Charge Delocalization Pathways in Persistent 1-Pyrenyl-, 4-Pyrenyl-, and 2-Pyrenylmethylcarbenium Ions as Models of PAH−Epoxide Ring Opening: NMR Studies in Superacids and AM1 Calculations[§]

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The relative stability, magnitude, and mode of charge delocalization into the pyrene moiety (Py) were evaluated for a series of tertiary and secondary 1-pyrenylmethylcarbenium ions $PyC^+R_1R_2$ and PyC^+R_3H (with $R_1 = R_2 =$ Me and Ph; $R_3 =$ Me, Ph, CH_2Ph, and $(CH_2)_{10}Me$), 4-pyrenylmethylcarbenium ions (with $R_1 = R_2 =$ Me; $R_3 =$ Me and Ph), and 2-pyrenylmethylcarbenium ions (with $R_1 = R_2 =$ Me). The carbocations were generated from the corresponding carbinols by protonation with FSO_3H/SO_2ClF. The primary 1-pyrenyl- and 2-pyrenylmethyl cations could not be generated by ionization of their primary alcohols. Within the tertiary and the secondary carbocations, π-charge delocalization into the pyrene moiety and the pyrenium ion character of the resulting carbocations increase in the order: 1-pyrenyl (α) > 4-pyrenyl ($\alpha\beta$) > 2-pyrenyl (β). The NMR characteristics of the resulting ions are discussed and compared. The connection between charge delocalization/stability in the regioisomeric pyrenylmethyl carbocations and the magnitude of carcinogenic activity in the benzannelated pyrenes, for which the bay-region diol−epoxides are the ultimate carcinogens, are discussed.

Introduction

Bay-region diol−epoxides have been identified as the ultimate metabolic carcinogens in several classes of polycyclic aromatic hydrocarbons (PAHs) en route to PAH−DNA adduct formation.[1−6]

The carbocationic character of the epoxide ring-opening process has been established in several solvolytic studies probing the rate, stereochemistry, and products.[7−14]

Early theoretical studies indicated increased stability for the bay-region dihydrotrihydroxycarbenium ions relative to their epoxides. Hückel and INDO calculations were carried out on the formation and delocalization energies of various PAH−carbocations.[15,16]

Whereas the need for more direct studies of suitable model PAH−carbocations has been realized, model PAH−CH_2X compounds bearing efficient leaving groups (like nitrosourea → $-N_2^+$) as precursors of arylmethylcarbenium ions proved to be too reactive for relative solution stability studies.[17] Interestingly the carbinols themselves may become active enzymatically via their corresponding chlorides[18,19] or sulfuric acid esters.[19−21]

Our work in mechanistic carcinogenesis has been concerned with generation and NMR studies of arenium ions of various classes of PAHs, having a varied degree of carcinogenic/mutagenic activity, with the aim of delineating their charge delocalization pathways and its modulation by substituents such as nitro and fluoro.[22−27]

In the present study we have generated from their carbinol precursors a series of regioisomeric tertiary and

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(1) Harvey, R. G. *Polycyclic Aromatic Hydrocarbons: Chemistry and Carcinogenicity*; Cambridge University Press: Cambridge, U.K., 1991.
(2) Levin, W.; Wood, A.; Chang, R.; Ryan, D.; Thomas, P.; Yagi, H.; Thakker, D.; Vyas, K.; Boyd, C.; Chu, S.-Y.; Conney, A.; Jerina, D. *Drug. Metabolism. Rev.* **1982**, *13*, 555.
(3) Koreeda, M.; Gopalaswamy, R. *J. Am. Chem. Soc.* **1995**, *117*, 10595.
(4) Lehr, R. E.; Singh, M.; Utermoehlen, C. *J. Org. Chem.* **1987**, *52*, 5576.
(5) Kiselyov, A. S.; Lee, H.; Harvey, R. G. *J. Org. Chem.* **1995**, *60*, 6123. Kiselyov, A. S.; Steinbrecher, T.; Harvey, R. G. *J. Org. Chem.* **1995**, *60*, 6129.
(6) Fu, P. P.; Harvey, R. G. *J. Org. Chem.* **1979**, *44*, 3778.
(7) Bruice, P. Y.; Bruice, T. C.; Dansette, P. M.; Selander, H. G.; Yagi, H.; Jerina, D. M. *J. Am. Chem. Soc.* **1976**, *98*, 2965. Bruice, P. Y.; Bruice, T. C.; Yagi, H.; Jerina, D. M. *J. Am. Chem. Soc.* **1976**, *98*, 2973. Nashed, N. T.; Sayer, J. M.; Jerina, D. M. *J. Am. Chem. Soc.* **1993**, *115*, 1723.
(8) Nashed, N. T.; Balani, S. K.; Loncharich, R. J.; Sayer, J. M.; Shipley, D. Y.; Mohan, R. S, Whalen, D. M.; Jerina, D. M. *J. Am. Chem. Soc.* **1991**, *113*, 3910.
(9) Nashed, N. T.; Bax, A.; Loncharich, R. J.; Sayer, J. M.; Jerina, D. M. *J. Am. Chem. Soc.* **1993**, *115*, 1711.
(10) Nashed, N. T.; Rao, T. V. S.; Jerina, D. M. *J. Org. Chem.* **1993**, *58*, 6344.
(11) Yagi, H.; Sayer, J. M.; Thakker, D. R.; Levin, W.; Jerina, D. M. *J. Am. Chem. Soc.* **1987**, *109*, 838.
(12) Keller, J. W.; Kundu, N. G.; Heidelberger, C. *J. Org. Chem.* **1976**, *41*, 3487.
(13) Hylarides, M. D.; Lyle, T. A.; Daub, G. H.; van der Jagt, D. L. *J. Org. Chem.* **1979**, *44*, 4652.
(14) Whalen, D. L.; Islam, N. B.; Gupta, S. C.; Sayer, J. M.; Jerina, D. M. *Polynuclear Aromatic Hydrocarbons: Measurements, Means and Metabolism*; Cooke, M., Loening, K., Merritt, J., Eds.; Battelle Press: Columbus, OH, 1991; pp 1021−1035.
(15) Lowe, J. P.; Silverman, B. D. *J. Am. Chem. Soc.* **1981**, *103*, 2852.
(16) Lowe, J. P.; Silverman, B. D. *J. Am. Chem. Soc.* **1984**, *106*, 5955.
(17) Lehmann, T.; Pool, B. L.; Kramer, T.; Weissler, M. In *Polynuclear Aromatic Hydrocarbons: Measurements, Means and Metabolism*; Cooke, M., Loening, K., Merritt, J., Eds.; Battelle Press: Columbus, OH, 1991; pp 527−535.
(18) Glatt, H.; Henschler, R; Phillips, D. H.; Blake, J. W.; Steinberg, P.; Seidel, A.; Oesch, F. *Environ. Health Perspect.* **1990**, *88*, 43.
(19) Glatt, H.; Henschler, R.; Frank, H.; Seidel, A.; Yang, C.; Abushqare, E.; Harvey, R. G. *Carcinogenesis* **1993**, *14*, 599.
(20) Watanabe, T.; Ishizuka, T.; Isobe, M. and Ozawa, N. *Science* **1982**, *215*, 403.
(21) Sierk, Y.-S.; Blomquist, J. C.; Liem, A.; Miller, J. A. *Carcinogenesis* **1990**, *11*, 1451.
(22) Review: Laali, K. K. *Chem. Rev.* **1996**, *96*, 1873.
(23) Laali, K. K.; Hansen, P. E. *Res. Chem. Intermed.* **1996**, *22*, 737.
(24) Laali, K. K.; Hansen, P. E.; Houser, J. J.; Zander, M. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1781.
(25) Laali, K. K.; Bolvig, S.; Hansen, P. E. *J. Chem. Soc., Perkin Trans. 2* **1995**, 537.
(26) Laali, K. K.; Hansen, P. E. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2249.
(27) Laali, K. K.; Hansen, P. E. *J. Org. Chem.* **1993**, *58*, 4096.

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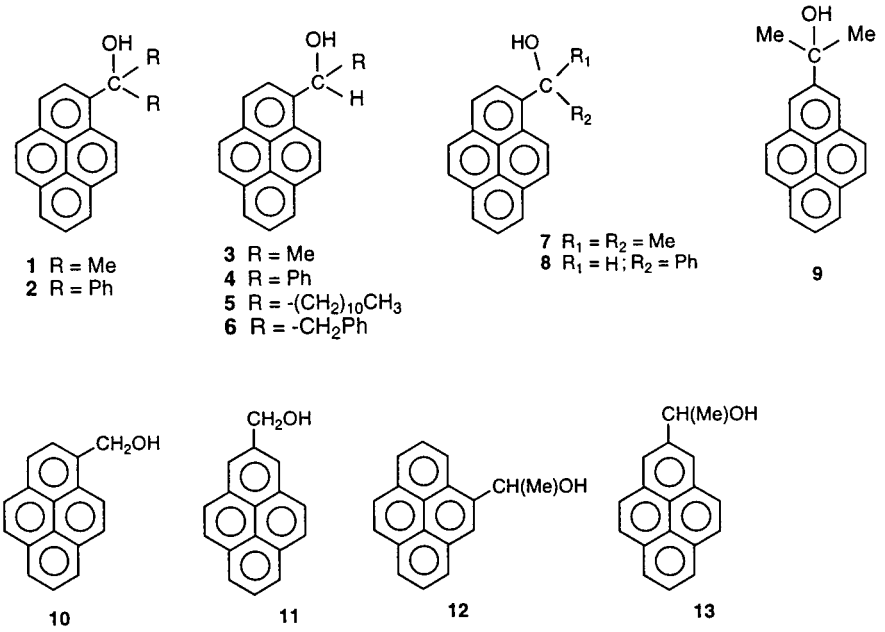

Figure 1. Carbinol precursors.

secondary methylcarbenium ions bearing 1-pyrenyl, 4-pyrenyl, and 2−pyrenyl substitutents. Charge delocalization into the pyrene moiety has been evaluated on the basis of the magnitude of the $\Delta\delta$C-13's and the chemical shift of the cation center.

We show that for both tertiary and secondary 1-pyrenylmethylcarbenium ions the positive charge is most effectively delocalized. Thus the pyrenium ion character of the resulting benzylic carbocations increases in the order 1-pyrenyl > 4-pyrenyl > 2-pyrenyl.

AM1 charges and energies for representative regioisomeric pyrenylmethylcarbenium ions and related models more closely resembling the PAH−epoxide ring opening intermediates have been calculated for comparison with experiment. The relationship between carbocation stability and carcinogenic activity is also addressed.

Results and Discussion

Carbinols **1**−**9** (Figure 1) are cleanly ionized in FSO_3H/SO_2ClF to give their corresponding pyrenylmethylcarbenium ions (Figure 2).

The ^{1}H NMR assignments are based on chemical shifts, multiplicities, coupling constants, and H−H COSY and H−C HETCOR relationships. This analysis is combined with recording of spectra at different temperatures and ion concentrations. The ^{1}H NMR chemical shifts show considerable variation as a function of temperature. For **1a**$^+$, irradiation of the two methyl resonances caused H-2 and H-10 to exhibit NOE effects in the NOED spectra. According to coupling constant trends H-2 is at lower frequency than H-10. This assigns the higher frequency Me resonance to the methyl group pointing toward H-10. The assignment of H-5, H-6, and H-8 may be interchanged as is often the case in this type of system. For **3a**$^+$, in the NOED spectrum, irradiation of the methyl resonance led to NOE effects at the C$^+$**H** and the H-2 resonance (assuming that the conformation is such that the methyl group points away from the more sterically hindered H-10 position). The ^{13}C NMR assignments were based on chemical shifts, off-resonance decoupling, and H−C HETCOR correlations. For **4** and **4a**$^+$, COLOC spectra have been recorded to assure the assignments of C-10a, C-1, C-1′, and C-2′ via couplings to C*H*(OH) or C$^+$H, respectively; C-3a is then assigned by default. The NMR data are summarized in Figures 3 and 4.

Tertiary 1-Pyrenylmethylcarbenium Ions 1a$^+$ and 2a$^+$ (Figures 3 and 4 and Table 1). Distinctly different colors are observed for these carbocations (Table 1). The C$^+$ center in **2a**$^+$ is 9.88 ppm more shielded as compared to that in the less sterically crowded **1a**$^+$. The 1-pyrenyl moiety is quite effective in charge delocalization; the pyrenium ion character of these benzylic carbocations is clearly revealed on the basis of $\Delta\delta^{13}$C values and the nonequivalence of the methyls, indicative of significant double-bond character in the Py−C$^+$ bond for **1a**$^+$.

For **2a**$^+$, charge delocalization into the phenyl groups is taking place, but π-participation by the 1-pyrenyl unit

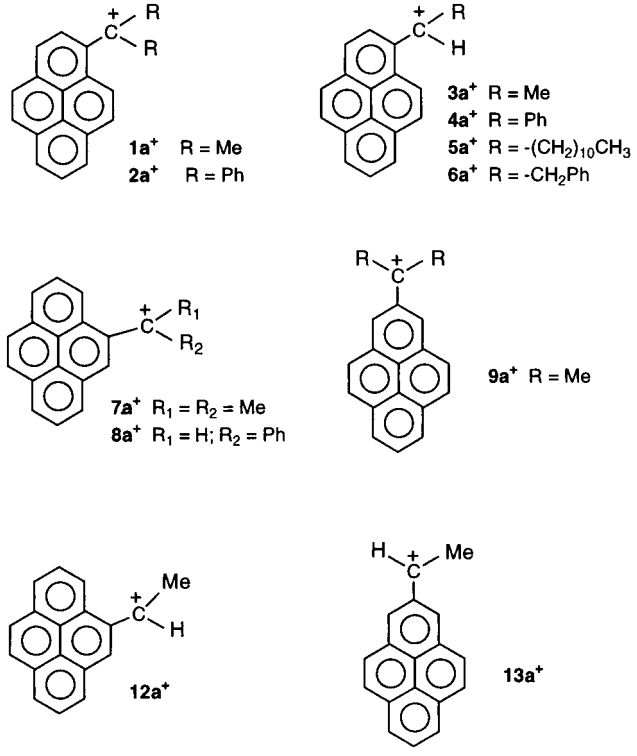

Figure 2. Regioisomeric tertiary and secondary prenylmethylcarbenium ions.

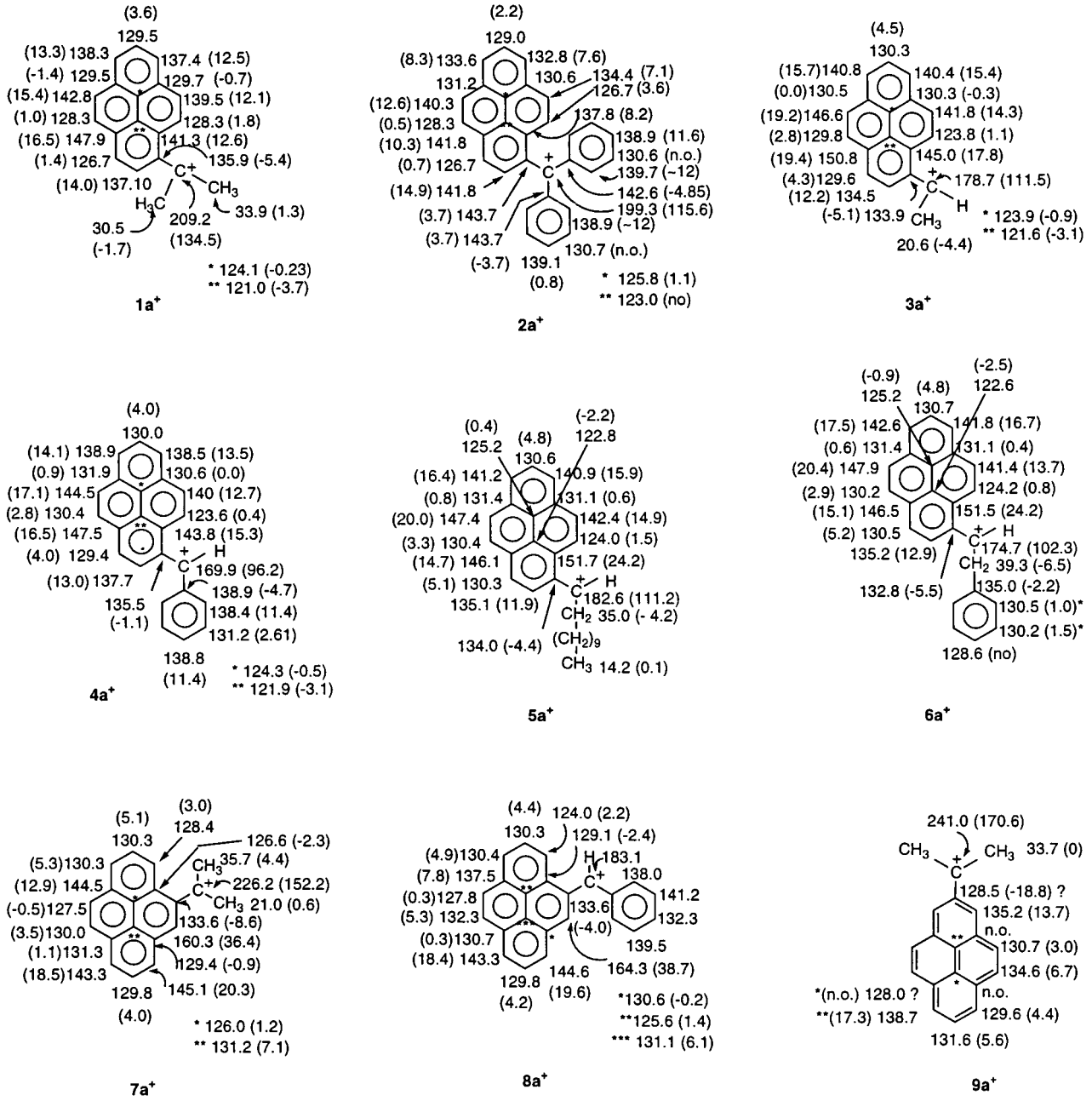

Figure 3. ^{13}C chemical shifts and $\Delta\delta^{13}C$ values (in parentheses). n.o. means not observed.

is much greater. Indeed, the C^+ center in the trityl cation is at 211 ppm,[28] ca. 11.7 ppm more downfield than that for **2a**$^+$.

Cation **2a**$^+$ whose conformational aspects we have recently studied[29] is so stable it can be generated by protonation with TFAH at room temperature, where the Py−C^+ rotation is fast but the phenyl groups rotate slowly. Hence the 1-pyrenyl protons are sharp and those of phenyls are quite broad.

The *ortho* and *peri* hydrogens (H-2, H-10) appear at 8.27 and 8.58 in **1a**$^+$ and at 7.78 and 7.71 ppm in **2a**$^+$. These proton shielding effects in **2a**$^+$ are probably caused by transannular shielding by the slowly rotating phenyl rings.

Secondary 1-Pyrenylmethylcarbenium Ions (Figure 3 and 4 and Table 1). We have provided four examples of secondary methylcarbenium ions having a 1-pyrenyl substitutent (**3a**$^+$−**6a**$^+$). Among these only **4a**$^+$ having a phenyl substitutent exhibited a blue color; others were red. The most deshielded carbocation carbon resonance is at 182.6 ppm (**5a**$^+$) and the most shielded at 169.9 ppm for the phenyl-substituted cation (**4a**$^+$). For the secondary carbocations, increased electron demand leads to enhanced π-participation by the 1-pyrenyl group, hence increased pyrenium ion character in the ions.

The charge delocalization mode into the 1-pyrenyl moiety for cations **3a**$^+$−**6a**$^+$ is quite similar, and a distinct charge alternation pathway can be deduced on the basis of the magnitude of $\Delta\delta^{13}C$ values. The C-10a carbon which is a ring fusion site is always more positive than the proton-bearing C-2.

The C*H*$^+$ chemical shifts varies between 9.30 (for **6a**$^+$) and 9.88 ppm (for **4a**$^+$). Enhanced pyrenium ion character of the secondary 1-pyrenylmethyl cations is also reflected in their more deshielded protons as compared

(28) Günther, H. In *NMR Spectroscopy*, 2nd ed.; Wiley: New York, 1995; p 500.
(29) Hansen, P. E.; Spanget-Larsen, J.; Laali, K. K. *J. Org. Chem.*, to be submitted.

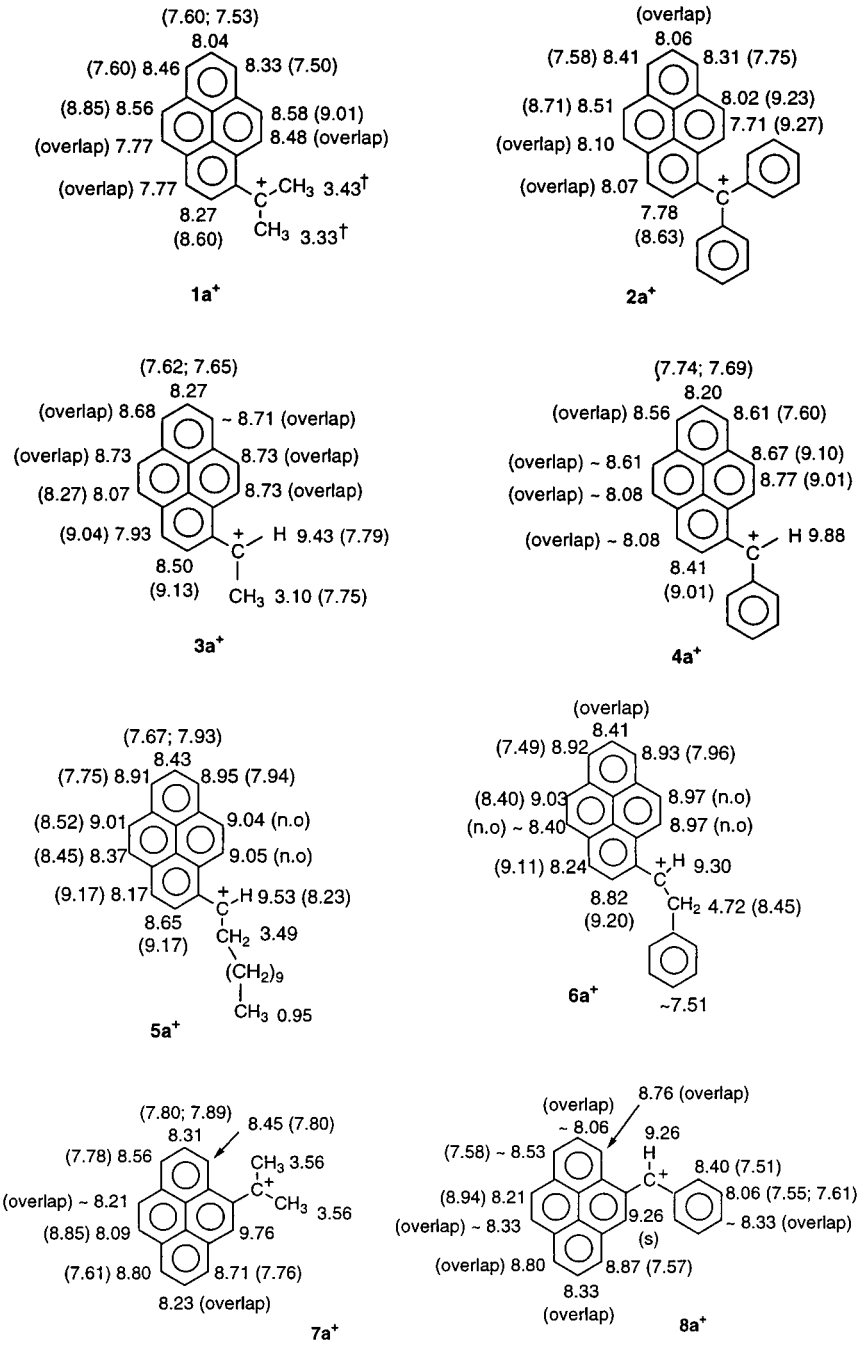

Figure 4. ^{1}H chemical shifts and H,H coupling constants (in parentheses).

Table 1. The Colors, $\delta_{^{13}C}$, $\delta_{^1H}$, and Total Deshieldings for Various Pyrene-Substituted Carbocations

carbocation	color	$\delta_{^{13}C}(C^+)$	$\delta_{^1H}(CH^+)$	total deshielding[a]
1a$^+$	burgendy-red	209.20		227.2
2a$^+$	green	199.32		~258[b]
3a$^+$	dark-red	178.68	9.43	229.2 (224.8)[c]
4a$^+$	blue	169.90	9.88	239.7
5a$^+$	deep-red	182.5	9.53	239.1[d]
6a$^+$	red	174.6	9.34	213.1[d]
7a$^+$	blue-green	226.20		258.2
8a$^+$	dark-red	183.09	9.26	265.3
9a$^+$	dark-red	243.95		~233.6

[a] For the individual contributions, see Figure 3. [b] C-2′ and C-10b contributions are not included. [c] The number in parentheses includes the contribution from the methyl group. [d] Changes on aliphatic carbons are not taken into account.

to the values for the tertiary cations. The *peri* protons are always more deshielded than those *ortho* to the carbocation substituent. The H-2/H-3 three-bond coupling constants have increased and the H-4/H-5 couplings have decreased compared to those of the carbinols. The H-6/H-7 and H-7/H-8 couplings have become nonequivalent (in accord with resonance structures derived from charge delocalization around the perimeter of the pyrene moiety). The H-2/H-3 vicinal coupling constants are usually larger than other couplings.

Primary 1-Pyrenylmethylcarbenium Ion. Attempts to generate the primary carbocation under the same conditions by ionization of **11** were unsuccessful; instead, very broad and yet deshielded NMR resonances were observed, indicative of ionization followed by alkylation to give dimers and oligomers presumably of the type $PyCH_2Py$ which are then ring protonated. Our observations are in line with previous reports that the primary benzyl cation $PhCH_2^+$ is not persistent, forming polybenzyl.[30] Hence additional stability gained by re-

placing a phenyl group for a 1-pyrenyl substituent is inadequate for the primary carbocation to become persistent.

Tertiary and Secondary 4-Pyrenylmethylcarbenium Ions (Figures 3 and 4 and Table 1). One example for each type (**7a**$^+$ and **8a**$^+$) has been provided. Ionization of the 4-carbinols **7** and **8** in the usual manner gave the corresponding carbocations as dark-red solutions. The 4-pyrenyl-substituted cations exhibit diminished π-participation by the 4-pyrenyl group and decreased stability. Thus the carbocation centers in **7a**$^+$ and **8a**$^+$ are 17 and 13.2 ppm more deshielded, respectively, as compared to the regioisomeric **1a**$^+$ and **4a**$^+$.

The magnitude of the $\Delta\delta^{13}$C values suggests a shorter conjugation path within the 4-pyrenyl unit with C-3a, C-5, C-6, and C-8 being most deshielded. The hydrogen-bearing C-5 rather than the ring fusion site (C-3a) sustains the most positive charge. Nevertheless, the double-bond character of the C_4-C^+ bond is evident by nonequivalence of the methyl groups in both ^{1}H and ^{13}C NMR spectra.

Tertiary 2-Pyrenyldimethylcarbenium Ion (Figures 3 and 4 and Table 1). Carbocation **9a**$^+$ was generated as a dark-red solution from its carbinol precursor. The carbocation center at 243.95 ppm represents the most deshielded, least delocalized, carbocation generated in this study.[31] The magnitude of $\Delta\delta^{13}$C values defines a conjugation path more or less confined to the *ortho* and *para* carbons. The symmetry element in the molecule does not allow the extent of C_2-C^+ double-bond character to be evaluated from the methyl nonequivalence perspective (see later discussion on AM1 work). Cation **9a**$^+$ showed tendency for ring protonation at higher temperatures.

Primary 2-pyrenylmethylcarbenium Ion. Not surprisingly, attempted generation of 2-PyCH_2^+ from **11** was unsuccessful; a mixture of the oxonium ion and ring-protonated **11** were observed instead.

AM1 Engergies and Carbon Charges in Pyrene-Substituted Methylcarbenium Ions. As a guiding tool and for comparison with our solution NMR studies, AM1 energies and charges were calculated for tertiary carbocations **1a**$^+$, **7a**$^+$, and **9a**$^+$, as well as for the secondary carbocations **3a**$^+$, **12a**$^+$, and **13a**$^+$.

In accord with NMR-based stability trends, AM1 predicts the relative stability order **3a**$^+$ ($\Delta H_f°$ = 237.60 kcal/mol) > **12a**$^+$ ($\Delta H_f°$ = 243.64 kcal/mol) > **13a**$^+$ ($\Delta H_f°$ = 245.54 kcal/mol) for the regioisomeric secondary pyrenyl(methyl)methylcarbenium ions.

Peri interactions in **7a**$^+$ raise its energy; hence for the regioisomeric tertiary pyrenyldimethylcarbenium ions, the relative stability order: **1a**$^+$ ($\Delta H_f°$ = 232.14 kcal/mol) > **9a**$^+$ ($\Delta H_f°$ = 234.74 kcal/mol) > **7a**$^+$ ($\Delta H_f°$ = 237.08 kcal/mol) was established.

A plot of $\Delta\delta^{13}$C- versus AM1-calculated changes in carbon charges (Δq_C(ion) − Δq_C(neutral)) (Supporting Information) shows a reasonable correspondence, with increasing deviation for carbons with larger $\Delta\delta^{13}$C values.[32a]

The 1-pyrenylmethylcarbenium ions show the most extensive charge alternation path and the largest degree of pyrenium ion character, followed by 4-pyrenyl- and 2-pyrenyl-substituted carbocations. AM1-calculated $C-C^+$ bond lengths for the tertiary [**1a**$^+$ (1.385 Å); **7a**$^+$ (1.393 Å); **9a**$^+$ (1.399 Å)] and secondary carbocations [**3a**$^+$ (1.370 Å); **12a**$^+$ (1.375 Å); **13a**$^+$ (1.381 Å)] concur with diminishing double-bond character in each sequence.

Carbocation Stability and Carcinogenic Activity. Benzo[*a*]pyrene and Benzo[*e*]pyrene. As highlighted in the Introduction, bay-region diol−epoxides are recognized as the ultimate carcinogens which bind covalently to DNA bases. There is compelling evidence that the PAH−epoxide ring opening process has carbocationic character. Bay-region diol−epoxides having steric crowding in the proximity of the epoxide are usually more carcinogenic.[10] The K-region and non-K-region epoxides react differently.[7]

Taking the same line of argument proposed by Weissler,[17] cation **14a**$^+$ derived from **14** can be simplified to **15a**$^+$, **16a**$^+$, and to **17a**$^+$ (Figure 5). Similarly, **14b**$^+$ can be simplified to **16b**$^+$ as a model. Cations **18c**$^+$ → **20c**$^+$ serve as models for epoxide ring opening of benzo[*e*]pyrene bay-region diol−epoxide **18**. These "model" carbocations are analogous to those generated in the present study.

Comparison of the AM1-calculated changes in carbon charges for cation **16a**$^+$ ($\Delta H_f°$ = 226.51 kcal/mol) and **1a**$^+$ (a specific example of the **14a**$^+$ cation type) show very similar patterns: Charge delocalization into the 1-pyrenyl moiety is quite extensive and there is significant pyrenium ion character. On the contrary, the delocalization pattern for **20c**$^+$ ($\Delta H_f°$ = 232.43 kcal/mol) is more limited and pyrenium ion character has diminished.

As our model studies did not take into account the role of the OH group β to the carbocation, we calculated (AM1) **15a**$^+$ and **19c**$^+$ with the OH group equatorial and axial. The pseudoequatorial OH is the conformation needed for hydride shift leading to phenol.[7] AM1 predicts that the β-hydroxy carbocation with an axial OH is slightly less favored over one with an equatorial OH (by 2.56 kcal/mol). For **19c**$^+$ the preference for equatorial OH is even less (1.2 kcal/mol). In both cases the pattern of AM1 carbon charges remain unchanged.

CNDO/2 calculations by Yeh et al.[32b] revealed that for the diol−epoxide of benzo[*a*]pyrene in the syn-diaxial conformation, **14a**, the 7-OH group influences the charge at C-9 and C-10 in such a manner that C-9 becomes the more positive. This influence is probably caused by hydrogen bonding. This feature is not reflected in the way the compound reacts in water. As CNDO/2 as well as AM1 calculations of this study are made in vacuo, the inclusion of OH groups at C-7 and C-8 is best avoided in the calculations.

The geometry of the diol−epoxides is likewise influenced by the OH groups at C-7 and C-8. Lehr et al.[33] concluded that a maximum overlap between the C−O bond of the epoxide and the π-orbitals of the aromatic system is preferable. A geometry with maximum overlap between the π-system of pyrene and the vacant ρ-orbital of the carbocation is obtained in our model compounds.

(30) Olah, G. A.; Prakash, G. K. S.; Sommer, J. *Superacids*; Wiley: New York, 1985; p 105.

(31) The ^{13}C chemical shift for the carbocation center in PhC^+Me_2 is at 255 ppm (see, for example: Heagy, M. D.; Olah, G. A.; Prakash, G. K. S.; Lomas, J. S. *J. Org. Chem.* **1995**, *60*, 7355).

(32) (a) The utility and limitations of AM1 (and other semiempirical methods) in dealing with charge have been examined for delocalized carbanions (Tolbert, L. M.; Ogle, M. E. *J. Am. Chem. Soc.* **1990**, *112*, 9519) and in several classes of PAH-arenium ions (see ref 24 and Laali, K. K.; Hollenstein, S.; Harvey, R. G.; Hansen, P. E. *J. Org. Chem.* **1997**, *62*, 4023). Whereas quantitative comparisons are unwise, qualitative use of such relationships is acceptable. (b) Yeh, C. Y.; Fu, P. P.; Belandl, F. A.; Harvey, R. G. *Bio. Org. Chem.* **1978**, 497.

(33) Lehr, R. E.; Kumar,S.; Levin, W.; Wood, A. W.; Chang, R.; Conney, A. H.; Yagi, H.; Sayer, J. M.; Jerina, D. M. *ACS Symp. Ser.* **1985**, *283*, 63

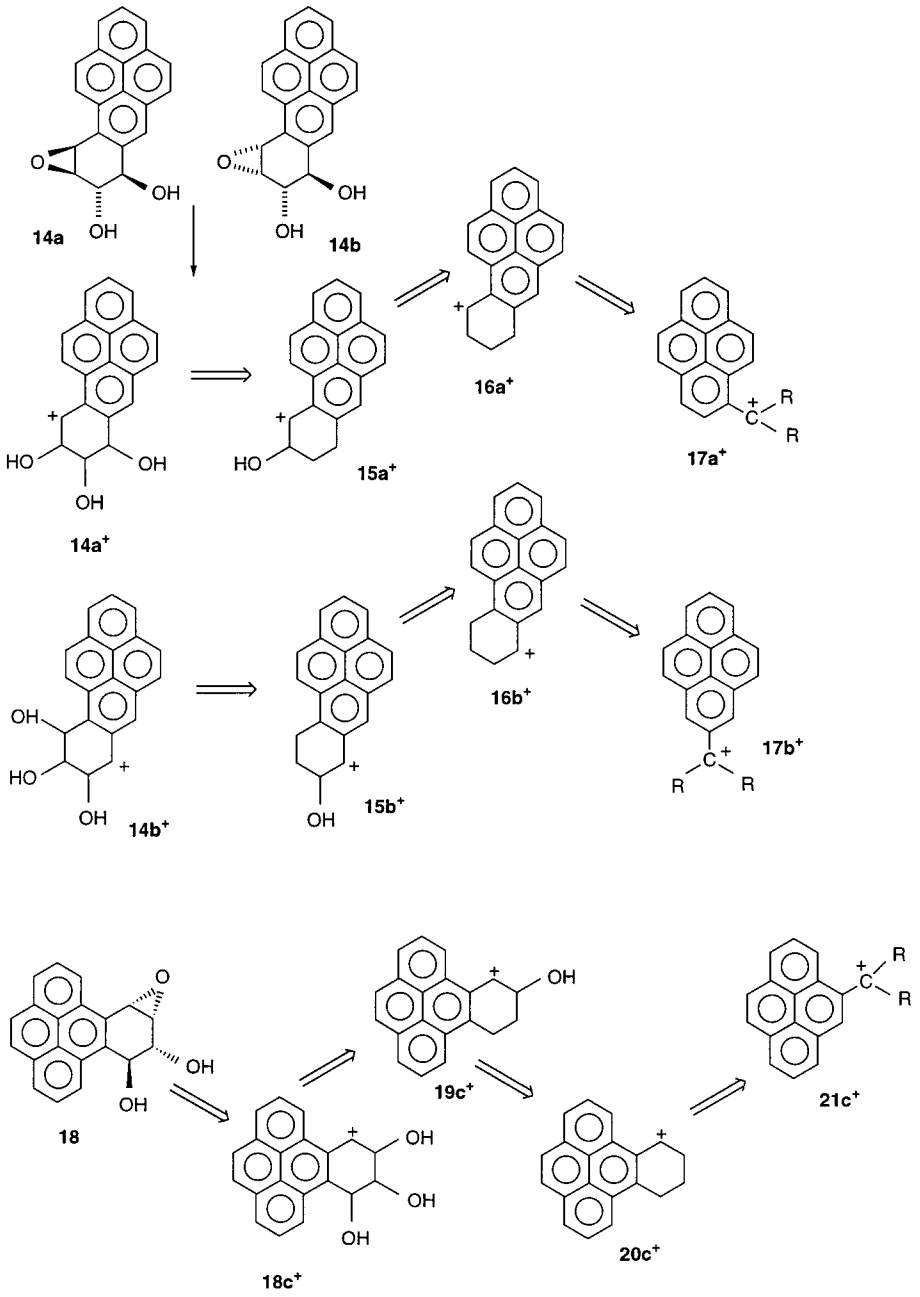

Figure 5. Analogy between "simplified" carbocations generated in this study and those formed by diol-epoxide ring opening.

Ab initio calculations of the MF-FSGO type on carbocation **14a**$^+$ were carried out sometime ago by Shipman.[34] Inspection of the ab initio π-charges for the triol carbenium ion clearly defines a charge alternation path similar to the models reported in the present study.

It is evident from the present study that the charge delocalization at positions away from the C$^+$ center is limited and chances of nucleophilic attack at the pyrene ring are small.

In summary, it appears that the carcinogenic activity in benzo[*a*]pyrene resulting from regiospecific binding to the 2-amino group of guanine via C-10, rather than, for example, C-7,[34b] may be traced to enhanced stability and the higly delocalized nature of **14a**$^+$ as compared to **14b**$^+$ (Figure 5). It can be further proposed that lack of carcinogenicity in benzo[*e*]pyrene could stem from lower relative stability of **18c**$^+$.

Our work has provided experimental evidence in support of "bay-region theory" under stable ion conditions.

Experimental Section

Synthesis of Carbinols. Tertiary carbinols **1**, **2**, **7**, and **9** were synthesized by reacting MeMgBr or PhMgBr with the corresponding acetyl- or benzoylpyrene, respectively.[35]

Secondary carbinols **3**, **6**, and **8** were prepared by $LiAlH_4$ reduction of the corresponding acetyl- and benzoylpyrenes.[19]

Secondary carbinols **5** (lauryl) and **6** (benzyl) were prepared in a similar fashion.

1-Acetyl- and 1-benzoylpyrene were prepared by standard Friedel−Crafts acylation and benzoylation of pyrene.[36] 2-Acetyl- and 4-acetylpyrene were synthesized by acetylation of hexahy-

(34) (a) Shipman, L. L. In *Polynuclear Aromatic Hydrocarbons*; Jones, P. W., Leber, P., Eds.; Ann Arbor, MI, 1979; pp 569−580. (b) Zegar, I. S.; Kim, S. J.; Johansen, T. N.; Horton, P. J.; Harris, C. M.; Harris, T. M.; Stone, M. P. *Biochemistry* **1996**, *35*, 6212.

(35) Lund, H.; Berg, A. *Kgl. Dan. Vidensk. Selsk.* **1941**, *18*, 1.

(36) Vollmann, H.; Becker, H.; Corell, M.; Streek, H. *Liebigs Ann. Chem.* **1937**, *531*, 1.

dropyrene and tetrahydropyrene, respectively, followed by aromatization with DDQ.[37]

The primary alcohols **10** and **11** were synthesized by $LiAlH_4$ reduction of the corresponding formylpyrenes.[19]

Characterization of the Carbinols. ^1H NMR ($CDCl_3$). **1**: δ 9.11 (d, J = 9.45 Hz, 1H) H-10; 8.15 (m, 2H) H-6, H-8; 8.07 (s, 1H) H-2; 8.06 (s, 1H) H-3; 8.06 (d, J = 9.45, 1H) H-9; 7.99 (s, 2H) H-4, H-5; 7.99 (t, J = 7.38, 1H) H-7 and 1.97 (s, 6H) CH_3.

2: NMR data reported elsewhere (ref 29).

3: δ 8.17 (d, J = 9.35 Hz, 1H) H-10; 8.10 (d, 1H) H-6; 8.10 (d, 1H) H-2 or H-3; 8.08 (d, 1H) H-8; 8.05 (d, 1H) H-3 or H-2; 7.98 (d, 1H) H-9; 7.94 (s, 2H) H-4, H-5; 7.93 (t, J = 7.42 Hz, 1H) H-7; 5.82 (q, J = 6.45 Hz, 1H); 2.62 (s (broad), 1H) OH; 1.68 (d, J = 6.61 Hz, 6H) CH_3.

4: δ 8.26 (d, J = 9.31 Hz, 1H) H-10; 8.15 (d, J = 7.28 Hz, 1H) H-6; 8.15 (d, J = 7.38 Hz, 1H) H-8; 8.14 (s, 2H) H-2, H-3; 8.02 (s, 2H) H-4, H-5; 8.00 (d, 1H) H-9; 7.96 (t, J = 7.50 Hz, 1H) H-7; 7.41 (dd, 1H) H-2′; 7.25 (m, 2H) H-3′ and H-4′; 6.81 (d (broad) J = 3.37 Hz, 1H) CH and 2.54 (d, J = 3.73 Hz, 1H) OH.

5: δ 8.28 (d, J = 9.4 Hz, 1H) H-10; ~8.16 (m, 2H) H-6, H-8; 8.15 (2H) H-2, H-3; 8.05 (d, J = 9.4 Hz, 1H) H-9; 8.02 (s) H-4, H-5; 7.99 (t, J = 7.7 Hz, 1H) H-7; 5.70 (t, 1H) H-1′; 2.22 (S, 1H) OH; 1.99 (p, CH) H-2′; ~1.24 (CH_2); 0.89 (s) CH_3.

6: δ 8.35 (d, J = 9.35 Hz, 1H) H-10; ~8.20 (m, 4H) H-2, H-3, H-6, H-8; 8.10 (d, J = 9.32 Hz, 1H) H-9; 8.05 (s, 2H) H-4, H-5; 8.00 (t, 1H) H-7; 7.28 (m, 3H) H-2′, H-3′, and H-4′; 5.98 (dt, 1H) CH; 3.34 (dd, J = 13.80 Hz, 1H) CH_2; 3.22 (dd, J = 13.80 Hz, 1) CH_2; 2.28 (d, J = 2.84 Hz, 1H) OH.

7: δ 8.94 (d, J = 7.92 Hz, 1H) H-3; 7.92 (d, 1H) H-1; ~7.92 (m, 2H) H-6, H-8; 7.91 (s, 1H) H-5; 7.84 (d,1H) H-9*, 7.81 (t, 1H) H-7; 7.83 (d, 1H) H-10*; 7.77 (t, 1H) H-2; 1.79 (s, 3H) CH_3.

8: δ 8.29 (s, 1H) H-5; 8.23 (d (broad) J = ~8 Hz, 1H) H-3; 8.19 (d, 1H) H-6; 8.18 (d, 1H) H-8; 8.12 (d (broad), 1H) H-1; 8.04 (s, 2H) H-9, H-10; 7.99 (t, J = 7.62 Hz, 1H) H-7; 7.88 (t, J = 7.33 Hz, 1H) H-2; 7.51 (dd, 2) H-2′; 7.29 (m, 2H) H-3′, H-4′; 6.67 (s, 1H) CH, 2.52 (s, 1H) OH.

9: δ 8.31 (s, 2H) H-1,H-3; 8.14 (d, J = 7.75 Hz, 2H) H-6, H-8; 8.02 (s, 4H) H-4, H-5, H-9, H-10; 7.97 (t, J = 7.7 Hz, 1H) H-7; 2.85 (s (broad), 1H) OH; 1.76 (s, 3H) CH_3.

10: δ 8.30 (d, J = 9.30 Hz, 1H) H-10; 8.16 (d, J = 7.8 Hz, 1H) H-6; 8.15 (d, J = 7.8 Hz, 1H) H-8; 8.09 (d, J = 9.29 Hz, 1H) H-9; 8.06 (d, J = 7.84 Hz, 1H) H-3; 8.01 (dd, J = 9.29 Hz, 2H) H-4,H-5; 7.98 (t, J = 7.75 Hz, 1H) H-7; 7.98 (d, J = 7.62 Hz, 1H) H-2; 5.34 (s, 2H) CH_2.

11: δ 8.17 (d, J = 9.12, 2H) H-6, H-8; 8.15 (s, 2H) H-1, H-5; 8.05 (s, 2H) H-4, H-10; 8.05 (d, 2H) H-5, H-9; ~7.99 (m, 1H) H-7; 5.12 (d, J = 5.55 Hz) CH_2; 1.94 (t, J = 5.66 Hz) OH.

12: δ 8.30 (d, J = 7.90 Hz, 1H) H-3; 8.20 (s, 1H) H-5; 8.13 (m, 3H) H-1, H-6, H-8; 8.04 (s, 2H) H-9, H-10; 7.97 (t, 1H) H-7; 7.97 (t,1H) H-2; 5.74 (q, J = 6.44 Hz) 2.15 (s (broad), 1H) OH; 1.78 (d, J = 6.30 Hz, 3H) CH_3.

^{13}C NMR $CDCl_3$ (data for **1**−**9** are incorporated into Figure 3). **11**: δ 138.56 C-2; 131.39, C-3a, C-10a; 131.09, C-5a, C-8a; 127.75, C-4, C-10; 127.30, C-5, C-9; 125.89, C-7; 125.10, C-6, C-8; 123.10, C-1, C-3.

FSO_3H (triple-distilled) and SO_2ClF (high-purity grade; in sealed ampules) were purchased from Aldrich and used without further purification.

Stable Ion Studies. To a cold slurry of the carbinol (ca. 80 mg) in SO_2ClF (ca. 0.5 mL) charged into a 10 mm NMR tube under argon was added a clear homogeneous solution of FSO_3H (1 mL) diluted in SO_2ClF (1 mL) at dry ice/acetone temperature with efficient vortex mixing. O-Protonation/ionization occurred rapidly forming colored solutions on contact. In some cases the resulting ion solutions were too viscous for NMR studies and had to be diluted further by addition of more SO_2ClF (ca. 0.5 mL). The resulting cold stock solutions were transferred by pouring directly from cold 10−5 mm NMR tubes which had been fully immersed into a dry ice/acetone bath and flushed with argon. A few drops of precooled CD_2Cl_2 added to the superacid solution (vortex mixing) served as lock and reference. The NMR spectra were recorded on a Bruker 250-AC instrument either at 250 MHz for ^1H or 62.889 MHz for ^{13}C spectra. COSY and HETCOR spectra were recorded as described earlier.[26] COLOC spectra were recorded with D2 = 2 × D3 = 82.5 ms. A total of 300 transients were used in each of the 32 increments with 2 Hz lines broadening in f2 and sine-bell apodization.

AM1 calculations were carried out using the Hyperchem package (Hypercube Inc, 1994) which is based on Dewar's model.

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Supporting Information Available: Plot of Δ_{qc} vs $\Delta\delta^{13}C$ (1 page). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from ACS; see any current masthead page for ordering information.

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(37) Moyle, M.; Ritchie, E. *Aust. J. Chem.* **1958**, *11*, 211.