is 14-aneN$_4$, to the case where L is trien. As pointed out,[36] this must be regarded as a lower limit because of the severe steric interactions which 14-aneN$_4$ produces for additional coordinated ligands, which is confirmed in our MM calculations.

H. Conclusions. In Table IV we have attempted to summarize the results of our MM calculations. The following general conclusions can be drawn:

(1) Trans-I (++++) forms are much more flexible than trans-III (++−−) forms; they are not readily able to accommodate octahedral coordination geometry, and they tend to cause the metal ion to lift out of the plane of the donor atoms. For 12-aneN$_4$ the trans-I is so much more stable than the trans-III configuration that the latter is unlikely to occur. For 13-aneN$_4$ the trans-I and trans-III are of about the same stability, while for 14-aneN$_4$ the trans-III is the most stable except at high (M–N > 2.29 Å) and low (M–N < 1.90 Å) bond lengths.

(2) van der Waals repulsions mean that ligands coordinated axially to the planar trans-III forms will experience considerable steric hindrance.

(3) Folding of 14-aneN$_4$ to give the cis-V structure will be favored for octahedral metal ions with M–N above 2.09 Å.

(4) The ideal bond length of Ni(II), and probably other metal ions, can vary as nitrogens are replaced by other donor atoms such as oxygen, as well as in response to gross distortion of coordination geometry, such as the tetragonal distortion present in [Ni(14-aneN$_4$)Cl$_2$]

Acknowledgment. We thank the Senate and Council Research Grants Committee of the University of the Witwatersrand and the Council for Scientific and Industrial Research for financial support. Jon Albain is thanked for carrying out the crystallographic data collection.

Registry No. [Cu(13-aneN$_3$O)Br]Br, 91711-59-0; [Ni(1-aneN$_4$)(NO$_3$)$_2$], 91711-60-3.

Supplementary Material Available: Table of temperature factors and observed and calculated structure factors (12 pages). Ordering information is given on any current masthead page.

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MO Theory of Ease of Formation of Carbocations Derived from Nonalternant Polycyclic Aromatic Hydrocarbons

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Abstract: The energy required for carbocation formation from diol epoxide derivatives of polycyclic aromatic hydrocarbons (PAHs) is of interest in understanding molecular carcinogenicity. Here we examine the effects upon such (computed) energies of changing from alternant to nonalternant PAHs. Quantum chemical calculations indicate that the presence of an external unsaturated five-membered ring on an otherwise alternant PAH makes "bay-region" carbocation formation more difficult. However, the presence of a *saturated* external five-membered ring has the opposite effect. A "peninsular" ring can undergo ionization in either of two ways, the resulting ions often having significantly different stabilities. Simple interactive-fragment frontier-orbital models are found to rationalize all of these results and to offer predictive shortcuts.

There is currently strong interest in relative stabilities of carbocations formed from polycyclic aromatic hydrocarbons (PAHs). A great deal of experimental evidence[1-6] supports the notion that, when certain PAHs undergoing metabolism in the body lead to cancer, the transition state for the reaction with DNA has carbocation character. (See Figure 1.) Quantum chemical calculations of relative ion stabilities by many groups indicate a general tendency for the most carcinogenic PAHs to be those with greatest computed ion stability,[6-24] relative to the diol epoxide precursor. This correlation between experimental carcinogenicity and computed ease of ion formation is imperfect, which is hardly surprising when we consider the involved nature of the overall biochemical process. Still, it is widely felt that knowledge of relative carbocation stability is one of the chief ingredients needed to rationalize or predict relative PAH carcinogenicities.

Our goal, in this and earlier papers,[13-18] is to understand and predict relative ease of carbocation formation. That is, if carbocation A is *computed* to be easier to form from a diol epoxide than carbocation B, what factors are responsible? Could we have predicted in advance that A is more easily formed? If it is also true that the PAH associated with carbocation A is more carcinogenic than that associated with B, then perhaps our explanation of the computed relative ease of ion formation is also an explanation for the relative experimental carcinogenicities. If the

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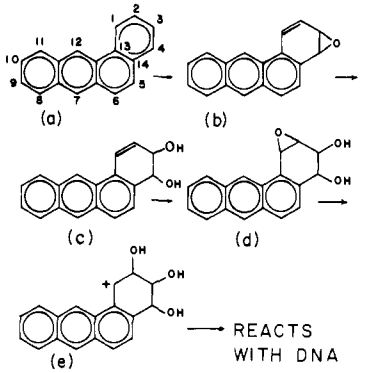

Figure 1. Possible reaction sequence wherein benz[*a*]anthracene (a) forms, in succession, an epoxide (b), a dihydrodiol, the "proximate" carcinogen (c), a dihydrodiolepoxide (d) which is thought to be an "ultimate carcinogen", an unstable triol carbocation (e), which reacts with a nucleotide on DNA.

carcinogenicity ranking is at variance with the computed ease of ion formation, we have an apparent exception to the assumption that ease of ion formation controls relative carcinogenicity. However, *this does not mean that our analysis of ion formation energy is invalid*, a point we emphasize due to frequent misunderstanding. While understanding cancer is an ultimate goal of the scientific community, our goal here is much more limited—to understand relative ease of carbocation formation from diol epoxides, which are found to correlate with PAH carcinogenicities in many cases.

Alternant PAHs have been found[2,6-13] to form the requisite carbocation more easily if the terminal ring undergoing oxidation is adjacent to a "bay region"—an inner corner of a phenanthrene segment, as between atoms 1, 13, and 12 of Figure 1a. We have shown elsewhere[13] that a "bay region" is necessary if the carbocation center is to be attached to an α carbon of the conjugated portion of the diol epoxide. Such α sites are generally more capable of stabilizing a carbocation than are β sites, as can be shown from elementary wavelength and bonding considerations in π MO theory.[13] The effects on energy of bay-region carbocation formation of PAH ring topology,[14,15] of methylation on the PAH,[16,17] and of heteroatom substitution *in* the PAH[18] have been dealt with in earlier papers. Here, we examine the effects on carbocation stability of alterations that turn the PAH into a *nonalternant* system.

Computational Methods

We are calculating relative ease of carbocation formation at various kinds of positions on saturated terminal rings in oxidized nonalternant PAHs. This problem is similar in some ways to that of calculating the relative solvolysis rates for substituted nonalternant PAHs, a problem which has been carefully studied by others.[25] A conclusion from that work is that, for reasonably reliable results over such a wide variety of sites, one must use a method which includes all valence electrons at the self-consistent field level and that neglect-of-overlap methods appear to be acceptable.[25] Therefore, we shall focus here on INDO results,[26] although simple Hückel results[27] will also be displayed for purposes of comparison and discussion. In certain cases, GAUSSIAN 70 STO-3G computations[28] have been performed also. We find, as reported in earlier papers,[16-18] that numerical trends at the INDO level are paralleled at the ab initio level.

Our model calculations for conversion of a diol epoxide to a triol carbocation utilize standard geometries for all cases, with bonds on the active terminal ring being saturated by hydrogen atoms. The calculations do not, therefore, distinguish differences in energy associated with the relative stability of conformers of the diol epoxide diasteromers, a subject of recent interest.[29,30]

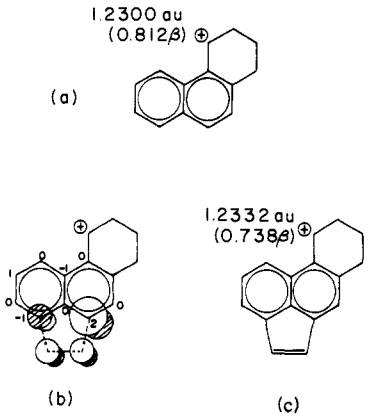

Figure 2. (a) INDO calculations indicate that 1.2300 au of energy is required to form the model bay-region carbocation of phenanthrene from the model bay-region diol epoxide. Simple Hückel calculations indicate that placing a CH_2^+ entity on the α position of naphthalene (which is the π-electron analogue for the bay-region ionization process) results in a π-energy lowering of 0.812β. (b) The integers around the ring system are relative LUMO coefficients for the naphthyl carbocation. The phase relation between π AOs in the naphthyl LUMO and in an ethene HOMO is depicted. (c) For acephenanthrylene, the INDO energy is 1.2332 au, and the π-electron delocalization energy is 0.738 β.

Acephenanthrylene and Related Molecules

Consider the problem of comparing the bay-region ionization energies of phenanthrene and acephenanthrylene (Figure 2). The conversion of the bay-region diol epoxide of phenanthrene (modeled by saturating the terminal ring with hydrogens) to the triol carbocation (analogously modeled) is computed by the INDO method to require 1.2300 au (figure 2a). Simple Hückel calculations indicate that the π-electron energy is *lowered* by 0.812β. Thus, the carbocation is computed by an all-valence-electron method to be less stable than its precursor, while the π electronic part of the energy, due to delocalization, is a stabilizing contribution. For acephenanthrylene (Figure 2c), we find that the INDO energy is greater (the ion is harder to form) and that the Hückel energy is smaller (the ion is less stabilized by π-electron delocalization). Thus, these INDO and Hückel data are in qualitative accord and support the notion[6-9] that π-electron delocalization energy is the dominant variable affecting ease of bay-region carbocation formation as we compare related molecules. A simple way to rationalize these results is to ask whether the phenanthrene-related ion should be made more or less difficult to form (in terms of π-delocalization energy) by affixing an ethene segment to form the five-membered ring. A rough approximation of this effect is provided by considering the interaction between

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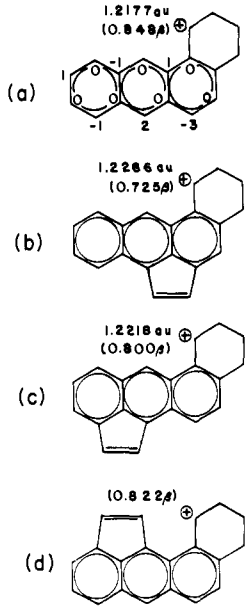


Figure 3. (a) Bay-region ion of benz[*a*]anthracene with relative LUMO coefficients (unnormalized). (b–d) INDO and Hückel bay-region ionization energies for various nonalternant systems related to benz[*a*]anthracene. (INDO calculations have not been performed for the sterically strained molecule (d).)

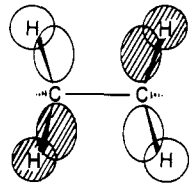
the LUMO of the cation and the HOMO of ethene (Figure 2b). Since the LUMO has phase disagreement between the points where ethene is to bond, and the ethene HOMO has phase agreement between the two ends, it is apparent that phase mismatch must occur between HOMO and LUMO. This should make it harder to form the ion, and both INDO and simple Hückel data are in agreement with this conclusion as Figure 2 shows.

A similar analysis applies to benz[*a*]anthracene-related nonalternants, as outlined in Figure 3. Here, we should expect the greatest destabilization to occur for ethene attachment at sites of largest LUMO absolute magnitude. Hückel and INDO data (the latter restricted to cases without steric complications) are in accord with expectation.

Carbocation π destabilization occurs in the above-described systems because the LUMO has a phase reversal (or else is zero) at the points of ethene attachment. Since all odd-alternant carbocation LUMOs possess these phase characteristics, we expect an external unsaturated five-membered ring generally to result in greater difficulty of bay-region carbocation formation.

Cholanthrene and Related Molecules

A class of molecules related to the acephenanthrylene types results by saturating the ethene segment with hydrogens. This gives molecules such as benz[*b*]acephenanthrene and cholanthrene (d and e of Table I), the latter compound being well-known in cancer research for its extreme carcinogenicity.[1,2] Computations at the INDO and GAUSSIAN 70 levels indicate that it is significantly easier for cholanthrene to form a bay-region carbocation than it is for benz[*a*]anthracene (Table I), i.e., that the presence of an attached *ethane*-like segment *stabilizes* the ion, relative to its precursor, in contrast to the *ethene*-like segment, which we have seen destabilizes it. The simple MO explanation for this reversal of effect is that the HOMO of ethane **1** is C–C antibonding, hence



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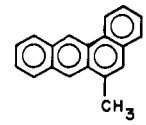
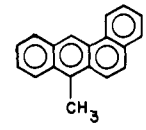
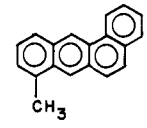
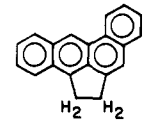
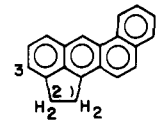
is able to phase-match the LUMO of the bay-region carbocation of benz[*a*]anthracene (Figure 2b). The ethane-like segment, however, is not a true π-system, and can only *hyperconjugate* with the carbocation. This computed hyperconjugative capability is shown in Table I for two possible attachment schemes of the ethane fragment on benz[*a*]anthracene. For comparison, we also show the effects of hyperconjugative stabilization by a methyl group at various locations. Comparison of the numbers in Table I shows that hyperconjugative stabilization by an ethane segment is greater when the segment is attached to sites where the LUMO coefficients have large absolute magnitude. It also shows that stabilization by an ethane segment exceeds the sum of stabilizations by independent methyl groups at the same two sites of attachment. This results from the fact that the HOMO of C_2H_6 is higher in energy than that of CH_4, due to the C–C antibonding interaction mentioned earlier. As a result of this higher HOMO energy and the phase agreement between ethane HOMO and ion LUMO, *phase-matched hyperconjugation* provides unusual computed ease of bay-region carbocation formation to benz[*b*]acephenanthrene and cholanthrene. (We do not include, in Table I, data for 6,7- or 7,8-dimethylbenzanthracenes or for the system produced when an ethane fragment is joined onto the 11,12 positions. In such cases, sizeable steric effects occur which we are unable to distinguish from the electronic effects being considered here, preventing a useful analysis.)

Table I. Calculated Extra Ease of Bay-Region Carbocation Formation (kcal mol^{-1}) Caused by Substitution on Benz[*a*]anthracene

	molecule	INDO	G70
(a)		4.8	2.8
(b)		1.8	1.9
(c)		0.00	0.57
(d)		9.9	7.2
(e)		4.1	3.5

If the ultimate carcinogenic form of cholanthrene and of benz[*b*]acephenanthrene is the bay-region diol epoxide of the otherwise unchanged parent molecule, then the calculated stabilization of the carbocation through phase-matched hyperconjugation offers a rationale for the observed high carcinogenicities of these molecules.[1,2,31] But the ultimate carcinogens are not yet identified. Experiments with the closely related molecule 3-methylcholanthrene indicate[2] that the 1-hydroxy or 2-hydroxy derivative of 3-methylcholanthrene forms prior to bay-region diol epoxide formation. However, replacing a hydrogen of the $-CH_2CH_2-$ group with a hydroxyl group does not result in loss

(31) Qualitative theory and INDO calculations agree that benz[*b*]acephenanthrene should form a bay-region carbocation more readily than cholanthrene. Yet it appears that cholanthrene is the more active of the two in animal tests. (See ref 2, p 25.) This suggests the presence of an additional, as yet unrecognized, factor influencing the relative activities of these substances.

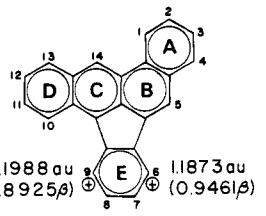


Figure 4. Dibenzo[*a*,*e*]fluoranthene, showing INDO results in au and Hückel results in terms of β. (All rings are depicted as unsaturated, but it is understood that ion formation occurs after a ring has become saturated.)

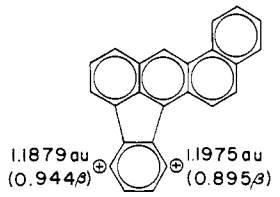


Figure 5. Dibenz[*a*,*j*]aceanthrylene.

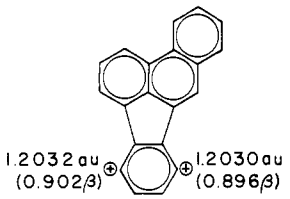


Figure 6. Benzo[*b*]fluoranthene.

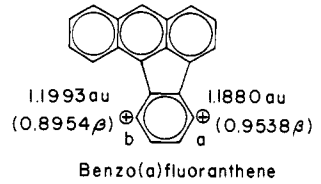


Figure 7. Benzo[*a*]fluoranthene.

of the high-energy C–C antibonding hyperconjugating MO. We find that the MO drops in energy by about $^1/_4$ eV and becomes polarized away from the oxygen and onto the carbon which is β to the hydroxyl group. As a result, hyperconjugative stabilization is greatest when the *terminal* carbon of the $-CH_2CHOH$ moiety (i.e., β to OH) bonds to the carbocation site with the larger LUMO coefficient. Our calculations indicate that the hyperconjugative stabilization of the carbocation is about the same for 2-hydroxycholanthrene as for cholanthrene itself, while 1-hydroxy substitution yields only about half as much hyperconjugative stabilization.

Carbocation Formation on Peninsular Rings

There is speculation that molecules like dibenzo[*a*,*e*]fluoranthene (Figure 4) may undergo carbocation formation on the *peninsular* ring (the E ring of Figure 4).[32] Such molecules could form ions on either side of the peninsular ring, and computations (Figures 5–8) show that their stabilities (relative to their respective precursors, throughout this discussion) can be rather different. It is quite easy to use simple MO concepts to predict whether a significant difference in stabilities is expected, and, if it is, which of the two possibilities will be more stable. To do this, we employ two facts. The first, coming from an earlier study,[13] is that a PAH is best able to conjugatively stabilize an attached positive ion if the point of attachment is an α' site on the PAH (a site which is adjacent to *two* fusion sites). The second-greatest stabilization occurs with attachment at an α site (adjacent to one fusion site)

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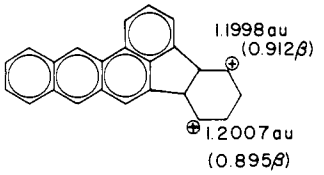

Figure 8. Peninsular ring ionization energies related to α sites on benz[*a*]anthracene.

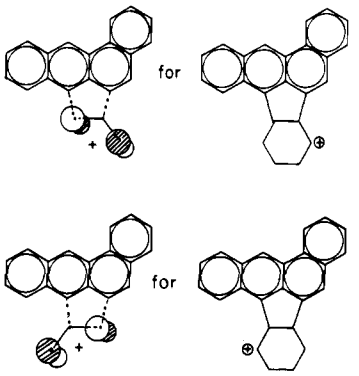

Figure 9. Relation between benz[*a*]anthracene-plus-allyl cation and possible peninsular ring ions of dibenz[*a*,*e*]fluoranthene.

and least stabilization with attachment at a β site (two bonds away from a fusion site). The second fact is that a peninsular ring carbocation can be regarded as an allyl ion attached to a PAH (as shown in Figure 9), allowing us to ask how the LUMO of the allyl ion can be most effectively stabilized by the PAH. Since the points of attachment for the allyl ion are its central carbon, where its LUMO vanishes, and one of its end carbons, where its LUMO is large, it is primarily the end-carbon interaction with the PAH that dominates. Hence, we expect that the greatest ion stability should result when the allyl moiety has its *end* carbon attached to an α' site on the PAH. If the alternative arrangements for the allyl are end-α' vs. end-α, the two computed energies should be quite different, with the former arrangement being more stable. This is the case in Figures 4, 5, and 7. If both arrangements are end-α' or both are end-α (as in the case of Figures 6 and 8), we cannot be confident in advance that a significant difference in stabilities exists or which arrangement is more stable.

Conclusions

We have shown that relative ease of carbocation formation computed by INDO and GAUSSIAN 70 STO-3G methods for certain classes of nonalternant PAH can be rationalized by using standard MO concepts and frontier orbital characteristics. These allow one to quickly estimate the effects of certain structural modifications on computed ease of carbocation formation. The relative ion stabilizing capabilities of α', α, and β positions, found earlier to explain the presence of a bay region in most carcinogenic PAHs, allows us to predict which of two peninsular carbocations will be more stable, relative to the appropriate diol epoxide precursors.

Registry No. 6-Methylbenz[*a*]anthracene, 316-14-3; 7-methylbenz[*a*]anthracene, 2541-69-7; 8-methylbenz[*a*]anthracene, 2381-31-9; 1,2-dihydrobenz[*e*]aceanthrylene, 3697-25-4; 1,2-dihydrobenz[*j*]aceanthrylene, 479-23-2; 1,2,3,4-tetrahydrophenanthrene carbocation, 91743-98-5; 7,8,9,10-tetrahydroacephenanthrylene carbocation, 91743-99-6; 1,2,3,4-tetrahydrobenz[*a*]anthracene carbocation, 91744-00-2; 4,5,6,7-tetrahydrobenz[*e*]aceanthylene carbocation, 91744-01-3; 7,8,9,10-tetrahydrobenz[*j*]aceanthrylene carbocation, 91759-10-3; 9,10,11,12-tetrahydrobenz[*l*]acenthrylene carbocation, 91743-97-4; dibenz[*a*,*e*]aceanthrylene 5-carbocation, 91743-87-2; dibenz[*a*,*j*]acenathrylene 12-carbocation, 91743-88-3; benz[*e*]acephenanthrylene 7-carbocation, 91743-89-4; benz[*a*]aceanthrylene 4-carbocation, 91743-90-7; 3b,4,5,6,7,7a-hexahydrodibenz[*e*,*k*]acephenanthrylene 7-carbocation, 91743-91-8; 3b,4,5,6,7,7a-hexahydrodibenz[*e*,*k*]acephenanthrylene 4-carbocation, 91743-92-9; benz[*a*]aceanthrylene 1-carbacation, 91743-93-0; benz[*e*]acephenanthrylene 4-carbocation, 91743-94-1; dibenz[*a*,*j*]aceanthrylene 9-carbocation, 91743-95-2; dibenz[*a*,*e*]aceanthrylene 8-carbocation, 91743-96-3.