This information is of great relevancy in preparing DB[a,l]P-nucleoside adducts with the purpose of determining the involvement of one-electron oxidation in the biological formation of adducts. Similar studies have demonstrated that B[a]P adducts are formed predominantly by one-electron oxidation in biological systems.[16]

Second, the DB[a,e]P radical cation is rather inert to nucleophilic substitution. This lack of reactivity presumably derives from a relatively high oxidation potential combined with steric hindrance at the *meso*-anthracenic position, which still possesses a fair degree of charge localization. Thus, formation of DB[a,e]P-DNA adducts is expected to be inefficient.

Third, DB[a,h]P, DB[a,i]P, and anthanthrene basically show similar behavior during oxidation by $Mn(OAc)_3$. Their rates of reaction are extremely fast, and disubstitution products are also present. This reflects the fact that all three PAH possess two identical *meso*-anthracenic positions available for nucleophilic substitution and relatively low anodic peak potentials.

Acknowledgment. This research was supported by Public Health Service Grants R01CA44686 and P01CA49210 from the National Cancer Institute and by institutional grant CA36727 from the National Cancer Institute. Mass spectral determinations were performed at the Midwest Center for Mass Spectrometry at the University of Nebraska in Lincoln.

Supplementary Material Available: ^1H NMR spectra of the products (18 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(16) Devanesan, P. D.; RamaKrishna, N. V. S.; Todorovic, R.; Rogan, E. G.; Cavalieri, E. L.; Jeong, H.; Jankowiak, R.; Small, G. J. *Chem. Res. Toxicol.* **1992**, *5*, 302-309.

Electrophilic Substitution of Methylene-Bridged Polycyclic Aromatic Hydrocarbons

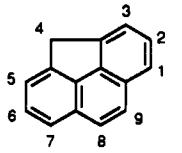
Elias Abu-Shqara, ChengXi Yang, and Ronald G. Harvey*

Ben May Institute, University of Chicago, Chicago, Illinois 60637

Received January 13, 1992

The electrophilic bromination and formylation of the methylene-bridged polycyclic aromatic hydrocarbons 11*H*-benz[*bc*]aceanthrylene (**2**), 4*H*-cyclopenta[*def*]chrysene (**3**), 13*H*-dibenz[*bc,l*]aceanthrylene (**4**), and 4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (**5**) were investigated. All reactions proceeded with high regioselectivity to afford predominantly a single major isomeric product. The sole exception was bromination of **3** which gave a small amount of a second isomeric product. The sites of electrophilic substitution were correlated with theoretical predictions from semiempirical molecular orbital calculations using the MNDO method. The observed sites of electrophilic substitution were in excellent agreement with the theoretical predictions in the cases of **2**-**4**. However, in the case of **5**, substitution took place in the 6-position, whereas the site predicted to be most reactive is the 5-position. In addition, the aryl aldehyde products were converted into the corresponding methyl derivatives for studies of their potential carcinogenicity.

Methylene-bridged polycyclic aromatic hydrocarbons (PAHs) are principal components of coal tar and crude petroleum, and significant levels occur as environmental pollutants.[1] However, few PAHs of this class are known, and their chemical properties are relatively unexplored.[2,3] As part of a program to investigate the chemistry and carcinogenic properties of the methylene-bridged polyarenes, we reported recently the syntheses of several PAHs of this class.[4] Syntheses of additional examples have been described by other investigators.[5] The available evidence suggests that the sites of electrophilic substitution of bridged hydrocarbons may differ significantly from those of the related unbridged polyarenes. Thus, electrophilic bromination,[6] acylation,[7] and nitration[8] of the prototype methylene-bridged hydrocarbon 4*H*-cyclopenta[*def*]-phenanthrene (**1**) take place preferentially in the 1-position. In contrast, analogous reactions of the parent aromatic ring system, phenanthrene, occur predominantly in the 9-position.



1

We now report electrophilic bromination and formylation of the methylene-bridged PAHs 11*H*-benz[*bc*]aceanthrylene (**2**), 4*H*-cyclopenta[*def*]chrysene (**3**), 13*H*-dibenz[*bc,l*]aceanthrylene (**4**), and 4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (**5**) (Figure 1). These hydrocarbons were synthesized by methods described previously.[4a-c] The observed sites of electrophilic substitution were correlated with theoretical predictions from semiempirical molecular

(1) (a) Blumer, M. *Sci. Am.* **1976**, *234*, 35. (b) Adams, J. D.; LaVoie, E. J.; Hoffmann, D. *J. Chromatogr. Sci.* **1982**, *20*, 274.
(2) Harvey, R. G. *Polycyclic Aromatic Hydrocarbons: Chemistry and Carcinogenesis*; Cambridge University Press: Cambridge, U.K., 1991.
(3) Clar, E. *Polycyclic Hydrocarbons*; Academic Press: New York, 1964.
(4) (a) Yang, C.; Harvey, R. G. *Tetrahedron*, in press. (b) Harvey, R. G.; Pataki, J.; Cortez, C.; DiRaddo, P.; Yang, C. *J. Org. Chem.* **1991**, *56*, 1210. (c) Ray, J.; Harvey, R. G. *J. Org. Chem.* **1983**, *48*, 1352. (d) Young, R. J.; Harvey, R. G. *Tetrahedron Lett.* **1989**, *30*, 6603. (e) Yang, C.; Harvey, R. G. *Poly. Arom. Compds.*, in press.
(5) (a) Lee-Ruff, E.; Kruk, H.; Katz, M. *J. Org. Chem.* **1984**, *49*, 553. (b) Lee-Ruff, E.; Kruk, H. *Poly. Arom. Compds.* **1991**, *1*, 191. Nagel, D. L.; Kupper, R.; Antonson, K.; Wallcave, L. *J. Org. Chem.* **1977**, *42*, 3626.
(6) Yoshida, M.; Minabe, M.; Suzuki, K. *J. Org. Chem.* **1979**, *44*, 3029.
(7) Yoshida, M.; Hishida, K.; Minabe, M.; Suzuki, K. *J. Org. Chem.* **1980**, *45*, 1783.
(8) Yoshida, M.; Nagayama, S.; Minabe, M.; Suzuki, K. *J. Org. Chem.* **1979**, *44*, 1915.

0022-3263/92/1957-3312$03.00/0

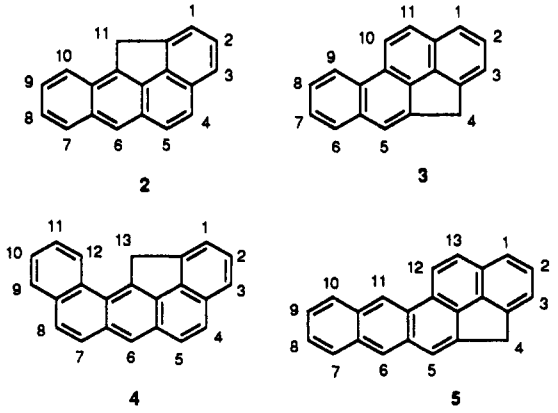


Figure 1. Structural formulae and numbering of methylene-bridged polyarenes: 11*H*-benz[*bc*]aceanthrylene (**2**), 4*H*-cyclopenta[*def*]chrysene (**3**), 13*H*-dibenz[*bc,l*]aceananthrylene (**4**), 4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (**5**).

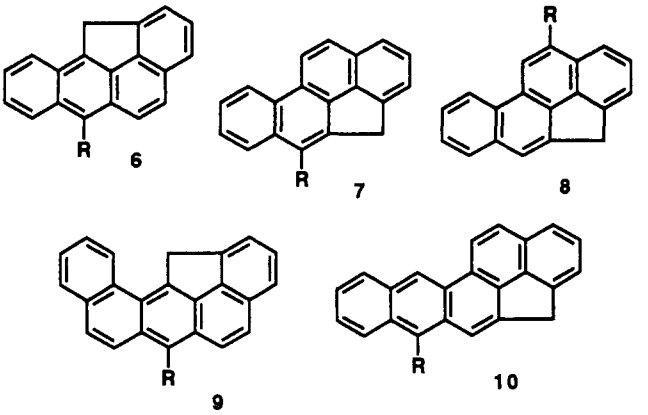
orbital calculations using the MNDO method.[9] The aryl aldehyde products were converted into the corresponding methyl derivatives for studies of their potential carcinogenicity.

Results

Bromination. Brominations of hydrocarbons **2–5** were carried out with bromine in CH_2Cl_2 at room temperature. The reactions were worked up immediately after loss of color which required only 10–15 min. In all cases the reactions were highly regioselective, affording predominantly a single isomeric monobromo-substituted product. The positions of substitution were determined by direct analysis of the high-resolution proton NMR spectrum of the products and confirmed by conversion of the brominated products to their deuterated analogs by reduction with lithium aluminum deuteride and comparison of the NMR spectra of the deuterated derivatives with those of the previously assigned parent polyarenes. This technique was utilized previously for structural assignment of the products of electrophilic bromination of polycyclic fluoranthenes.[10]

Bromination of 11*H*-benz[*bc*]aceanthrylene (**2**) gave a single major monobromo isomer in 95% yield. Analysis of its 300-MHz ^{1}H NMR spectrum showed the absence of the singlet peak at δ 8.33 ppm corresponding to the H_6 peak of **2** and the downfield shift of the adjacent H_5 and H_7 signals from δ ~7.80 and 8.21 ppm, respectively, to δ 8.01 and 8.64 ppm, respectively. On this basis, the structure of the product is assigned as 6-bromo-11*H*-benz[*bc*]aceanthrylene (**6a**). Comparison of the NMR spectrum of the monodeuterio analog obtained from the bromo compound with that of the parent hydrocarbon confirmed this structural assignment. The spectra closely matched one another with the only significant difference being the virtual disappearance of the H_6 signal in the spectrum of deuterated derivative.

Bromination of 4*H*-cyclopenta[*def*]chrysene (**3**) furnished a 10:1 mixture of 5-bromo- and 11-bromo-4*H*-cyclopenta[*def*]chrysene (**7a** and **8a**) in 85% yield. Attempts to separate these isomers by HPLC were not successful. The structural assignments were deduced from the proton NMR spectrum of the mixture. The major component showed the absence of the characteristic singlet



a: R = Br; **b**: R = D; **c**: R = CHO; **d** R = CH_3

at δ 7.97 for the H_5 signal of the parent hydrocarbon, indicating substitution in the 5-position. The marked downfield shift of the H_6 signal from δ 8.06 to ~8.55 was consistent with this assignment. This was further supported by the lack of change in the H_1, H_{10}, and H_{11} peaks, indicating that substitution has not taken place in the alternative 11-position (equivalent to the 6-position of chrysene). The most revealing feature of the spectrum of the minor component was the appearance of the H_{10} signal as a singlet rather than a doublet shifted downfield from δ 8.52 to 8.75, allowing its assignment as 11-bromo-4*H*-cyclopenta[*def*]chrysene (**8a**). These assignments were confirmed by analysis of the NMR spectra of the deuterated products which closely matched that of **3** with the only significant differences being the expected decrease of the H_5 peak for **7a** and the H_{11} signal for **8a**.

Bromination of 13*H*-dibenz[*bc,l*]aceanthrylene (**4**) afforded a single monobromo derivative in 87% yield. Its ^{1}H NMR spectrum was consistent with substitution in the 6-position. Most notably, the singlet peak at δ 8.31 for the H_6 proton of the parent hydrocarbon was lacking, and the adjacent H_5 and H_7 proton signals were shifted downfield to δ 8.10 and 8.55, respectively. Further confirmation for the assignment of this product as **9a** was provided by the NMR spectrum of the deuterated product **9b**, which was identical with that of **4** except for a marked decrease of the singlet peak at δ 8.31 for the H_6 proton.

Bromination of 4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (**5**) also furnished a single monobromo derivative (91% yield). This was assigned as 6-bromo-4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (**10a**) on the basis of its ^{1}H NMR spectrum which showed loss of the singlet peak at δ 8.55 for the H_6 proton of **5** and downfield shift of the H_5 singlet and the H_7 doublet proton signals from the region δ 7.66–8.20 in **5** to δ 8.54–8.58 in the brominated product (it was not possible to assign precise chemical shifts due to overlapping). It was also clear that substitution had not taken place in the 5-position, since this would have resulted in a shift in only one peri hydrogen peak (H_6), and this was contrary to observation. Assignment of **10a** was confirmed by analysis of the NMR spectrum of its deuterated derivative which closely matched that of **5** except for a large decrease in the H_6 proton signal.

Formylation. Formylations of PAHs **2–5** were carried out with 1,1-dichloromethyl methyl ether and $TiCl_4$ in methylene chloride at 0 °C by a modification of the method of Rieche.[11] Formylation was highly regioselective in all cases, affording a single monoaldehyde product. The

(9) Hites, R.; Simonsick, W. J., Jr. *Calculated Molecular Properties of Polycyclic Aromatic Hydrocarbons*; Elsevier: New York, 1987.
(10) Minabe, M.; Cho, B. P.; Harvey, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 3809.
(11) Reiche, A.; Gross, H.; Hoft, E. *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. V, p 49. Reiche, A.; Gross, H.; Hoft, E. *Chem. Ber.* **1960**, *93*, 88.

positions of substitution were identical with the principal sites of bromination of these PAHs.

Formylation of **2** furnished a single major aryl aldehyde (87% yield) identified as 6-formyl-11*H*-benz[*bc*]aceanthrylene (**6c**). Its 300-MHz ^{1}H NMR spectrum showed a characteristic aldehyde peak at low field (δ 11.27), absence of the singlet peak at δ 8.33 ppm corresponding to the H_6 peak of **2**, and the strong downfield shift of the adjacent H_5 and H_7 proton signals from $\delta \sim 7.60$ and ~ 8.21, respectively, to δ 8.56 and 9.16, respectively.

Formylation of **3** gave a single aldehyde product (71%) identified as 5-formyl-4*H*-cyclopenta[*def*]chrysene (**7c**). Analysis of its ^{1}H NMR spectrum showed the presence of an aldehyde peak at low field (δ 10.94) and the absence of the singlet at δ 7.97 for the H_5 signal of **3**, indicating substitution in the 5-position. Assignment as **7c** was supported by the strong downfield shift of the H_6 signal from δ 8.06 to 9.19 and the relatively minimal changes in the chemical shifts and couplings of the H_1, H_{10}, and H_{11} peaks, indicating that substitution had not occurred in the 11-position (equivalent to the 6-position of chrysene).

Formylation of **4** also yielded a single product (85%) which was identified as 6-formyl-13*H*-dibenz[*bc*,*l*]aceanthrylene (**9c**). NMR analysis revealed the presence of an aldehyde peak at δ 11.02, the absence of a singlet at δ 8.31 for the H_6 signal of **4**, and the downfield shift of the H_5 and H_7 signals to δ 8.42 and 8.55, respectively. This pattern is only consistent with substitution in the 6-position and structure **9c**.

Finally, formylation of **5** furnished 6-formyl-4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (**10c**) (84%) as the sole product. This assignment was supported by the presence of an aldehyde peak at δ 11.40 and the absence of the singlet at δ 8.55 for the H_6 signal of **5**. Additional support was provided by the strong downfield shift of the H_5 singlet and the H_7 doublet signals from the region δ 7.66–8.20 in **5** to δ 8.79 and 8.74 in **10c**. It was also clear that substitution had not taken place in the 5-position, since this have resulted in a shift in only one peri hydrogen peak (H_6), contrary to the observed finding.

Methyl Derivatives. Methyl substitution in appropriate molecular regions of unbridged polyarenes frequently results in substantial enhancement of carcinogenic activity.[2,12,13] Thus, while benz[*a*]anthracene, dibenz[*a*,*j*]anthracene, and chrysene exhibit only weak borderline activity, 7-methylbenz[*a*]anthracene, 7-methyldibenz[*a*,*j*]anthracene, and 5-methylchrysene are highly potent carcinogens. It is unknown whether methyl substitution of bridged hydrocarbons results in a similar enhancement of biological activity. Therefore, it was of interest to convert the bridged aryl aldehydes **6c–10c** into the corresponding methyl derivatives, **6d–10d**, for biological testing. This was readily accomplished by deoxygenation with sodium cyanoborohydride in the presence of zinc iodide.[14]

Discussion

Electrophilic substitution of the methylene bridged hydrocarbons **2–5** proceeded with high regioselectivity to afford predominantly a single major isomeric product from both bromination and formylation. Only in the case of bromination of **3** was a small amount of a second isomer isolated. It is possible that small percentages of minor isomers were produced in other cases but were not detected.

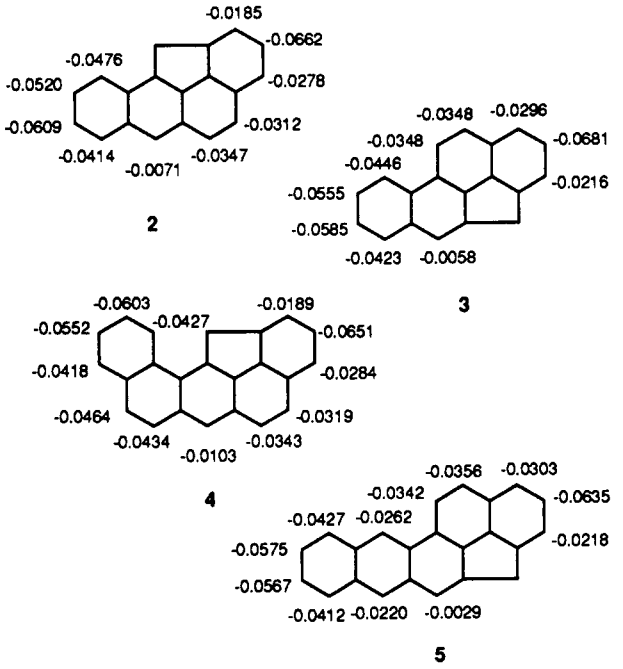


Figure 2. Net atomic charges calculated by the semiempirical MNDO method.[9]

The sites of substitution of methylene bridged polyarenes are theoretically predictable by theoretical molecular orbital methods using the semiempirical MNDO method.[9] However, the accuracy of the predictions has not been determined due to the deficiency of published information from experimental studies. For the hydrocarbons **2–5**, the calculated values of the net atomic charges for all ring positions are given in Figure 2. According to the theory, the carbon atoms with the lowest charges are predicted to be the most reactive for electrophilic substitution. It is assumed in these calculations that the PAH ring systems are planar. This is likely, except in the case of **4** wherein there is likely strong steric interaction between the benzo ring of **4** and the methylene bridge. In this respect **4** closely ressembles 12-methyl- and 7,12-dimethylbenz[*a*]anthracene which are known to be distorted from planarity.[15] The experimentally observed sites of bromination and formylation in the cases of **2–4** are in excellent agreement with the theoretical predictions. In the case of **2** and **4**, the net atomic charges are lowest in the 6-positions, –0.0071 and –0.0103, respectively, and this is the observed exclusive site of substitution. In the case of **3**, the lowest atomic charge (–0.0058) is in the 5-position, and it is the principal site of bromination and formylation, but a small amount of bromination also takes place in the 11-position remote from the bridge. This may be partially a consequence of steric crowding in the 5-position. However, in the case of **5**, the observed site of substitution is the 6-position, whereas the site predicted to be most reactive is the 5-position. The net atomic charges at these positions are –0.0220 and –0.0029, respectively. This may be partially a steric effect due to the proximity of the methylene adjacent to the predicted size of substitution. However, no similar effect was observed in the case of **3**

(12) DiGiovanni, J.; Diamond, L.; Harvey, R. G.; Slaga, T. J. *Carcinogenesis* **1983**, *4*, 403–407.

(13) Hecht, S. S.; Amin, S.; Melikian, A.; LaVoie, E. J.; Hoffmann, D. In *Polycyclic Hydrocarbons and Carcinogenesis*; Harvey, R. G., Ed.; ACS Monograph 283; American Chemical Society: Washington, D.C., 1985; pp 85–105.

(14) Lau, C. K.; Dufresne, C.; Belanger, P. C.; Pietre, S.; Scheigetz, J. *J. Org. Chem.* **1986**, *51*, 3038.

(15) Glusker, J. P. In *Polycyclic Hydrocarbons and Carcinogenesis*; Harvey, R. G., Ed.; ACS Monograph 283; American Chemical Society: Washington, D.C., 1985; pp 125–185.

which undergoes facile substitution adjacent to the methylene bridge. The sites of substitution of **2–4** also accord with the sites of substitution of the parent polycyclic ring systems.[2,3] Information on the electrophilic substitution of **5** is not available, but chromic acid oxidation occurs at the 6-position,[2,3] the observed site of substitution.

Experimental Section

General Methods. The proton NMR spectra were obtained on a Varian EM360 spectrometer or the University of Chicago 300-MHz NMR spectrometer in $CDCl_3$ with tetramethylsilane as internal standard unless stated otherwise. Integration was consistent with all structural assignments. Ultraviolet spectra were taken on a Perkin-Elmer Lambda 5 spectrometer.

NMR Spectral Data of 2–5. **2**: (300 MHz) δ 8.33 (s, 1, H_6), 8.21 (overlapping ds, 2, $H_{7,10}$), 7.75–7.87 (m, 4, $H_{1,3,4,5}$), 7.60–7.66 (m, 3, $H_{2,8,9}$), 4.60 (s, 2, CH_2). **3**: δ 8.67 (d, 1, H_9, J = 8.04 Hz), 8.52 (d, 1, H_{10}, J = 8.84 Hz), 8.06 (d, 1, H_6, J = 7.44 Hz), 8.00 (d, 1, H_{11}, J = 8.84 Hz), 7.97 (s, 1, H_5), 7.88 (t, 1, H_1), 7.60–7.72 (m, 4, Ar), 4.43 (s, 2, CH_2). **4**: δ 8.93 (d, 1, H_{12}, J = 8.19 Hz), 8.31 (s, 1, H_6), 7.63–7.98 (m, 10, Ar), 4.87 (s, 2, CH_2). **5**: δ 9.17 (s, 1, H_{11}), 8.63 (d, 1 H_{12}, J = 8.76 Hz), 8.55 (s, 1, H_6), 7.66–8.20 (m, 5, Ar), 7.55–7.60 (m, 4, Ar), 4.46 (s, 2, CH_2).

Bromination. The general procedure may be illustrated by the reaction of **2**. To a solution of **2** (100 mg, 0.41 mmol) in 5 mL of dry CH_2Cl_2 at room temperature was added a solution of 0.83 mL of Br_2 (0.5 M in CH_2Cl_2) over 10 min. The solution was stirred for an additional 10 min, 20 mL of CH_2Cl_2 was added, and the mixture was washed with 50 mL of 50% aqueous $Na_2S_2O_5$. The organic layer was separated, washed again with water, and dried over $MgSO_4$. Evaporation of the solvent gave pure 6-bromo-11*H*-benz[*bc*]aceanthrylene (**6a**) (124 mg, 95%), mp 175 °C (cyclohexane): NMR δ 8.64 (m, 1, H_7), 8.14 (m, 1, H_{10}), 8.01 (d, 1, H_5, $J_{4,5}$ = 9.2 Hz), 7.74–7.85 (m, 3, $H_{1,3,4}$), 7.60–7.68 (m, 3, $H_{2,8,9}$), 4.47 (s, 2, CH_2). Anal. Calcd for $C_{19}H_{11}Br$: C, 71.49; H, 3.47; Br, 25.03. Found: C, 71.83; H, 3.66; Br, 24.81.

5-Bromo- and 11-Bromo-4*H*-cyclopenta[*def*]chrysene (7a and 8a). Bromination of **3** (300 mg, 1.25 mmol) by the same procedure (reaction time 15 min) afforded 340 mg (85%) of a 10:1 mixture of **7a** and **8a** (based on the ^1H NMR spectrum), mp 156–158 °C. The ^1H NMR spectrum of the major product **7a** showed the absence of the singlet at δ 7.97 assigned to H_5 of **3** and the shift of the adjacent H_6 signal downfield from δ 8.06 to ~8.55. Significantly, the H_{11}, H_1, and H_{10} peaks of the major component remained essentially unchanged, indicating that substitution has not taken place in the 11-position. The minor product **8a** was distinguished by a small shift of its methylene proton signal to higher field (δ 4.46 vs 4.43) and the appearance of H_{10} as a singlet shifted downfield to δ 8.75. Anal. Calcd for $C_{19}H_{11}Br$: C, 71.49; H, 3.47; Br, 25.03. Found: C, 71.22; H, 3.52; Br, 24.91.

6-Bromo-13*H*-dibenz[*bc*,*l*]aceanthrylene (9a). Bromination of **4** (100 mg, 0.34 mmol) by the same procedure (reaction time 15 min) afforded **9a** (110 mg, 87%): yellow needles, mp 240–242 °C (benzene): NMR δ 8.87 (d, 1, H_{12}, J = 8.3 Hz), 8.55 (d, 1, H_7, $J_{7,8}$ = 9.1 Hz), 8.10 (d, 1, H_5, $J_{4,5}$ = 9.0 Hz), 7.94 (dd, 1, H_9, $J_{9,10}$ = 9.0 Hz), 7.88 (d, 1, H_8, $J_{7,8}$ = 9.1 Hz), 7.67–7.86 (m, 6, Ar), 4.75 (s, 2, CH_2). Anal. Calcd for $C_{23}H_{13}Br$: C, 74.81; H, 3.54; Br, 21.64. Found: C, 74.58; H, 3.62; Br, 21.52.

6-Bromo-4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (10a). Bromination of **5** (100 mg, 0.34 mmol) by the same procedure (reaction time 15 min) afforded **10a** (116 mg, 91%), yellow-green needles, mp 225–227 °C (benzene): NMR δ 9.06 (s, 1, H_{11}), 8.54–8.58 (m, 3, $H_{5,7,12}$), 8.07 (d, 1, H_{10}, $J_{9,10}$ = 8.0 Hz), 8.01 (d, 1, H_{13}, $J_{12,13}$ = 8.8 Hz), 7.86 (d, 1, H_1, $J_{1,2}$ = 7.2 Hz), 7.56–7.66 (m, 4, Ar), 4.40 (s, 2, CH_2). Anal. Calcd for $C_{23}H_{13}Br$: C, 74.81; H, 3.54; Br, 21.64. Found: C, 74.55; H, 3.68; Br, 21.38.

Preparation of Deuterated Derivatives. The preparation of 6-deuterio-11*H*-benz[*bc*]aceanthrylene (**6b**) is typical. To a suspension of $LiAlH_4$ in 5 mL of refluxing anhydrous THF under an argon atmosphere was added a solution of **6a** (100 mg, 0.31 mmol) in 5 mL of dry THF. The color became blue. The mixture was heated at reflux for 12 h and then cooled in an ice bath, and reaction was quenched by the addition of ice. Ether (30 mL) was added and a solution of 20% NaOH. The usual workup afforded **6b** (62 mg, 82%) with ~60% deuterium incorporation, mp 124–125 °C. The NMR spectrum of **6b** closely matched that of **2** except for the marked decrease of the singlet peak at δ 8.33.

Formylation. The general procedure may be illustrated by the formylation of **2**. A solution of **2** (143 mg, 0.59 mmol) in 10 mL of dry under argon was cooled to 0 °C, 1.19 mL of a solution of $TiCl_4$ (1.0 M in CH_2Cl_2) was added, and the solution turned blue. To this solution was added 0.1 mL of Cl_2CHOCH_3 over 10 min. The resulting solution was stirred for 1 h at 0 °C and for an additional 2 h at room temperature and then cooled in an ice bath, and 5 mL of cold 10% HCl and 20 mL of CH_2Cl_2 were added. The organic layer was washed with water, dried, evaporated to dryness, and crystallized from cyclohexane to afford 6-formyl-11*H*-benz[*bc*]aceanthrylene (**6c**) (135 mg, 85%) as pale yellow needles, mp 166 °C (cyclohexane): IR (Nujol) 1600 cm^{-1} (CHO); NMR δ 11.27 (s, 1, CHO), 9.16 (d, 1, H_7, J = 8.9 Hz), 8.56 (d, 1, H_5, J = 9.3 Hz), 8.08 (dd, 1, H_{10}, J = 9.0 Hz, J = 1.1 Hz), 7.59–7.86 (m, 6, Ar), 4.31 (s, 2, CH_2). Anal. Calcd for $C_{20}H_{12}O$: C, 89.52; H, 4.50. Found: C, 89.27; H, 4.56.

5-Formyl-4*H*-cyclopenta[*def*]chrysene (7c). Formylation of **3** (200 mg, 0.83 mmol) by the same procedure provided a solid which on recrystallization from CH_2Cl_2 yielded pure 5-formyl-4*H*-cyclopenta[*def*]chrysene (**7c**) (159 mg, 71%), mp 168–170 °C: IR (Nujol) 1660 cm^{-1} (CHO); NMR δ 10.94 (s, 1, CHO), 9.19 (dd, 1, H_6, J = 9.7 Hz, J = 4.8 Hz), 8.60 (dd, 1, H_9, J = 9.2 Hz, J = 4.0 Hz), 8.38 (d, 1, H_{10}, J = 8.8 Hz), 8.07 (d, 1, H_{11}, J = 8.8 Hz), 7.70–7.89 (m, 5, Ar), 4.59 (s, 2, CH_2); MS *m*/*e* (rel intensity) 268 (M^+, 93), 240 (40), 239 (100), 237 (25).

6-Formyl-13*H*-dibenz[*bc*,*l*]aceanthrylene (9c). Formylation of **4** (176 mg, 0.61 mmol) by the same procedure afforded a yellow solid which on recrystallization from CH_2Cl_2 gave pure **9c** (165 mg, 85%), mp 233 °C: IR (Nujol) 1660 cm^{-1} (CHO); NMR δ 11.02 (s, 1, CHO), 8.55 (d, 1, H_7, $J_{7,8}$ = 9.2 Hz), 8.42 (d, 1, H_5, $J_{4,5}$ = 9.2 Hz), 8.37 (dd, 1, H_{12}, $J_{11,12}$ = 9.3 Hz, $J_{10,12}$ = 3.6 Hz), 7.79 (dd, 1, H_9, $J_{9,10}$ = 9.2 Hz, $J_{9,11}$ = 2.4 Hz), 7.72 (d, 1, H_8, $J_{7,8}$ = 9.2 Hz), 7.71 (d, 1, H_3, $J_{2,3}$ = 7.3 Hz), 7.54–7.81 (m, 5, Ar), 4.79 (s, 2, CH_2). Anal. Calcd for $C_{24}H_{14}O$: C, 90.54; H, 4.43. Found: C, 90.43; H, 4.46.

6-Formyl-4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (10c). Formylation of **5** (245 mg, 0.77 mmol) by the same procedure gave crude **10c** which was purified by chromatography on silica gel to yield pure **10c** (460 mg, 84%), mp 220–222 °C (benzene): IR (Nujol) 1680 cm^{-1} (CHO); NMR δ 11.40 (s, 1, CHO), 9.10 (s, 1, H_{11}), 8.79 (d, 1, H_7, $J_{7,8}$ = 8.6 Hz), 8.74 (s, 1, H_5), 8.46 (d, 1, H_{12}, $J_{12,13}$ = 8.8 Hz), 8.06 (dd, 1, H_{10}, $J_{9,10}$ = 8.7 Hz, $J_{8,10}$ = 1.0 Hz), 7.97 (d, 1, H_{13}, $J_{12,13}$ = 8.8 Hz), 7.84 (d, 1, H_1, $J_{1,2}$ = 7.8 Hz), 7.58–7.68 (m, 4, Ar), 4.27 (s, 2, CH_2); MS *m*/*e* (rel intensity) 318 (M^+, 100), 290 (50), 289 (98), 145 (18).

General Procedure for Deoxygenation of Aldehydes. To a solution of **6c** (80 mg, 0.28 mmol) in 5 mL of dry CH_2Cl_2 under argon were added ZnI_2 (134 mg, 0.42 mmol) and $NaBH_3CN$ (132 mg, 2.09 mmol). The mixture was stirred at room temperature and monitored by TLC on silica gel. After 12 h, the solution was cooled in an ice bath and 5 mL of 6 N HCl was added. The organic layer was washed with water, separated, dried, and evaporated to dryness. The residue was chromatographed on silica gel. Elution with hexane gave 6-methyl-11*H*-benz[*bc*]aceanthrylene (**6d**) (55 mg, 78%), mp 176 °C (hexane): NMR δ 8.37 (dd, 1, H_7, J = 9.9 Hz, J = 2.2 Hz), 8.18 (dd, 1, H_{10}, J = 9.2 Hz, J = 2.5 Hz), 7.98 (d, 1, H_5, J = 9.2 Hz), 7.58–7.77 (m, 6, Ar), 4.49 (s, 2, CH_2), 3.04 (s, 3, CH_3); UV λ_{max} (EtOH) 393 (ε 6170), 373 (9190), 357 (11 445), 310 (11 190), 292 (69 225), 259 (47 140), 233 (34 550), 221 (42 475), 206 (43 155). Anal. Calcd for $C_{20}H_{14}$: C, 94.45; H, 5.54. Found: C, 94.17; H, 5.67.

Reduction of **7c** (45 mg, 0.17 mmol) by the same procedure (reaction time 48 h) furnished 5-methyl-4*H*-cyclopenta[*def*]-chrysene (**7d**) (37 mg, 87%) as a white solid, mp 171–172 °C: NMR δ 8.76 (d, 1, H_9, $J_{8,9}$ = 7.5 Hz), 8.54 (d, 1, H_{10}, $J_{10,11}$ = 9.2 Hz), 8.29 (d, 1, H_6, $J_{6,7}$ = 7.8 Hz), 7.99 (d, 1, H_{11}, $J_{10,11}$ = 9.2 Hz), 7.90 (d, 1, H_1, J = 6.8 Hz), 7.69–7.75 (m, 4, Ar), 4.46 (s, 2, CH_2), 2.90 (s, 3, CH_3); UV λ_{max} (EtOH) 329 (ε 14 050), 314 (12 530), 303 (12 780), 269 (105 735), 219 (29 885). Anal. Calcd for $C_{20}H_{14}$: C, 94.45; H, 5.54. Found: C, 94.27; H, 5.72.

Reduction of **9c** (100 mg, 0.31 mmol) by the same procedure (reaction time 10 h) yielded 6-methyl-13*H*-dibenz[*bc*,*l*]ace-

anthrylene (**9d**) (81 mg, 82%) as a white solid, mp 205–206 °C (benzene): NMR δ 8.92 (d, 1, H_{12}, $J_{11,12}$ = 8.2 Hz), 8.22 (d, 1, H_7, $J_{7,8}$ = 9.3 Hz), 8.05 (d, 1, H_5, $J_{4,5}$ = 9.1 Hz), 7.90 (d, 1, H_9, $J_{9,10}$ = 7.6 Hz), 7.67–7.85 (m, 8, Ar), 4.79 (s, 2, CH_2), 3.04 (s, 3, CH_3); UV λ_{max} (EtOH) 393 (ε 8830), 292 (12530), 303 (99450), 287 (89525), 257 (62055), 233 (49635), 221 (61030), 206 (62000). Anal. Calcd for $C_{24}H_{16}$: C, 94.70; H, 5.29. Found: C, 94.65; H, 5.32.

Reduction of **10c** (245 mg, 0.77 mmol) by the same procedure (reaction time 18 h) afforded 6-methyl-4*H*-benzo[*b*]cyclopenta[*mno*]chrysene (**10d**) (204 mg, 87%) as pale yellow crystals, mp 202–204 °C (benzene): NMR δ 9.09 (s, 1, H_{11}), 8.66 (d, 1, H_{12}, $J_{12,13}$ = 8.8 Hz), 8.35–8.38 (overlapping d + s, 2, $H_{5,7}$), 8.15 (dd, 1, H_{10}, $J_{9,10}$ = 8.6 Hz, $J_{8,10}$ = 2.0 Hz), 8.02 (d, 1, H_{13}, $J_{12,13}$ = 8.8 Hz), 7.88 (dd, 1, H_1, $J_{1,2}$ = 8.3 Hz, $J_{1,3}$ = 1.6 Hz), 7.55–7.67 (m, 3, Ar), 4.54 (s, 2, CH_2), 3.19 (s, 3, CH_3); UV λ_{max} (EtOH) 396 (ε 9130), 373 (10285), 355 (6515), 335 (6090), 308 (33175), 288 (12650), 245 (35700), 214 (19055), 201 (21670). Anal. Calcd for $C_{24}H_{16}$: C, 94.70; H, 5.29. Found: C, 94.74; H, 5.52.

Acknowledgment. This research was supported by a grant from the National Institute of Environmental Health Sciences (ES 04266).

Registry No. **2**, 202-94-8; **3**, 202-98-2; **4**, 141046-06-2; **5**, 141046-07-3; **6a**, 141046-08-4; **6c**, 141046-09-5; **6d**, 63041-88-3; **7a**, 141046-10-8; **7c**, 141046-11-9; **7d**, 141046-12-0; **8a**, 141046-13-1; **9a**, 141046-14-2; **9c**, 141046-15-3; **9d**, 141046-16-4; **10a**, 141046-17-5; **10c**, 141046-18-6; **10d**, 141046-19-7.

Photochemistry of *N*-(Benzoylimino)-1,2,4-triazolium and *N*-(Benzoylimino)pyridinium Ylides: A Source of Benzoylnitrene Useful in Photolabeling and Photo-Cross-Linking Experiments

Charles R. Arnold, Tracy Melvin, William M. Nelson, and Gary B. Schuster*

Department of Chemistry, Roger Adams Laboratory, University of Illinois, Urbana, Illinois 61801

Received January 17, 1992

The photochemistry of substituted 1-(benzoylimino)pyridinium and 4-(*N*-benzoylimino)-1,2,4-triazolium ylides was investigated to judge their capacity to give aroylnitrenes and their suitability for use in photolabeling experiments. Evidence presented indicates that the triplet states of the ylides cleave to generate aroylnitrenes. In an attempt to enhance triplet formation, nitro- and acetyl-substituted pyridinium ylides were examined. Their irradiation does not give nitrenes in meaningful yield. However, irradiation of the triazolium ylides gives nitrenes in excellent yield. The mechanism of these reactions was probed, and additional evidence is obtained that supports the proposal that benzoylnitrene is a singlet in its ground state. The triazolium ylides may be suitable reagents for photolabeling applications.

Introduction

Photochemical generation of an intermediate with high reactivity toward intermolecular covalent bond formation is the basis for many chemical and biochemical marking methods.[1] In the most often used procedures, photolysis of a diazo compound, a diazirine, or an azide gives a carbene or nitrene which may subsequently be incorporated into the targeted substrate.[2] The azides most commonly used in this application are substituted aryl azides. However, in recent years it has been clearly shown that photolysis of such azides usually leads to formation of dehydroazepines—not nitrenes.[3] When a nucleophilic group is present at the targeted site, the dehydroazepines may be sufficiently reactive to meet the objectives of the procedure, but often this is not the case. In general, the photolysis of an aryl azide will not give an intermediate of sufficient reactivity to ensure its reaction at the site of creation irrespective of the chemical composition of the site. With this restriction in mind, we undertook research aimed at the development of new reagents and intermediates that could achieve the objective of global reactivity. In this connection, global reactivity of an intermediate is defined as rapid, irreversible reaction with unactivated, carbon-bound hydrogen to form a covalent bond at the targeted site.

Earlier work on this project revealed that aroylnitrenes exhibit the desired chemical reactivity toward carbon–hydrogen bonds.[4] These intermediates display chemical and physical properties that led us to conclude that they have singlet spin multiplicity in the ground state. As singlets, the aroylnitrenes are strongly electrophilic and insert concertedly into carbon–hydrogen bonds. Unfortunately, photolysis of aroyl azides, the most commonly used reaction for generation of an aroylnitrene, leads to approximately equal amounts of the nitrene formed by nitrogen elimination and the isocyanate formed from the photo-Curtius rearrangement of a singlet excited state of the azide.[5] The isocyanate is a comparatively weak electrophile that can migrate from the site of its creation before it is trapped by a nucleophilic group.

Triplet sensitization of the aroyl azide stops formation of the isocyanate and gives singlet nitrene-trapping products in essentially quantitative yield.[4] Two intersystem crossing reactions facilitate this process: the sensitizer excited singlet state is converted to its triplet before energy transfer to the aroyl azide, and the triplet nitrene formed by nitrogen loss from the azide intersystem crosses to its singlet ground state before the intermolecular reaction occurs. It is possible to carry out the triplet "sensitization" intramolecularly. Light absorbed by the ketone chromophore of 4-acetylbenzoyl azide, for example, leads to reaction of the azide group and formation of singlet nitr-

(1) Chowdry, V.; Westheimer, F. H. *Annu. Rev. Biochem.* **1962**, 237, PC3006. Brunner, J. *Methods Enzymol.* **1989**, 172, 628.

(2) Bayley, H.; Staros, J. V. In *Azides and Nitrenes*; Scriven, E. F. V., Ed.; Academic Press: New York, 1984.

(3) Liang, T.-Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1987**, *109*, 7803. Li, Y.-Z.; Kirby, J. P.; George, M.; Poliakoff, M.; Schuster, G. B. *J. Am. Chem. Soc.* **1988**, *110*, 8092. Schuster, G. B.; Platz, M. *Adv. Photochem.*, in press.

(4) (a) Ingaki, M.; Shingaki, T.; Nagai, T. *Chem. Lett.* **1982**, 9. (b) Autrey, T.; Schuster, G. B. *J. Am. Chem. Soc.* **1987**, *109*, 5814. (c) Sigman, M. E.; Autrey, T.; Schuster, G. B. *J. Am. Chem. Soc.* **1988**, *110*, 4297.

(5) Lwowski, W. In *Azides and Nitrenes*; Scriven, E. F. V., Ed.; Academic Press: New York, 1984; Chapter 4.

0022-3263/92/1957-3316$03.00/0