Radical Cations of Benzo[a]pyrene and 6-Substituted Derivatives: Synthesis and Reaction with Nucleophiles

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Radical cations of benzo[a]pyrene (BP) and 6-substituted derivatives were synthesized by two methods: reaction of the hydrocarbon with I_2 and $AgClO_4$ in benzene, and reaction of the hydrocarbon with $NOBF_4$ in CH_3CN/CH_2Cl_2. Both the radical cation perchlorates and tetrafluoroborates were stable for prolonged periods of time when stored under argon at subzero temperatures. The radical cations were reacted with nucleophiles of various strengths, namely H_2O, AcO^- and F^-, as a means of best characterizing these intermediates, as well as determining their chemical properties. Reaction of BP, 6-FBP, 6-ClBP, and 6-BrBP radical cation perchlorates with H_2O produced BP 1,6- 3,6-, and 6,12-dione, whereas the radical cation derived from 6-CH_3BP yielded 6-CH_2OHBP. When $BP^{\bullet+}ClO_4^-$ and 6-$FBP^{\bullet+}ClO_4^-$ were reacted with NaOAc in H_2O/CH_3CN (9:1), 6-OAcBP was formed, in addition to the quinones. 6-$ClBP^{\bullet+}ClO_4^-$ formed a small amount of 1-OAc-6-ClBP and 3-OAc-6-ClBP, in addition to the diones, whereas for 6-$BrBP^{\bullet+}ClO_4^-$ and 6-$CH_3BP^{\bullet+}ClO_4^-$ the reaction products were BP diones and 6-CH_2OHBP, respectively. Reactions conducted under anhydrous conditions, using tetramethylammonium acetate in CH_3CN, gave similar results, except that no quinones were formed. These results confirm the reactivity of nucleophiles at the positions of high charge localization in the $BP^{\bullet+}$, i.e. C-6, followed by C-1 and C-3.

Introduction

A substantial body of experimental evidence indicates that the formation of a covalent bond between chemical carcinogens and cellular macromolecules represents the first critical step in the multistage process eventually leading to tumor formation.[1,2] Most chemical carcinogens are not active *per se*, but require metabolic activation to produce reactive intermediates capable of binding covalently to target macromolecules, in particular DNA, and initiate cancer. The common unifying feature of these critical intermediates is their electrophilic character.[1,2]

Polycyclic aromatic hydrocarbons (PAH) undergo two main pathways of bioactivation: one-electron oxidation and monooxygention.[3,4] The former yields radical cations, the latter produces oxygenated metabolites.

To establish radical cations as key intermediates in metabolic activation of PAH, several chemical approaches have been investigated. Electrochemical oxidation of benzo[a]pyrene (BP) in the presence of deoxyguanosine (dG) or deoxyadenosine (dA) forms adducts in which BP is bound at C-6 to the nucleoside.[5,6] Some of these adducts are obtained when the binding of BP to DNA is catalyzed by horseradish peroxidase or rat liver microsomal cytochrome P450.[5,7,8]

Manganic oxidation of BP in acetic acid shows that nucleophilic attack of acetate ion occurs regioselectively at C-6, the position of greatest charge density in the BP radical cation.[9] Furthermore, metabolic formation of BP quinones catalyzed by cytochrome P450,[10] horseradish peroxidase,[11] or prostaglandin H synthase[11] occurs via the BP radical cation intermediate.

Because of the nature of the manganic acetate system, the radical cation generated is immediately trapped by acetate ion, thus preventing the use of other nucleophiles. A valid alternative is to synthesize the radical cation as a solid salt, isolate it, and investigate its reaction with various nucleophiles.

Synthesis of radical cation perchlorates by oxidation with I_2 and $AgClO_4$ or radical cation tetrafluoroborates by oxidation with $NOBF_4$ has previously been successful only for perylene[12,13] and thianthrene.[14] In this paper, we report the reaction of both radical cation perchlorates and tetrafluoroborates of BP and 6-substituted BPs with various nucleophiles as a means of characterizing some properties of these intermediates, which could complement the results obtained by generation of PAH radical cations by electrochemical and manganic oxidations.

Experimental Section

All ^{1}H-NMR spectra were recorded in $CDCl_3$ with $(CH_3)_4Si$ as an internal standard on a Varian XL-300 instrument at 300 MHz. Support for the chemical shift assignments was

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obtained by spin–spin decoupling and two-dimensional chemical shift correlation spectroscopy (2-D COSY). Mass spectra were recorded at the Midwest Center for Mass Spectrometry, University of Nebraska–Lincoln, on a Kratos MS-50 instrument. PAH were analyzed by TLC on silica gel (Eastman Chromagram) in the following solvent systems: hexane, hexane/benzene (7:3 and 1:1), benzene, and CH_2Cl_2/hexane (7:3 and 8:2). HPLC analyses were conducted on a Waters (Milford, MA) 600E solvent delivery system equipped with a Waters 700 WISP autoinjector. Effluents were monitored for UV absorbance with a Waters 990 photodiode array detector, and the data were collected on a NEC APC-IV Powermate 2 computer. Analytical runs were conducted on a YMC (Overland Park, KS) ODS-AQ 5 μm column (6.0 × 250 mm). The mobile phase was a linear 60-min gradient from 40% water in methanol to 100% methanol at a flow rate of 1 mL/min. Yields of reaction products were calculated from peak areas using detection wavelengths corresponding to absorbance maxima for all products. Cyclic voltammetry experiments were performed with a Bioanalytical Systems Model CV-27 voltammograph (Lafayette, IN). The supporting electrolyte was 0.2 M tetra-n-butylammonium tetrafluoroborate in CH_3CN. Solutions (2–5 mM) were analyzed at a platinum electrode. The electrode potential was scanned between 0 and +2.50 V at a 200 mV/s scan rate. Anodic peak potentials were measured vs a Ag/AgCl reference electrode. Voltammograms were recorded on a Houston Omnigraphic Model 100 X-Y recorder (Houston, TX).

Chemicals. Melting points are uncorrected. Benzene was distilled over Na, CH_2Cl_2 over P_2O_5 and CH_3CN over CaH_2; iodine was purified by sublimation. All other reagents were analytical grade and were used with no further purification. $AgClO_4$ was obtained from Alfa Products (Danvers, MA) and $NOBF_4$ from Aldrich Chemical Corporation (Milwaukee, WI). BP (Aldrich) was purified by column chromatography on alumina eluted with hexane/benzene (1:1) and recrystallized from benzene/CH_3OH, mp 176–178 °C. 6-CH_3BP was synthesized by the method of Dewhurst and Kitchen[15] and purified as previously described,[16] mp 215–216 °C. 6-FBP, 6-ClBP, and 6-BrBP were synthesized and purified as previously described.[9] Tetramethylammonium dihydrogen trifluoride was purchased from Ozark-Mahoning (Tulsa, OK). All other tetraalkylammonium salts were purchased from Aldrich. Anhydrous tetra-n-butylammonium fluoride was prepared according to a published procedure.[17] Because of their hygroscopic nature, these salts were stored and handled under argon in a dry box. **Caution**: BP, 6-CH_3BP, 6-FBP, 6-ClBP, and 6-BrBP are hazardous chemicals. They are handled according to NIH guidelines.[18]

Synthesis of Radical Cation Perchlorates. Synthesis of radical cations of BP and derivatives was based on the method of Sato et al.[12] and Ristagno and Shine[13] under modified experimental conditions. To a solution of the hydrocarbon (1 mmol) in a minimal volume of benzene (5–40 mL), were subsequently added solutions of $AgClO_4$ (1 mmol) in benzene (7.5 mL) and iodine (0.45 mmol) in benzene (2 mL) under argon with vigorous stirring. A black precipitate containing the hydrocarbon radical cation perchlorate adsorbed on AgI immediately formed. Stirring was continued for 1 min. The reaction mixture was transferred under argon into centrifuge tubes; argon was bubbled in, the tubes were sealed, and the black solid was collected in a low speed centrifuge. The benzene was decanted, an equal volume of dry benzene was added, and centrifugation was repeated to remove unreacted iodine and hydrocarbon. This procedure was performed 3–4 times until the benzene was colorless. After a final wash with hexane, the black solid was dried in vacuum. The radical cation perchlorate was iodometrically assayed with potentiometric end point detection by using a platinum working electrode along with a Ag/AgCl reference electrode. The black solids could be stored at subzero temperatures under argon for a period of months with no appreciable decomposition.

Synthesis of BP Radical Cation Tetrafluoroborate. The synthesis of $BP^{\bullet+}BF_4^-$ was a modification of published methods.[19,20] Two separate solutions of BP (1 mmol) in dry CH_2Cl_2 (25 mL) and $NOBF_4$ in dry CH_3CN (7 mL) were prepared in a dry box. The vials were sealed and moved to a fume hood. The two solutions were then transferred through a syringe into the reaction apparatus: the former into a three-neck 100 mL flask and the latter into a liquid addition funnel. The hydrocarbon solution was stirred and an argon stream was passed over the solution (to remove NO/NO_2), while the $NOBF_4$ solution was added dropwise, yielding immediate darkening and partial precipitation of the $BP^{\bullet+}BF_4^-$ as a black solid. At the end of the addition, the mixture was stirred for 2 min. Hexane (50 mL) was added to fully precipitate the $BP^{\bullet+}BF_4^-$, which was then transferred under argon into a centrifuge tube. The solid was collected in a low speed centrifuge. The liquid phase was decanted, equal volumes (ca. 50 mL) of dried CH_2Cl_2 and hexane were added, and centrifugation was repeated. The washing was repeated 3–4 times. The resulting black solid was dried in vacuum for 4 h, weighed, and assayed as before.

Reaction of Radical Cations with Nucleophiles. Reactions in Aqueous Medium. With NaOAc (15 mmol) dissolved in H_2O/CH_3CN (9:1, 7 mL), the radical cation perchlorate (1 mmol) was added as a solid and stirring was continued for 15 min. The acidity of the reaction medium strongly increased with time. At the end of the reaction, the solid was removed by filtration and washed with 100 mL of $CHCl_3/CH_3OH$ mixture (1:1). Unless otherwise specified, the crude mixture obtained by removal of the solvent was chromatographed on a column of silica gel by using gradient mixtures of hexane, benzene, and acetone. The purity of all reaction products was monitored by reverse phase HPLC and TLC prior to NMR spectroscopy and mass spectrometric analysis.

The solid radical cation salt was reacted with H_2O by stirring for 15 min, followed by separation of the reaction products as described above.

Anhydrous Reactions with Organic Nucleophilic Salts. Solid PAH radical cation salts (ca. 50 mg) were weighed in an argon dry box into a one-neck reaction flask and tetraalkylammonium salts into crimp-top vials. Flasks and vials were then sealed with rubber septa and transferred to a fume hood. Dry CH_3CN was added to the nucleophile through a syringe and the mixture was sonicated until a clear solution was obtained. These solutions were generally 0.15–0.20 M in nucleophile. Under positive argon pressure the CH_3CN/nucleophile solution was added through a syringe to the radical cation salt and stirring was applied. The molar ratio of radical cation/nucleophile was always 1:15. Discoloration occurred almost immediately, and the resulting solution became orange-brown with time, sometimes yielding precipitation of solid. The reaction mixture was stirred for 0.5–1 h, mixed with 15–20 mL of THF, and filtered through a Celite pad; solvents were then removed under reduced pressure. Product isolation was carried out as described above. Products were also identified and quantitated by HPLC retention time and comparison of UV spectra with authentic samples.

Results and Discussion

Radical Cation Perchlorates. Sato et al.[12] and Ristagno and Shine[13] previously synthesized the perylene radical cation perchlorate by using CH_2Cl_2 as the solvent. Under similar conditions, but using benzene as the solvent, the synthesis of radical cation perchlorates was extended in our laboratory to BP and some of its

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Table 1. Yields and Iodometric Assays of BP and 6-Substituted BP Radical Cation Perchlorates

radical cation	% isolated yield	% iodometric assay
$BP^{\bullet+}ClO_4^-{\cdot}AgI$	90	51
$6\text{-}FBP^{\bullet+}ClO_4^-{\cdot}AgI$	63	59
$6\text{-}ClBP^{\bullet+}ClO_4^-{\cdot}AgI$	64	50
$6\text{-}BrBP^{\bullet+}ClO_4^-{\cdot}AgI$	62	52
$6\text{-}CH_3BP^{\bullet+}ClO_4^-{\cdot}AgI$	46	69

substituted derivatives. The isolated yields of radical cation perchlorates and the results of iodometric assay used to measure the percent of $BP^{\bullet+}$ in the solid were obtained (Table 1). Elemental analysis confirmed that the radical cation was a complex with AgI (1:1): calc. 40.96% C, 2.06% H, 18.39% Ag, 21.64% I; found 39.63% C, 2.21% H, 18.85% Ag, 22.32% I.

The solvents CH_2Cl_2, CH_3CN, CH_3NO_2 and benzene were tested, and the last found to be the best solvent. To the best of our knowledge, this work represents the first synthesis of BP radical cation in a stable form as a perchlorate, silver iodide-complexed salt. We are well aware of the potential explosion hazard intrinsic to the use of organic perchlorates. Explosion of a sample of thianthrene radical cation during handling has been reported.[14] However, we have carried out approximately 100 preparations of PAH radical cation perchlorates and never encountered any problems. BP radical cation perchlorate is soluble, at least in part, in CH_3CN and CH_3NO_2, sparingly soluble in CH_2Cl_2 and benzene, and insoluble in aliphatic hydrocarbons. Although soluble, the radical cation perchlorate rapidly decomposes in dimethylformamide, as judged by discoloration of the solution. It is generally stated that aromatic hydrocarbon radical cations can react with CH_3CN, yielding acetamidation products of the type ArNHAc.[21] BP radical cation perchlorates stirred in dry CH_3CN under argon formed highly fluorescent products; however, the same products were formed in benzene and CH_2Cl_2, suggesting that acetamido derivatives were not formed. The most abundant of these products was isolated and purified. MS analysis yielded a mass (502 *m/z*) and a formula ($C_{20}H_{22}$) consistent with the structure of a BP dimer. However, NMR analysis showed a very complex shift pattern, suggesting the presence of at least three dimers, most likely the 6-6′, 6-1′ and 6-3′. These dimers are side products detected in every subsequent reaction of the radical cations, and are likely to be already present in the black solid. As mentioned above, elemental analysis shows that the radical cation is complexed 1:1 with AgI. While the elemental analysis assay is useful in determining the stoichiometry of elements present, it cannot distinguish between BP and $BP^{\bullet+}$ in the black solid, since both have identical molecular weights. To determine the percentage of radical cation in the solid, the radical cation complex was reacted with an excess of NaI in CH_3CN (0.5 M solution). Due to its low oxidation potential (anodic peak potential +0.68 V in CH_3CN), iodide ion quantitatively reduces the radical cation to the parent hydrocarbon structure and does not act as a nucleophile. The reaction mixture could then be analyzed for I_2 via $Na_2S_2O_4$ titration; the end-point was detected electrochemically. All radical cation perchlorates were stable for months in solid form, stored in sealed vials under argon at subzero temperatures. In fact, year-old samples showed no appreciable decrease in reactivity.

BP Radical Cation Tetrafluoroborate. Although radical cation complexes adsorbed on AgI tend to be very stable, the presence of the insoluble AgI can cause experimental problems. Thus, synthesis of radical cation salts free of AgI was undertaken. Electrocrystallization at a platinum electrode succeeded in forming PAH radical cation salts in some instances.[21] No stable solid material could be isolated for BP. One-electron oxidation of BP was easily accomplished by tris(p-bromophenyl)aminium hexachloroantimonate, according to the procedure by Bauld et al.[22] However, due to the presence of nucleophilic chloride ions in solution, BP was largely converted into 6-ClBP. Use of nitrosonium tetrafluoroborate, $NOBF_4$, previously used to prepare radical cation tetrafluoroborates of aromatics and heteroaromatics, was then considered.[20,21]

Using the original experimental procedure, nitrosation/nitration of the aromatic substrate during formation of the radical cation could not be prevented. However, with slightly modified conditions the synthesis of BP radical cation tetrafluoroborate was achieved in 90% yield that contained 87% radical cation as determined by iodometric assay. Elemental analysis of the $BP^{\bullet+}BF_4^-$ complex was difficult due to the tendency of tetrafluoroborate salts to lose BF_3 when placed under vacuum.[17] When the sample was dried overnight under high vacuum (0.1 mm Hg) elemental analysis showed almost complete loss of boron: 74.54% C, 3.99% H, 9.45% F, 0.095% B. When the sample was dried for only 1 h at high vacuum, the analysis showed an increase in boron: 78.31% C, 4.37% H, 10.31% F, 1.06% B. Neither analysis agreed with the theoretical values for $BP^{\bullet+}BF_4^-$: 70.84% C, 3.57% H, 3.19% B, 22.41% H. Thus, reactions involving $BP^{\bullet+}BF_4^-$ are best conducted with freshly prepared solutions. BP radical cation is soluble in CH_3CN, partly soluble in CH_2Cl_2 or benzene, and insoluble in aliphatic hydrocarbons. Like the radical cation perchlorates, the radical cation tetrafluoroborates could be stored for extended periods of time under argon at subzero temperatures.

Reaction with Nucleophiles. To understand some of the chemical properties of these intermediates, reactions with various nucleophiles were undertaken. Radical cations can react with nucleophiles according to two different mechanisms: electron transfer and/or nucleophilic addition. The former occurs when the oxidation potential of the nucleophile is lower than that of the hydrocarbon precursor of the radical cation. Thus, the radical cation is capable of oxidizing the nucleophile (generally, in the case of an anion, to a radical or neutral species). The latter mechanism occurs when the oxidation potential of the nucleophile is higher than the parent hydrocarbon structure. In this case the radical cation undergoes nucleophilic addition, yielding a substituted derivative. When the parent hydrocarbon and the nucleophile have comparable oxidation potentials, both mechanisms can, in principle, occur at the same time. Therefore, all hydrocarbons used in this study were analyzed by cyclic voltammetry. Their anodic peak potentials were measured and compared to the potentials obtained for selected nucleophilic species (Table 2).

Thus, it is reasonable to assume that fluoride and acetate ions, because of their high anodic peak potentials, react with the radical cations of all five hydrocarbons exclusively through the nucleophilic substitution pathway. On the contrary, nitrite ion most likely undergoes

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Table 2. Potentials of BP, BP Derivatives, and Selected Nucleophiles

hydrocarbon	anodic peak potential[a]	nucleophile	anodic peak potential
BP	+1.62	$(CH_3)_4NF{\cdot}2HF$	>+2.50
6-FBP	+1.57	$(CH_3)_4NOAc$	+1.97
6-ClBP	+1.65	$(CH_3)_4NCl$	+1.38
6-BrBP	+1.65	$(CH_3)_4NSCN$	+1.13
6-CH_3BP	+1.34	$(CH_3)_4NNO_2$	+0.72
		NaI	+0.68

[a] Potentials were measured by using a Pt working electrode against an Ag/AgCl reference electrode in CH_3CN containing 0.2 M $(Bu)_4NBF_4$ at a scan rate of 200 mV/s.

electron transfer, reducing the radical cations to their parent hydrocarbons and, in turn, being oxidized to nitrite radical or even to neutral nitrogen dioxide. Evidence for the presence of the latter species was indeed obtained experimentally. When nitrite salt was added to a solution of BP radical cation perchlorate, a brown gas immediately formed above the solution, corresponding to the formation of nitrogen dioxide. This also resulted in formation of nitrated BP derivatives, namely 6- and 1-nitroBP, as determined by comparison with authentic samples. In fact, as electron transfer occurs, BP radical cation is reduced to the parent BP and nitrite ion is oxidized to nitrogen dioxide. The latter can then carry out electrophilic nitration of the electron-rich neutral hydrocarbon.

Further study of radical cation perchlorates and tetrafluoroborates was restricted to the acetate and fluoride nucleophiles. The five hydrocarbons considered in this work were previously studied by one-electron oxidation catalyzed by manganic acetate, a model system in which radical cations generated by oxidation are immediately trapped by acetate ion, yielding acetoxy-substituted products.[9] It was, therefore, particularly meaningful to study the reactivity of preformed radical cations in comparison to the same species generated *in situ* in the presence of the nucleophile. Fluoride ion was tested with BP and 6-ClBP radical cations for the important synthetic implications of these reactions.

Nucleophilic reactions were conducted in both aqueous and anhydrous systems. The former employed water-soluble nucleophiles (inorganic salts, such as sodium acetate) in an aqueous/organic medium (CH_3CN/H_2O 1:9) to solubilize both the radical cation salts and the nucleophiles. The latter used organic nucleophilic salts (tetraalkylammonium salts) in organic anhydrous medium, CH_3CN.

The major drawback to the aqueous medium is that water itself is nucleophilic and reacts with radical cations, yielding predominantly BP diones and other hydroxylated products. Thus, all reactions were contaminated by the competing reaction with water. Nonetheless, this system deserves some attention, in view of future studies. To react radical cations with nucleophiles of biological macromolecules (i.e., proteins, DNA), partially aqueous solutions must be used. The results of nucleophilic substitution of the radical cation perchlorates of BP, 6-halogeno derivatives and 6-CH_3BP in aqueous medium are summarized in Table 3. The only products obtained from the reaction of H_2O with the radical cation perchlorates of BP and 6-halogeno derivatives were BP 1,6-, 3,6-, and 6,12-dione. The only product obtained from 6-$CH_3BP^{\bullet+}ClO_4^-$ was 6-CH_2OHBP. The data indicate that nucleophilic attack of H_2O occurs at C-6 in the radical cation of BP and 6-halogeno derivatives

Table 3. Nucleophilic Substitution on Radical Cations of BP and 6-Substituted BP by H_2O or NaOAc in CH_3CN/H_2O (1:9)

	products formed with two nucleophiles[a,b]			
radical cation perchlorate	H_2O	(% yield)	NaOAc	(% yield)
$BP^{\bullet+}ClO_4^-$	diones	29	6-OAcBP	11
			diones	29
6-$FBP^{\bullet+}ClO_4^-$	diones	31	6-OAcBP	1
			diones	35
6-$ClBP^{\bullet+}ClO_4^-$	diones	14	(1,3)-OAc-6-ClBP	3
			diones	12
6-$BrBP^{\bullet+}ClO_4^-$	diones	10	diones	12
6-$CH_3BP^{\bullet+}ClO_4^-$	6-CH_2OHBP	5	6-CH_2OHBP	5

[a] The remainder of the product in all reactions is the parent PAH. [b] NMR spectra for all products have been published.[9]

and at the 6-methyl group in 6-$CH_3BP^{\bullet+}ClO_4^-$. These results are in agreement with those obtained by manganic oxidation of the same PAH[9] or by anodic oxidation of BP in H_2O.[23] In reactions of the radical cation perchlorates of BP and 6-halogeno derivatives with the other nucleophile, NaOAc, BP diones were still the major products formed, because H_2O was present as solvent. For the same reason, 6-CH_2OHBP was the major product from 6-$CH_3BP^{\bullet+}ClO_4^-$. The relatively weak nucleophile AcO^- displayed high selectivity with $BP^{\bullet+}ClO_4^-$ at C-6, the position of greatest charge density in the $BP^{\bullet+}$.[9,24]

The parent hydrocarbon is the major species observed when radical cations of both perchlorates and tetrafluoroborates are reacted with nucleophiles. The mechanism proposed by Ristagno and Shine[13] shows that the addition of H_2O to the $BP^{\bullet+}$ occurs with a stoichiometry of six radical cations for every molecule of quinone formed. The yield of diones is higher than theoretically calculated because some of the oxygenated intermediates in the route to quinones, starting with 6-OHBP, can be autoxidized to quinones without involvement of $BP^{\bullet+}$.[13]

In principle, the anhydrous medium would be expected to yield effective nucleophilic reactions. However, the limitation in this case is the tendency of radical cations to form dimeric products. Two different procedures were used for these reactions, one employing solid, previously isolated radical cation salts and the other using freshly prepared solutions containing radical cation salts just synthesized. Similar results were obtained with either method. The results of nucleophilic reactions of both the perchlorate and tetrafluoroborate radical cations are shown in Table 4. For both AcO^- and F^- nucleophiles, the yield of substituted products was higher than obtained in reactions performed in an aqueous environment. Reaction with AcO^- produced small amounts of diacetates as secondary products, presumably from oxidation of the initial acetate product. Although the $BP^{\bullet+}BF_4^-$ black solid contained a higher percentage of radical cation (as determined by iodometric titration), reactions with both AcO^- and F^- showed no improvement over those with the $BP^{\bullet+}ClO_4^-{\cdot}AgI$ complex. This presumably occurs because $BP^{\bullet+}BF_4^-$ is less stable in CH_3CN, completely decomposing to BP dimers in ca. 15 min. Formation of quinones was generally 1% or less for both perchlorate and tetrafluoroborate salts. However, dimers were detected by both TLC and HPLC.

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Table 4. Nucleophilic Substitution on Radical Cations of BP and 6-Substituted BP by Selected Nucleophiles under Anhydrous Conditions

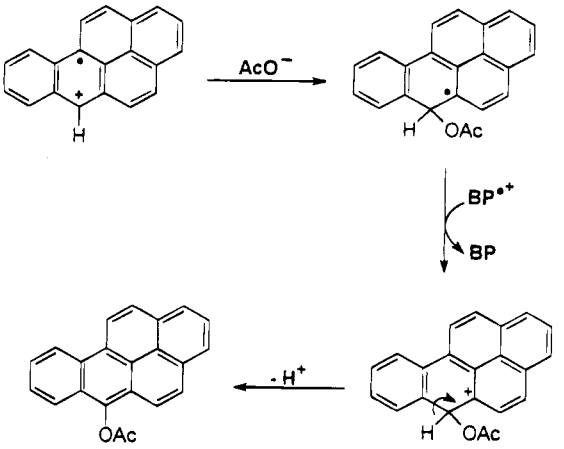
	products formed with two nucleophiles[a]			
radical cation perchlorate	$(CH_3)_4NOAc$	(% yield)	$(CH_3)_4NF\cdot 2HF$	(% yield)
$BP^{\bullet+}ClO_4^-$	6-OAcBP	17	6-FBP	25
	diacetates	3		
	diones	1		
$6\text{-}CH_3BP^{\bullet+}ClO_4^-$	$6\text{-}CH_2OAcBP$	6		0
	$6\text{-}CH_2OHBP$	17		
$BP^{\bullet+}BF_4^-$	6-OAcBP	18	6-FBP	20
	diacetates	2		
	diones	3		

[a] The remainder of the product in all reactions is the parent PAH and dimers.

The ECE mechanism (electron transfer, chemical attack, electron transfer) has been invoked to explain anodic substitution and addition reactions of aromatic hydrocarbons.[25] A similar mechanism can be hypothesized for the formation of 6-OAcBP via nucleophilic attack of AcO^- on $BP^{\bullet+}$ (Scheme 1). Oxidation of BP to form the radical cation involves the first electron transfer. Reaction of AcO^- at C-6 of BP represents the chemical attack. The radical generated is further oxidized by another molecule of $BP^{\bullet+}$ in the second electron transfer. The latter is reduced to BP, whereas the acetoxy-substituted radical is oxidized to an arenium ion, which by loss of a proton yields 6-OAcBP. When nucleophilic attack of AcO^- on $BP^{\bullet+}$ was conducted under anhydrous conditions, formation of diacetate products was observed, albeit in low yields (Table 4). The diacetates are formed when the initial 6-OAcBP is further oxidized by $BP^{\bullet+}$, repeating the process described above and further consuming $BP^{\bullet+}$.

(25) Manning, G.; Parker, V. D.; Adams, R. N. *J. Am. Chem. Soc.* **1969**, *91*, 4584–4585.

Scheme 1. Proposed Mechanism for Formation of 6-OAcBP from $BP^{\bullet+}$ and AcO^-.



Conclusions

Radical cations of BP and 6-substituted derivatives were synthesized by reaction of the PAH in benzene with I_2 and $AgClO_4$, and reaction in CH_2Cl_2/CH_3CN with $NOBF_4$. The radical cation perchlorates were isolated as complexes with AgI, whereas the tetrafluoroborates were free of AgI and, therefore, displayed greater solubility in organic solvents; both were stable for prolonged periods when stored at subzero temperatures under argon. The pattern of nucleophilic substitution, when these radical cations are reacted with nucleophiles of various strength, reflects the distribution of positive charge localization in the radical cation. High selectivity for the position of greatest charge localization, C-6, is displayed by H_2O, AcO^- and F^-.

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