Complete ^1H and ^{13}C NMR Assignment of Polycyclic Aromatic Fluoranthenes by Long-Range Optimized Homo- and Heteronuclear Correlation Spectroscopy

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Complete assignment of the ^1H and ^{13}C resonances of the representative polyaromatic fluoranthenes indeno[1,2,3-*hi*]chrysene (1), indeno[1,2,3-*cd*]pyrene (2), and benzo[*b*]fluoranthene (3) are accomplished by 2D-NMR analysis utilizing a combination of long-range homo- and heteronuclear shift correlation techniques (LR-COSY and LR-HETCOR). A number of characteristic inter-ring couplings (epi, peri, and through-space couplings, etc.) play an important role in assigning the proton signals.

Introduction

Interest in the higher polyaromatic derivatives of fluoranthene is dictated by recent evidence that nonalternant hydrocarbons of this class are widespread environmental pollutants, some members of which are mutagenic and/or carcinogenic.[1] Remarkably little is known concerning the chemistry of the polycyclic fluoranthenes, and their patterns of electrophilic substitution are virtually unknown.[2] A general synthetic route for the preparation of hydrocarbons of this class was reported in a preliminary communication,[3] and further details are presented in the accompanying paper.[4]

Herein we report methods for the complete proton and carbon signal assignment of selected polycyclic fluoranthenes using long-range optimized homo- and heteronuclear correlation NMR spectroscopic techniques. These NMR methods are potentially useful for investigations of the patterns of electrophilic substitution of polycyclic fluoranthenes and other complex hydrocarbon ring systems and for assignment of the structures of their metabolites in mammalian cells.

Complete assignments of the proton and carbon spectra of polycyclic aromatic hydrocarbons (PAHs) by conventional NMR experiments (double resonance, ring current effect, deuterium substitution, etc.) are frequently hampered by the severe overlap of the ^1H resonances due to the similarity in coupling networks in different parts of the molecule. Moreover, the ^{13}C signals of PAHs occur in a relatively narrow range (14–22 ppm), and about half of these belong to nonprotonated carbon atoms.[5] One approach to this problem utilizes double quantum coherence experiments (INADEQUATE) which make it possible to exploit natural abundance ^{13}C–^{13}C spin couplings to derive carbon–carbon connectivity networks.[6] However, this technique is often impractical for polyaromatic compounds due to its relatively low sensitivity. Recently, several alternative methodologies have been developed that make use of combinations of 2D-NMR techniques. These include 2D-NOE (NOESY),[7] relayed coherence transfer (RCT2D),[8] one-dimensional polarization transfer (INAPT),[9] multiple quantum filtration (MQF),[9] and a long-range C–H shift correlation experiment (LR-HETCOR).[11] The versatility of the latter technique makes it particularly attractive for the complete assignment of the proton and/or carbon NMR spectra of congested polyaromatic systems, and this method has been improved further by various modifications (TANGO, COLOC, and BIRD sequences).[12]

This study examines the utility of a combination of long-range optimized ^1H–^1H correlation and ^{13}C–^1H shift correlation spectroscopy for the complete ^1H and ^{13}C assignment of selected polycyclic fluoranthene compounds, namely, indeno[1,2,3-*hi*]chrysene (1), indeno[1,2,3-*cd*]pyrene (2), and benzo[*b*]fluoranthene (3), whose structures and numbering systems are shown below.

Results

Assignment of Indeno[1,2,3-*hi*]chrysene (1). The 500-MHz ^1H NMR spectrum (Figure 1a) of indeno[1,2,3-*hi*]chrysene (1) spans from 7.4 to 9.2 ppm and reveals four groups of signals: 9.2–8.5 ppm (4 protons), 8.1–7.9 ppm (5 protons), 7.8–7.6 ppm (3 protons), and around 7.4 ppm (2 protons). The assignment of the proton spectrum can be carried out almost completely on the basis of long-range COSY (LR-COSY) in addition to normal COSY experiments.[13] The latter (Figure 2a) connect the protons that belong to the various spin systems in the molecule, i.e., one 1 (H5,6),1 AMX (H7,8,9), and 2 ABMX (H1,2,3,4 from the chrysene ring and H10,11,12,13 from the indeno ring) systems but do not allow an unequivocal assignment of the spectrum.

We start with the assumptions that H1, H6, H7, and H14 resonate most downfield because of their repulsive

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[1] *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*: *Polynuclear Aromatic Compounds*; Vol. 32, Part 1, IARC: Lyons, France, 1983.

[2] Clar, E. *Polycyclic Hydrocarbons*; Academic Press: New York, 1964.

[3] Cho, B. P.; Harvey, R. G. *Tetrahedron Lett.* **1987**, *28*, 861, 2906.

[4] Cho, B. P.; Harvey, R. G. *J. Org. Chem.*, previous paper in this issue.

[5] Jones, A. J.; Alger, T. D.; Grant, D. M.; Litchman, W. M. *J. Am. Chem. Soc.* **1970**, *92*, 2386.

[6] Bax, A.; Freeman, R.; Kempsell, S. P. *J. Am. Chem. Soc.* **1980**, *102*, 4849.

[7] Yu, C.; Levy, G. C. *J. Am. Chem. Soc.* **1984**, *106*, 6533.

[8] (a) Musmar, M. J.; Martin, G. E.; Gampe, R. T., Jr.; Lee, M. L.; Hurd, R. E.; Tedjamulia, M. L.; Kudo, H.; Castle, R. N. *J. Heterocycl. Chem.* **1985**, *22*, 219. (b) Musmar, M. J.; Zektzer, A. S.; Martin, G. E.; Gampe, R. T., Jr.; Lee, M. L. Castle, R. N.; Hurd, R. E. *Magn. Reson. Chem.* **1987**, *24*, 1039. (c) Musmar, M. J.; Martin, G. E.; Tedjamulia, M. L.; Kudo, H.; Castle, R. N.; Lee, M. L. *J. Heterocycl. Chem.* **1984**, *21*, 929. (d) Kessler, H.; Bermel, W.; Griesinger, C.; Hertl, P.; Streich, E.; Reiker, A. *J. Org. Chem.* **1986**, *51*, 596.

[9] Bax, A.; Ferretti, J. A.; Nashed, N.; Jerina, D. M. *J. Org. Chem.* **1985**, *50*, 3029.

[10] Williamson, D. S.; Cremonesi, P.; Cavalieri, E.; Nagel, D. L.; Markin, R. S.; Cohen, S. M. *J. Org. Chem.* **1986**, *51*, 5210.

[11] (a) Jans, A. W. H.; Tintle, C.; Cornelisse, J.; Lugtenburg, J. *Magn. Reson. Chem.* **1986**, *24*, 101. (b) Quast, M. J.; Ezell, E. L.; Martin, G. E.; Lee, M. L.; Tedjamulia, M. L.; Stuart, J. G.; Castle, R. N. *J. Heterocycl. Chem.* **1985**, *22*, 1453.

[12] Zektzer, A. S.; Quast, M. J.; Linz, G. S.; Martin, G. E.; McKenny, J. D.; Johnston, M. D., Jr.; Castle, R. N. *Magn. Reson. Chem.* **1986**, *24*, 1083 and references cited therein.

[13] Bax, A. *Two-Dimensional Magnetic Resonance in Liquids*; Reidel: Boston, 1982; Chapter 2.

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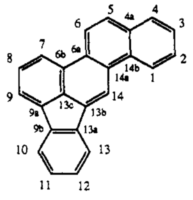
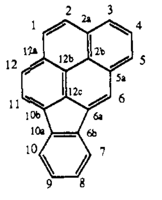
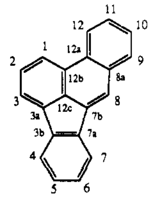


Indeno[1,2,3-hi]chrysene
1



Indeno[1,2,3-cd]pyrene
2



Benz[e]acephenanthrylene
3

van der Waals interaction (bay region) and that the singlet at 9.19 ppm must be due to H14. From the high resolution COSY-45 spectrum (Figure 2a) the ortho (vicinal) coupling gives rise to strong cross peaks in the spectrum. It appears that the protons absorbing at 8.52 and 7.98 ppm are both coupled with the proton at 7.78 ppm; in addition, they show a weak coupling with each other. This must be the H7,8,9 network, because it is the only possible isolated AMX system in the molecule. The proton absorbing at 8.66 ppm shows a strong coupling with the proton at 8.00 ppm and a weak coupling with a bay region singlet at 9.19 ppm (H14). The latter weak interaction is assumed to be due to five-bond zig-zag coupling between the H14 and H6. This epi coupling, as well as other long-range coupling, is commonly observed in PAH derivatives,[14] and long-range interactions of this type are illustrated in Figure 3 for 1. Since these small couplings are not seen in the low-resolution COSY spectrum (not shown), they can be easily recognized as long-range couplings. Thus, there are six pairs of off diagonal peaks for the bay region protons, of which three pairs are much stronger than the others. The remaining bay region proton signal at 8.90 ppm must be H1. The latter reveals a series of strong connectivities between the vicinal protons H1/H2 (7.74 ppm), H2/H3 (7.64 ppm), and H3/H4 (7.99 ppm), plus the weaker H1/H3 coupling.

In order to confirm the above-mentioned long-range couplings and to search for others, the τ delay ($D_3 = 0.2$ s) was inserted as described in the Experimental Section. The resulting spectrum (LR-COSY), shown beneath the normal COSY spectrum (Figure 2b), reveals additional interesting long-range couplings as well as the expected meta couplings. It is worth noting that the H14/H6, H7/H9, and H1/H3 contours are intensified; in addition, new epi coupling between H1/H5 is observed. Similar epi zig-zag long-range ^6J coupling is frequently observed in other PAH molecules. Thus, the LR-COSY experiment (spectrum not shown) on benz[*def*]indeno[1,2,3-*hi*]chrysene (4) clearly revealed the ^6J couplings (H5/H13 and H4/H14). More importantly, connectivities between H1 and H14 and H6 and H7 were observed, suggesting that coupling due to van der Waals interaction across the two bay regions takes place.[15] Such through-space coupling is rare but can play a crucial role in the assignment of protons for this class of compounds.[16] The above-mentioned long-range couplings are believed to be also responsible for the broadening of the signals of protons of H1,4,5,6,7,10,14.

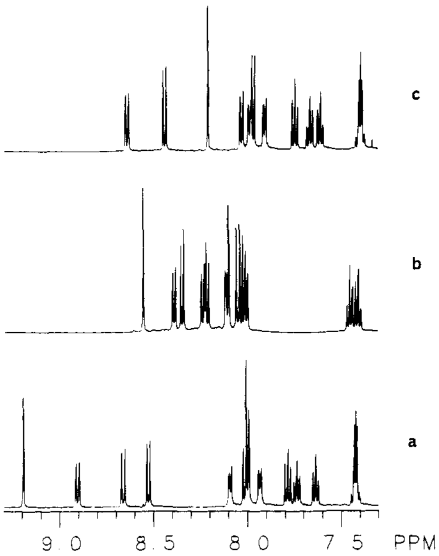
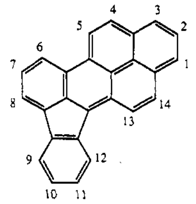


Figure 1. Proton NMR spectra (500 MHz) of (a) indeno[1,2,3-*hi*]chrysene (1), (b) indeno[1,2,3-*cd*]pyrene (2), and (c) benzo[*b*]fluoranthene (3) in $CDCl_3$.



Benz[def]indeno[1,2,3-hi]chrysene
4

While the assignment of the protons associated in the chrysene portion of the molecule is reasonably clear, the unambiguous identification of the indeno ring protons (H10–13) is less straightforward because of the absence of the long-range coupling between the protons of the indeno ring and other aromatic protons. If it is assumed that the protons absorbing at 7.42 and 7.43 ppm are due to H11 and/or H12, the chemical shifts of the adjacent protons at H10 and H13 can be located at 7.93 and/or 8.08 ppm. However, it is not clear which is from the COSY experiment alone. This assignment can be completed by performing the long-range shift correlation (LR-HETCOR) experiment described below.[17]

The normal carbon spectrum reveals only 23 of the 24 expected carbon signals (Figure 4c). The identification of the missing quaternary carbon can easily be done by a simple APT experiment (Figure 4a,b).[18] Notice the reduced intensity of the carbon signal at 128.77 ppm (arrow) in the middle spectrum. For the assignment of the ^{13}C spectrum of 1, we perform a normal (HETCOR)[19] (not shown) and a long-range (LR-HETCOR) ^{13}C–^1H shift correlation experiment,[17] shown in Figure 5. The observation of long-range $^3J_{CH}$ couplings in the LR-HETCOR was optimized as 7 Hz, and the relevant long-range correlations are indicated.[20]

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[14] Jarvis, M. W.; Moritz, A. G. *Aust. J. Chem.* **1971**, *24*, 89.

[15] Barfield, M.; Karplus, M. *J. Am. Chem. Soc.* **1969**, *91*, 1.

[16] (a) Sydnes, L. K.; Skjetne, T. *Magn. Reson. Chem.* **1986**, *24*, 317. (b) Perin-Roussel, O.; Croisy-Delcey, M.; Mispelter, J.; Saguem, S.; Chalvet, O.; Ekert, B.; Fouquet, J.; Jacquignon, P.; Lhoste, J.-M.; Muel, B.; Zajdela, F. E. *Cancer Res.* **1980**, *40*, 1742.

[17] (a) Kessler, H.; Griesinger, C.; Zarbock, J.; Loosli, H. R. *J. Magn. Reson.* **1984**, *57*, 331. (b) Bauer, C.; Freeman, R.; Wimperis, S. *J. Magn. Reson.* **1984**, *58*, 526.

[18] Patt, S. L.; Shoolery, J. N. *J. Magn. Reson.* **1982**, *46*, 535.

[19] Bax, A.; Morris, G. A. *J. Magn. Reson.* **1981**, *42*, 501.

[20] (a) Hansen, P. E. *Org. Magn. Reson.* **1979**, *12*, 109. (b) Kissane, P. J.; Johns, S. R.; Willing, R. I.; Sasse, W. H. F. *Aust. J. Chem.* **1976**, *29*, 1613. (c) Johns, S. R.; Willing, R. I. *Aust. J. Chem.* **1976**, *29*, 1617.

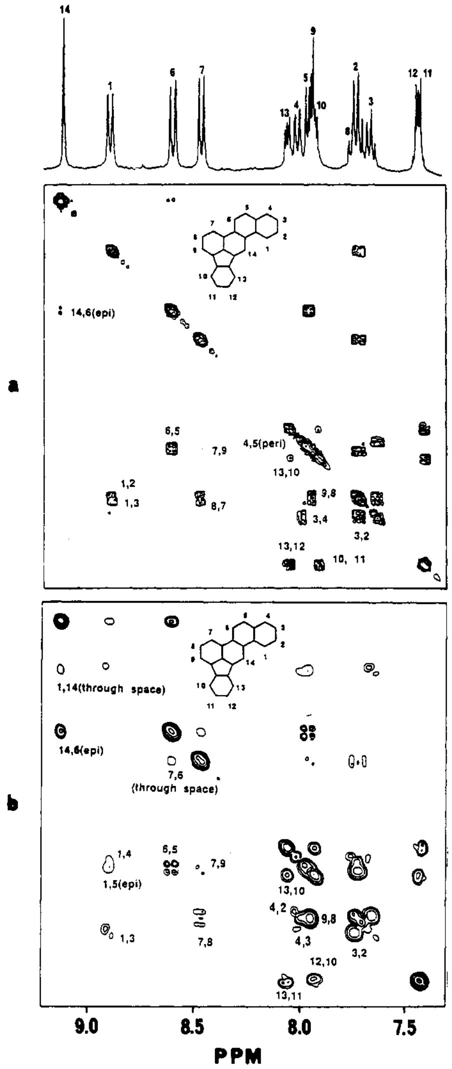
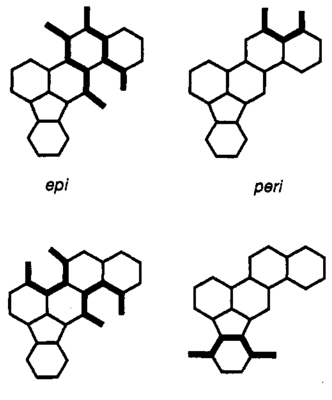


Figure 2. Homonuclear correlated (COSY) spectra of 1. The top spectrum (a) is a regular COSY spectrum. The bottom (b) spectrum is a long-range COSY (LR-COSY) spectrum for which the long-range cross peaks are emphasized using the τ delay ($D_3 = 0.2$ s).


epi peri

through-space para

Figure 3. Modes of long-range coupling illustrated for 1.

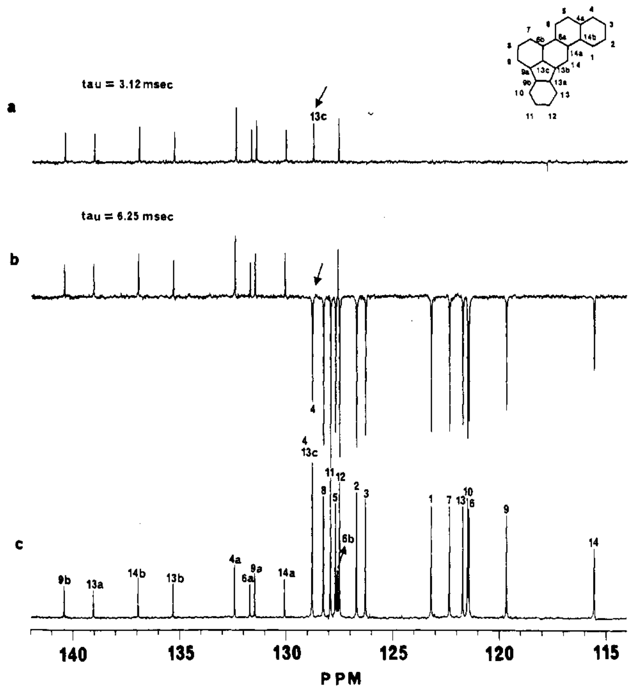


Figure 4. APT spectra of 1: (a) shows the signals due to nonprotonated carbons; (b) shows quaternary carbons in positive phase and monoprotonated carbons in negative phase; (c) is normal broad-band carbon spectrum.

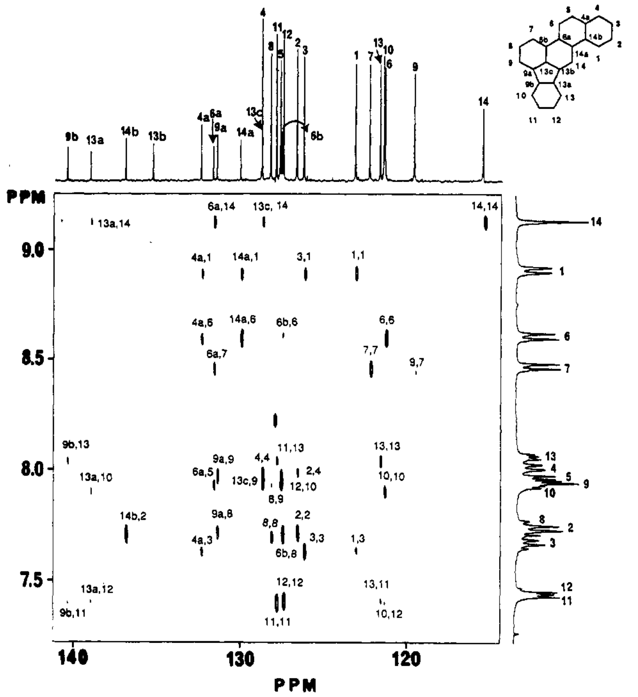


Figure 5. Long-range $^1H-^{13}C$ chemical shift correlation spectrum (LR-HETCOR) of 1; $SW_1 = 895$ Hz; $SW_2 = 2829$ Hz; NT = 96.

From Figure 5, the carbon signals that resonate at the lowest field (140.43 and 139.04 ppm) are easily assigned as C9b and C13a, respectively, because the former peak shows the expected three-bond C–H couplings with H11,13 and the latter with H10,12,14. Consistent with these assignments, H11 and H12 also show $^3J_{CH}$ couplings with C13 and C10, respectively. These assignments enable us to differentiate the two indeno ring protons (H11 and H12), which are difficult to assign by the COSY experiment alone. Likewise, the quaternary carbon signals of C14b (H2), C4a (H1,3,6), C6a (H7,5,14), C9a (H8), C14a (H1,6), and C6b (H6,8) show the expected $^3J_{CH}$ couplings and were assigned in the usual manner. The remaining signals (C13b and C13c) can be identified by the fact that C13b shows the expected single connectivity with H13 (this can be seen only in a higher contour map), while C13c (which resides under C4) shows $^3J_{CH}$ coupling with H14 and H9. The complete proton and carbon chemical shifts of compound 1 are listed in Table I.

Table I. ^{13}C and ^{1}H Chemical Shift Assignments of Indeno[1,2,3-*hi*]chrysene (1), Indeno[1,2,3-*cd*]pyrene (2), and Benzo[*b*]fluoranthene (3)[a]

1			2			3		
no.	^{13}C shift, ppm	^{1}H shift, ppm	no.	^{13}C shift, ppm	^{1}H shift, ppm	no.	^{13}C shift, ppm	^{1}H shift, ppm
1	123.199	8.90	1	126.639	8.10	1	121.529	8.42
2	126.692	7.74	2	127.145	8.04	2	128.072	7.73
3	126.282	7.64	2a	130.424		3	119.439	7.95
4	128.770	7.99	2b	123.168		3a	136.878	
4a	132.420		3	126.772	8.22	3b	140.598	
5	127.690	8.00	4	126.483	8.03	4	121.167	7.90
6	121.408	8.66	5	128.532	8.37	5	127.972	7.40
6a	131.696		5a	132.003		6	127.325	7.39
6b	127.587		6	121.384	8.53	7	121.852	7.97
7	122.330	8.52	6a	135.643		7a	138.458	
8	128.257	7.78	6b	139.054		7b	134.938	
9	119.651	7.98	7	122.553	8.10	8	121.392	8.17
9a	131.463		8	126.808	7.40	8a	133.905	
9b	140.432		9	128.242	7.45	9	130.112	8.01
10	121.485	7.93	10	121.553	8.00	10	126.641	7.60
11	127.915	7.42	10a	141.887		11	126.890	7.66
12	127.492	7.43	10b	133.027		12	123.034	8.62
13	121.715	8.08	11	119.600	8.33	12a	130.609	
13a	139.044		12	124.819	8.20	12b	127.450	
13b	135.305		12a	130.581		12c	132.002	
13c	128.770		12b	121.649				
14	115.542	9.19	12c	130.629				
14a	130.062							

[a] The proton chemical shifts of these compounds may vary depending upon concentration.

It should be noted that several $^{3}J_{CH}$ couplings, such as C9b-H6, C13b-H13, C14b-H4, C14b-H5, and C9a-H10, are notably absent, whereas a few $^{2}J_{CH}$ couplings, such as C9a-H9 and C8-H9, are observed in the LR-HETCOR spectrum. This phenomenon is a consequence of the fact that these couplings fall outside of the optimized value (~7 Hz) selected for this experiment. Thus, $^{3}J_{CH}$ is normally in the range of 4–10 Hz, and $^{2}J_{CH}$ and $^{4}J_{CH}$ are usually less than 4 and 2 Hz, respectively.[21] In addition, the magnitude of peri $^{3}J_{CH}$ coupling, such as C5-H4, is known to be generally lower than meta $^{3}J_{CH}$ couplings.[20c] It has been shown in other cases that the missing contours could be detected by using a different pulse sequence.[11a,12] This was not required in the present case, since the spectrum gave enough contours to assign all the ^{1}H and ^{13}C signals with the aid of LR-COSY.

Assignment of Indeno[1,2,3-*cd*]pyrene (2). Assignment of the proton signals of indeno[1,2,3-*cd*]pyrene (2)[22] offers somewhat more difficulty because of the overlap of signals due to the similarity of the two AX systems and the lack of distinguishable bay-region protons (Figure 1b). Nevertheless, the ready identification of the H6 singlet and a number of useful long-range couplings allows the spectral assignment to proceed along similar lines to that described for indeno[1,2,3-*hi*]chrysene.

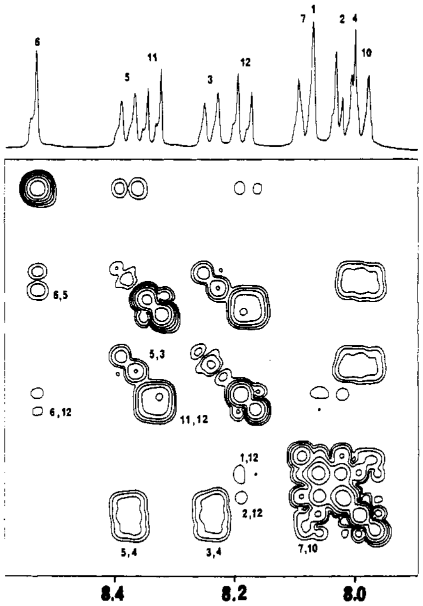


Figure 6. Partial LR-COSY spectrum of 2.

We start with the assumptions that H6 is the singlet that appears most downfield (8.53 ppm) and the H8 and H9 resonances appear most upfield (7.40 or 7.45 ppm). If these assumptions are incorrect, it will lead to contradictory results in the LR-HETCOR experiment. From the normal COSY spectrum (not shown) the H7 and H10 signals can be located either at 8.10 or 8.00 ppm. The expanded LR-COSY (Figure 6) shows that the doublets absorbing at 8.37 and 8.22 ppm are both coupled with the proton at 8.03 ppm; in addition, they are weakly coupled to each other. This must belong to the only AMX system of the molecule (H3,4,5). While the higher field signal (8.03 ppm) may be assigned as H4 on the basis of its chemical shift, it is not possible to differentiate H3 and H5. The two pair of signals due to H1/H2 and H11/H12 can be easily identified from the normal COSY spectrum, because they form isolated AX spin pairs, but again it is not clear which is which. However, the LR-COSY spectrum in Figure 6 provides some insight into differentiating these AX systems. Thus, the H6 singlet shows two different long-range couplings, one of which is peri (H6/5) and the second an unusual coupling through seven bonds between H6 and H12. In addition, H12 is also coupled with H2 through five bonds. Such non-zig-zag long-range couplings are rare but have been previously observed in a few PAHs, including derivatives of naphthalene,[23] benzo[*c*]phenanthrene,[24] and nitrobenzo[*e*]pyrene.[16a] ^{5}J coupling

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[21] Chang, C.-J.; Floss, H. G.; Steck, W. *J. Org. Chem.* **1977**, *42*, 1337.

[22] Karcher, W.; Fordham, R. J.; Dubois, J. J.; Glaude, P. G. J. M.; Ligthart, J. A. M. *Spectral Atlas of Polycyclic Aromatic Compounds*; Reidel: Boston, 1985.

[23] Crecely, R. W.; Goldstein, J. H. *Org. Magn. Reson.* **1970**, *2*, 613.

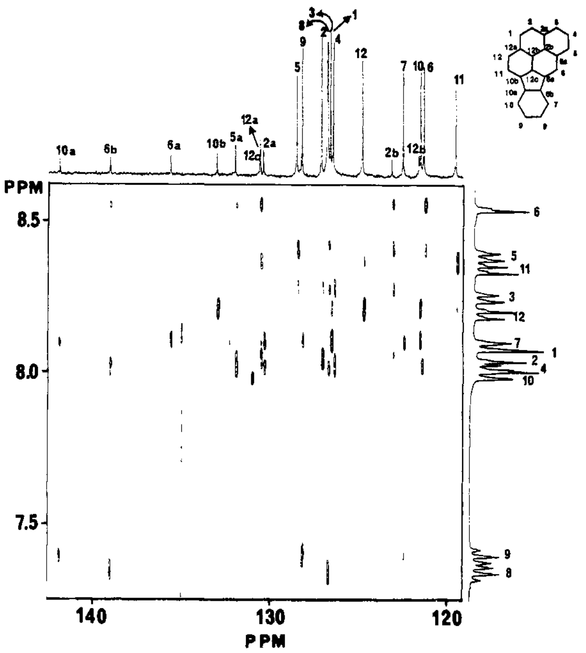

Figure 7. Long-range ^{1}H–^{13}C chemical shift correlation spectrum (LR-HETCOR) of **2**; SW_1 = 581 Hz; SW_2 = 2481 Hz; NT = 208.

is known to be much larger than ^4J couplings, with the exception of meta couplings.[25] In addition, H12 shows peri coupling with H1.

These assignments are supported by a LR-HETCOR experiment (Figure 7) which also serves to clarify the ambiguity of the ABMX system (H7–10) of the indeno ring component. Thus, the two most downfield quaternary carbons (141.88 and 139.05 ppm) may be identified as C10a and C6b on the basis of their observed connectivities with H7 and H9, and with H6, H10, and H8, respectively. The carbon at 135.64 ppm may be assigned as C6a because of its unique $^3J_{CH}$ coupling with H7. It is worthy of note that several weak $^2J_{CH}$ couplings are also observed, i.e. C5a-H6, C12a-H1, C4-H3, and C12-H11, etc., probably for the same reason discussed for compound **1**. The assignment of the remaining carbon signals is accomplished by using a combination of normal and long-range HETCOR experiments in the manner described for compound **1** and listed in Table I.

Assignment of Benzo[*b*]fluoranthene (3).[26] The complete assignment of benzo[*b*]fluoranthene (**3**)[22,27] is also readily carried out by the methods described in the preceding sections for **1** and **2**. The basic assumptions are that the singlet peak at 8.17 ppm is H8 and the doublets that appear furthest downfield are the bay-region protons, H1 and H12 (Figure 1c). Thus, H1 is differentiated from the other bay-region proton H12 on the basis of its LR-COSY spectrum (Figure 8), which shows couplings with the signals at 7.73 ppm and 7.95 ppm which indicate that it is part of the AMX system (H,2,3). On the other hand, H12 shows several long-range couplings with H8 (epi), H9 (para), H10 (meta), as well as ortho coupling with H11, consistent with it being part of the ABMX system (H9,10,11,12). Analysis of the LR-HETCOR spectrum (Figure 9) by methods similar to those utilized previously for **1** and **2** allows a definite assignment of all the remaining proton and carbon signals. The assigned proton and carbon chemical shifts are included in Table I.[27]

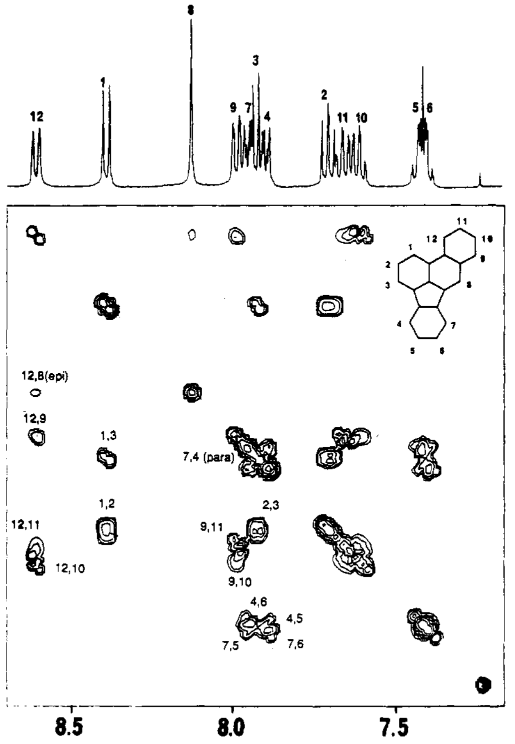

Figure 8. LR-COSY spectrum of **3**.

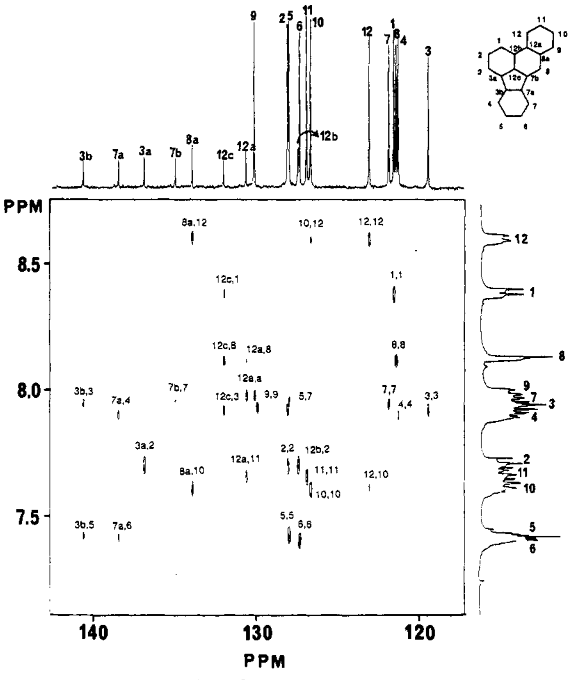

Figure 9. Long-range ^{1}H–^{13}C chemical shift correlation spectrum (LR-HETCOR) of **3**; SW_1 = 660 Hz; SW_2 = 2561 Hz; NT = 40.

Discussion

Complete assignment of the ^{1}H and ^{13}C resonances of the three representative polycyclic fluoranthene hydrocarbons indeno[1,2,3-*hi*]chrysene, benzo[*b*]fluoranthene, and indeno[1,2,3-*cd*]pyrene is readily and unambiguously accomplished by application of a combination of LR-COSY and LR-HETCOR two-dimensional NMR techniques as outlined in the preceding section. Consistent with previous

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(24) Martin, R. H.; Defay, N.; Geerts-Evrard, F. *Tetrahedron* **1965**, *21*, 2435.

(25) Barfield, M.; Chakrabarti, B. *Chem. Rev.* **1969**, *69*, 757.

(26) This hydrocarbon is named benz[*e*]acephenanthrylene in Chemical Abstracts.

(27) For previous NMR data for **3**, see: (a) Bartle, K. D.; Jones, D. W.; Matthews, R. S. *Spectrochim. Acta* **1969**, *25A*, 1603. (b) Jones, D. W.; Matthews, R. S.; Bartle, K. D. *Spectrochim. Acta* **1974**, *30A*, 489.

observations for other classes of PAHs, the bay-region protons of these polycyclic fluoranthenes generally resonate at the lowest field in the proton spectra. In contrast, the terminal indeno ring protons (the AB portion of ABMX) generally appear at highest field, indicative of minimal electron delocalization from the benzenoid ring to the rest of the fused polyaromatic ring system. In this connection, it is interesting to observe that the resonances of the quaternary carbons of the indeno ring generally appear at the lower field than the quaternary carbons of the polycyclic ring system to which the indeno ring is fused.

The afore-mentioned methods for the complete assignment of the ^1H and ^{13}C chemical shifts in the NMR spectra of polycyclic fluoranthenes have already proven invaluable for the determination of the previously unknown patterns of substitution of this class of nonalternant PAHs. In preliminary studies of the electrophilic substitution of the polyaromatic fluoranthenes,[28] it was established that bromination of **1**, **2**, and **3** occurs predominantly in the 5-, 12-, and 1-positions, respectively. The isomeric assignments were made by comparison of the proton and carbon spectra of the parent hydrocarbon with that of the deuteriated analogue that was obtained from the major bromo derivative by treatment with butyllithium and D_2O. Full details of these and other related syntheses will be reported in due course.

Experimental Section

The syntheses of the compounds used in this paper are described in the accompanying paper.[4] All compounds were dissolved in 0.4 mL of $CDCl_3$ using 5-mm tubes. The sample quantities are 10 mg of **1**, 30 mg of **2**, and 25 mg of **3**. The 500-MHz 1D-proton NMR spectra were recorded on the University of Chicago 500-MHz spectrometer at 20 °C. The 2D-NMR experiments were performed on a Varian XL-400 instrument operating at 400 MHz for protons and at 100 MHz for carbon. The 2D ^1H NMR spectra were obtained by using a decoupler coil. The 90° ^1H pulse from the decoupler was calibrated as 84 μs by taking $^1/_4(\gamma H_2/2\pi)$. The 90° ^{13}C observe pulse was 14.3 μs.

The ^{13}C chemical shifts are reported in ppm from TMS with the center ^{13}C resonance of $CDCl_3$ as an internal reference for ^{13}C (77.0 ppm) and with the small amount of residual $^1HCCl_3$ as an internal reference for the proton spectrum (7.24 ppm). All COSY spectra were obtained by using Jeener's two-pulse sequence $90°–D_3–t_1–PW–$acquire. Forty transients were acquired for each 128 t_1 values, with a data set of 1024 × 1024 (256 × 256 for low resolution) complex data points in both dimensions. A τ delay ($D_3 = 0.20$ s, $D_3 = {}^1/_{2}J$) was used to obtain the LR-COSY spectra. The second mixing pulse (PW) in all the COSY experiments was set at 60 °C to deemphasize the diagonal peaks. Free induction decays were subjected to "pseudo-echo" processing,[29] and diagonal folding was applied to the final spectrum.

The normal and long-range ^1H-^{13}C shift correlation spectra (HETCOR and LR-HETCOR, respectively) were recorded by using the sequence $90°_H–{}^1/_2t_1–180°_C–{}^1/_2t_1–D_3–90°_C90°_H–D_4–$acquire ($t_2$) (proton BB decoupling). The data matrix was composed of 512 × 1024 data points, and 128 increments were made. The recycle time was 3-s and the other parameters, proton (SW_1) and carbon (SW_2) sweep width, and number of transients (NT) of each spectrum, are specified under the figures. For LR-HETCOR, the delays D_3 and D_4 of 71 and 48 ms (i.e., $^1J_{CH} = 160$ Hz, $^3J_{CH} = 7$ Hz), were used to pick out the two- and three-bond couplings discussed in the text.

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Registry No. **1**, 111189-32-3; **2**, 193-39-5; **3**, 205-99-2; **4**, 111189-33-4.

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(28) Minabe, M.; Cho, B. P.; Harvey, R. G., unpublished results.

(29) Bax, A.; Freeman, R.; Morris, G. A. *J. Magn. Reson.* **1981**, *43*, 333.