Rotational Barriers and Conformational Studies in 9-Arylxanthyl Derivatives

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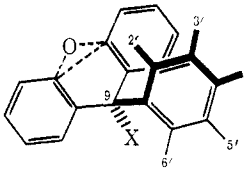
Abstract: The temperature-dependent nmr spectra of 9-(2,4,6-trimethylphenyl)xanthene (III-H), 9-(2,6-dimethylphenyl)xanthenol (II-OH), and 9-(2-methylphenyl)xanthene (I-H) were investigated in detail. The observed exchange of methyl environments is attributed to hindered rotation about the 9-aryl bond. Exchange rates were calculated by comparing experimental spectra with theoretically calculated spectra over a range of temperatures, and gave $\Delta F_{25°}^{\ddagger}$ of 17.6, 10.9, and 9.4 kcal/mol for III-H, II-OH, and I-H, respectively. A comparison is drawn of the similarities and differences for the rotational barriers and chemical shifts of these and other xanthyl derivatives with the recently investigated 9-arylfluorenyl system. Interpretation of the spectral results in terms of nonbonded interactions in both the ground and transition states is discussed in some detail for both systems. The striking differences between barriers of analogous compounds of the xanthyl and fluorenyl series are explained by the greater conformational mobility in the former. The preferred axial-phenyl conformation suggested for the xanthyl compounds is discussed in relation to the conformationally analogous 9,10-dihydroanthracenyl system. The attempted detection of an optically active xanthyl cation is briefly reported.

These studies of the 9-arylxanthyl system originated from an interest in their role as carbonium ion precursors; in particular they appeared promising as an entry into studies of the preparation and properties of an optically active 9-arylxanthyl carbonium ion. Though this latter goal was not realized (*vide infra*), nmr studies on the covalent 9-arylxanthyl compounds revealed a novel rotational barrier which was consequently investigated in some detail. Concurrently, an analogous barrier was discovered in the closely related 9-arylfluorenyl system, and reported independently by three different groups.[1-4]

It is our purpose here to compare and contrast the rotational processes of the 9-arylxanthyl with the reported fluorenyl systems, to comment on the nature and mechanism of the rotational process, and to consider the role of conformational effects in the 9-arylxanthyl system.

Table I. Chemical Shifts[a] (δ)



	Xanthyl					Fluorenyl[b]				
	CH$_3$ at position					CH$_3$ at position				
9-Aryl substituent	2'	3'	4'	6'	9-H	2'	3'	4'	6'	9-H
Carbinols (X = OH)										
I, 2'-methyl	1.62[c]			*c*		1.25[c]			*c*	
II, 2',6'-dimethyl	1.35[d]			2.93[d]		1.15			2.90	
III, 2',4',6'-trimethyl	1.33		2.25	2.98		1.17		2.25	2.90	
IV, 3'-methyl		2.25[e]								
V, 4'-methyl			2.25							
VI, 2'-ethyl	0.37[c]			*c*						
Hydrocarbons (X = H)										
I, 2'-methyl	*c*			2.32[c,f]	5.59[c,f]	1.13[g]			2.69[g]	4.90, 5.30
II, 2',6'-dimethyl	1.63			2.58	*h*	1.13			2.69	5.50
III, 2',4',6'-trimethyl	1.60		2.27	2.53	5.9	1.10		2.25	2.64	5.47
IV, 3'-methyl							2.21[e]			4.97
V, 4'-methyl								2.27		4.98
VI, 2'-ethyl	*c*			1.10[c]	*h*					

[a] Probe temperature (~36°) unless specified otherwise. [b] Data for the carbinols from Chandross and Sheley[1] and for the hydrocarbons from Siddall and Stewart[2,3] at 0°. [c] δ listed under site of the more predominant rotamer in the equilibrium mixture of the two possible forms. See Discussion. [d] At −65°. At probe temperature a single methyl resonance at δ 2.14 is observed. [e] Average δ of methyl protons at the 3' and 5' positions since aryl rotation is rapid, and no isomer preference is expected. [f] Chemical shift at −65°. At −100° the signals of the 2' and 6' rotamers are observed for the methyl protons at δ 1.66 and 2.73 and for the methine proton at 5.67 and 5.48. [g] Two methyl signals of the 2' and 6' rotamers were observed[2] at 0° with the 6' isomer predominating to the extent of 61.5% (K_{eq} = 1.6). [h] Obscured by solvent band.

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[1] E. A. Chandross and C. F. Sheley, Jr., *J. Amer. Chem. Soc.*, **90**, 4345 (1968).

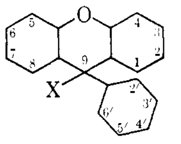
[2] T. H. Siddall, III, and W. E. Stewart, *J. Org. Chem.*, **34**, 233 (1969).

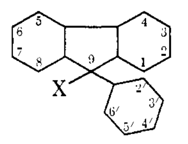
[3] T. H. Siddall, III, and W. E. Stewart, *Tetrahedron Lett.*, 5011 (1968).

[4] A. Rieker and H. Kessler, *ibid.*, 1227 (1969).

Results

The nmr spectra of compounds studied in this work (I–VI) are summarized in Table I and, for purposes of comparison, the data are also listed for the corresponding fluorenyl systems (Fl-I–Fl-V) recently reported by others.[1–4]





	2'	3'	4'	6'
I–X	CH_3	H	H	H
II–X	CH_3	H	H	CH_3
III–X	CH_3	H	CH_3	CH_3
IV–X	H	CH_3	H	H
V–X	H	H	CH_3	H
VI–X	C_2H_5	H	H	H

X = OH, H, or Cl
Fl = 9-arylfluorenyl

The presence of discrete signals for the 2'- and 6'-methyl substituents in the xanthyl compounds II-H and III-H at room temperature and II-OH and III-OH at low temperature clearly indicates the existence of a barrier to rotation about the 9-aryl sp^2–sp^3 bond. An increase in temperature leads to broadening and eventual coalescence of these 2'- and 6'-methyl signals, as expected for rotational processes in which rotamers are being rapidly equilibrated on the nmr time scale.

Activation parameters for methyl exchange in the xanthyl compounds are shown in Table II. Also listed in Table II are the chemical shift ($\nu_{6'\text{-CH}_3} - \nu_{2'\text{-CH}_3}$), coalescence temperatures, as well as the corresponding values for analogous fluorenyl compounds as obtained by others. Kinetic parameters were determined by comparison of experimental spectra with calculated spectra at a series of temperatures. Arrhenius plots of these data are shown in Figure 1; limits of error estimated from the least squares analyses are ±0.5 kcal/mol.

Table II. Kinetic Data[a]

Compound	Xanthyl $\Delta F_{25°}^{\ddagger}$	Xanthyl $\Delta S_{25°}^{\ddagger}$	Xanthyl T_c, °C	Xanthyl $\Delta\nu^c$	Fluorenyl[b] $\Delta F_{200°}^{\ddagger}$	Fluorenyl[b] T_c, °C	Fluorenyl[b] $\Delta\nu^c$
II-OH	10.9	5.8	−20	99	21.3	200	105
III-H	17.6	5.2	~95	56	>26	>200	92
I-H	9.4	−2.5	~−75	64	16.3[d]		90

[a] Energies of activation are in kilocalories per mole and entropies of activation are in entropy units. Estimated errors for the xanthyl compounds are ±0.5 kcal/mol and ±2 eu. [b] Reference 2. [c] $\nu_{6'\text{-CH}_3} - \nu_{2'\text{-CH}_3}$ at 60 MHz. [d] At 60°.

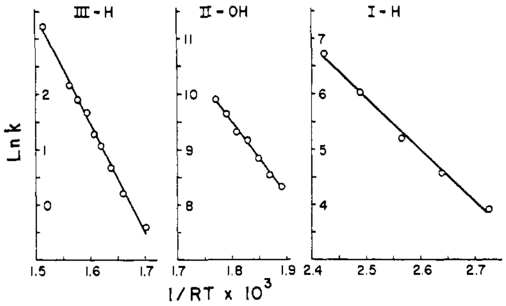


Figure 1. Arrhenius plots ($1/RT \times 10^3$ *vs.* $\ln k$ (sec^{-1})) for methyl exchange in compounds III-H, II-OH, and I-H.

Discussion

Comparison of Xanthyl and Fluorenyl Systems. In general, the presence and detection of the rotational barrier about the xanthyl 9-aryl bond arises from steric and anisotropic considerations qualitatively similar to those for the 9-arylfluorenes; however, greater conformational mobility and variation in nonbonded interactions lead to important differences and these will be discussed in detail.

The structure in Table I represents the similar ground-state configuration of the 9-arylxanthyl and fluorenyl compounds. Space-filling molecular models[5] clearly demonstrate the similar steric requirements in both molecules. As shown in this figure, steric requirements force the 9-aryl ring to be approximately perpendicular to the fluorenyl or average xanthyl plane, leading to very different chemical and magnetic environments for the *o*-methyl groups in the 2' and 6' positions. In the absence of rotation the 2'-methyl is located in the shielding zone of the π clouds of the multiaromatic rings, in contrast to the 6'-methyl which is held in close proximity to the 9-X group and approximately in the plane of this aromatic component. Thus, the large differences in the chemical shifts of the 2'- and 6'-methyls are readily understood in terms of their individual proximity to the shielding and deshielding zones of the xanthyl or fluorenyl components. Johnson and Bovey's[6] calculations, previously carried out in reference to the fluorenyl system,[1] are presumably applicable here as well, but are superfluous since the above assignments have been rigorously established by application of the nuclear Overhauser effect on III-H; the 32% enhancement of the 9-H proton signal, observed upon irradiation of the low-field methyl, identifies the latter as the more proximate methyl group at the 6' position.

In the di-*o*-methyl-substituted compounds, II-OH, II-H, III-OH, III-H, Fl-II-OH, Fl-II-H, Fl-III-OH, and Fl-III-H, equal populations of diastereomeric methyls offer no difficulty in recognizing and interpreting the rotational barriers as long as slow rotation on the nmr time scale can be achieved in an accessible temperature range. The observation that the nonequivalence of the two methyl groups may be removed by heating requires rapid rotation on the nmr time scale, a process which time-averages the methyl environments and leads to a single resonance found at the exact average of the individual methyl signals. In contrast to the 2'- and 6'-methyls, the 4'-methyls of the 9-mesitylxanthene (III-H) and xanthenol (III-OH) have normal aromatic methyl chemical shifts and line shapes which are independent of temperature, as required by symmetry considerations.

The situation differs with the mono-*o*-methyl compounds, in which methyl may assume either a 2' or 6'

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(5) CPK atomic models (The Ealing Corporation, Cambridge, Mass.) are particularly well suited for the study of steric interactions in crowded systems.

(6) C. E. Johnson, Jr., and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).

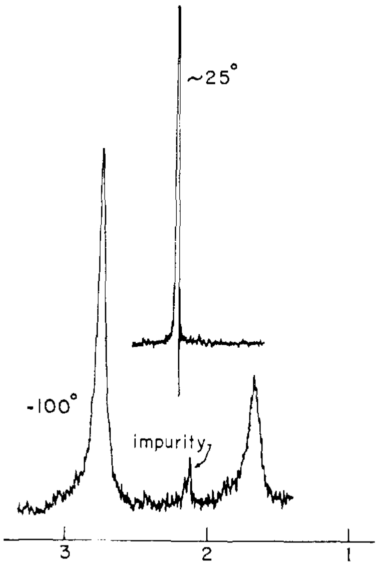
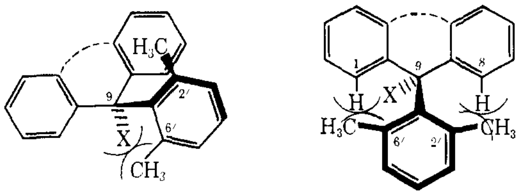


Figure 2. 100-MHz nmr spectrum of the methyl region of I-H in CD_2Cl_2 showing limits of fast (25°) and slow exchange (−100°). For the slow-exchange spectrum the more intense low-field resonance is assigned to the 6′-methyl.

position. The resulting diastereomeric rotamers are now of unequal energy and this leads to unequal population distribution. As seen in Table I for compound Fl-I-H near ambient temperature, Siddall and Stewart[2] were able to detect a mixture of the two possible ground-state conformers in which the rotamer with methyl at the 6′ position predominates. As expected, the methyl resonances of the individual mono-*o*-methyl rotamers of Fl-I-H are close to those found for the 2′- and 6′-methyls of the di-*o*-methyl derivatives, Fl-II-H and Fl-III-H. In the present work only a single resonance is observed near ambient temperature for the mono-*o*-methyl compounds I-H and I-OH. Such a single methyl signal can be the result of either (i) rapid rotation in which the individual methyl environments of the two diastereomeric rotamers are averaged or (ii) slow rotation in which an energetically favored rotamer overwhelmingly dominates.

From the observation that the chemical shifts of the single methyl resonances in I-H and I-OH are between the chemical shifts expected for the individual rotamers, we can conclude that fast rotation (i) and not the thermodynamic constraint (ii) applies. Using the limiting chemical shifts as obtained from the appropriate dimethyl derivative, and assuming the usual relation between mole fraction and chemical shift,[7] the favored isomer for I-OH has methyl at the 2′ position (83%, $K_{eq} = 4.9$) while I-H has methyl at the 6′ position (63%, $K_{eq} = 1.7$). This conclusion was confirmed for I-H by direct low-temperature nmr observation of both rotamers (see Figure 2, −100°) in the approximate proportions calculated above from the time-averaged chemical shift (see Figure 2, 25°). This chemical shift argument can be used to interpret the data reported by Chandross and Sheley[1] for the mono-*o*-methyl alcohol Fl-I-OH. The chemical shift of Fl-I-OH (δ 1.25 at probe temperature) is too close to that which would be expected for the pure 2′ isomer to decide whether condition i or ii applies. However, from the constancy of the chemical shift values of the 2′-methyl protons in other derivatives (see Fl-II-OH, H, and Fl-III-OH, H) it seems likely that rotation is fast and that the 2′ rotamer is favored to the extent of $>90\%$.



3a

3b

Figure 3. Ground (**3a**) and transition (**3b**) states for aryl rotation in both xanthyl and fluorenyl compounds.

Similarly, the assertion[1] that the lack of line broadening at high temperature in the nmr spectrum of 9-chloro-9-*o*-tolylfluorene (Fl-I-Cl) proves the absence of rotation in this compound is invalid on the basis of the above discussion. In fact, the chemical shift of the methyl in this compound (δ 1.25) in comparison to the 2′- and 6′-methyls of nonrotating dimethyl compounds (δ 1.10 and 2.95 in Fl-II-Cl, respectively) again suggests that fast rotation is occurring and that the 2′ rotamer is present to $>90\%$.

The Effect of 9-X Substituents. Mechanism of Rotation. There is a dramatic difference in the rotational barriers in both the xanthyl and fluorenyl compounds with variation of the size of the 9-X substituents (Table II). A comparison of the barriers in the di-*o*-methyl-substituted hydrocarbon (X = H) and alcohol (X = OH) in both systems shows that introduction of the larger 9-X group lowers the barrier by ~7 and >5 kcal/mol, respectively. Superficially this observation of increased barrier with decreasing size of 9-X substituent seems anomalous and an explanation of this phenomenon requires a detailed examination of the mechanism for exchange of methyls.

The observation of two nonequivalent methyls at low temperature which coalesce to a single band at high temperature clearly defines the respective ground- and transition-state configurations. The ground state, as previously deduced from a consideration of chemical shifts and space-filling models, has the 9-aryl ring approximately perpendicular to the xanthyl plane (see Figure 3a). The transition state, reached by a 90° rotation about the 9-aryl bond in either direction, leads to a high-energy array in which the molecular plane of symmetry bisects the plane of the aryl ring, and the two *ortho* methyls are equivalent. To attain this transition state the molecule encounters severe steric interactions between the *ortho*-9-aryl substituents and the 1- and 8-hydrogens (see Figure 3b). This interpretation agrees with that outlined by Siddall and Stewart[2] for the fluorenyl case.

Chandross and Sheley[1] have proposed an entirely different mechanism for the methyl exchange. On the basis of the observation of a considerably lower rotational barrier when Cl is substituted for either OH or H in the 9 position, they eliminate steric inhibition to rotation about the 9-aryl bond as a source of the barrier. They suggest instead an ionization–recombination mechanism in which methyl exchange is accomplished

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(7) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Magnetic Resonance Spectroscopy," Vol. I, Pergamon Press, New York, N. Y., p 485.

by inversion at the 9-carbon *via* a carbonium ion pair intermediate, a conclusion apparently supported by the ease with which Fl-III-Cl and Fl-III-OH are converted to the 9-mesitylfluorenyl-9 cation detectable by optical spectroscopy. However, since polarity of solvent is known to be of major influence for processes involving carbonium ion intermediates while the rotational barrier of Fl-III-Cl was solvent independent, they were forced to postulate that inversion involved only tight ion pairs. Though it would be difficult to rigorously eliminate such an intermediate, we are not aware of any precedent to support the concept of tight ion pairs as applied to stable, isolable carbonium ion salts. This would be particularly relevant to the xanthyl compounds which form even more stable carbonium ions. It has now been found that the barrier for the xanthyl compounds is not affected by change in solvent polarity and that the addition of CF_3COOH to the point where the carbonium ion is actually observable in the nmr leads to no significant change for the methyl exchange rates in the carbinol, II-OH. Presumably Chandross and Sheley[1] would attribute the absence of rotation in the hydrocarbon Fl-II-H to its sterically insurmountable barrier, unalleviated by the ability of this molecule to ionize and invert. In fact, as is shown for the xanthyl hydrocarbon, III-H, where ionization is equally implausible, rotation does occur and the barrier depends only upon steric factors to be discussed below.

The elimination of steric factors as the source of the barrier to rotation of the 9-aryl group on the basis of the effect of the steric size of the 9-substituent, as was concluded by Chandross and Sheley,[1] is invalid.[8] Though they state that "the primary barrier to rotation comes as a result of steric interactions between the 2′- and 6′-methyls and the 1 and 8 ring protons of fluorene rather than because of any substituent on the C-9 carbon," they use the inverse correlation of size of the 9-X substituent with $\Delta F^{\neq}$ to eliminate transition state **3b**. In point of fact and as clearly demonstrated by a consideration of the relative steric influences in the ground and transition state (Figure 3), substitution at C-9 has a primary influence only on the energy of the ground state and little or no influence on the energy of the transition state. The inverse substituent effects observed both in the fluorenyl and xanthyl systems (*i.e.*, the barrier increases with decreasing size of 9-X substituent) are thus readily interpreted as an increase in ground-state energy with increased size of X, relative to the transition state which remains unaffected. Similar conclusions in favor of a transition state involving a rotational mechanism rather than an inversion mechanism were independently reached by Rieker and Kessler[4] and by Siddall and Stewart.[2]

The mono-*o*-methyl compounds are informative concerning the energy of both the ground and transition state. Our conclusion that the barrier to rotation is considerably smaller in all the mono-*o*-methylxanthyl and -fluorenyl compounds is in accord with the removal of one of the two major interactions in the transition state. Similar ground-state energies for mono- and *o*,*o*′-dimethyl xanthylhydrocarbons (I-H, II-H), as suggested by the nearly equal equilibrium distribution of the two rotamers of I-H, would be expected to lead to an approximately 50% reduction in the barrier of the monomethyl as compared to the dimethyl compounds. This is substantiated by a comparison of $\Delta F^{\neq}$ for I-H and II-H in Table II. Similar reasoning applied to the fluorenyl case provides an additional argument against an ionization–recombination mechanism. This mechanism, on the basis of the observation[1] that the mono-*o*-methyl compound, Fl-I-Cl, ionizes slower than the corresponding more sterically encumbered di-*o*-methyl derivatives, requires a greater rotational barrier for the former. The experimental facts are otherwise: Fl-III-Cl requires a temperature greater than 80° for fast rotation,[1] while we have concluded that Fl-I-Cl is rotating rapidly at ambient temperature.

As noted earlier, steric interactions in the ground state between the 9-X and mono-*o*-methyl substituents affect the population distribution between the 2′ and 6′ rotamers. Increasing the size of X in going from the hydrocarbon to the carbinol leads to substantially increased population of the 2′ isomer at the expense of the 6′ isomer. This can only be due to relief of steric compression between the 6′ and 9-X substituents.[9] Parenthetically, we note that this difference in conformer populations ($\Delta F°$(6′ isomer, I-OH) $-$ $\Delta F°$(6′ isomer, I-H) $\cong$ 1.2 kcal/mol) should act to equalize the ground-state energies of these two compounds and that we would therefore expect the rotational barriers to be more nearly alike here than in the 2′,6′-dimethyl compounds in which ground-state differences account for a 6 kcal/mol difference in the barrier. A similar trend is noted for the mono-*o*-ethyl derivatives where the 2′ isomer is seen to be favored in the alcohol VI-OH (δ_{CH_3} 0.37, δ_{CH_2} 1.83) relative to the hydrocarbon VI-H (δ_{CH_3} 1.10, δ_{CH_2} 2.72) when comparison is made to normal chemical shifts as found in the ethyl group of ethylbenzene (δ_{CH_3} 1.25, δ_{CH_2} 2.68).

Conformational Effects. The major difference between corresponding derivatives of the previously investigated fluorenyl compounds[1-4] and the present xanthyl series is readily apparent from Table II; the coalescence temperatures of II-OH and Fl-II-OH differ by more than 200° and account for $\sim$10 kcal/mol difference in $\Delta F^{\neq}$ and a difference at least as large is likely between III-H and Fl-III-H. We can account for these dramatic differences by consideration of conformational alternatives available to the xanthyl but not to the fluorenyl system. Construction of Drieding models shows that, in common with other six-membered cyclic 1,4-dienes with at least one sp^3 center, the central ring of the xanthyl compounds must exist in a boat conformation in its most stable ground state. For unsubstituted xanthene, interconversion between two identical conformations by a boat-to-boat ring-flipping process is illustrated for the central ring in Figure 4. Inversion between the two boat forms is expected to be a very facile process by analogy with the 9,10-dihydroanthracenes, in which attempts to detect this

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(8) However, we cannot at this time eliminate the unlikely possibility that the exchange in the fluorenes and xanthenes proceeds *via* independent mechanisms. We agree with Dr. Chandross (personal communication) that the finding of a similar or lower barrier for a 9-alkyl-9-mesitylfluorene than for Fl-III-Cl would effectively eliminate any mechanism involving ionization. Unfortunately, such compounds appear to be synthetically inaccessible.

(9) Another manifestation of this steric crowding between the 9-X and *o*-aryl substituents is reflected in our inability to insert substituents as large as CH_3 at the 9 position in the 9-(2′,6′-dimethylphenyl) compounds by standard synthetic techniques.

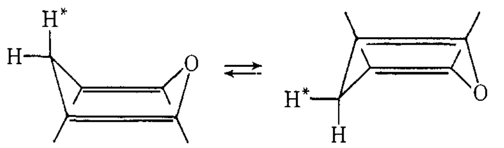
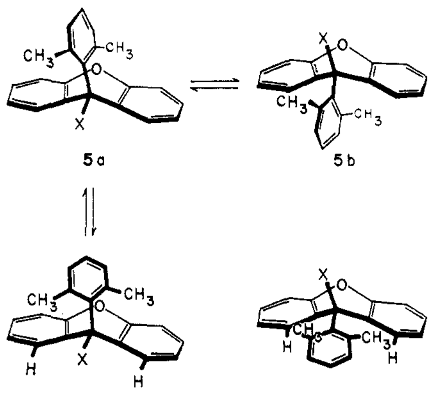


Figure 4.



5a 5b 5c 5d

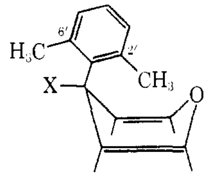
Figure 5. Ground state with phenyl substituent axial (**5a**) or equatorial (**5b**). Transition state with phenyl substituent axial (**5c**) or equatorial (**5d**).

barrier at low temperature have thus far been unsuccessful.[10,11] Substitution of medium size groups at the 9 position such as OH and aryl would have relatively little effect on the energetics of this boat-to-boat interconversion which we postulate would be fast under all temperatures encountered in our studies.

Though interconverting rapidly, the 9-arylxanthenes and xanthenols can exist in two energetically different ground-state conformations, with phenyl axial[12] as in Figure 5a and phenyl equatorial[12] as in Figure 5b. Consideration of steric interactions encountered by the 9-aryl substituents in the rotational process necessary to interconvert the *o*-methyl substituents suggests that these interactions are minimized in the axial isomer **5a** (transition state **5c**) and maximized in the equatorial isomer **5b** (transition state **5d**). In the transition state for rotation in the axial conformer (**5c**) the distance between the barrier-inducing *ortho*-methyls and the 1,8-hydrogens is large compared to the corresponding equatorial transition state (**5d**) in which extreme hindrance precludes rotation.[13] The situation in the fluorenes where the central ring is planar would be expected to be in between these two extremes. We therefore conclude that the axial boat conformation available to the xanthyl but not the fluorenyl system leads to the lower barriers exhibited by the former.

We believe, as will be amplified below, that, in fact, the axial conformer (**5a**) where rotation is more facile is the favored conformation. However, we emphasize that this fact is irrelevant to the argument so long as interconversion of the two conformers (**5a** $\rightleftharpoons$ **5b**) is a process requiring considerably less energy than the rotational process which exchanges the methyls (**5a** $\rightleftharpoons$ **5c**).

Our conclusion that the axial conformation is the favored one was arrived at by comparison of the chemical shifts of the 2′- and 6′-methyls in the two series of compounds. The very similar environments of the 6′-methyl protons in both the xanthyl and fluorenyl compounds is reflected in their similar chemical shifts (Table I). They appear at δ 2.95 ± 0.05 in the alcohols and replacement of the electronegative hydroxyl group by hydrogen shifts both series upfield to δ 2.60 ± 0.10. This is in contrast to the shifts observed for the 2′-methyl protons which, rather than being in the vicinity of the 9-substituent, are over the aromatic portion. Though similar effects upon the 2′-methyl due to the shielding by the aromatic rings would have been expected in both the xanthyls and fluorenyls, instead we find significant downfield shifts in the xanthyl compounds. This amounts to 0.5 ppm for the xanthyl hydrocarbons (II-H and III-H) and is best explained on the basis of a preferred axial conformation where the 2′-methyl is in close proximity to the ether oxygen as shown in **6**. For the 2′-methyls of the corresponding xanthenols the downfield shift relative to the corresponding fluorenols is smaller (0.3 ppm) than that observed with the hydrocarbons. We relate this to the previously noted ground-state destabilization introduced by the larger OH. Models suggest that the 6′-methyl–9-hydroxy interaction can be relieved by a slight twisting of the 9-phenyl group in its axial conformation. This leads to a more skewed ground state and places the 2′-methyl further from the oxygen and more nearly over the aryl shielding zone and accounts for the observed reduction in chemical shift difference.



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Corroborative evidence for a favored axial phenyl conformation is found in the downfield shift of the equatorial 9-H of III-H as compared to Fl-III-H; the lower field resonance of the xanthyl 9-proton follows from its close proximity to the deshielding zone of the xanthyl aromatic rings. Finally, in the carbinols the presence of equatorial phenyl, *i.e.*, axial hydroxyl, would be expected to produce an infrared-detectable concentration of intramolecularly hydrogen-bonded hydroxyl (see **7**). The infrared spectra of I-OH and III-OH showed only the presence of nonbonded hydroxyl as a sharp band at 3600 cm^{-1} in dilute CCl_4 solution, suggesting that the population of equatorial phenyl is too small to observe, or less likely, that equa-

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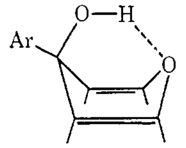
(10) W. B. Smith and B. A. Shoulders [*J. Phys. Chem.*, **69**, 2022 (1965)] examined the nmr spectrum of 9,10-dihydroanthracene down to −60°. We have extended this down to −100° with similar results.

(11) (a) D. Nicholls and M. Szwarc, *J. Amer. Chem. Soc.*, **88**, 5757 (1966); (b) D. Nicholls and M. Szwarc, *Proc. Roy. Soc., Ser. A*, 301, 231 (1967).

(12) Atoms or groups in the 9 position of xanthenes and in the 9 and 10 positions of 9,10-dihydroanthracenes are described frequently as pseudo- or quasi-axial or equatorial, but for simplicity we refer to such substituents as axial or equatorial.

(13) The alternative possibility of rate-determining conformational ring flip with fast phenyl rotation could in principle fit the nmr results. However, this can be ruled out by (a) the barrier is observed in the fluorenyl compounds where conformational effects are impossible, (b) the unlikely possibility that this conformational process could have a barrier as high as those observed, and (c) the requirement of fortuitously equal population of axial and equatorial conformers.



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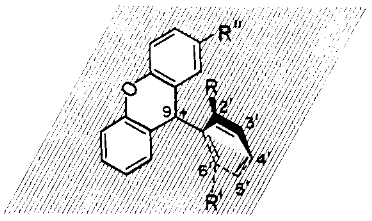
torial phenyl is present but with a hydrogen bond too weak for detection.

The deduction that the preferred conformation in this mobile xanthyl ring system is that with phenyl axial led us to draw a parallel with the analogously substituted 9,10-dihydroanthracenyl system. We would expect, from a consideration of models, that they have similar geometry and conformational inversion barriers, resulting from similar steric interactions in both ground and transition states. A considerable body of literature has accumulated in recent years concerning inversional barriers of 9-substituted 9,10-dihydroanthracenes. There is general agreement that with 9-substituents smaller than *t*-butyl the inversional barrier is very low,[10,14,15] though it appears to us that in at least two cases[11,16] the experimental reasoning used to substantiate this is specious. For 9,10-disubstituted 9,10-dihydroanthracenes only one report suggests the possibility of a barrier high enough to permit the isolation of conformers.[17] This seemed highly unlikely to us and has been repudiated by the very recent work of MacMillan and Walker.[18] In only one drastically modified anthracenyl system has the presence of a conformational barrier been unequivocally observed: the introduction of moderately bulky substituents on the methylene and/or 1,8-ring positions of 9,10-dihydro-9,9-dimethyl-10-methyleneanthracenes leads to nmr detectable inversion barriers.[19,20]

Conformational preference for 9-mono- and 9,10-disubstituted 9,10-dihydroanthracenes has also been the object of numerous recent studies. A definitive analysis of the steric interactions which lead to conformational preferences in such systems has been presented by Beckett and Mulley.[14] They explicitly point out that equatorial groups are subject to greater nonbonded interactions than the corresponding axial groups, and that this leads to a preferred axial conformation. This experimentally supported conclusion has been ignored by some recent investigators,[11,15,16] who have erroneously assumed that cyclohexane conformational preferences are applicable in this system and consequently have incorrectly relegated the bulky group to the equatorial position. Two very recent communications[18,21] reaffirm the original conclusions of Beckett and Mulley[14] and, in particular, MacMillan[18] indicates an intention of a general reappraisal of this entire subject. Our conclusion that the axial phenyl conformation is preferred in the 9-arylxanthyls is in accord with the similar steric interactions in both systems, and agrees with the conclusions of Beckett and Mulley.[14]

Chirality in the Xanthyl Carbonium Ion. The original motivation for this investigation arose from attempts to synthesize or detect by nmr techniques a stable dissymmetric carbonium ion in which chirality is inherent at the carbonium ion site. We chose derivatives of the 9-arylxanthyl carbonium ions because of their synthetic accessibility, their thermodynamic stability, and the presence of steric factors which are necessary for the introduction and maintenance of the dissymmetry. The synthesis[22] and stability[23] of xanthyl cations are described elsewhere, and the latter is discussed here only so far as it supplies information on the ground-state conformation of the 9-arylxanthyl cations.

Consideration of models clearly shows that in common with the previously discussed 9-sp^3 xanthyl series, the 9-sp^2 carbonium ion also must have phenyl perpendicular to the xanthyl moiety in its ground-state configuration (as in **8**). Experimental confirmation for this conclusion is clearly evident from the fact that carbonium ion stabilization energies (ΔF_{R}-) for 3′- and 4′-substituted 9-arylxanthyl cations correlate with σ^0 rather than with σ^+.[22] Assuming an average planar conformation for the xanthyl portion we note that steric interactions in the transition state between the 2′ and 6′ and 1 and 8 substituents are considerably larger for rotation about the 9-aryl bond in the cation than in the previously discussed tetrahedral compounds. Further, conformational factors cannot relieve the transition state interactions to nearly the same extent in the cation. In fact, considering the likely possibility that the ether oxygen in the cation is more nearly sp^2-hybridized due to electron demand at the carbonium ion site, the cation no longer will exist in a boat conformation, thus eliminating the possibility of conformational relief of transition-state nonbonded interactions. We conclude, then, that if steric interactions in the ground state of the trigonal and tetrahedral xanthyl compounds are at all similar, the former will have a significantly larger rotational barrier.



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On the above basis we felt justified in constructing dissymmetric 9-arylxanthyl carbonium ions with the expectation that the chirality inherent in this system would be maintained in a readily accessible temperature range. In contrast to the 9-sp^3 covalent xanthyl compounds where nmr studies allowed the detection of diastereomeric *o*-methyls, the symmetry elements of the carbonium ion are such that substituents in the 2′ and 6′ positions are now equivalent (see **8**, R = R′). To create chirality in the cation it is necessary to destroy both mirror planes of **8** by asymmetrically substituting

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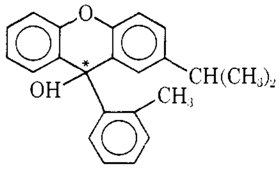
both the xanthyl and 9-aryl rings (**8**, R, R″ = alkyl, R′ = H). In the absence of aryl rotation, the resulting rotamers are now enantiomers rather than diastereomers, and for nmr detection require a diastereotopic probe.[24] The carbinol precursors to such potential chiral carbonium ions were prepared with a 2-isopropyl group and a 2′-methyl as in **9** and a 1,2-benzo and 2′-ethyl as in **10**. These covalent xanthenols **9** and **10** are also chiral, but by virtue of the asymmetric center at C-9, and accordingly exhibit the diastereotopic character of the isopropyl methyls in **9** and the methylene protons in **10** by a 1.5- and 2.5-Hz splitting in their respective 100-MHz spectra.[25] However, the carbonium ions prepared from these carbinols did not exhibit nonequivalent methyls of the 2-isopropyl group or methylene protons of the ethyl group even at −90°. We attribute this to a reduction in anisochronous character of these groups rather than to a low rotational barrier about the 9-aryl bond. It is possible that the use of a more sensitive probe group would detect such enantiomeric carbonium ions, and the feasibility of such an approach has been considerably strengthened by the detection of an analogous barrier in suitably substituted trityl cations.[26]



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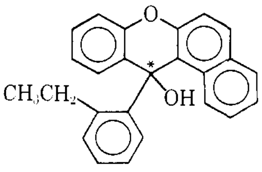

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Experimental Section

1. **Syntheses.** Commercially available chemicals used in the preparation of the 9-arylxanthyl alcohols were obtained as follows: *o*-, *m*-, and *p*-bromotoluene (Columbia Organic Chemicals); 2-bromo-*m*-xylene (Aldrich); and 2-bromomesitylene and xanthen-9-one (Eastman). All compounds synthesized gave nmr and infrared spectra consistent with the proposed structures. Melting points are uncorrected. Elementary analyses were performed by Galbraith Laboratories.

a. **Xanthenols.** These were prepared by reaction of xanthen-9-ones with aryl Grignards in tetrahydrofuran (THF). Owing to the low solubility of xanthenone in THF, this solid was usually added directly to the Grignard and the resulting suspension stirred overnight followed by the usual work-up procedure. Crude reaction products were isolated and recrystallized. Yields were generally 50–75%. The melting points of xanthenols with the following substituents agreed with those reported in the literature: 9-*o*-tolyl,[27] 9-*p*-tolyl,[28] and 9-*m*-tolyl.[29] 9-(2,6-Dimethylphenyl)xanthenol is reported elsewhere.[22] Other xanthenol derivatives have the following physical properties: 9-mesityl, mp 192.5–193.5° dec (*Anal.* Calcd for $C_{22}H_{20}O_2$: C, 83.51; H, 6.37. Found: C, 83.36; H, 6.39), 2-isopropyl-9-*o*-tolyl, mp 97.5–99°, and 1,2-benzo-9-(2-ethylphenyl), mp 170–173°.

b. **Xanthenes.** The alcohols were reduced to the hydrocarbons using acetic acid and zinc as described by Reilly and Drumm.[30] The hydrocarbons were recrystallized from a methylene chloride-methanol mixture. Elemental analyses were as follows: 9-(2-methylphenyl)xanthene (*Anal.* Calcd for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 87.82; H, 5.99) and 9-(2,6-dimethylphenyl)-xanthene (*Anal.* Calcd for $C_{21}H_{18}O$: C, 88.08; H, 6.34. Found: C, 87.78; H, 6.30). Elemental analyses and spectral evidence were relied upon for characterization, since melting points were not reproducible in some cases.

c. **Xanthen-9-ones.** 1,2-Benzoxanthone was prepared by the procedure of Dilthey and coworkers[31] and had mp 142° (lit. 142°[31]). 2-Isopropylxanthone was prepared by treatment of 7 g of *o*-(*p*-isopropylphenoxy)benzoic acid with 80 ml of acetic anhydride and 1.5 ml of concentrated sulfuric acid at 100° for 1.5 hr. After cooling and extraction with ether an oil was obtained. Recrystallization from methanol–water and again from methylene chloride–petroleum ether yielded 5 g of white solid, mp 84.5–85.5°. The starting material, *o*-(*p*-isopropylphenoxy)benzoic acid, was prepared from *o*-chlorobenzoic acid and *p*-isopropylphenol (Dow Chemical Co.) by a procedure similar to that described by DeTar and Hlynsky.[32] Recrystallization from benzene–petroleum ether gave a solid in 50% overall yield with mp 114.5–115.5° (*Anal.* Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.71; H, 6.22).

2. **Nmr Measurements.** The chemical shift data listed in Table I for the 9-arylxanthyl compounds and the rate data for the Arrhenius plots of Figure 1 were obtained on ∼2–10% solutions in chloroform-*d* or methylene chloride-d_2 using a Varian A56/60 or HA100 spectrometer.

Rates of methyl exchange between magnetically nonequivalent sites were obtained from a comparison of experimental spectra to theoretically calculated spectra. The spectral calculations were carried out using either EXCH10[33] on a IBM 7094 computer or a modified version of this program on an IBM 1130 and plotted using a Calcomp plotter. Temperature calibrations above −60° were obtained using methanol peak separations. Below −60° temperatures were measured using a special toluene thermometer mounted in a conventional spinning nmr tube,[34] in which calibrations agreed well with those obtained above −50° by Van Geet.[35]

The exchange rates for II-OH were obtained at 60 MHz in methylene chloride solution primarily in the temperature range above coalescence due to its limited solubility at lower temperatures; however, chemical shifts in the slow-exchange limit were obtained at −65° on a more dilute solution with the HA100 spectrometer. The hydroxyl proton resonance normally found in the methyl region of the spectrum was removed by deuteration. Rate data for III-H were obtained in deuteriochloroform solution at 60 MHz over the temperature range between coalescence and the slow-exchange limit. For compound I-H, where the 2′- and 6′-methyl sites are unequally populated, the isomer equilibrium was obtained by integration (planimeter) of the two distinct methyl signals at several temperatures below coalescence and extrapolated to higher temperatures in the range of the kinetic studies. Over this range, $\Delta G°$ for the equilibrium, $2'$ isomer $\rightleftarrows$ $6'$ isomer, is ∼−0.3 kcal/mol. The $\Delta G_{25°}^{\ddagger}$ values, which differ by this amount, are reported as an average value in Table II.

The nuclear Overhauser experiment was performed at probe temperature on a thoroughly degassed $CDCl_3$ solution of III-H at 100 MHz using TMS as lock signal. Irradiation of the low-field (6′) and high-field (2′) methyl signals produced enhancements of the 9-H signal of 33 and 15%, respectively. The latter enhancement by

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[24] (a) K. Mislow and M. Raban [in "Topics in Stereochemistry," Vol. I, Interscience Publishers, New York, N. Y., 1967, p 19 ff] define diastereotopic. (b) We note, however, that it is possible to detect the rotational barrier in a xanthyl cation such as **8** (R = R′ = CH_2X, R″ ≠ H) in which the rotamers are neither enantiomers nor diastereomers; thus identical diastereotopic probe groups substituted in the 2′ and 6′ positions can detect the absence of rotation though the molecule is inherently achiral.

[25] (a) Though not actually observed, slow aryl rotation can, as a consequence of the diastereomeric rotamers thus produced, lead to four isopropyl methyl doublets in **9** and four methylene quartets in **10**. (b) J. C. Martin (personal communication) has pointed out that the presence of magnetic nonequivalence of the isopropyl methyls in **9** also offers evidence against an ionization–recombination mechanism in the xanthenols. Fast rotation at room temperature for **9**, as previously shown for I-OH, is expected on the basis of their similar constitution. An ionization–recombination mechanism for this fast rotation would require loss of the asymmetry at C-9 with concomitant absence of isopropyl nonequivalence in **9**.

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[34] We thank S. W. Tobey of this laboratory for making this apparatus available to us.

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the spatially more distant 2′-methyl is expected as a result of a small but significant methyl exchange rate at this temperature (23°).

Solvent effects were semiquantitatively examined by comparison of the line widths of the exchange broadened di-*o*-methyls of II-OH at several temperatures. At +10°, the half-height line widths in CD_2Cl_2 and DMSO-d_6 were 5.50 and 5.15 Hz, respectively, and at ambient temperature in CD_2Cl_2, $CDCl_3$, and DMSO, 2.90, 4.20, and 2.65 Hz at 100 MHz. These differences represent rate variations of less than a factor of about 3, and for this range of solvent polarities are considered insignificant.

The effect of the presence of carbonium ion on the exchange process of II-OH was examined by combining equimolar amounts of this carbinol (δ(av CH_3 at 30°) = 2.1) and its carbonium ion tetrafluoroborate (δ(30°) = 1.90). The line widths of the CH_3's of II-OH (9.5 and 17.5 Hz at 100 MHz in CD_2Cl_2 at +1.5 and −8°, respectively) are close to those expected for the carbinol alone. It was further noted that the addition of a fractional equivalent of CF_3COOH to II-OH near −10° generated an observable amount of the carbonium ion distinct from carbinol for which the line width was approximately that expected for II-OH alone in CD_2Cl_2.

Acknowledgment. We thank D. Dix for assistance in carrying out and interpreting the nuclear Overhauser experiment.

Nuclear Magnetic Resonance Studies on the Conformations of 2-Substituted 1,3-Oxathiolanes

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Abstract: From analysis of coupling constants for a series of 2-substituted and 2,2-disubstituted 1,3-oxathiolanes, it has been possible to conclude that there is one highly preferred conformation but that rapid pseudorotation is occurring. The latter is confirmed by a low-temperature nmr study of 2-ethyl-1,3-oxathiolanes. The envelope conformations (**1** and **2**) most consistent with the observed coupling constants for monosubstituted oxathiolanes have the R group directed away from the center of the ring with either C-5 or O-1 as the flap atom. Postulated collision complexes based on these conformations explain the observed solvent shifts.

Low barriers to pseudorotation and the consequent profusion of nearly equi-energy conformers complicate the conformational analysis of five-membered rings,[2a] thus accounting for the dearth of information on such materials. Particularly lacking are data on five-membered sulfur-containing heterocycles.

On the basis of a derived barrier height of 2.8 kcal/mol for thiophane[2b] and assuming distorted cyclopentane geometries, conformational calculations indicated the C_2 form should be favored over the C_s conformer.[3] This low barrier for thiophane pseudorotation has been supported by recent studies,[4] and similar results were found for pyrrolidine and tetrahydrofuran.

Recent X-ray diffraction studies of ethylene sulfate indicate C_2 symmetry in the solid state with the C–C bond forming an angle of 20.6 ± 0.5° with the ring OSO plane.[5] The thiophane ring of the 1 : 1 thiophane–bromine complex appears planar on single crystal X-ray analysis, but this is attributed to the superposition of images from two static or dynamically interconverting C_s ring enantiomers.[6] By contrast in the crystal structure of cholestan-4-one-3-spiro(2,5-oxathiolane) the oxathiolane ring exists in a slightly distorted envelope conformation with the methylene carbon atom adjacent to oxygen lying 0.5 Å out of the plane defined by the other four atoms and with a torsional angle of 34.3° between the two carbon atoms.[7] The conclusion that 2-substituted 1,3-oxathiolanes exist in an envelope conformation not undergoing pseudorotation and with the oxygen atom out of the plane of the other atoms was reached by Pasto and coworkers upon interpretation of nmr spectra.[8]

Our conformational studies of the highly flexible 2-substituted 1,3-oxathiolane ring system were undertaken in order to understand some reactions of these compounds,[9,10] but we were also aware of the potential to obtain information about the pseudorotation of the ring afforded by the magnetically nonequivalent protons of the insulated ethylene group in the chiral molecule. Thus our studies were designed not only to define a dominant conformation of 1,3-oxathiolanes if any existed, but also to determine whether rapid pseudorotation were occurring on the nmr time scale.

Results

2-Ethyl-1,3-oxathiolane. The nmr spectrum of 2-ethyl-1,3-oxathiolane at 60 MHz in carbon tetrachloride

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[1] (a) Polytechnic Institute of Brooklyn; (b) Bell Telephone Laboratories.

[2] (a) See, for example, E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, Chapter 2; C. Romers, C. Altona, H. R. Buys, and E. Havinga, "Topics in Stereochemistry," E. L. Eliel and N. L. Allinger, Ed., Vol. 4, Interscience, New York, N. Y., 1969, Chapter 2; (b) W. N. Hubbard, H. C. Finta, D. W. Scott, J. P. McCullough, C. Katz, M. E. Gross, J. F. Messerly, R. E. Pennington, and G. Waddington, *J. Amer. Chem. Soc.*, **74**, 6025 (1952).

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