8,10,10-Tetramethyl-9,10-dihydroanthracenes[a]

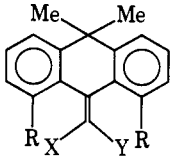
Compound	Group irradiated	(δ)	H_{obsd}	(δ)	Intensity increased,[b] %
12	aryl CH_3–	(2.35)	–CH–	(4.81)	28
			$-CH_2-$	(3.38)	2.8
	$-CH_2-$	(3.38)	–CH–	(4.81)	5
			aryl CH_3	(2.35)	−3
			axial CH_3	(1.34)	+3
			eq CH_3	(1.63)	0
11	aryl CH_3–	(2.50)	–CH–	(4.75)	16
			$-CH_2-$	(3.65)	−2.5

[a] In $CDCl_3$. [b] $100[(A - A_0)/A_0]$; estimated accuracy is ±3%.

Ring Inversion Studies. Examination of the NMR spectra of **1a** at temperatures from −21 to 55° in $CDCl_3$ revealed the usual pattern of broadening and the eventual coalescence of the two equal intensity 10,10-dimethyl signals. Addition of iodine or picric acid (10%) did not affect the energy barrier to ring inversion significantly. On the other hand, the two (well-separated) 10,10-dimethyl signals in compounds **1b, 1c,** and **1d** remained sharp even when the temperature was raised to 190°, and therefore only a lower limit can be set for $\Delta G^{\ddagger}$. We have also examined the ring inversion process for 9-(isopropylidene)-10,10-dimethyl-9,10-dihydroanthracene (**2**).

In Table II are listed the kinetic parameters of the above ring-inversion studies and some related compounds reported previously. For the sake of comparison, all values of $\Delta G^{\ddagger}$ are calculated by the Gutowsky–Holm relationship[18] at T_c and considered to be accurate to within ±0.1 kcal/mol.[19] Although Arrhenius activation energies can be calculated, we have refrained from placing much reliance on such values because of several sources of error involved.[20-22] As is apparent from Table II, several interesting points can be drawn: (i) examination of the free energies of activation for a series of different substituents at the methylene position leads to the following general order of inhibition to ring inversion:[23] $-CH_2-$ (ring) > Br > Cl > CH_3 > phenyl > COOME ≫ H. A similar partial order has been observed in the hindered rotation of ortho-substituted biphenyls[24] and, more recently, in dithiametacyclophanes[25] and trineopentylbenzenes,[26] Br > CH_3 > Cl ≫ H, which places the CH_3 group between Br and Cl. The small capacity of the methyl group to interfere with passage through the planar transition state in the present system is surprising if one considers the order of size of the groups (van der Waals radii: CH_2[28] 2.0, CH_3[29] 1.95, Br[28] 1.92, Cl[28] 1.77, and H[28] 1.20). Before possible sources for the difference observed are evaluated, some assumptions must be made. It is assumed that the ground-state energies due to nonbinding atomic interactions are the same in all compounds under consideration and that the differences in barrier to inversion originate from differences in energy of the transition states. It is also assumed that the nonbonded interactions between the exocyclic methylene substituents and 1,8-aryl substituents are the dominant interactions giving rise to the potential barrier for ring inversion. On the basis of analogy with racemization of substituted biphenyls, a planar transition state has been proposed[3-5] in which the bond angles are distorted and bonds stretched in order to reduce the nonbonded interactions. In general, one or more of the following factors might be involved for the determination of the extent of the nonbonded interactions, i.e., the energy barrier to inver-

Table II. Activation Parameters for Ring Inversion in Some 10,10-Dimethyl-9-methylene-9,10-dihydroanthracenes



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Compd	R	X	Y	$\Delta\nu_{max}$, hertz	T_c (°C)	k, sec^{-1}	$\Delta G^{\ddagger}$, kcal/mol	Ref
1a	Me	H	H	26.0	39.5	57.8	15.8	*a*
2	H	Me	Me	29.8	45.5	66.2	16.0	*a*
14a	Cl	H	H	29.1	ca. 41	64.6	15.8	*b, c*
					(39.5)		(15.8)	*d*
14b	H	Cl	Cl	27.7	ca. 65.9	61.5	17.2	*b, c*
					(45.5)		(17.1)	*d*
14c	H	Br	Br	25.6	91.1	56.9	18.5	*b, c, e*
					(45.5)		(18.6)	*d*
14d	H	$-(CH_2)_2-X-(CH_2)_2-$ ($X = NCH_3$)					21	*f*
14e	H	Br	H	(15)	<−30		<9	*e*
14f	H	Br	C_6H_5	15.8	32	35.1	15.7	*e*
14g	H	Br	COOMe	27.6	27	61.3	15.1	*e*
1b	Me	H	Br	(18.3)	190	<40.7	>24	*a*
1c	Me	H	Cl	(19.0)	190	<42.2	>24	*a*
1d	Me	H	$-SC_6H_5$	(16.5)	190	<36.7	>24	*a*
14h	Cl	H	Br	(27.6)	180	<61.3	>23	*b*
14i	Cl	Cl	Cl	(22.8)	190	<50.6	>24	*b*

[a] Present work. [b] Reference 5c. [c] Reference 4. [d] Calculated from ref 5c and 4. [e] Reference 3. [f] Reference 27.

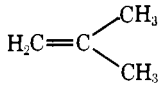
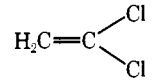
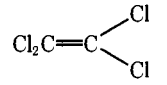
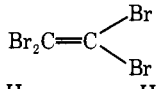
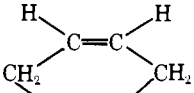
sion: (1) the relative size of the substituents (the van der Waals radii); (2) the modification of the bond length between the methylene carbon and vinyl substituents; (3) the variation of the valency bond angle between the double bond and the vinyl substituents, thus changing the effective size of the group; (4) the modification of the bond length of the double bond due to different nature of the vinyl substituents.

No structural information for any methylenedihydroanthracene being available at present,[30] it is difficult to assess the significance of each factor to the barrier of ring inversion quantitatively, but structural data for substituted ethylenes (Table III) lead to the conclusion that the presence of a substituent (Br, CH_3, Cl) on the olefin does not alter the bond length of the double bond and that the bond angle between the double bond and the substituent remains very nearly constant (the differences are less than the experimental uncertainties).

In the first-order approximation, it is reasonable to assume that the olefinic bond length and bond angle (∠CCX) remain constant in the methylenedihydroanthracene series. Consequently, factors 3 and 4 are not significant for the determination of barrier to ring inversion. It is implied that a longer bond (C-X) and larger size of the vinyl substituent should result in a higher barrier to ring inversion. On this basis, the energy barriers of compounds **2** and **14d** are expected to be somewhat smaller than that of the bromo compound **14c** and comparable to that of the chloro compound **14b**. The fact that compound **14d** gave a somewhat higher barrier (21 kcal/mol) than the bromo compound **14c** (18.5 kcal/mol) can be explained in terms of greater rigidity of the six-membered ring which is more difficultly deformed in the planar transition state of ring inversion. The lower barrier of the methyl group (**2**, 16.0 kcal/mol, 45.5°) in comparison with the chloro substituent (**14b**, 17.2 kcal/mol, 65.9°) can be a result of a synchronous rotation possible in the methyl group. Such a "cogwheel effect" of the methyl group has been observed in the study of hindered rotation in some α,α,o,o'-tetrasubstituted toluenes[31] whose barrier to rotation has the same order as Br > Cl > CH_3. This inherent effect of the methyl group may be partially responsible for the similarity in rates of inversion of 1,8-aryl substituted compounds **1a** and **14a**.

It is of interest that the inversion rate of **2** is slower than that of **1a**. It seems to be a general phenomenon that substituents at the methylene positions give higher barriers to inversion than the same substituents at the 1,8-aryl positions. A similar observation has been made for the chloro analogs.[4,5c] Such a difference can be explained in terms of greater ease of bond angle distortion at the 1,8-aryl positions than the methylene carbon in the planar transition states since the ground state energies due to nonbonding interactions are nearly equal in both compounds. The cogwheel effect of the methyl group might also partially explain the smaller difference in energy barriers to ring inversion between **1a** and **2** than that between the chloro counterparts **14a** and **14b**. It is also of interest to observe that, as the free energies for ring inversion in compounds **1a** and **2** are quite similar (15.8 kcal/mol at 39.5–45.5°), the free energy for rotation in 2,2′-dimethylbiphenyl[32] is much higher (17.4 kcal/mol at −35° or 18.1 kcal/mol at 25°). It has been pointed out[3] that the transition states and steric interactions in both systems, methylenedihydroanthracene and biphenyl, are very similar. This implies that, when the effective steric bulk of a group is considered, the appropriate mechanism of the particular interaction in question should be taken into account. This has been amplified in a recent study on triarylmethanes.[33] Furthermore, although the cylindrically symmetrical halogens and the "three-pronged" CH_3 groups are not strictly comparable, it seems clear from the present study that the effective steric bulk of CH_3 in relation to Cl and Br not only depends on the molecular system studied[26] but also the orientation of interaction and the degree of "cogwheel effect" involved. As expected, the inversion rates of compounds **1b**, **1c**, and **1d** are "frozen" on the NMR time scale at temperatures as high as 190°. Further examination of their NMR spectra at 190° revealed that the arylmethyl signals remained sharp and separated

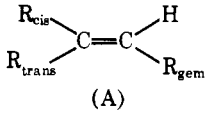
Table III. Bond Angles and Bond Lengths in Some Substituted Ethylenes

Compd	Method[a]	C=C, Å	∠CCX, deg	C–X, Å	Ref
	A	1.34	122.1	1.507	*b*
	A	1.330	122.1	1.507	*c*
	B	1.331	124.0	1.505	*d*
	B	1.32	122.8	1.71	*e*
	B	1.33	123	1.72	*f*
	B	1.30 ± 0.03	123.5 ± 0.75		*g*
	B	1.26	121.5	1.883	*h*
	B	1.41	121.2	1.881	*h*
	A	1.34	123.3	1.51	*i*

[a] A, microwave; B, electron diffraction. [b] V. W. Laurie, *J. Chem. Phys.*, 34, 1516 (1961); [c] L. H. Scharpen and V. W. Laurie, 39, 1732 (1963). [d] L. S. Bartell and R. A. Bonham, *ibid.*, 32, 824 (1960). [e] R. L. Livingston, C. N. R. Rao, L. H. Kaplan, and L. Rocks. *J. Am. Chem. Soc.*, 80, 5368 (1958). [f] C. N. R. Rao and R. L. Livingston, *Curr. Sci.*, 27, 330 (1958). [g] I. L. Karle and J. Karle, *J. Chem. Phys.*, 20, 63 (1952). [h] T. Dahl and O. Hassel, *Acta Chem. Scand.*, 22, 2851 (1968). [i] L. H. Scharpen, J. E. Wollrab, and D. P. Ames, *J. Chem. Phys.*, 49, 2368 (1968).

as did those of the 10,10-dimethyl groups. Their free energies of activation were estimated to have a minimum value of 24 kcal/mol. An obvious conclusion is that the energy barriers to rotation of the carbon–carbon double bond and inversion of the central ring for these compounds are high enough for resolution of optical antipodes or isolation of geometric invertomers.[34] In the following paper in this issue, we will report the preparation and separation of (a)-ethyl and (e)-ethyl atropisomers of 9-(bromomethylene)-10-ethyl-1,8,10-trimethyl-9,10-dihydroanthracene, whose free energy of activation has found to be 28.2 kcal/mol at 107°.

Correlation of the Chemical Shifts of Vinyl Protons in Methylene-9,10-dihydroanthracene System. An Empirical Approach. Recently, several groups of chemists have derived additive shielding parameters for ethylenic protons which reproduced the vast majority of experimentally obtained chemical shifts with a surprisingly high accuracy.[35,36] Assuming that the total shielding experienced by a vinyl proton is simply the sum of the shielding effects exerted by all of the substituents present, the resonance position of the vinyl proton in such molecules (A) can be calculated from eq 1:



(A)

$$\delta_{ppm} = \text{base value} + \sum_i Z_i = \delta_{ethylene} + Z_{gem} + Z_{cis} + Z_{trans} \quad (1)$$

In this equation, the chemical shift of ethylene is taken as the base value, and Z_{gem}, Z_{cis}, and Z_{trans} are the shielding constants for substituents (R) in the gem, cis, and trans relationship to the proton. In a system (such as monosubstituted methylenedihydroanthracenes) where only the R_{gem} substituents vary, eq 1 can be written as:

$$\delta_{ppm} = Z_{gem} + (\delta_{ethylene} + Z_{cis} + Z_{trans}) = Z_{gem} + \text{constant} \quad (2)$$

In this work, we apply such shielding parameters Z_{gem} to correlate and estimate the chemical shifts of the vinyl protons in a series of monosubstituted methylenedihydroanthracenes by eq 3:

$$\delta_{ppm} = mZ_{gem} + \delta_{basic} \quad (3)$$

In this equation, Z_{gem} are the substituent shielding coefficients for the effect of substituents on a vinyl proton attached to the same carbon atom. The symbol m is the slope of the line when δ_{ppm} is plotted vs. Z_{gem} and should have a value of 1.00 if the shielding coefficients Z_{gem} of the ethylenic system were exact in applying to our system. The interception of the line at $Z_{gem} = 0.00$ gives the value of δ_{basic}. Theoretically speaking, δ_{basic} is the chemical shift of the vinyl protons in the parent compound since the shielding coefficient for hydrogen is taken as zero. In our calculations we have employed only one set of shielding coefficients revised recently[35b] because this set covered 43 functional groups and reproduced at least 4298 chemical shifts. In Table IV, we have tabulated the Z_{gem} coefficients for various substituents and the observed chemical shifts of the vinyl protons in the 9-methylene-10,10-dimethyl-9,19-dihydroanthracenes and 9-methylene-1,8,10,10-tetramethyl-9,10-dihydroanthracenes.

Using linear regression analysis,[37] we have obtained a linear equation for the 9-methylene-10,10-dimethyl-9,10-dihydroanthracene system:

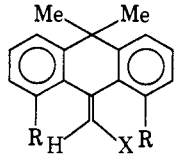
$$\delta_{ppm} = 0.99Z_{gem} + 5.56 \quad (4)$$

The r factor is 0.98. As we can see, the correction factor m (0.99) has a value very close to 1.00. This is an indication that these Z_{gem} coefficients are almost perfect for this particular system. Furthermore, the additivity approximation is also valid in the present case.

For the 9-methylene-1,8,10,10-tetramethyl-9,10-dihydroanthracene system with a three-point plot, we have derived eq 5 with an r factor of 0.98.

$$\delta_{ppm} = 0.75Z_{gem} + 5.65 \quad (5)$$

Table IV. Z_{gem} Shielding Coefficients and the Observed Chemical Shifts of Vinyl Protons in Methylenedihydroanthracenes



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X	Z_{gem}	Compd (R = H)	δ_{ppm}[a]	Compd (R = Me)	δ_{ppm}[b]
H	0.00	15a	5.60	1a	5.65
Br	1.07	14e	6.70	1b	6.55
Cl	1.08	15b	6.66	1c	6.37
SC_5H_6		15c	6.78	1d	6.53
COOH	0.80	15d	6.30[b]		
$COOCH_3$	0.78	15e	6.21		

[a] In CCl_4. [b] In $CDCl_3$.

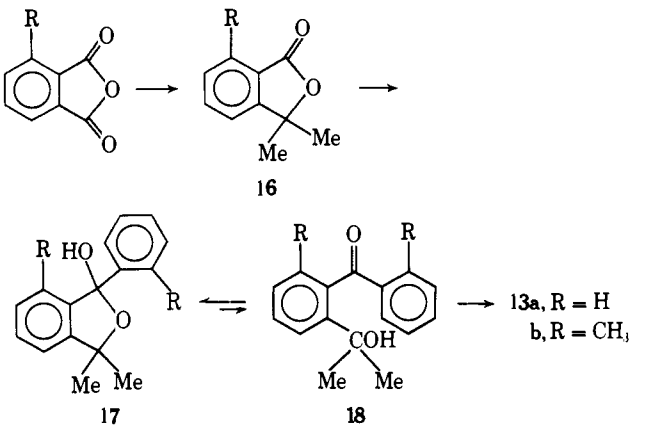
In this equation, the correction factor of 0.75 deviates from 1.00. This implies that the Z_{gem} coefficients are not applicable to this particular system and they required modification by multiplication by a factor of 0.75. Such differences, as pointed out in the polysubstituted ethylene systems,[35c,36] are caused by steric and electronic interactions between substituents. There is little doubt that such severe interactions are due to the spatial proximity of the substituents at the methylene and aryl positions. It is tempting to speculate that the geometry of the double bond was twisted significantly. It is also interesting to notice that, as we compared the chemical shifts of the vinyl protons in compound **15a** and **1a**, the presence of the two methyl groups in the 1,8-aryl positions only caused 0.05 ppm more deshielding.

As a test of the validity of the above approach and the accuracy of the equations, we have calculated the Z_{gem} coefficient for the SC_5H_6 substituent from eq 4 and found a value of 1.23. This coefficient was used to estimate the chemical shift of the vinyl proton for compound **1d** in our second series. From eq 5, there was obtained a value of 6.57 ppm which agrees well with the observed value (6.53 ppm).

In conclusion, the above equations provide not only a means of testing the validity of the Z_{gem} coefficients and the additivity relationship but also a convenient method to estimate the chemical shifts of the vinyl protons in these systems. The good agreement between the calculated and the observed chemical shifts demonstrates the validity of our approach.

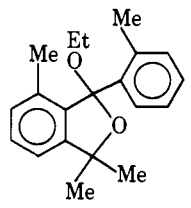
Novel Reactions of Hydroxyphthalans. During the synthetic studies, the possibility of converting hydroxyphthalans into anthrones and dihydroanthracenes was also explored. Our first synthetic approach is outlined in Scheme II. Although cyclodehydration by hydrogen chloride in glacial acetic acid or concentrated sulfuric acid had been unsuccessful,[38] it was hoped that a suitable reagent might be found. 3,3-Dimethyl-1-phenyl-1-hydroxyphthalan **17a** was prepared.[38] Spectroscopic data revealed that it exists predominantly or entirely in the ring form **17a**, rather than the chain form **18a** in agreement with the position of other keto-lactol equilibria.[39,40] Furthermore, derivatives of the chain form **18a** in this system have been prepared.[41] Conversion of **17a** to **13a** in 10% yield was successful using polyphosphoric acid (PPA) as the cyclodehydrating agent. Treatment of **17a** with sulfuric acid under various conditions gave only starting material. If a stable oxonium ion[42] were formed under the reaction conditions (stable salts of **17a** such as perchlorate have been isolated[43]), it would explain why the reaction did not proceed further and, on

Scheme II

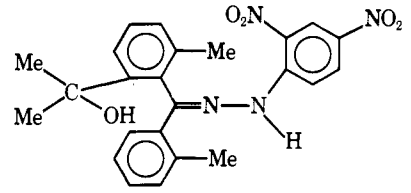


quenching with water, the starting material was regenerated and might also account for the failure of Barnett and coworkers.[38] Hydroxyphthalan **17b** was similarly prepared. However, reaction of **17b** with PPA gave only 2% yield of anthrone **13b**.

It is known that hydroxyphthalan **17a** reacts with semicarbazide to give high yield of semicarbazone.[43] Our alternative approach involved preparation of the corresponding semicarbazone and Wolff-Kishner reduction.[44] Wolff-Kishner reduction of the semicarbazone **19** by way of the Huang-Minlon reduction modification[45] gave 94–100% yield of an oil which was identified as the alcohol **21** (Scheme III). Cyclization of **21** with 70% sulfuric acid gave the desired product **22**, thus providing a new synthetically useful route to this compound. Application of the above route to the preparation of 1,8,10,10-tetramethyl-9,10-dihydroanthracene (**10**) met with difficulties. Treatment of hydroxyphthalan **17b** with semicarbazide hydrochloride in ethanol gave no expected semicarbazone **20** but a new product **23** which could also be prepared just by heating **17b** in ethanol. This stable ethoxy product **23** did not react further with semicarbazide, but did react with 2,4-dinitrophenylhydrazine to give the same hydrazone **24** prepared from **17b**.



23



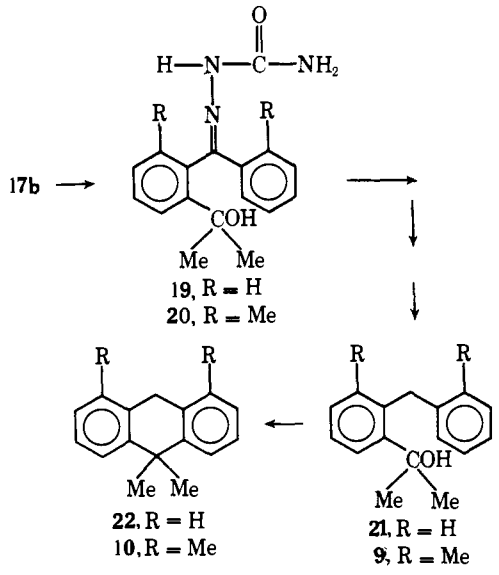
24

Preliminary experiments indicated that the semicarbazone **20** could be prepared in aprotic solvent such as dimethyl sulfoxide (Me_2SO). Wolff-Kishner reduction of the semicarbazone **20** by way of Huang-Minlon reduction modification[45] gave the expected alcohol **9** which upon cyclodehydration gave 1,8,10,10-tetramethyl-9,10-dihydroanthracene (**10**).

Experimental Section

Melting points were obtained with a Thomas-Hoover capillary melting point apparatus and are corrected. Infrared (ir) spectra (10% solutions) were obtained with a Perkin-Elmer Model 137 Infracord or by Mr. R. L. Thrift and his associates with a Perkin-Elmer Model 521 spectrophotometer. A number of nuclear magnetic resonance (NMR) spectra (7–20% solutions) were recorded by Mr. R. L. Thrift and his associates with Varian Associates Model A-60-A, 56/60, Ha-100, or Hr-220 instruments. Reported values are on the scale using Me_4Si as an internal standard. Ultraviolet (uv) spectra were obtained with a Perkin-Elmer Model Cole-

Scheme III



man 124 spectrophotometer or a Cary Model 14M spectrophotometer. The mass spectra were run on an Atlas CH-4, MAT CH-5,[46] or MAT SM-1B[46] by Mr. J. Wrona, Dr. J. C. Cook, and their associates. Elemental analyses were performed by Mr. J. Nemeth and his associates of the University of Illinois Microanalytical Laboratory. All compounds marked with an asterisk had elemental analyses within acceptable limits. All thin-layer chromatography (TLC) tests were performed on Eastman Silica Gel Sheets (6060) with benzene, unless otherwise indicated. The sheets were developed with an ultraviolet lamp. Anhydrous ether was prepared by distillation over lithium aluminum hydride. Anhydrous tetrahydrofuran (THF) and glyme were distilled over sodium hydride before use. A general work-up procedure involved the following steps: the organic extracts were combined, washed thoroughly with saturated NaCl, dried over $MgSO_4$, and finally evaporation of solvent under reduced pressure.

3-Methylphthalic Anhydride (3). Treatment of 152.4 g of maleic anhydride (1.55 mol, freshly distilled, bp 194–195°) with 173.5 g of piperylene (n^{20}D 1.4212, Aldrich; estimated[47] 60% trans isomer present) in benzene followed by aromatization with bromine in glacial acetic acid, according to the method of Newman and McCleary,[48] gave 75–85% of the desired anhydride **3**: mp 114.5–116.0° (lit.[48] mp 114.5–117°; lit.[49] mp 112–114°; lit.[50] mp 111–113°); ir ($CHCl_3$) 1850, 1780, and 900 cm^{-1}.

6-Methyl-2-(2-methylbenzoyl)benzoic Acid (4).* The procedure described by Newman et al.[48,51] gave (91%) of solid, mp 86–97°, whose NMR spectrum ($CDCl_3$) indicated a mixture of compounds **4** and **5** in a 4 to 1 ratio. This material was used for the next step without further purification.

Pure keto acid **4** was separated by extraction of the above ether-benzene solution of keto acids with a 10% solution of sodium bicarbonate. Acidification of the bicarbonate solution followed by extraction with ether. After work-up, recrystallization from ether-hexane gave 100% isomerically pure sample of **4**: mp 116.5–118.0° (lit.[9a] 117°); ir (KBr) 3020 (broad, -COOH), 1700 (-COO-), and 1660 cm^{-1} (-CO-) (no absorption corresponding to the hydroxy group was observed in chloroform or in Nujol); uv (absolute ethanol) λ_{max} 287 (ϵ 2.67 × 10^3) and 250 (8.54 × 10^3); NMR ($CDCl_3$) δ 2.40 (s, 3 H, CH_3), 2.49 (s, 3 H, CH_3), 6.90–7.50 (m, 7 H, aromatic), and 10.81 (broad, 1 H, COOH).

3-Methyl-2-(2-methylbenzoyl)benzoic Acid (5).* The conditions reported by Cristol and Caspar[9a] gave very low yield of the desired acid. Milder conditions for the reverse Hayashi rearrangement[9] were used. A mixture of the crude keto acids of the preceding section (16.0 g) was dissolved in 280 ml of 70% sulfuric acid at 80°, with stirring, during 0.5 hr. The deep red solution was stirred for another 5 hr, poured into ice-water, and extracted with ether. After washing with saturated aqueous sodium chloride, the ethereal solution was extracted with a 5% solution of NaOH (200 ml in three portions). After decolorization with charcoal, the aqueous solution was filtered, acidified, and extracted with ether. After work-up, there remained 13.6 g (85%) of **5**, mp 138–152°. Recrystallization from ether-hexane gave 10.1 g (63%) of the desired pure **5**, mp 158.0–160.5°. Further recrystallization from ether-hexane gave an analytical sample: mp 162–163° (lit.[9a] 161–162°); ir (KBr) 3020 (broad, -COOH), 1670 (-COO-), and 1669 cm^{-1} (-CO-) (no hydroxy absorptions and significant changes in carbonyl regions were observed in chloroform on Nujol); uv (absolute ethanol) λ_{max} 287 (ϵ 3.32 × 10^3) and 245 (ϵ 1.34 × 10^4); NMR ($CDCl_3$) δ 2.19 (s, 3 H, CH_3), 2.66 (s, 3 H, CH_3), 6.90–7.50 (m, 6 H, aromatic), 7.60–8.00 (m, 1 H, aromatic), 11.40 (broad, 1 H, COOH).

3-Methyl-2-(2-methylbenzyl)benzoic Acid (6).* The procedure, essentially that described by Cristol and Caspar,[9a] gave a 100% yield of 3-methyl-2-(2-methylbenzyl)benzoic acid (**6**), mp 160–166°. Several recrystallizations from acetone-hexane gave an analytical sample: mp 161.0–162.5° (lit.[9a] 161–162°); ir ($CHCl_3$) 2950 (broad, -COOH) and 1690 cm^{-1} (-COO-).

Ethyl 3-Methyl-2-(2-methylbenzyl)benzoate (7).* To a solution of 3-methyl-2-(2-methylbenzyl)benzoic acid (**6**) (2.40 g, 0.01 mol) in 45 ml of absolute ethanol and benzene (4:5) in a flask fitted with a Dean-Stark trap was added 24 drops of concentrated sulfuric acid. The solution was heated under reflux for 7 hr, and then 30 ml of solvent was distilled off. A fresh solution of 25 ml of absolute ethanol and benzene (4:1) was added. After refluxing for another 1 hr, most of the solvent was distilled off. Benzene was added and the solution was concentrated again. A solution of 25 ml of absolute ethanol–benzene (3:2) was added, and reflux was continued for another 22 hr. The solvent was partially distilled, and the solution was poured into an aqueous solution saturated with sodium chloride. The aqueous layer was separated and extracted with benzene. After work-up there remained 2.4 g (90%) of white solid, mp 48.5–49.5°. One recrystallization from absolute ethanol gave an analytical sample of **7**: ir (CCl_4) 1720 cm^{-1} (ester); NMR (CCl_4) δ 1.11 (t, J = 7 Hz, 3 H, CH_3), 2.16 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 4.09 (q, J = 7 Hz, 2 H, CH_2), 4.20 (s, 2 H, CH_2), and 6.1–7.8 (m, 7 H, aromatic).

3-Methyl-2-(2-methylbenzyl)-α,α-dimethylbenzyl Alcohol (9). This compound was prepared by treatment of the ester **5** with methyllithium. A typical experiment follows. A solution of 3.1 g (0.011 mol) of ethyl ester **7** in 25 ml of anhydrous ether was added to a well-stirred ethereal solution of methyllithium (1.91 M;[52] 55 ml amounts of 0.11 mol) over a period of 10 min. After reflux for 12 hr, a small sample was taken out and quenched with water. A TLC test in benzene indicated two spots corresponding to the ketone **8** and the desired alcohol **9**, the ketone being the major component. Another 55.0 ml (0.11 mol) of methyllithium in ether was added, and the reaction mixture was heated under reflux for another 12 hr. A TLC test indicated the reaction was not yet complete. Another 55.0 ml (0.11 mol) of methyllithium in ether was added. After a total of 60 hr of reflux, the reaction did not seem to be complete and the TLC test indicated very little change. At this point, the whole mixture was decomposed with an equivalent amount of absolute ethanol. After a solution of methyllithium in ether (50 ml, 0.1 mol) was added, the reaction mixture was heated under reflux with stirring for 3 hr. After work-up, there remained 3.0 g (100%) of the desired alcohol **9** as an oil: (CCl_4) 3600 (hydroxy), 1380, and 1360 cm^{-1} (*gem*-dimethyl) (no carbonyl absorption); NMR ($CDCl_3$) δ 1.58 (s, 6 H, CH_3), 1.68 (s, 1 H, -OH; disappeared after shaking with D_2O), 2.08 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 4.33 (s, 2 H, CH_2), 6.30–7.50 (m, 7 H, aromatic).

1,8,10,10-Tetramethyl-9,10-dihydroanthracene (10).* A mixture of 4.7 g (0.018 mol) of the above crude alcohol **9** in 72 g of polyphosphoric acid (PPA) was stirred with a glass rod for 30 min at room temperature. The reaction was slightly exothermic. The yellow mixture was decomposed with ice-water, filtered, and dried. There was obtained 4.15 g (95%) of the desired product, mp 95–104°. Recrystallization from absolute ethanol gave an analytical sample: mp 109.0–110.0°; ir (CCl_4) 1380, 1360 (*gem*-dimethyl), and 1135 cm^{-1}; uv (cyclohexane) λ_{max} 264 nm (ϵ 428) and $\lambda_{shoulder}$ 270 (326); NMR (CCl_4) δ 1.58 (s, 6 H, CH_3), 2.38 (s, 6 H, CH_3), and 3.78 (s, 2 H, CH_2), 6.8–7.35 (m, 6 H, aromatic); mass spec (70 eV). M^+ at *m/e* 236 ($C_{18}H_{20}$).

9-Hydroxymethyl-1,8,10,10-tetramethyl-9,10-dihydroanthracene (11).* The apparatus was flame dried before use. To an ice-cold solution of 2.2 g (9.2 mmol) of dihydroanthracene **10** in 30 ml of anhydrous THF was added 7.0 ml of *n*-butyllithium (1.61 M,[52]

1.12 mmol) in hexane. The solution assumed a deep red color and was stirred for 0.5 hr at 0°. Powdered paraformaldehyde (0.7 g) was added. The color of the solution gradually disappeared during 10 min of stirring at 0°. After the solution was allowed to warm to room temperature and kept stirring for 1 hr, it was quenched with a saturated solution of sodium chloride and extracted thoroughly with ether. After work-up, there was obtained 2.40 g of white solid, mp 122–136°. Recrystallization from pentane gave 1.9 g (71–77%) of alcohol, **11**, mp 145.5–148°. Recrystallization once more from pentane gave an analytical sample, mp 147.5–148.5°; ir ($CHCl_3$) 3580 cm^{-1} (OH); uv ($CHCl_3$) λ_{max} nm 264 (ϵ 394) and $\lambda_{shoulder}$ 270 (309); NMR ($CDCl_3$) δ 1.40 (s, 1 H, OH; disappeared after shaking with D_2O), 1.64, 1.70 (s, 6 H, CH_3), 2.48 (s, 6 H, CH_3), 3.55 (d, 2 H, CH_2, J = 6.5 Hz), 4.66 (t, 1 H, CH, J = 6.5 Hz), and 6.85–7.50 (m, 6 H, aromatic).

Tosylate (12)* of 9-Hydroxymethyl-1,8,10,10-tetramethyl-9,10,dihydroanthracene. To an ice-salt cooled solution of 1.95 g (7.35 mmol) of the primary alcohol **11** in 8 ml of dry pyridine (dried over potassium hydroxide) was added portionwise 1.55 g (8.15 mmol) of tosyl chloride (Eastman) over a period of 10 min with stirring. The mixture was stirred until solution was complete and then placed in a refrigerator (−6°) for 18 hr. The solution was diluted with 30 ml of 20% hydrochloric acid in 20 ml of ice. The ester which crystallized was collected on a Buchner funnel and washed thoroughly with water. After drying in vacuum there was obtained 2.85 g (92.5%) of the desired product, mp 159.5–164°. Recrystallization twice from ether pentane gave an analytical sample, mp 149° dec; ir ($CHCl_3$) 1600, 1460, 1360, 1190, 1175, 1100, 880, and 560 cm^{-1}; uv ($CHCl_3$) λ_{max} 263 nm (ϵ 457) and $\lambda_{shoulder}$ 269 (381); NMR ($CDCl_3$) δ 1.37 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.47 (s, 6 H, CH_3), 3.90 (d, 2 H, CH_2, J = 6.5 Hz), 4.83 (t, 1 H, CH, J = 6.5 Hz), 6.90–7.49 (m, 10 H, aromatic).

9-Methylene-1,8,10,10-tetramethyl-9,10-dihydroanthracene (1a).* The apparatus was dried by flame before use. To a solution of 0.8 g (2 mmol) of tosylate **12** in 8 ml of dry glyme (distilled over sodium hydride) at 60° was added with stirring 0.425 g of potassium *tert*-butoxide. After 10 min or so, the reaction mixture became very viscous and 2 ml of dry glyme was added. The reaction was stirred for another 10 min. A TLC test showed the reaction was complete. The reaction was quenched with saturated NaCl and extracted with pentane. After work-up, there remained 0.43 g (91.5%) of the desired product, mp 91–94°. Recrystallization from methanol and ether–methanol gave an analytical sample: mp 95.0–96.0°; ir (CCl_4) 3080, 2980 (C–H stretching doublet asymmetric and symmetric $C{=}CH_2$); uv (cyclohexane) λ_{max} 256 nm (ϵ 1.36 × 10^4); NMR ($CDCl_3$) δ 1.64 (broad, 6 H, CH_3), 2.58 (s, 6 H, CH_3), 5.65 (s, 2 H, CH), and 6.95–7.45 (m, 6 H, aromatic); mass spec (70 eV) M^+ at *m/e* 248 ($C_{19}H_{20}$).

9-(Bromomethylene)-1,8,10,10-tetramethyl-9,10-dihydroanthracene (1b). The synthesis was patterned after that previously reported.[3] To a stirred solution of methylene compound **1a** (0.5 g, 2 mmol) in 6 ml of carbon tetrachloride was added over a 3-min period 1.2 ml of a fresh carbon tetrachloride solution of bromine (0.65 g of bromine dissolved in 2.4 ml of carbon tetrachloride; 1.2 ml contains 0.325 g, 4 mmol, of bromine). The solution was stirred at room temperature for 9 hr and then heated under reflux for 3 hr. Distillation of the solvent gave 0.68 g of a tan residue. Chromatography on 25 g of alumina (Merk) and elution with cyclohexane–ether (4:1) gave 0.59 g (90%) of **1b**, mp 114–118°. Recrystallization twice from 95% ethanol gave an analytical sample: mp 128–129°; ir (CCl_4) 1380, 1360 (*gem*-dimethyl), and 700 cm^{-1}; uv (cyclohexane) λ_{max} 259.0 nm (ϵ 1.49 × 10^4); NMR ($CDCl_3$) δ 1.40 (s, 3 H, CH_3), 1.82 (s, 3 H, CH_3), 2.50, 2.69 (s, 6 H, CH_3), 6.55 (s, 1 H, C=CH), and 7.0–7.5 (m, 6 H, aromatic); mass spec (70 eV) M^+ at *m/e* 328 and 326 ($C_{19}H_{19}Br$).

9-(Chloromethylene)-1,8,10,10-tetramethyl-9,10-dihydroanthracene (1c).* The method of synthesis was patterned after that previously reported.[3] To a stirred solution of methylene compound **1a** (0.009 g, 2 mmol) in 10 ml of carbon tetrachloride at ice-salt temperature was added over a 10-min period 3.0 ml of a fresh carbon tetrachloride solution of chlorine (2.0 g of liquid chlorine diluted to 20.0 ml with carbon tetrachloride; 3.0 ml contains 0.3 g, 0.25 mmol, of chlorine). The solution was stirred for an additional 2.5 hr at 0°, and evaporation of solvent gave 0.63 g of a tan residue which was purified by chromatography on alumina. Elution with cyclohexane gave 0.45 g (80%) of the monochloromethylene compound **1a**, mp 100–110°. Recrystallization once from 95% ethanol gave a sample, mp 115–116.5°. Further purification from preparative TLC (silica gel, pentane) followed by recrystallization from ether–methanol gave **1c**: ir (CCl_4) 830 cm^{-1} (C=CH); uv (cyclohexane) λ_{max} 255.0 nm (ϵ 1.31 × 10^4); NMR ($CDCl_3$) δ 1.40 (s, 3 H, CH_3), 1.83 (s, 3 H, CH_3), 2.51 (s, 6 H, CH_3; separated into two peaks in 220 MHz spectrum with a separation of 10 Hz), 6.37 (s, 1 H, C=CH), 7.02–7.50 (m, 6 H, aromatic); mass spec (70 eV) M^+ at *m/e* 284 and 282 ($C_{19}H_{19}Cl$).

9-(Phenylthiomethylene)-1,8,10,10-tetramethyl-9,10-dihydroanthracene (1d).* The conditions used were similar to that of Beltrame and coworkers.[54] Thiophenol (11.0 g, 0.1 mol) was added to a mixture of sodium (2.3 g, 0.1 mol) in 75 ml of anhydrous ether. The mixture was stirred at room temperature for 5 hr. Then the white salt was filtered and washed thoroughly with ether to get rid of the unreacted thiophenol. Any unreacted sodium metal was separated from the salt which when dried in air weighed 13 g. To a stirred solution of sodium thiophenoxide (0.15 g, 1.13 mmol) in 5 ml of *N,N*-dimethylacetamide at 150°, there was added 0.3085 g of **1b** (0.92 mmol) over a period of 5 min. The solution assumed a red color and was heated at 160° for 8 hr. After cooling with an ice bath, the precipitated salt was filtered off. The solution was extracted with ether, and the ethereal extract was washed thoroughly with water. After work-up, there was obtained 0.3058 g of red residue. After eluting on a preparative TLC (silica gel) with pentane (developed four times), the red residue was separated into four well-defined bands. The most nonpolar band was identified as the starting material (0.1678 g, 54.4% recovery). The second band (0.1128 g, 33.6% yield) was identified as the desired product: uv spectrum (cyclohexane) λ_{max} 308 nm (ϵ 1.97 × 10^4) and 240 (1.32 × 10^4); ir spectrum (CCl_4) 1585, 1483, 1478, 1445, 1380, 1362, and 687 cm^{-1}; NMR ($CDCl_3$) 1.45 (3 H, CH_3), 1.83 (3 H, CH_3), 2.55, 2.57 (6 H, CH_3), 6.53 (1 H, C=CH) and 6.9–7.5 (m, 11 H, aromatic protons); mass spec (70 eV) M^+ at *m/e* 356 ($C_{25}H_{24}S$). The third band (0.0050 g) and the unmoved fourth band (0.0243 g) assumed a red color and were not investigated further.

3-Acetyl-2-(2-methylbenzyl)toluene (8).* The procedure used was similar to that reported by House and Bare.[55] The apparatus was dried by flame before use. To a cold (0°), vigorously stirred solution of 24.1 g (0.1 mol) of 3-methyl-2-(2-methylbenzyl)benzoic acid (**6**) in 600 ml of anhydrous ether was added, dropwise during 30 min, 140 ml of a titrated[52] ethereal solution of methyllithium (0.23 mol; Matheson Coleman and Bell). The resulting pink solution was stirred at room temperature for 4 hr, and then 50-ml aliquots were removed from the reaction mixture and added, dropwise with stirring, to fresh portions of ice and aqueous ammonium chloride solution. After work-up, there was obtained 21.95 g (93%) of the ketone, mp 64–65°. Two recrystallizations from ether–hexane gave an analytical sample: mp 65.0–66.0°; ir ($CHCl_3$) 1785 cm^{-1} (C=O); NMR (CCl_4) δ 2.17 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 2.35 (s, 3 H, CH_3), 4.10 (s, 2 H, CH_2), and 6.1–7.8 (m, 7 H, aromatic).

Reaction of 3-Acetyl-2-(2-methylbenzyl)toluene (8) with Methyllithium. (i) To a solution of 1.5 g (6.3 mmol) of ketone **8** in 30 ml of anhydrous ether under nitrogen was added an ethereal solution of methyllithium (8.3 ml, 12.6 mmol titrated).[52] After stirring at room temperature for 0.5 hr, the solution was heated under reflux for 1 hr. After work-up, only a small amount of the desired alcohol **9** was detected by a TLC test.

(ii) To a well-stirred solution of methyllithium (15.5 ml, 25 mmol) in ether was added a solution of 0.6 g (2.5 mmol) of ketone **8** in 4 ml of anhydrous ether. The mixture was heated under reflux for 6 hr. After work-up, only a small amount of alcohol **9** was formed as indicated by TLC.

9-(Isopropylidene)-10,10-dimethyl-9,10-dihydroanthracene (2).* This material was prepared from 10,10-dimethylanthrone (**13a**) and isopropylmagnesium bromide in the following two-step reaction.[5c] 10,10-Dimethylanthrone (**13a**) (1.00 g, 4.84 mmol) in 24 ml of ether–benzene (2:1) was added over a 30-min period to isopropylmagnesium bromide prepared from 0.582 g (24.0 mg-atoms) of magnesium turnings in 7 ml of ether and 2.95 g (24.0 mmol) of isopropyl bromide in 3 ml of ether under argon at 0° for 4 hr. The solution was poured onto crushed ice containing 2 g of ammonium chloride. After work-up, there remained 1.14 g of semisolid material which was subjected to dehydration by the method of Gar-

bisch[56] in 30 ml of a hot 20% concentrated sulfuric acid in glacial acetic acid solution. The reaction mixture was poured onto ice and extracted with ether. After work-up, there was obtained a dark oil which was purified by chromatography on alumina (cyclohexane eluent) to give 0.286 g (24% yield) of the desired olefin, mp 118–122°. Repeated recrystallizations from methanol gave an analytical sample: mp 122.5–123.0°; ir (KBr) 1465, 1450, 1385, 1370, 1360, 950, 770 cm^{-1}; uv (cyclohexane) λ_{max} 266 nm (ϵ 1.50 × 10^4) and 235 (1.31 × 10^4); NMR (tetrachloroethylene) δ 1.35 (broad), 1.75 (broad, 6 H, CH_3), 2.05 (s, 6 H, CH_3), and 6.8–7.4 (m, 8 H, aromatic); mass spec (70 eV) M^+ at *m/e* 248 ($C_{19}H_{20}$). Peak matching at high resolution identified the molecular ion as $C_{19}H_{20}$ (calcd 248.1565; found, 248.1565).

3,3-Dimethylphthalide (16a). Treatment of 2 molecular equiv of methylmagnesium iodide with 1 equiv of finely powdered phthalic anhydride in anhydrous ether[57] gave the phthalide: mp 67.5–68.0° (lit.[57] mp 67–68°); ir (CCl_4) 1770 (lactone), 1385, and 1378 cm^{-1} (*gem*-dimethyl).

3,3-Dimethyl-1-phenyl-1-hydroxyphthalan (17a).* Treatment of phenylmagnesium bromide with 3,3-dimethylphthalide in anhydrous ether[38] gave an 80% yield of phthalan: mp 116.0–117.0° (lit.[38] 118°); ir ($CHCl_3$) 3585 (hydroxy), 1385, 1370 (*gem*-dimethyl) [but no carbonyl absorptions even in the solid state (KBr)]; NMR ($CDCl_3$) δ 1.65 (s, 6 H, CH_3), and 3.54 (s, 1 H, OH), 7.22–7.62 (m, 9 H, aromatic) (on shaking with D_2O, the peak at 3.54 disappeared).

10,10-Dimethylanthrone (13a).* The reaction conditions were optimized. A mixture of hydroxyphthalan **17a** (1.0463 g, 4.33 mmol) and polyphosphoric acid (PPA, 15.0 g) was heated at 150° for 22 hr with stirring and under nitrogen. The dark red mixture was decomposed with water and then extracted with benzene. After work-up, there remained 0.87 g of a dark brown residue. [A TLC test indicated two spots (R_f 0.28; R_f 0.48). The small spot (R_f 0.28) was identified as the desired anthrone. No starting material was detected.] Chromatography on silica gel and elution with benzene gave 0.1278 g of crystals which were further purified by vacuum sublimation at 80° (1.5 mm) to give 0.0960 g (10%) of **13a:** mp 101.5–102.0° (lit.[3] mp 102–103°); ir (KBr) 1655 cm^{-1} (C=O).

2-(1-Hydroxy-1-methylethyl)benzophenone Semicarbazone (19). The semicarbazone was prepared according to the general method for Shriner, Fuson, and Curtin.[58] To 6.0 g (0.025 mol) of hydroxyphthalan **17a,** 70 ml of ethanol, and 40 ml of water were added a few drops of ethanol to remove the turbidity. Then 9.0 g of sodium acetate and 6.0 g of semicarbazide hydrochloride were added. The clear solution was heated on a steam bath (82°) for 1 hr with stirring. After cooling with ice-water and scratching, the turbid solution was left at room temperature overnight. The white precipitate was collected by suction filtration and washed thoroughly with ice-cooled water. After drying over P_2O_5 under vacuum, there was obtained 6.65 g (dilution of the mother liquor with water gave another 0.85 g of the desired product or a total yield 94%) of desired semicarbazone **19:** mp 140.0–141.0° (lit.[43] mp 140–141°); ir ($CHCl_3$) 3530, 3480, (shoulder), 3395, 3405 (shoulder), 1680, 1380, and 1360 cm^{-1}.

2-Benzyl-α,α-dimethylbenzyl Alcohol (21).* This alcohol was obtained by Wolff-Kishner reduction of the above semicarbazone **19** in the following manner. A mixture of potassium hydroxide (3.0 g) in 30 ml of ethylene glycol (bp 194–200°) was heated carefully with a small flame until the potassium hydroxide began to melt and go into solution; then the heat was removed until the exothermic dissolution was completed After the solution was cooled at 80–100°, there was added 4.50 g (0.015 mol) of the semicarbazone **19** and 0.3 ml of water. The flask was then fitted with a condenser, magnetic stirrer, and electric mantle. The mixture was cautiously heated. Ammonia gas began to evolve at 134°. The mixture was then heated under reflux (162°) for 3 hr. After lifting the condenser to evaporate the water vapor, the solution was heated under reflux (187°) for another 3 hr. It was then poured into 150 ml of ice-water, neutralized with hydrochloric acid, and extracted thoroughly with ether. After work-up, there was obtained 3.2 g (84%) of a greenish oil which upon standing gradually solidified (mp 57–62°). Recrystallization from pentane gave an analytical sample: mp 64.0–65.0° (lit.[59] 66–67°); ir spectrum (CCl_4) 3600 (OH), 1385, 1365 (*gem*-dimethyl), and 1130 cm^{-1}.

9,9-Dimethyl-9,10-dihydroanthracene (22).* The method was that described by Davis et al.[59] A solution of alcohol **21** (0.9664 g, 4.3 mmol) in 2.7 ml of 70% sulfuric acid was heated on a steam bath for 1.5 hr. After quenching with water, the mixture was extracted with benzene. After work-up, there remained 0.80 g (93%) of an oily material which crystallized to a white solid, mp 47.5–50.0°. Recrystallization from 95% ethanol gave an analytical sample: mp 49.5–50.5° [lit.[60] (an oil[59]) mp 51–52°]; ir (CCl_4) 1385 and 1362 cm^{-1} (*gem*-dimethyl).

3,3,7-Trimethylphthalide (16b).* The material was prepared by a method similar to that described by Jones and Desio[61] for the mono-C-methylation of 3-methylphthalic anhydride with methylmagnesium iodide. Anhydride **3** (25.0 g, 0.15 mol) in 200 ml of anhydrous ether and benzene (1:1) was treated with 2 equiv of methylmagnesium bromide which was prepared from 8.0 g of magnesium turnings and 42.6 g of methyl iodide in 200 ml of anhydrous ether. After work-up, it gave 12.0 g (44.5%) of **16b,** mp 53–56°. Recrystallization twice from benzene–pentane gave an analytical sample: mp 64.0–65.0° (lit.[62] mp 60.5°); ir (CCl_4) 1760 (lactone), 1385, 1370 (*gem*-dimethyl), and 1040 cm^{-1}.

3,3,7-Trimethyl-1-(*o*-tolyl)-1-hydroxyphthalan (17b).* The procedure followed was the same as that used for the preparation of hydroxyphthalan **17a.** The Grignard reagent was prepared from 1.10 g (0.041 g-atom) of magnesium turnings and 7.30 g (0.042 mol) of *o*-bromotoluene in 50 ml of anhydrous ether. Treatment of this Grignard reagent with a solution of 5.0 g (0.02 mol) of 3,3,7-trimethylphthalide (**16b**) in 100 ml of anhydrous ether gave 7.84 g of an orange oil. Chromatography on 220 g of alumina (Merck) and elution with *n*-hexane gave 7.3 g (100%) of the desired product as a pale, greenish, glass-like material. Additional drying under vacuum for 6 hr gave an analytical sample: ir ($CHCl_3$) 3570 (OH), 1380, 1365 (*gem*-dimethyl), and 1010–980 cm^{-1}; NMR ($CDCl_3$) δ 1.51 (s, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 1.98 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3), 3.00 (s, 1 H, OH), and 6.9–7.7 (m, 7 **H**, aromatic).

2,2′-Dimethyl-6-(1-hydroxy-1-methylethyl)benzophenone 2,4-Dinitrophenylhydrazone (24).* The general method of Shriner, Fuson, and Curtin[58] was used. A solution of 0.3 g of hydroxyphthalan **17b** in 7 ml of absolute ethanol and 0.35 g of 2,4-dinitrophenylhydrazine was heated by a small flame until boiling began. After 20 drops of concentrated hydrochloric acid was added, the solution assumed a bright red color. After 5 min of additional heating, the solution was cooled and the red precipitate was collected. The crude hydrazone melted at 205–207°. Recrystallization from ethyl acetate gave red needles, mp 201.0–202.0° dec.

1,8,10,10-Tetramethylanthrone (13b).* The method used was patterned after the synthesis for anthrone **13a.** Treatment of 1.0322 g (0.004 mol) of hydroxyphthalan **17b** (1.0322 g, 0.004 mol) and PPA (40.4 g) at 150° under nitrogen for 24 hr gave 0.8184 g of crude product. Vacuum sublimation at 150° (1.5 mm) gave 0.0167 g (1.7%) of the desired anthrone as a viscous yellow oily material. The analytical sample was held under vacuum for 4 hr. The ir spectrum ($CHCl_3$) showed carbonyl absorption at 1650 cm^{-1}.

1-Ethoxy-3,3,7-trimethyl-1-(*o*-tolyl)phthalan (23).* A crude sample of hydroxylphthalan **17b** (19.9 g, 0.07 mol) prepared from 12.5 g (0.071 mol) of 3-methylphthalic anhydride was dissolved in 30 ml of warm ethanol. Water was added till turbidity occurred. The turbidity was removed by adding more ethanol. Crystallization at room temperature gave 15.8 g (77%) of crystals which were identified as compound **23:** mp 110.0–111.5°; ir ($CHCl_3$) 1380, 1360 (*gem*-dimethyl), 1095, and 1130 cm^{-1}; NMR ($CDCl_3$) δ 1.19 (t, J = 7 Hz), overlapping with δ 1.18 (s, 6 H, CH_3), 1.58 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), and 2.68 (s, 3 H, CH_3), 6.6–7.5 (m, 7 H, aromatic), and two sets of octets centered at δ 3.08 and 3.58 (J = 7 Hz and J' = 2 Hz, 2 H, $-CH_2-$ next to an optically active center were nonequivalent). Under similar reaction conditions, 3,3-dimethyl-1-phenyl-1-hydroxylphthalan (**26a**) did not react with ethanol.

Attempted Reaction of 1-Ethoxy-3,3,7-trimethyl-1-(*o*-tolyl)-phthalan (23) with Semicarbazide Hydrochloride. A solution of ethoxyphthalan **23** (0.50 g), semicarbazide hydrochloride (0.5 g), and sodium acetate (0.75 g) in 15 ml of ethanol and 5 ml of water was heated under reflux for 3 days. After work-up, no semicarbazone **20** could be isolated.

Reaction of 1-Ethoxy-3,3,7-trimethyl-1-(*o*-tolyl)phthalan (23) with 2,4-Dinitrophenylhydrazine. The procedure used was essen-

tially that described by Shriner, Fuson, and Curtin.[58] A mixture of ethoxyphthalan **23** (2.0 g, 6.75 mmol) and 2,4-dinitrophenylhydrazine (1.5 g) was dissolved in 150 ml of absolute ethanol in which 50 drops of concentrated hydrochloric acid had been added. After refluxing for 2 hr, it was filtered, concentrated, and cooled. There was isolated 2.44 g (80.6%) of orange-red crystals, mp 208.5–209.5°, which were identified as hydrazone **24.**

2,2′-Dimethyl-6-(1-hydroxy-1-methyl)benzophenone Semicarbazone (20). To a solution of hydroxyphthalan **17b** (0.9 g, 0.00336 mol) in 14 ml of dimethyl sulfoxide (Me_2SO) at 80° was added dropwise an aqueous solution of semicarbazide hydrochloride (0.9 g) and sodium acetate (1.35 g) in 7 ml of water. The clear solution was heated at 100° for 3 hr and precipitate began to form. After standing at room temperature overnight, the turbid solution was diluted with water. There was isolated 0.95 g (86.2%) of the desired semicarbazone which was resubmitted to the reaction conditions to ensure that reaction was complete. After drying there was obtained 0.9 g of semicarbazone: mp 184–186° dec; ir ($CHCl_3$) 3530, 3480, 3410, 330, 1690, 1560, 1450, 1385, and 1365 cm^{-1}.

Reduction of Semicarbazone 20. The procedure used was the same as that described for the reduction of semicarbazone **19.** Evaporation of solvent gave 84% yield of an oil whose NMR spectrum ($CDCl_2$) revealed peaks corresponding to alcohol **9**. Cyclodehydration of **9** with 70% H_2SO_4 at 90° gave 54% of crude 1,8,10,10-tetramethyl-9,10-dihydroanthracene (**10**).

Nuclear Overhauser Effect (NOE) Measurement. The spectra of compounds **11** and **12** were run as filtered (fine sintered glass) and carefully degassed $CDCl_3$ solutions, in concentrations of 5–10%. A small amount of Me_4Si was added as an internal lock. The measurements were performed with a HA-100 instrument.[63]

The nuclear Overhauser enhancements were measured as the differences in the integrated intensities of a specific signal caused by double irradiation at the proton signal noted and at a blank region of the spectrum (i.e., off-resonance) consecutively, using the same irradiating power. The enhancements listed in Table I were calculated from the average of at least eight integrals and have a precision of ±3%.

Variable-Temperature Nuclear Magnetic Resonance Study. Variable-temperature NMR spectra were recorded with a Varian Associates 56-60A spectrometer equipped with a V-6040 variable-temperature probe. The probe temperature was measured by means of a copper-constantan thermocouple placed in a dummy nuclear magnetic resonance tube fitted with a 56-60A spinner. Sample temperatures are believed to be accurate to ±1°. High temperature (140–190°) measurements were based on the chemical-shift separation of the protons of ethylene glycol using the temperature-shift correlation chart. Coalescence temperatures, at which a broad and flat-topped peak is observed, were determined to ±0.5° by numerous readings immediately above and below the apparent coalescence temperature.

Samples of **1a** and **2** for the low temperature study were 10% solutions in $CDCl_3$ and tetrachloroethylene, respectively, containing Me_4Si as internal standard. The solutions were filtered into an A-60 NMR tube through sintered glass, degassed by several of the usual freeze–pump–thaw cycles, and then sealed under vacuum. Samples of **1b, 1c,** and **1d,** for the high temperature measurements, were prepared as 10% solutions in diphenyl ether. External standard Me_4Si was used.

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Isolable Stereoisomeric Methylenedihydroanthracenes. The Synthesis and Behavior toward Nucleophilic Displacement of Conformationally Isomeric 9-(Bromomethylene)-10-ethyl-1,8,10-trimethyl-9,10-dihydroanthracenes[1,2]

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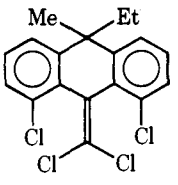
Abstract: Two stereoisomeric 9-(bromomethylene)-10-ethyl-1,8,10-trimethyl-9,10-dihydroanthracenes (**2**) have been prepared and separated and found to be stable at room temperature because of slow boat-boat inversion of the center ring. The rates of interconversion (to an equilibrium mixture containing 12% (e)-ethyl- and 88% (a)-ethyl-**2**) of the two isomers in tetrachloroethylene have been found to be first order with $k_1 + k_{-1} = 7 \times 10^{-4}$ sec^{-1} at 107° (ca. 4×10^4 times faster than 9-(dichloromethylene)-10-ethyl-10-methyl-1,8-dichloro-9,10-dihydroanthracene (**1**)). The free energy of activation was estimated to be 28.2 kcal/mol. A new type of reaction stereochemistry has been investigated, in which the original conformation of the 10-ethyl and 10-methyl groups in (a)-ethyl-**2** was retained during nucleophilic substitution by lithium diphenylphosphide at the vinyl carbon atom.

Earlier NMR studies[3-5] of restricted boat-boat interconversion for a number of substituted 9-methylene-10,10-dimethyl-9,10-dihydroanthracenes have been made. It has furthermore been demonstrated[6] that when four chlorine atoms, substituents of moderate steric size, were introduced onto the methylene carbon atom and the 1- and 8-aryl positions of 9-methylene-10-ethyl-10-methyl-9,10-dihydroanthracene, two stereoisomers, (a)-ethyl- and (e)-ethyl-**1**,



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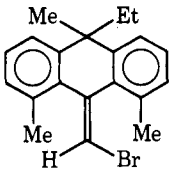

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could be separated and were found to be stable at room temperature. The introduction of a single substituent of sufficient bulk at the methylene position in the corresponding 1,8-dimethyl substituted compound, 9-methylene-1,8,10,10-tetramethyl-9,10-dihydroanthracene, should increase the barrier to ring inversion sufficiently to permit the isolation of stereoisomers. The present study was directed toward the synthesis of stereoisomeric 9-(bromomethylene)-10-ethyl-1,8,10-trimethyl-9,10-dihydroanthracene (**2**) to see whether it could be separated into (a)-ethyl- and (e)-ethyl isomers, and also in order to investigate replacement reactions at the vinyl carbon.[7] Thus, the presence of an intermediate with sufficiently reduced steric requirement would result in boat-boat interconversion concomitant with replacement. Compound **2** has the further potential interest that it could, in principle, be resolved into two pairs of optically active isomers interconvertible by a change of the configuration at the olefinic carbon atom.

The synthetic sequence for the preparation of a mixture of (a)-ethyl-**2** and (e)-ethyl-**2** modeled after that employed for the synthesis of the 10,10-dimethyl homologs, is outlined in Scheme I. The structure assignments of compounds **7**, **8**, **9**, and **10** were established by NMR studies.[8] At ambient temperatures the NMR spectrum of methylene compound **11** indicated that the rate of interconversion of (a)-ethyl and (e)-ethyl isomers was fast on the NMR time scale, and only time-averaged signals could be seen. On the other hand, the NMR spectrum of compound **2** revealed the presence of a mixture of (a)-ethyl- and (e)-ethyl isomers. The (a)-ethyl isomer could be separated by crystallization from methanol. The (e)-ethyl isomer was very difficult to separate and was obtained by chromatography on alumina impregnated with 25% silver nitrate and elution with hexane. Configurational assignments to (a)-ethyl and (e)-ethyl isomers are based on comparison of the NMR spectra with the known spectra of the (e)-ethyl- and (a)-ethyl-**1**.[6]

The rates of isomerization of (a)-ethyl- and (e)-ethyl-**2**