Stable Ion Study of Regioisomeric Carboxonium-Substituted Pyrenium Ions: Directive Effects, Charge Delocalization Mode, and Conformational Aspects

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Received February 11, 2000

Regioisomeric monoacyl- and monobenzoyl-substituted pyrenes are diprotonated in $FSO_3H{\cdot}SbF_5$ (4:1)/SO_2ClF to give persistent carboxonium−pyrenium dications, whereas diacetyl- and dibenzoylpyrenes are diprotonated to give dicarboxonium dications. The resulting dications were studied by low-temperature NMR at 500 MHz. Conformational aspects of the carboxonium group in various regioisomers are addressed by a combination of NOED spectra and 2D-NMR and AM1 calculations. Charge delocalization pathways are gauged and compared on the basis of the magnitude of $\Delta\delta$ ^{13}C values.

Introduction

The mechanism of intercalation of the bay-region *anti*-diolepoxide of benz[*a*]pyrene BaP into DNA has been shown to involve rate-determining protonation to form an intercalated triol−arenium ion.[1] The resulting carbocation undergoes two types of reactions: a DNA-catalyzed hydrolysis as the major pathway to give an intercalated tetraol and the biologically more significant covalent binding to DNA as a minor pathway. Hydrolysis of the bay-region *cis*-diolepoxide of BaP is pH dependent and is catalyzed by DNA and by synthetic polynucleotides.[2] The epoxide must be protonated before or during the rate-determining step(s). It was suggested that a physically bound diolepoxide reacts to form a physically bound benzylic carbocation in the rate-determining step.[2] The monohydrogen phosphate group on the nucleotide acts as general acid, and stacking interactions between the PAH-diolepoxide and the base contribute to catalysis.[3]

In continuation of our studies on PAH arenium ions and α-PAH substituted carbocations,[4−7] modeling the electrophiles from carcinogens (representative examples are depicted in Scheme 1), we showed that the origin of increased biological potency in different classes of PAH-epoxides could be traced to the relative stabilities of the resulting α-PAH-substituted carbocations, which can be gauged via charge delocalization mapping in the resulting arenium ions. A carbocation-based structure−activity relationship can also provide reasonable predictions of potency based on substituent effects in the arenium ions. For example, in α-pyrenylmethylcarbenium ions the carbocation stability order (**1a**$^+$ > **1b**$^+$ > **1c**$^+$) could explain the difference in biological potency between benzo[*a*]pyrene BaP and benzo[*e*]pyrene BeP based on magnitude of π-participation and arenium ion character (compare **2a**$^+$, **2b**$^+$, **2c**$^+$). A carbocation-based model would predict that hydrolysis of BaP 7,8-epoxide must be very much S_N2-like because the 2-pyrenylmethylcarbenium ion is relatively unstable. This is compatible with the finding that 9,10-diol-7,8-epoxide (precursor to **2c**$^+$) is not a carcinogen.[8]

In our studies with benz[*a*]anthracenium cations BA,[6] we found that the substituent effect on carbocation stability correlates in a number of cases with the available biological structure/activity relationships. In these studies, carbocations such as **5**$^+$, **6**$^+$, and **7**$^+$ serve as models for metabolic electrophiles formed through hydroxymethylation of BA and oxygenation at the ethano bridge in 3-methylcholanthrene 3MC,[9] whereas carbocations **8**$^+$ and **9**$^+$ represent models for the K-region epoxide ring opening in BA. Since mesomeric oxonium ion character is prominent in carboxonium ions,[10] α-PAH-substituted carboxonium cations may serve as models for arenium ions formed via PAH-epoxides ring opening under solvolytic conditions, which might be more relevant to biological systems (see **3**$^+$ and **4**$^+$).

The objective of the present study was to use regioisomeric carboxonium ions as strongly electron-withdrawing substituents on a pyrene ring in order to test the degree of π-participation as a function of substitution position as well as their directive effects. On the basis of our previous work,[4] it was anticipated that the relative stability order 1-carboxonium (α) > 4-carboxonium (αβ) > 2-carboxonium (β) might operate, and on this basis we predicted that with the 2-carboxonium substituent further electrophilic attack on the pyrene should be most

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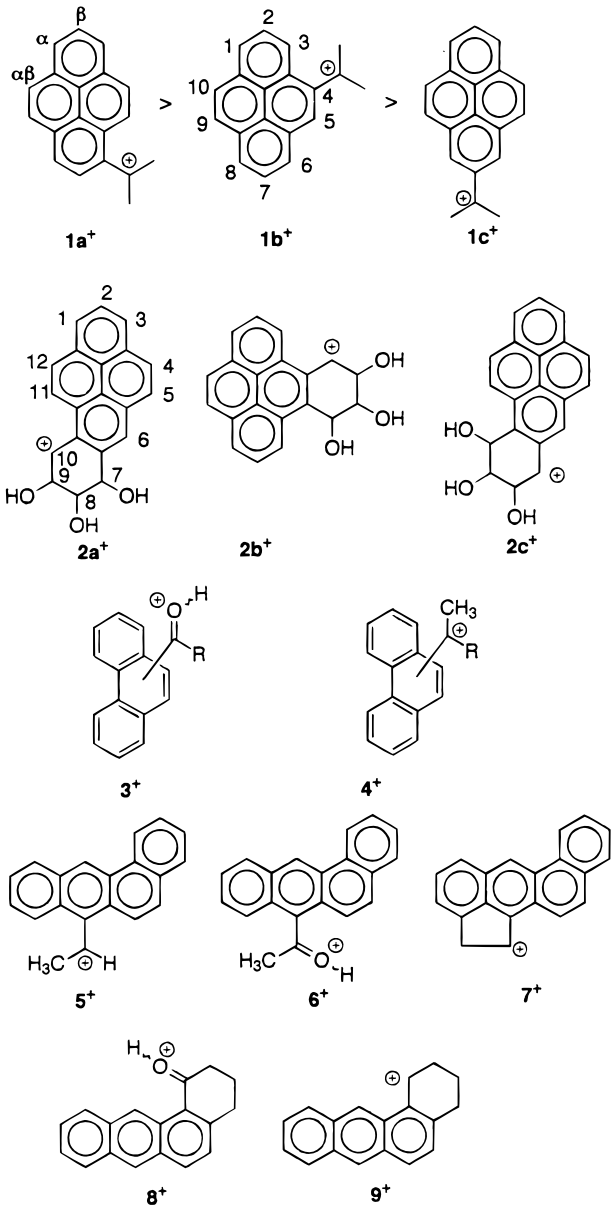
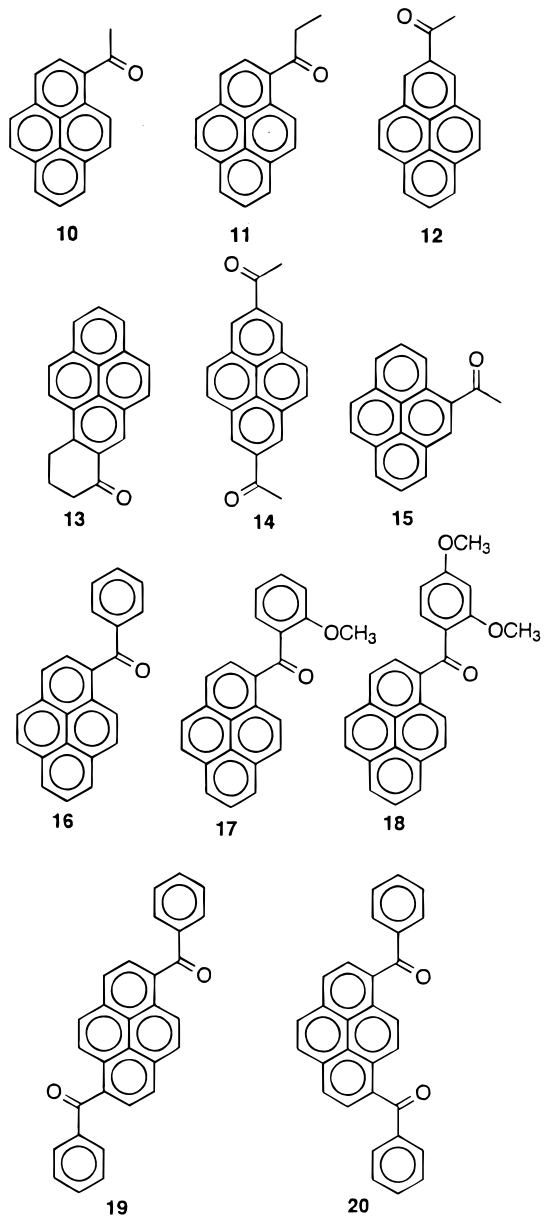
10.1021/jo0001939 CCC: $19.00
Published on Web 05/12/2000

Scheme 1



Scheme 2



favored, leading to carboxonium−pyrenium dications in superacid media. The study reported herein deals with generation and charge delocalization mapping in the resulting dications and their study by 500 MHz NMR, which also provided insight into the conformational aspects of the carboxonium group in different regioisomers based on NOED spectra.

Results and Discussion

In the initial phase of this project, several low-temperature protonations were carried out and examined by NMR at 250 MHz. At first, we explored monoprotonation in FSO_3H/SO_2ClF using regioisomeric acetyl- and benzoylpyrenes as substrates (see Scheme 2). Whereas the CO*H*$^+$ resonances were observed as separate signals, NMR spectra indicated competing ring protonation to form exchanging carboxonium−pyrenium dications even at ca. −70 °C. In addition, in many cases mixtures were formed giving rise to complex spectra for which only partial assignments could be made. In the case of 2-acetylpyrene **12**, addition of a few drops of higher acidity (H_o) superacid $FSO_3H{\cdot}SbF_5$ (4:1) shifted the equilibrium completely to the dication, thus reducing the complexity of the NMR spectra (see further discussion). Significant overall improvement was achieved by working at 500 MHz. The discussion, therefore, focuses only on these results, where protonation studies were carried out in $FSO_3H{\cdot}SbF_5$ (4:1)/SO_2ClF to give carboxonium−pyrenium dications and dicarboxonium ions. With **19** and **20**, protonations were also carried out with FSO_3H/SO_2ClF, where conformationally averaged dioxonium dications were obtained (see Scheme 3).

NMR Assignments of the Carbocations and Their Precursors. Detailed NMR assignments for the resulting dications and their neutral precursors were based on ^{1}H, ^{13}C, H/H COSY, C/H HETCOR, and NOED spectral data. Assignments for compounds **10** and **15**, which had appeared in the literature,[11] were refined. In several cases, COLOC spectra assisted the specific assignment

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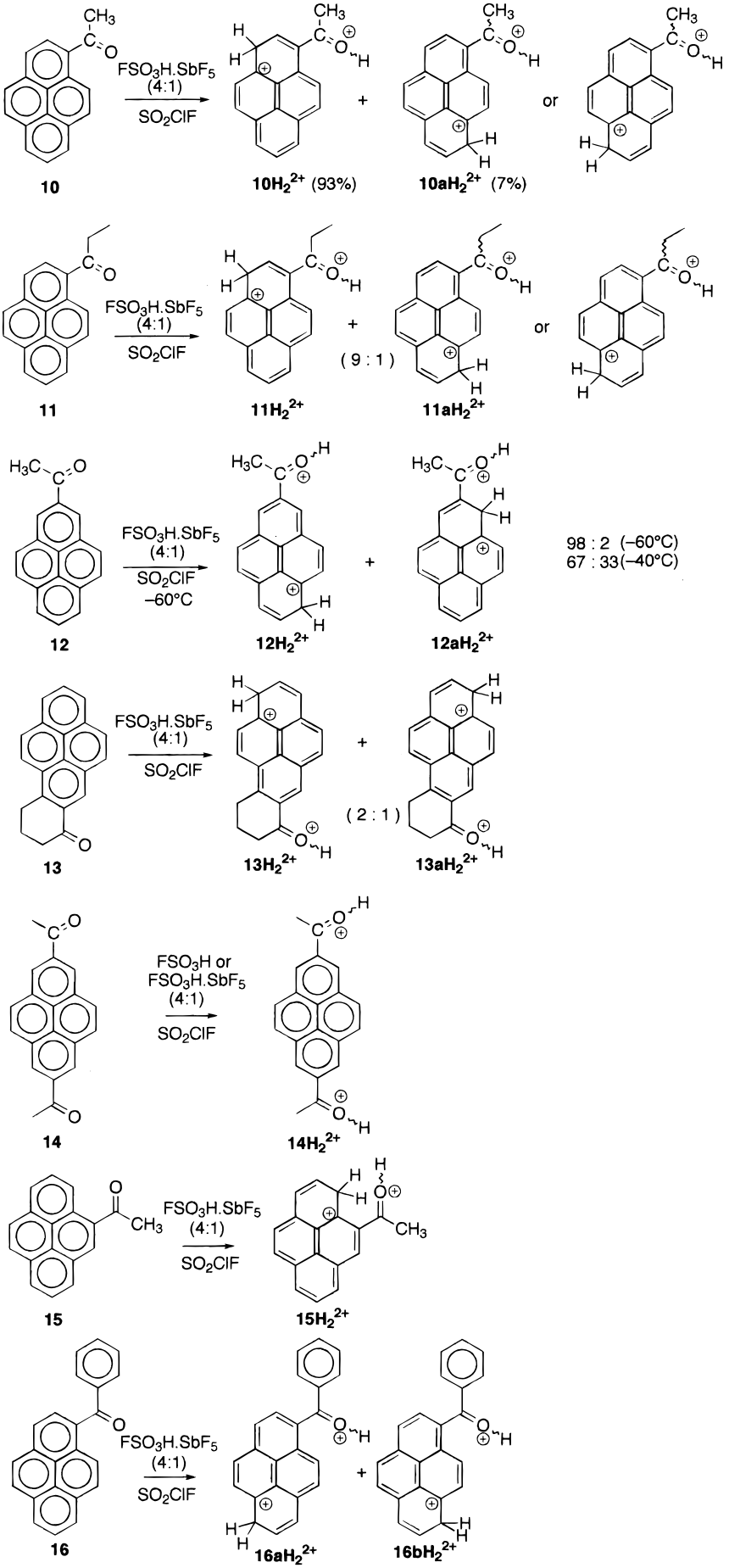
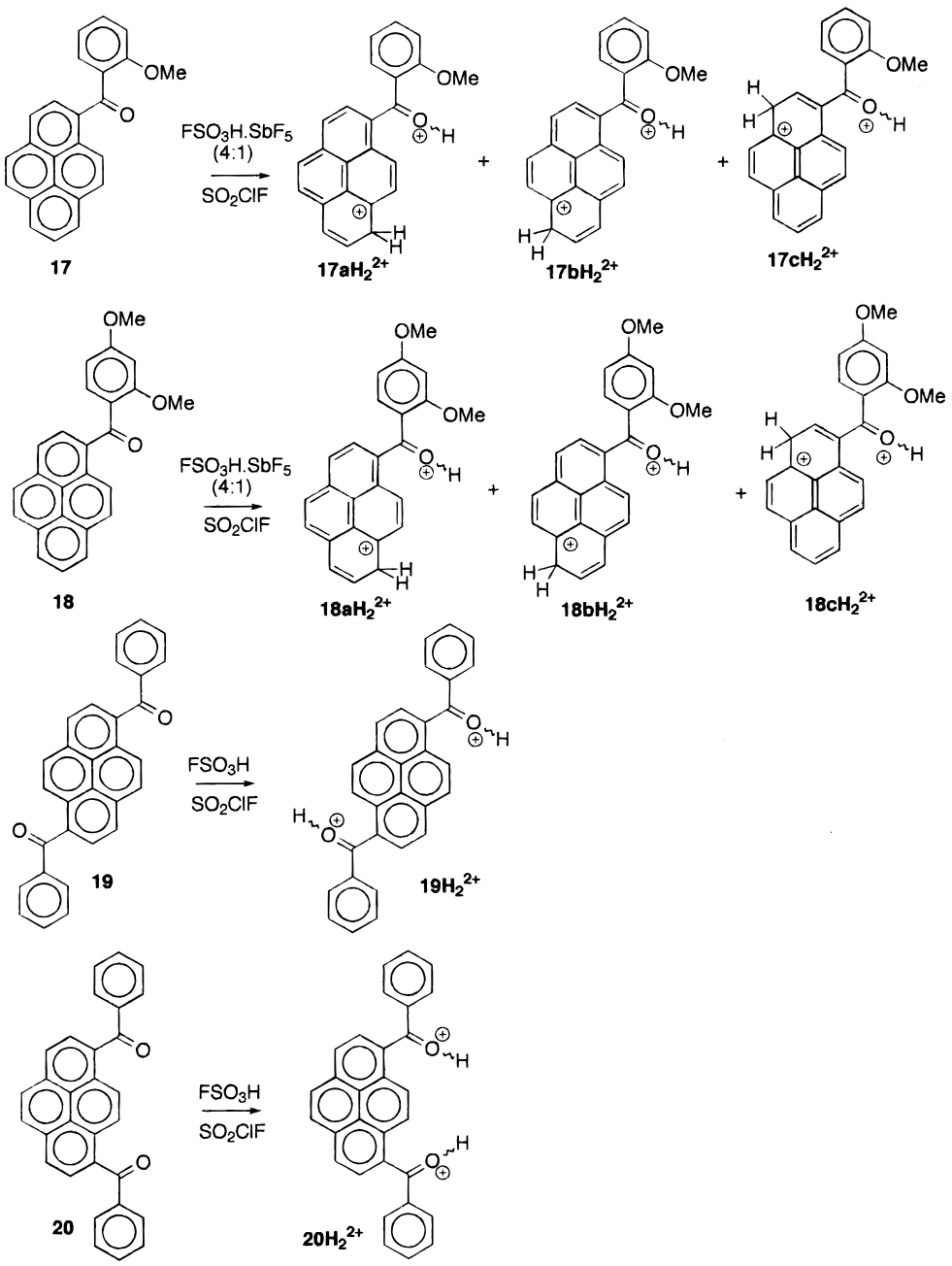
Scheme 3


FSO3H.SbF5 (4:1) SO2ClF
10
10H2 2+ (93%)
10aH2 2+ (7%)
or
11
11H2 2+
11aH2 2+
(9 : 1)
12
12H2 2+
12aH2 2+
FSO3H.SbF5 (4:1) SO2ClF –60°C
98 : 2 (–60°C)
67 : 33 (–40°C)
13
13H2 2+
13aH2 2+
(2 : 1)
FSO3H or FSO3H.SbF5 (4:1) SO2ClF
14
14H2 2+
15
15H2 2+
16
16aH2 2+
16bH2 2+

Scheme 3 (continued)



of some of the ring junction carbons (via ^3J C/H correlations) in the neutrals. For the dications, low-temperature COLOC measurements were mostly impractical due to the possibility of decomposition during long acquisitions; hence, specific assignments of the ring junction carbons remain tentative. However, these could be grouped based on the overall charge delocalization pattern and in comparison with previously established patterns with other pyrenium mono- and dications (in some cases, additional subgrouping was attempted by qualitative comparison with the overall trends based on AM1). In the case of **10**, low-temperature COLOC experiment was successful allowing specific assignments of C-3a/C-10a, C-10b/C-10c, and C-5a to be made.

These data are summarized in Figures 1 and 2.

Protonation of 1-Acetylpyrene 10. The major dication is **10H**$_2^{2+}$ (93%), where ring protonation occurs at C-3 and there is a minor dication **10aH**$_2^{2+}$ (7%) due to protonation at one of the remote α-positions (C-6 or C-8). Prolonged storage of the sample did not result in noticeable variations in the ratio of the two dications and further increase in temperature (−20 °C over 1 h period) led to gradual deterioration of the spectra due to decomposition and polymer formation. AM1 predicts that ring protonation at C-4 is slightly favored (∼2 kcal) over the observed C-3 protonation and that the dications formed by protonation at C-6/C-8 are no more than 0.5 kcal higher in energy than the observed **10H**$_2^{2+}$. The CO*H*$^+$ resonance appears as a singlet at δ 14.83 and the ring C*H*$_2$ at δ 5.32. The *C*OH$^+$ moves from δ 202.3 in **10** to δ 223.9 in the carboxonium ion with the ring *C*H$_2$ appearing at δ 40.7. There is an NOE between the methyl group and the H-2 broad singlet at δ 9.67 (this is the most deshielded aromatic proton resonance), which establishes the "*in*" configuration for the carboxonium group in the α position (Scheme 4). Since NOE effects are also

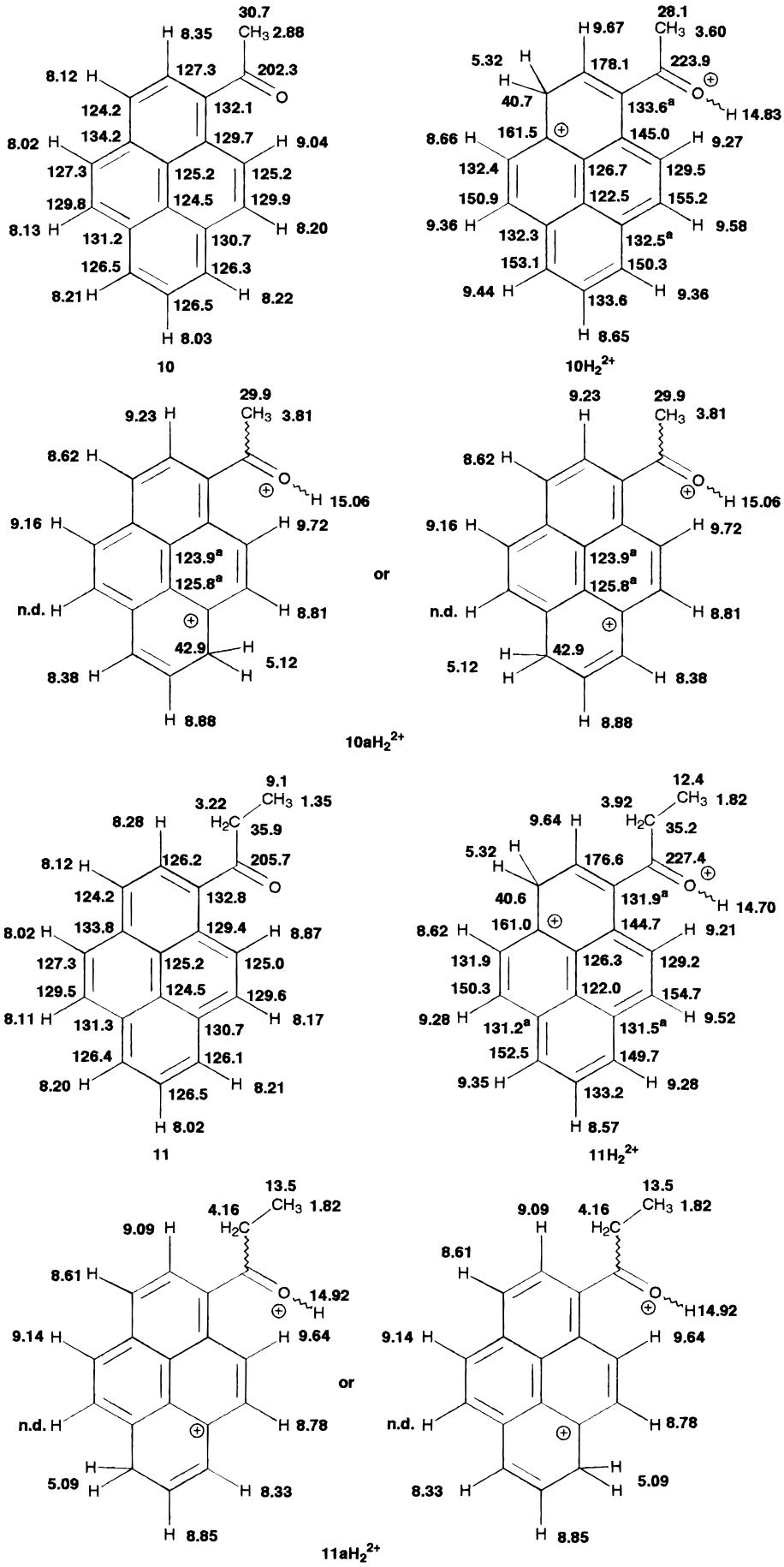


Figure 1. NMR assignments for the dications and their precursors (a, b, c, and e denote interchangeable assignments within a compound; d denotes relative assignment in line with AM1).

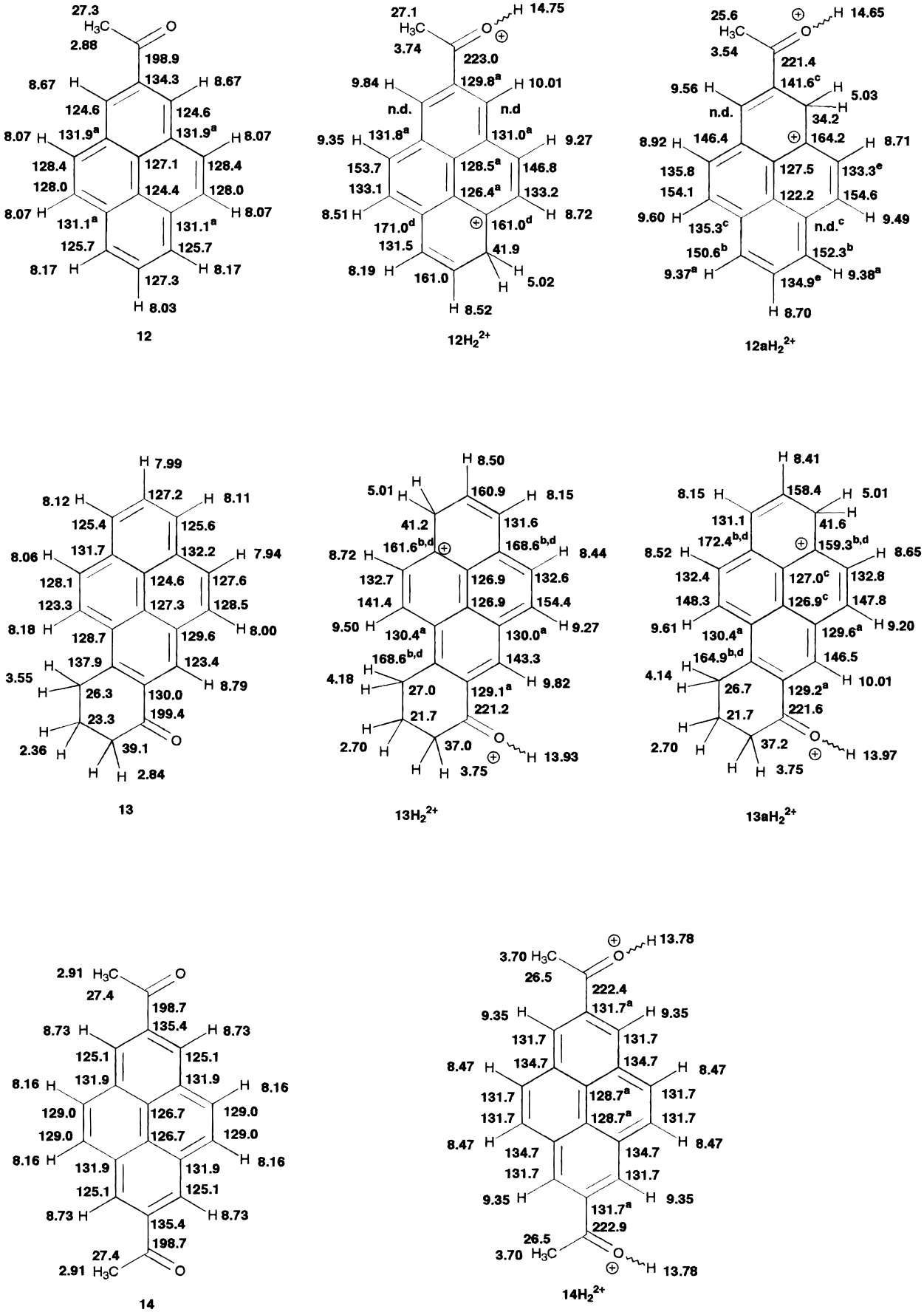
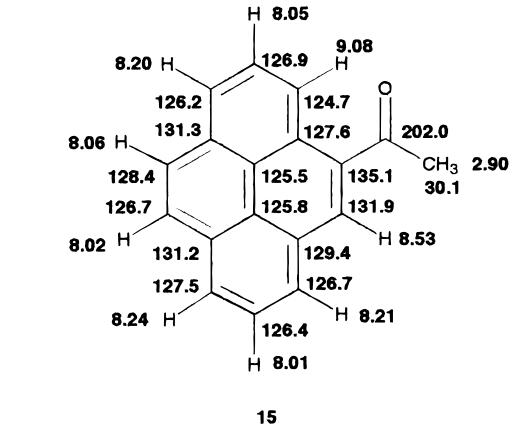


Figure 1 (continued)



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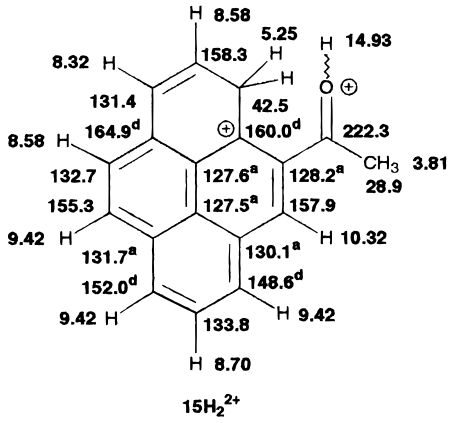
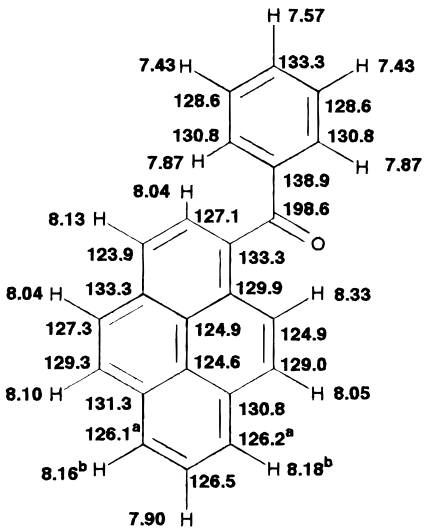
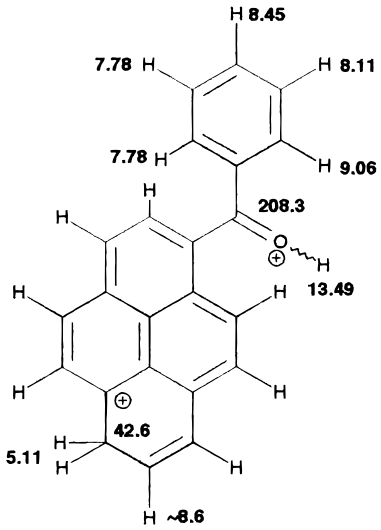


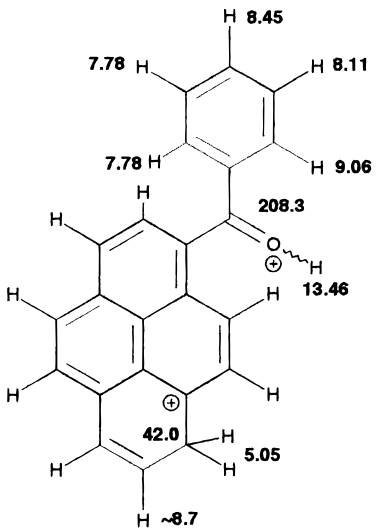
$15H_2^{2+}$



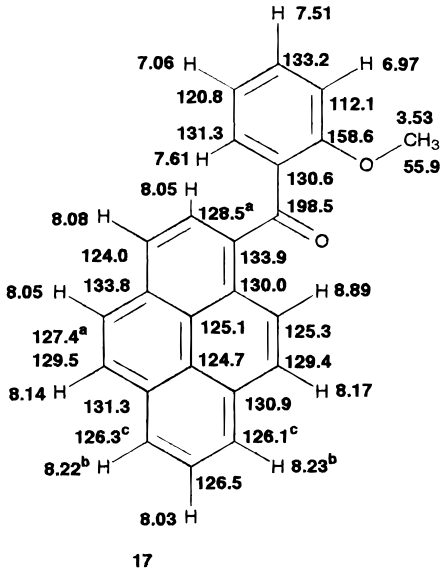
16



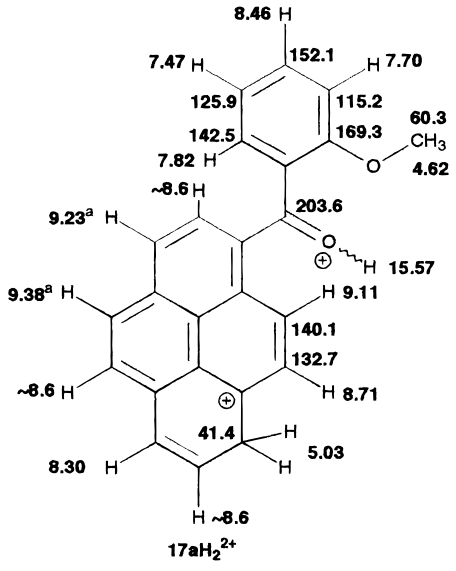
$16aH_2^{2+}$



$16bH_2^{2+}$



17



$17aH_2^{2+}$

Figure 1 (continued)

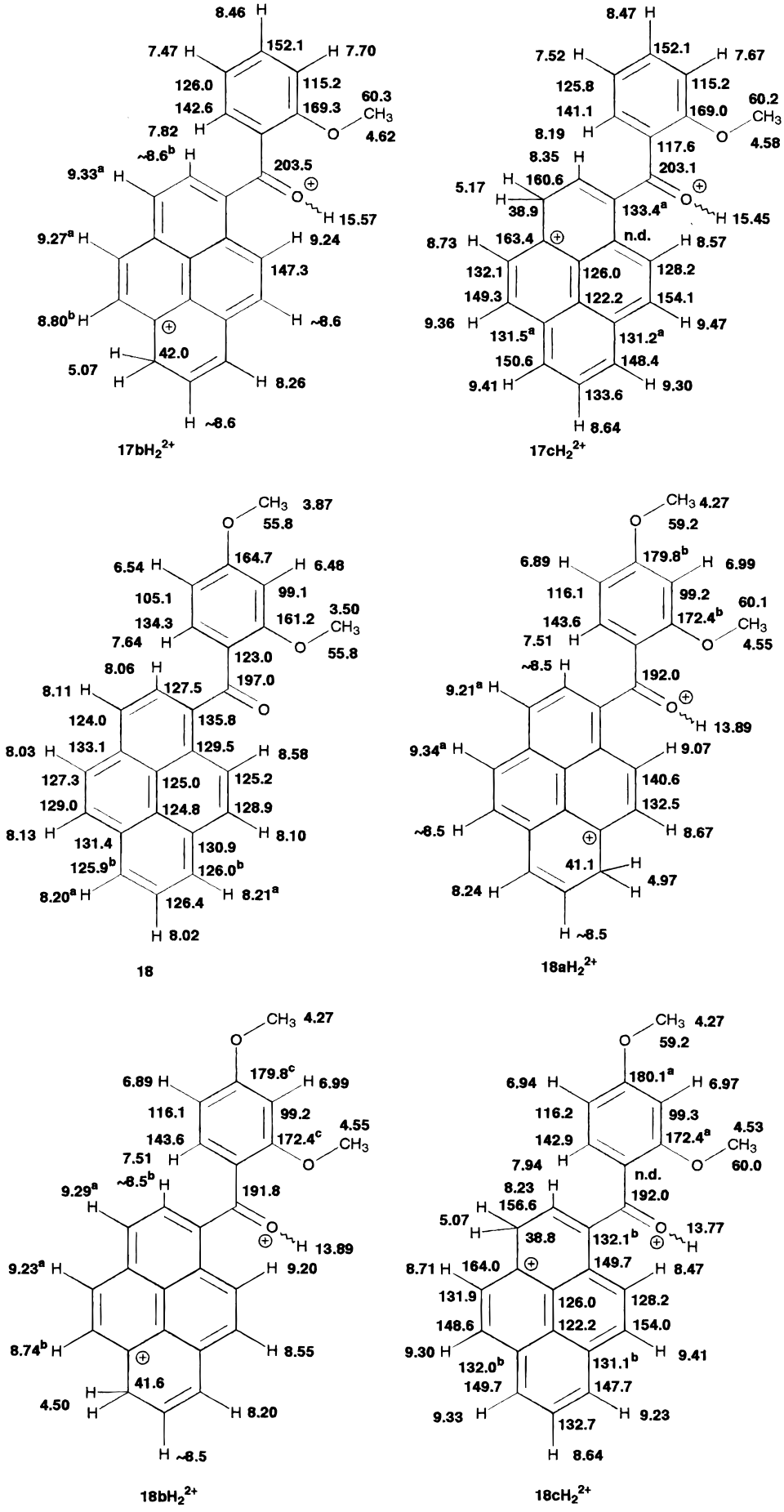


Figure 1 (continued)

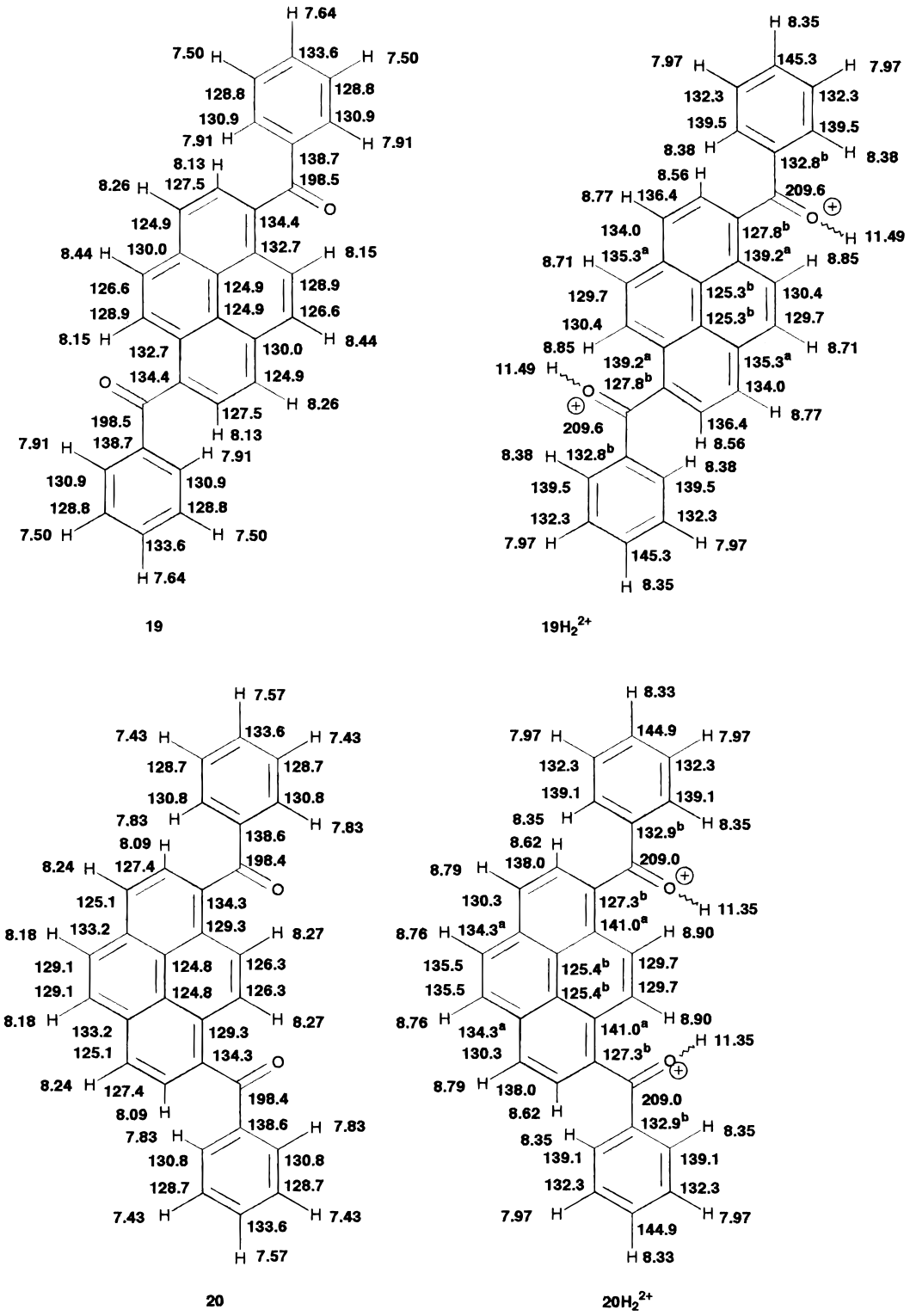
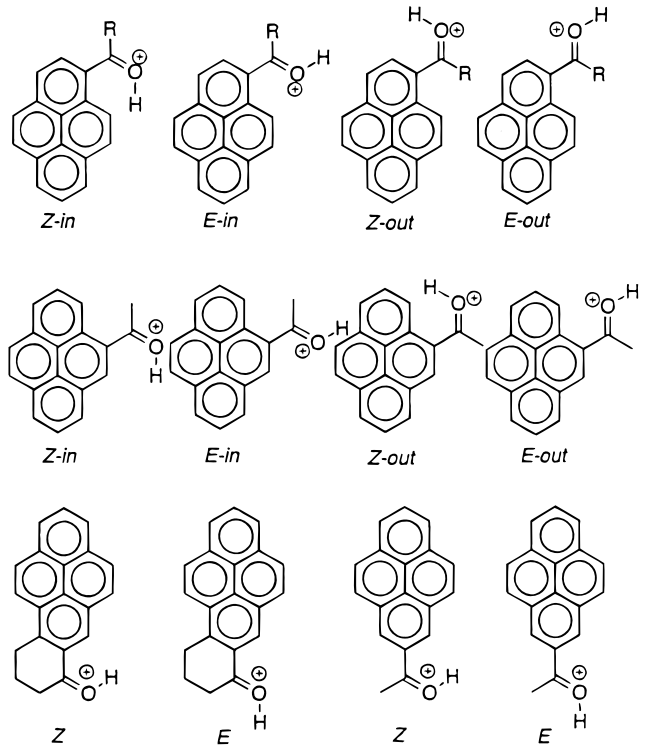


Figure 2. NMR assignments for the dibenzoyl−carboxonium dications (a and b denote interchangeable assignments within a compound).

observed between CO*H*$^+$ and the C*H*$_3$ group and *peri*-H-10 at δ 9.27, it can be concluded that there is rapid equilibrium between the *E-in*/*Z-in* pair on the NMR time scale. Judging from the weak enhancement of H-10 upon irradiation of the CO*H*$^+$ resonance compared to a large increase in the C*H*$_3$ resonance, it may be suggested that the *E*-form (Scheme 4) is predominant; AM1 predicts an energy difference of 0.5 kcal/mol between *E-in*/*Z-in* forms in their corresponding monocarboxonium ions. An NOE was also observed between the ring C*H*$_2$ and the *peri*-H-4 (at δ 8.66). It is relevant to note that in 1-acetylpyrene itself the methyl group exhibits NOE with both H-2 and the *peri* H-10 consistent with free rotation of the acetyl group at rt. The presence of **10aH**$_2^{2+}$ as a minor species is supported by the detection of additional CO*H*$^+$ (δ 15.06), methyl, and the ring CH$_2$ together with several resolved aromatic protons.

Protonation of 1-Propanoylpyrene 11. Low-tem-

Scheme 4



perature protonation of **11** gave a 9:1 mixture of $\mathbf{11H_2}^{2+}$ and $\mathbf{11aH_2}^{2+}$ showing behavior very similar to that of **10**. Dication $\mathbf{11H_2}^{2+}$ has its CO*H*$^+$ at δ 14.70 and the ring C*H*$_2$ at δ 5.32. Concurrent NOE between the propanoyl methylene protons and the ring H-2, between the Et group and CO*H*$^+$, and between CO*H*$^+$ and the ring H-10 establishes the carboxonium group as a rapidly equilibrating *E-in*/*Z-in* mixture. However, NOE enhancement in H-10 was relatively larger than that of the Et group upon irradiation of CO*H*$^+$, suggesting that the *Z-in* form is preferred. The major dication has its *C*OH$^+$ at δ 227.4 and the most deshielded aromatic resonance (δ 176.6) is the C-2. The minor dication ($\mathbf{11aH_2}^{2+}$) has its CO*H*$^+$ at δ 14.92 and ring CH_2 at δ 5.09 and exhibits a separate propanoyl Et group and several small but resolved aromatic resonances.

Protonation of 2-Acetylpyrene 12. With the carboxonium group at C-2 (β position), ring protonation occurs at a remote α position to give $\mathbf{12H_2}^{2+}$ (98%). Whereas only traces of $\mathbf{12aH_2}^{2+}$ is present in the spectra recorded at −60 °C, a gradual increase in the latter is observed with increasing temperature so that at −40 °C, 33% of the mixture is due to the C-1-protonated species. For $\mathbf{12H_2}^{2+}$, the CO*H*$^+$ resonance is observed at δ14.75 and *C*OH$^+$ is deshielded by 24.1 ppm relative to the precursor. Concurrent NOE are observed between CO*H*$^+$ and H-1/H-3 and between the methyl group and CO*H*$^+$/H-1, H-3. The data are compatible with a rapid equilibrium between the *E* and *Z* forms (Scheme 4). However, NOE enhancement in H-1/H-3 upon irradiation of CO*H*$^+$ was considerably less than that of the methyl group, suggesting that the *E* form was predominant. Several *peri*-NOE effects are also detected (H-5/H-6, CH_2/H-9, and H-10/H-1). The most deshielded aromatic protons are those of H-1/H-3, which are observed at δ 10.01 and 9.84. In the ^{1}H NMR spectrum recorded at −60 °C the H-1/H-3 protons are somewhat broader than other resonances. In the ^{13}C spectrum, the C-1/C-3 are not detectable and the most deshielded resonances observed (those of C-4, C-5a, C-7, C-8a, and C-10) appear noticeably broader than the rest; at −40 °C they sharpen but C-1/C-3 remain obscure. These effects indicate that rotation of the PAH-carboxonium bond is not completely averaged at −60 °C, which diminishes the symmetry of the system on the NMR time scale despite the fact that there is less effective conjugation from the 2-position, which is expected to reduce π-participation into the carboxonium group. The minor dication $\mathbf{12aH_2}^{2+}$ has a slightly different *C*OH$^+$ and the same CO*H*$^+$. Its H-3 is at δ 9.56 which, also shows NOE with the methyl group. The presence of a small NOE between the methyl group and the ring C*H*$_2$ is also detected. In concert with experiment, AM1 predicts that C-6/C-8 protonation is preferred over C-1 protonation by ca. 4.5 kcal/mol with the former having nearly identical energies. For the C-1-protonated dication, the *E*-configuration of the carboxonium group is favored over *Z* by ca. 2.5 kcal/mol. Quenching of the superacid solution returned the skeletally intact **12**.

Protonation of 9,10-Dihydrobenzo[*a*]pyren-7(8*H*)-one 13. The most deshielded proton in the neutral compound is H-6 (δ 8.79) (in keeping with the numbering system in BaP), which exhibits NOE with *peri* H-5. NOE effect is also detectable between H-3/H-4. Low-temperature reaction with $FSO_3H{\cdot}SbF_5$ (4:1)/SO_2ClF results in clean formation of two regioisomeric carboxonium-arenium dications $\mathbf{13H_2}^{2+}$ and $\mathbf{13aH_2}^{2+}$ by protonation at C-1 and at C-3 in 2:1 ratio. AM1 predicts that these are the most favored sites and that the resulting dications should have very similar energies. The finding that the *E*- and *Z*-configurations (Scheme 4) of the carboxonium group have very similar energies based on AM1, with the *Z*-configuration (proton pointing toward H-6) being slightly favored, is apparently borne out by the observation of concurrent NOE between CO*H*$^+$ and H-6/CH_2 for both dications. There is also NOE between the protonation site and the ortho/peri protons for both dications as well as a long-range NOE between CO*H*$^+$ and H-5. Because of structural similarity, the $\mathbf{13H_2}^{2+}$/$\mathbf{13aH_2}^{2+}$ mixture gives rise to protons and carbons in very similar environments (several coinciding ones) and, hence, a complex set of resonances which are barely resolved at 500 MHz. The *C*OH$^+$ groups appear at δ 221.2/221.6, CO*H*$^+$ at 13.93/13.97, and H-6 at δ 9.82/10.01, with the latter overlapping with H_3O^+ signal (present in the superacid).

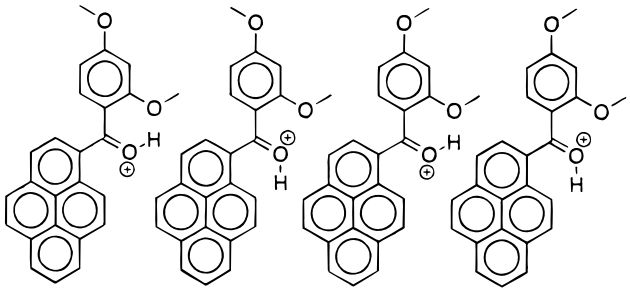
Protonation of 2,7-Diacetylpyrene 14. Since the carboxonium group at β-position is less effectively conjugated it was of interest to explore whether a dioxonium−arenium trication could be generated. Low-temperature protonation of **14**, however, led only to a dioxonium ion $\mathbf{14H_2}^{2+}$ along with side reactions which increased with time and prevented complete NMR assignments. The ^{1}H NMR spectrum of the symmetrical dioxonium ion exhibits just two aromatic singlets (δ 9.35, 8.47) and the CO*H*$^+$ at δ 13.78 using $FSO_3H{\cdot}SbF_5$ (4:1) (CO*H*$^+$ is at δ 11.3 in FSO_3H). Magnitude of CO*H*$^+$ deshielding in $\mathbf{14H_2}^{2+}$ is similar to $\mathbf{12H_2}^{2+}$. NOE enhancements were observed among acetyl methyl protons, H-1, H-3, and COH$^+$. It was found that NOE enhancement in H-1/H-3 was weaker than that of acetyl methyl protons upon irradiation of CO*H*$^+$, indicative of preference of the *E* form.

Protonation of 4-Acetylpyrene 15. The presence of NOE between the *Me*CO group and H-5 is noted in **15** at rt. This compound is cleanly diprotonated to give $\mathbf{15H_2}^{2+}$.

In concert with experiment, AM1 predicts that among all other possible ring protonation sites $\mathbf{15H_2}^{2+}$ is most favored. The CO*H*$^+$ is observed as a singlet at δ 14.93 and exhibits NOE with the CH_2 and the acetyl methyl but not with H-5. Additional NOE is observed between the *Me*CO and H-5 and between CH_2 and H-2 and CO*H*$^+$ at δ 222.3 ($\Delta\delta = 20.3$). On this basis, it can be concluded that the carboxonium group in the $\alpha\beta$ position exits as an *E-out*/*Z-out* mixture (Scheme 4*)*. The NOE enhancement in C*H*$_2$ upon the irradiation of CO*H*$^+$ was less intense than that of acetyl methyl protons, suggesting that the *E-out* form was predominant. AM1 predicts that the *E-out* form is 1.4 kcal/mol lower in energy than *Z-out* in the monoprotonated **15** and that *E-in*/*Z-in* forms are less favorable. In the ^{13}C NMR spectrum all 15 aromatic resonances are nicely resolved (164.9−127.5 ppm) and *C*OH$^+$ is seen at δ 222.3. Quenching of the dication solution returned the intact precursor.

Protonation Studies on the Monobenzoyl Derivatives 16−18. Low-temperature protonation of **16** gave a mixture consisting of two major and several minor oxonium−arenium dications. The major ions exhibited CO*H*$^+$ resonances at δ 13.46/13.49, a coinciding *C*OH$^+$ peak, at δ 208.3, and CH_2's at δ 5.05/5.11. On the basis of AM1, protonation at C-3 is expected to be most favored, with those of C-5, C-6, and C-8 predicted to have almost identical energies (these are higher than C-3 protonation by about 1.2 kcal/mol). This is in line with the formation of a dication mixture. However, the major isomer could be assigned to either the C-6-($\mathbf{16aH_2}^{2+}$) or the C-8-protonated species ($\mathbf{16bH_2}^{2+}$). In addition, it is seen from the ^{1}H NMR spectra that the free rotation around the CO−C-1′ (in the phenyl ring) bond is slowed so that H-2′/H-6′ and H-3′/H-5′ have different chemical shifts. Low regioselectivity in ring protonation is also encountered with the 2-methoxybenzoyl derivative **17**, where a mixture of three dications was formed, showing O*C*H$_3$ groups at δ 60.3, 60.2, CH_2's at δ 41.4, 42.0, 38.9 and *C*OH$^+$ at δ 203.6, 203.5, 203.1. Only partial assignments could be made (Figure 1). The ratio of three dications $\mathbf{17aH_2}^{2+}$, $\mathbf{17bH_2}^{2+}$, and $\mathbf{17cH_2}^{2+}$ changed over time with $\mathbf{17cH_2}^{2+}$ (initially a minor component) increasing at the expense of others. The latter dication could be assigned to the C-3 protonated species. Concurrent NOE enhancements were observed between the methoxy protons and CO*H*$^+$, between the methoxy protons and H-3′ of the phenyl ring, and between CO*H*$^+$ and H-10 of the pyrene ring for $\mathbf{17aH_2}^{2+}$, $\mathbf{17bH_2}^{2+}$, and $\mathbf{17cH_2}^{2+}$. The data are compatible with a rapid equilibrium between the *E*/*Z* forms of CO*H*$^+$. The chemical shift pattern at the pyrenyl ring of $\mathbf{17cH_2}^{2+}$ is similar to that of $\mathbf{10H_2}^{2+}$. AM1 favors protonation at C-3, C-5, C-6, and C-8 almost equally (all within 1.4 kcal/mol). With the 2,4-dimethoxybenzoyl derivative **18**, a mixture of three dications $\mathbf{18aH_2}^{2+}$, $\mathbf{18bH_2}^{2+}$, $\mathbf{18cH_2}^{2+}$ was similarly formed, whose ratios again changed over time, with $\mathbf{18cH_2}^{2+}$ (initially minor) increasing at the expense of others in the mixture. The latter could be assigned to the C-3 protonated species. Concurrent NOE enhancements were observed between the *p*-methoxy protons (at δ 4.27) and H-3′ of the phenyl ring (at δ 6.97/6.99), between the *o*-methoxy protons (at δ 4.53/4.55) and H-3′ of the phenyl ring and between CO*H* and H-10 of the pyrene ring for $\mathbf{18aH_2}^{2+}$, $\mathbf{18bH_2}^{2+}$, and $\mathbf{18cH_2}^{2+}$. Furthermore, irradiation of the CO*H*$^+$ proton resonance gave clear NOE effects at the O*C*H$_3$ resonance, suggesting the spacial proximity of the OH and OCH$_3$ moieties.

Scheme 5



a , b , c , d

Conformations *a*−*d* of the carboxonium group (Scheme 5) in a monocation were examined by AM1; *a* and *c* were clearly preferred over *b* and *d*. Ring protonation energies for *a* was also examined those of C-3/C-6/C-8 were within 0.5 kcal/mol. The chemical shift pattern of $\mathbf{18cH_2}^{2+}$ is similar to that of $\mathbf{17cH_2}^{2+}$. The proton resonances for $\mathbf{18aH_2}^{2+}$/$\mathbf{18bH_2}^{2+}$ were assigned following subtraction of resonances for the major dication $\mathbf{18cH_2}^{2+}$, and $\mathbf{17aH_2}^{2+}$/$\mathbf{17bH_2}^{2+}$ were assigned by analogy.

Protonation of 1,6- (19) and 1,8-Dibenzoylpyrene (20). In an attempt to generate dioxonium−arenium trications or oxonium−arenium dications, initial studies were performed in $FSO_3H{\cdot}SbF_5$ (4:1)/SO_2ClF but in both cases conformationally frozen mixtures (typically four or five) of dioxonium dications were formed with no indication for ring protonation. Increasing temperature or prolonged reaction times led to extensive side reactions and broadening. We therefore reexamined these dioxonium ions using FSO_3H/SO_2ClF to prevent side reactions while performing VT-NMR studies. With $\mathbf{19H_2}^{2+}$ at −60 °C, hindered rotation of the protonated benzoyl group leads to broad resonances in both ^{1}H and ^{13}C NMR spectra while peaks for the pyrene moiety remain sharp except for the peri H-5/H-10, which are broad and most deshielded. The CO*H*$^+$ is also broad whereas *C*OH$^+$ appears sharp. At −50 °C, the phenyl ortho/meta protons and pyrene-peri protons are still broad. At −30 °C, the meta protons sharpen, and at −20 °C only the phenyl ortho protons are broad. The data indicate that although the carboxonium group is dynamic, it is still not completely free. More information was provided through NOE (at −20 °C). The CO*H*$^+$ exhibits NOE with both peri and ortho protons of the pyrene moiety as well as with the benzoyl ortho protons, showing that the *in* and *out* forms are equilibrating. AM1 computes their relative energies to within 1 kcal/mol. The dynamics of the protonated benzoyl group in **20** are rather similar, where hindered rotation is observed in the ortho benzoyl protons and the peri H-9/H-10. At −20 °C, ^{1}H NMR spectra indicate that the protonated benzoyl groups is dynamically averaged, but the ^{13}C resonances for the ortho carbons of the benzoyl group and the pyrene C-2/C-7 are noticeably broader than other signals. The AM1-minimized structures of $\mathbf{19H_2}^{2+}$ and $\mathbf{20H_2}^{2+}$ indicate severe tilting of the protonated benzoyl groups out of the plane of the pyrene ring. The COH group is not planar relative to either the phenyl or pyrenyl group, but the torsion angle between the carbonyl group and phenyl group was smaller than that between the carbonyl group and pyrenyl group.

Comparison of the Protonation Sites among Various Regioisomers. The 1-acetyl- (**10**) and 1-propionyl-

pyrene (**11**) are protonated at the carbonyl carbons and subsequently at C-3, in opposition to the 1-benzoylpyrene (**16**), which is ring protonated at the α-position of the nonsubstituted end (C-6/C-8). For the *β*-substituted derivatives (**12**, **13**), ring protonation also takes place at the α-position of the nonsubstituted ring at low temperature. For the α*β*-substituted derivative (**15**), protonation again occurs at the α position. Electrophilic substitution in pyrene normally leads to 1,6- and 1,8-derivatives as found in bromination,[12] nitration,[13] and acetylation[14] with only small amounts of the 1,3-disubstituted derivative being isolated. Protonation of 1-isopropylpyrene under stable ion conditions gave predominant C-6/C-8 protonation (the C-3 protonated cation was present only as a minor species).[15] Protonation studies of 1-fluoro- and 4-fluoropyrene led to attack at the α-position in the nonsubstituted ring,[16] whereas 2-fluoro- and 2-alkylpyrenes are protonated in the same ring.[15,16]

Notable exceptions are found in Friedel−Crafts acetylation of 1-acetylpyrene (forming 35% of the C-3 substituted derivative)[11b] and in sulfonation of pyrenesulfonic acid (predominant disulfonation at C-3).[17] The present results showing predominant protonation at C-3 in **10** and **11** reflect the strong mesomeric electron-withdrawing power of the carboxonium group leading to electron depletion primarily from C-6/C-8 positions. Formation of a Lewis acid-bound carboxonium group under Friedel−Crafts conditions would rationalize the reported C-3 substitution product. A sulfo substituent is also strongly deactivating and should have a similar influence. [Reported formation of significant amounts of the 3-nitro derivative in the nitration of 1-methylpyrene (Chow, F. L.; Garner, R. C.; Martin, C. N.; Mann, B. E. *Magn. Reson. Chem*. **1985**, *23*, 771) is clearly unusual.] That the protonated benzoyl group behaves differently may possibly be ascribed to steric factors and to the fact that positive charge resides in the benzene ring as discussed in the following section.

Comparative Discussion of Charge Delocalization Mode. Magnitude of Δ*δ* values for the *C*OH$^+$ (about 22 ppm except for the benzoyl derivatives) clearly points to oxonium ion character of the carboxonium groups. For the carboxonium−pyrenium dications, with the carboxonium group in the α position (as in **10H$_2$**$^{2+}$ and **11H$_2$**$^{2+}$) there is extensive charge delocalization and alternation at the pyrenium moiety with largest Δ*δ* values at C-2, C-5/C-9, C-6/C-8, and C-10a/C-3a. The C-2 and C-3a, which are ortho/para to the carboxonium group and ortho to the protonation site, are more deshielded than C-10a (para to protonation site; ortho to carboxonium group). Dications **12H$_2$**$^{2+}$, **13H$_2$**$^{2+}$/**13aH$_2$**$^{2+}$ represent models of charge interaction between a carboxonium group in the *β*-position and a pyrenium cation of α-attack. Dication **12H$_2$**$^{2+}$ exhibits a charge delocalization path that is very similar to those of **10H$_2$**$^{2+}$ and **11H$_2$**$^{2+}$ and its overall charge distribution is very much pyrenium ion like. In the case of **15H$_2$**$^{2+}$ charge interaction is realized between a carboxonium group in the α*β* position and a pyrenium ion of α attack. Again, the overall charge delocalization path remains similar to an α-pyrenium ion.

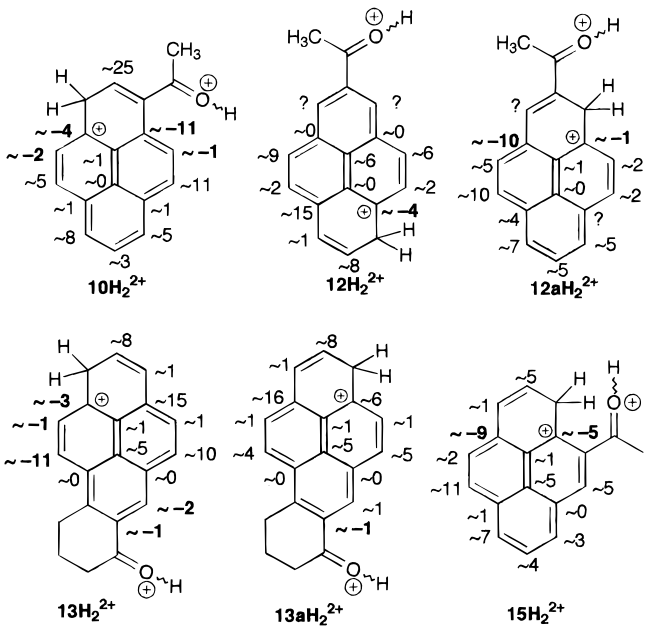


Figure 3. Δδ^{13}C as compared to parent pyrenium ion of α-attack.

To gauge substituent effects, it is instructive to compare Δ*δ* values in regioisomeric dications with parent α-pyrenium ion PyH$^+$ (in the present study PyH$^+$ was generated and reexamined at 500 MHz; detailed NMR assignments using 300 MHz NMR was previously reported).[18] The trends are sketched in Figure 3. It is clear that the carboxonium group in the α position interacts more strongly with the pyrenium ion. An interesting feature is the induced shielding of some of the carbon resonances (see Figure 3). Although a number of these appear to be due to steric effects, others are more subtle. With the α-benzoyl derivatives, although only partial NMR assignments were possible due to complexity of the spectra, it can be deduced that charge delocalization involves mostly the phenyl group (Figure 1). This is also supported by comparison of Δ*δ*COH for **10**, **16**, **17**, and **18**. In the latter three Δ*δ*COH is less than for other α-substituted derivatives. This can be ascribed to increased delocalization of charge, which is optimal in **16**−**18** for which steric effects probably combined with hydrogen bonding (in the case of methoxy-substituted derivatives) (see Scheme 5) increase the coplanarity of the COH$^+$ group and the phenyl ring. Limited charge delocalization from the *β*-position into pyrene can be clearly observed in the dioxonium dication **14H$_2$**$^{2+}$. In the isomeric dibenzoyl derivatives charge delocalization is primarily into the phenyl groups. The origin of this effect is possibly steric inhibition to delocalization as the benzoyl H$^+$ moiety is twisted out of the pyrene ring plane; this is corroborated via AM1 calculations.

It can be concluded that the carboxonium group is a robust electron-withdrawing substituent whose electronic response is sensitive to steric factors. It can be used to modulate charge delocalization into PAHs and their carbocations as a function of substitution position.

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Experimental Section

NMR Spectroscopy. NMR spectra were recorded on a 500 MHz instrument at Kent using a 5 mm broadband probe. Some spectra were recorded at 250 MHz at Roskilde. The stable ion spectra (^{1}H, H/H COSY, ^{13}C, C/H HETCOR, and NOED) were collected between −70 and −20 °C. NOED spectra were obtained by using cyclenoe pulse sequence with irradiation of several protons. NMR spectra of the parent compounds (**10**−**20**) were run at r.t. in $CDCl_3$ solvent. Carboxonium−pyrenium dications were generated in $FSO_3H{\cdot}SbF_5$ (4:1)/SO_2ClF, whereas dioxonium dications were studied in FSO_3H/SO_2ClF.

Materials. Compounds **10** and **13** and hexahydropyrene were high-purity samples purchased from Aldrich. Other substrates (all known compounds) were available from previous studies in our laboratories. They had been prepared by conventional acylation and benzoylation of pyrene (→ 1-isomer),[14] hexahydropyrene (→ the 4-isomer) and tetrahydropyrene (→ the 2-isomer). The 2,7-diacetylpyrene was synthesized by standard Friedel−Crafts acetylation of tetrahydropyrene and subsequent aromatization. It was purified by chromatography [SiO_2; $CHCl_3$−pentane (1:1)]. Tetrahydropyrene was obtained from a raw mixture containing pyrene, hexahydropyrene and tetrahydropyrene. The mixture was refluxed over lithium in THF for two days and subsequently quenched with water. The resulting crude mixture was separated by chromatography over silica using $CHCl_3$−pentane (1:1).

FSO_3H (Allied or Aldrich) and SbF_5 (Fluorochem and Aldrich) were freshly distilled in an all-glass distillation unit under dry nitrogen at atmospheric pressure and stored in Nalgene bottles with Teflon seals. $FSO_3H{\cdot}SbF_5$ (4:1) was prepared under argon by transfer of freshly distilled SbF_5 into a Nalgene bottle and by direct addition of the required amount of FSO_3H, which was weighed inside a second Nalgene bottle. SO_2ClF was prepared from SO_2ClF with NH_4F and TFAH using a modified procedure of Prakash et al.[19] Other commercially available reagents were used as received.

General Procedure for Stable Ion Generation. SO_2ClF (ca. 0.3 mL) was distilled into a 5 mm NMR tube containing the substrate (40 mg) cooled to dry ice/acetone temperature. To the resulting suspension was carefully added the precooled superacid (3−6 drops) under a dry nitrogen atmosphere with efficient mixing (vortex) until homogeneous. Finally, three drops of precooled CD_2Cl_2 was added on top of the solution and mixed to give a homogeneous solution. The resulting ion solutions were all deep-red in color except for **13**, which was dark-green. In the case of α-benzoyl derivatives **16**, **17**, and **18**, small amounts of dark-solid was formed.

Quenching Experiments. The superacid solution was carefully poured into ice−bicarbonate. The organic material was extracted with ether, and the extract was washed with 10% NaCl and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was analyzed by NMR. AM1 calculations were performed with the Hyperchem package version 5.1 (Hypercube Inc., 1999) or Insight II Release 97.0 (MSI).

Acknowledgment. Support of our work in the area of reactive intermediates of carcinogenesis of PAHs by the NCI of NIH (R15 CA 78235-01A1) is gratefully acknowledged. We thank Dr. M. Gangoda for NMR assistance and Prof. A. Berg for making available compounds **16**−**20**.

Supporting Information Available: Selected NMR spectra for the protonation of **10**, **12**, **15**, and **19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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