and the solvent was evaporated to gave the unstable indolenine **22**, which was used directly in the next step: IR ($CHCl_3$) ν_{max} 2860, 2790, 2730, 1695, 1600, and 1575 cm^{-1}.

Compound **22** (0.020 g, 0.068 mmol) was dissolved in ethanol (10 mL). Concentrated hydrochloric acid (1 mL) was added, and the resulting mixture was stirred at reflux for 12 h. After cooling, the solvent was evaporated, 5% sodium carbonate solution was added, and the mixture was extracted three times with CH_2Cl_2. The organic extract was dried over sodium sulfate and concentrated. The crude product was purified by flash chromatography on silica gel (elution with AcOEt–MeOH, 95:5) and gave compound **2** (0.017 g, yield = 85%): amorphous; IR ($CHCl_3$) ν_{max} 3350, 2850, 2780, 2720, 1705, 1600 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.2–2.0 (m, 10 H), 2.2–3.3 (m, 7 H + 1 H exchangeable with D_2O), 6.7 (d, 1 H, J = 7.5 Hz), 6.8 (t, 1 H, J = 7.5 Hz), 7.05 (t, 1 H, J = 7.5 Hz), 7.18 (d, 1 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 216.6, 149.2, 143.5, 127.6, 122.2, 120.6, 111.3, 67.2, 65.2, 57.1, 51.2, 48.5, 47.8, 46.9, 35.4, 27.1, 26.2, 23.9, 17.3; MS m/z (relative intensity) 294 (100), 279 (10), 266 (12), 252 (45), 238 (20), 166 (10), 144 (12), 143 (12), 138 (40), 130 (10), 123 (10), 109 (60); exact mass m/z 294.1729 (calcd for $C_{19}H_{22}N_2O$ m/z 294.1732).

Acknowledgment. We thank Dr. N. Kunesch for communicating the IR, ^1H NMR, ^{13}C NMR and MS spectra of 17-oxoaspidofractinine before publication. We thank also Dr. G. Dauphin for his help in recording the high-field NMR spectra and for fruitful discussions concerning attributions in 2D NMR. Finally we wish to thank B. Perrin for technical assistance throughout this work.

Preparation of 4- and 10-Fluorobenzo[*j*]fluoranthene via Cyclodehydration of Acetals and Cyclopropanecarboxaldehydes

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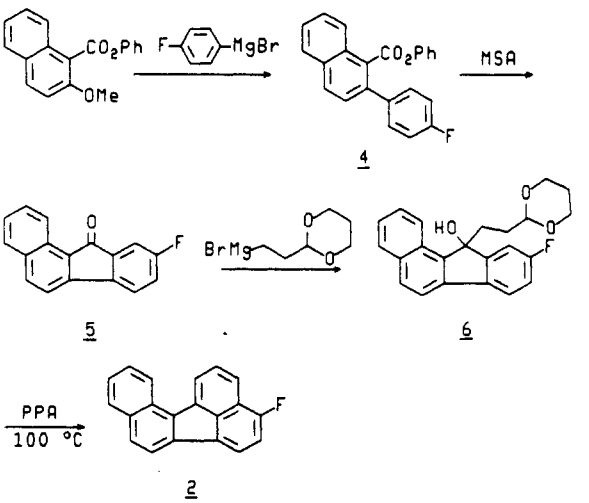
Two procedures have been developed for the synthesis of 4-fluorobenzo[*j*]fluoranthene (4-fluoroBjF) and 10-fluoroBjF. Reaction of 9-fluoro-11*H*-benzo[*a*]fluoren-11-one (**5**) with the Grignard reagent prepared from 2-(2-bromoethyl)-1,3-dioxane provided hydroxy acetal **6** in quantitative yield. Cyclodehydration with polyphosphoric acid (PPA) at 110 °C gave 4-fluoroBjF in 35% yield. This represents an improvement over previous methods for preparing BjF derivatives substituted in the B ring. The preparation of 10-fluoroBjF represents a new synthetic entry into the BjF ring system. 1-(4-Fluorophenyl)acenaphthylene (**8**) was treated with ethyl diazoacetate in the presence of copper bronze to give a mixture of *anti*- and *syn*-cyclopropanecarboxylates **9** and **10** in the ratio of 2:1. Reaction with iodotrimethylsilane gave the ring-opened ester attached at the 2-position of the substituted acenaphthylene. Reduction to the aldehyde followed by cyclodehydration with PPA at 100 °C gave 10-fluoroBjF in 58% yield. Alternatively, the cyclopropyl esters could be reduced directly to the aldehydes, which underwent efficient ring opening and cyclodehydration in PPA at 100 °C to 10-fluoroBjF in 53–57% yield.

Introduction

Benzo[*j*]fluoranthene (**1**) (BjF) (Figure 1) is a nonalternant polycyclic aromatic hydrocarbon that is tumorigenic to mice when applied topically and is carcinogenic when administered ip to newborn mice.[1] Studies in our laboratory have shown that two dihydrodiol metabolites, BjF-4,5-diol and BjF-9,10-diol, have tumorigenic activity under these bioassay conditions. While BjF-4,5-diol is more tumorigenic than BjF-9,10-diol, the latter is formed to a greater extent in vivo in mouse skin.[1a,c] The effect of fluorine substitution on biological activity will be evaluated to ascertain the relative contribution of these two major sites of metabolic activation of BjF to its overall tumorigenic activity. Fluorine frequently inhibits metabolism at the bond to which it is attached. In this report we describe the synthesis of 4-fluoroBjF (**2**) and 10-fluoroBjF (**3**) via cyclodehydration of acetals and cyclopropanecarboxaldehydes. The synthesis of **3** represents a new entry into the BjF ring system.

Scheme I. Synthesis of 4-Fluorobenzo[*j*]fluoranthene



Results and Discussion

9-Fluoro-11*H*-benzo[*a*]fluoren-11-one (**5**) was judged to be a suitable starting material for the synthesis of **2** (Scheme I). Previous syntheses of BjF derivatives substituted in either the A or B ring relied on alkylation of benzo[*a*]fluorene derivatives and required a total of nine steps.[2] It was envisioned that a much more concise synthesis could be devised by reacting a three-carbon nu-

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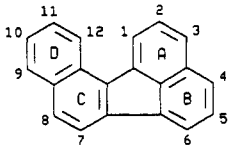

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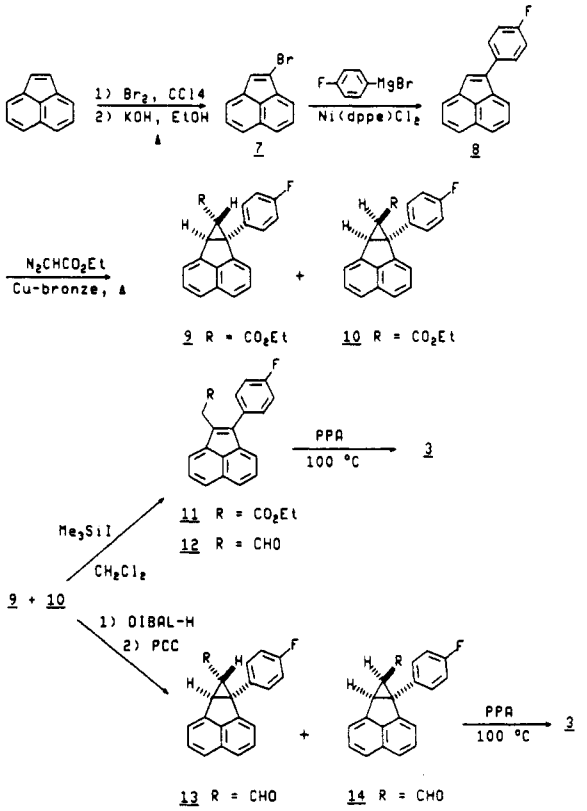
Figure 1. Structure and numbering of benzo[j]fluoranthene (1).

cleophile, bearing a latent electrophilic center at the opposite end, with an appropriate benzo[a]fluorenone derivative. Treatment with acid would release the electrophile, which would then acylate at the 10-position, forming a BjF derivative. The synthesis of requisite benzo[a]-fluorenone derivative **5** was accomplished in two steps. Displacement of the methoxy group from phenyl 2-methoxy-1-naphthoate[3] by (4-fluorophenyl)magnesium bromide gave **4** in 77% yield. Dissolution of **4** in methanesulfonic acid results in hydrolysis of the bulky phenyl ester and ring-closure to **5** in 59% yield. The location of the fluorine at the 9-position of **5** is confirmed by its ^{13}C NMR spectrum. Carbon resonances at 121.60, 120.39, and 112.40 with C–F coupling constants of 7.8 Hz, 23.3 Hz, and 24.1 Hz indicate that the fluorine is flanked at both ortho positions by protonated carbons and that there is one protonated carbon located meta to the fluorine. The three-carbon nucleophile selected for reaction with ketone **5** was the Grignard reagent prepared from 2-(2-bromoethyl)-1,3-dioxane, which provided hydroxy acetal **6** in quantitative yield. This high conversion was achieved only when an excess of the Grignard reagent was employed in the reaction. Cyclodehydration of **6** was accomplished by treatment with polyphosphoric acid (PPA) at 110 °C, giving 4-fluoroBjF (**2**) in 35% yield. Several other catalysts, including methanesulfonic acid, boron trifluoride etherate, and Amberlyst-15 resin, were evaluated for effecting this transformation. In each case lower yields of **2** were realized and several difficult to separate byproducts were formed. It had been observed in a previous study that extensive seven-membered ring formation occurred upon attempted cyclization of a benzo[a]fluorene derivative bearing a propionic acid chain at the 11-position.[2] Evidence that the product from the cyclization is **2** and not the seven-membered ring compound is obtained from the ^{13}C NMR spectrum. Protonated carbon resonances (determined from an APT experiment) were observed at 121.82 ppm and 112.21 ppm with C–F coupling constants of 8.2 Hz and 21.5 Hz. This is indicative of one ortho and one meta proton in the substituted ring. Had the cyclization been directed toward seven-membered ring formation, a similar pattern as that observed for **5** would have been evident.

The plan for the synthesis of 10-fluoroBjF begins with an acenaphthylene derivative having a 4-fluorophenyl substituent attached at the 1-position. A two-carbon unit with an electrophilic center would be attached regioselectively at the 2-position. This electrophile would be positioned so that it could attack the 4-fluorophenyl ring to complete the synthesis of the BjF derivative. The synthesis of **3** is outlined in Scheme II. Initial attempts to prepare the requisite 1-arylacenaphthylene **8** relied on reaction of 1(2*H*)-acenaphthenone with (4-fluorophenyl)-magnesium bromide followed by dehydration. The yield of the Grignard reaction was extremely poor due to the propensity of this ketone to enolize.[4] The use of cerium

Scheme II. Synthesis of 10-Fluorobenzo[j]fluoranthene



chloride to lower the basicity of the organometallic reagent[5] did not offer any significant improvement in yield. An alternant method was investigated which relies on the ability of Ni(II) to couple Grignard reagents with aryl and vinyl halides.[6] The vinyl halide required for this approach was 1-bromoacenaphthylene (**7**), which was prepared by bromination of acenaphthylene (75% yield) followed by dehydrobromination with ethanolic potassium hydroxide (98% yield). The coupling of **7** with (4-fluorophenyl)-magnesium bromide to give **8** was catalyzed by [bis(diphenylphosphino)ethane]nickel(II) chloride and proceeded in 71% yield. It was anticipated that a cyclopropanecarboxylate fused at the 1,2-position of **8** would be a good choice for the two-carbon unit needed to complete the BjF skeleton. Electrophilic ring opening was expected to occur in the direction that would form the more stable diarylmethylcarbonium ion. Cyclopropanation of **8** was accomplished by treatment with ethyl diazoacetate in the presence of copper bronze. Several other transition-metal catalysts that are known to effect diazoacetate cyclopropanations under mild conditions were also evaluated.[7] Among the catalysts tested were $PdCl_2$, $Pd(OAc)_2$, and Cu_2Cl_2. While each of these was found effective at catalyzing the reaction with **8**, copper bronze gave the highest yield (49%). The product was actually a mixture of two diastereomers, **9** and **10**, which were formed in the ratio of 2:1. In addition, a mixture of diethyl fumarate and maleate was also formed, presumably as a result of carbene coupling. These byproducts were easily removed by Kugelrohr distillation. Examination of the ^1H NMR spectrum of **9** and **10** provides a clear indication of the orientation

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(5) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392.
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(7) (a) Doyle, M. P.; Dorow, R. L.; Tamblyn, W. H.; Buhro, W. E. *Tetrahedron Lett.* **1982**, *23*, 2261. (b) Lottes, A. C.; Landgrebe, J. A.; Larsen, K. *Tetrahedron Lett.* **1989**, *30*, 4093.

of the ester group with respect to the naphthalene ring system. While the CH_2 and CH_3 groups of the anti isomer **9** absorb at 4.0 and 1.10 ppm, these same protons absorb at higher field (3.06 and 0.68 ppm) in the syn isomer **10** as a result of shielding by the large aromatic naphthalene ring. In addition, the methine proton adjacent to the ester group of **9** absorbs upfield from that of **10** due to shielding by the naphthalene ring. Ring opening of a mixture of **9** and **10** was effected cleanly by treatment with iodotrimethylsilane[8] in CH_2Cl_2, giving a single product, in 85% yield. This product was identified as **11** on the basis of its ^1H and ^{13}C NMR spectrum. Reduction of the ester with DIBAL-H in toluene at −65 °C gave aldehyde **12** along with a significant amount of the carbinol, which was oxidized back to **12** with pyridinium chlorochromate (PCC). Cyclodehydration of **12** was accomplished cleanly upon being heated in PPA at 100 °C and gave **3** in 58% yield. The UV spectrum of **3** closely resembles a spectrum of BjF. Location of the fluorine at the 10-position was determined by ^1H and ^{13}C NMR. Three protonated carbons with C–F splitting were observed at 127.04, 117.65, and 112.75 ppm, which had C–F coupling constants of 8.7, 25.0, and 20.2 Hz. The magnitude of these coupling constants indicates that fluorine is flanked by two protons with an additional proton located at a meta position. A HETCOR experiment indicated that the absorption at 127.04 ppm (J_{CF} = 8.7 Hz) correlates with the most downfield proton in the ^1H NMR spectrum (H_{12}). This confirms the identity of **3** as 10-fluoroBjF. One troubling aspect of this approach to **3** was the difficulty in purifying ring-opened ester **11** and its derived aldehyde **12**. A likely explanation for this is the acidic nature of the methylene group, which is prone to enolization. To circumvent this, we investigated the use of cyclopropyl aldehydes **13** and **14** for the cyclodehydration reaction. Esters **9** and **10** were reduced with excess DIBAL-H to their respective carbinols, which were then oxidized to **13** and **14** with PCC in 72% and 57% yields, respectively, for the two steps. Both of these aldehydes proved to be easily purified and could be crystallized. Treatment of either **13** or **14** with PPA at 100 °C gave clean conversion to **3** in yields of 53 or 57%. Cyclization of syn isomer **14** requires that ring opening precede acylation. This is not a requirement for anti isomer **13**, although the similarity in yields for the two compounds suggests that reactions proceed through a common intermediate. While these diastereomers were handled separately in the present account, separation of **13** and **14** is not necessary and the mixture has been used with equal effect. This synthesis represents a new entry into the BjF ring system and specifically provides a method for the rapid preparation of derivatives substituted in the D ring.

Experimental Section

Ether, THF, and benzene were distilled from sodium–benzophenone. [Bis(diphenylphosphino)ethane]nickel(II) chloride was purchased from Alfa and was dried under vacuum at 67 °C overnight prior to use. All other reagents were obtained from Aldrich Chemical Co., Milwaukee, WI. Melting points were determined on a Thomas Uni-Melt apparatus and are uncorrected. NMR spectra were recorded on a Varian Gemini 200 spectrometer at 200 MHz for ^1H NMR and at 50 MHz for ^{13}C NMR in $CDCl_3$. APT and HETCOR experiments were performed by using standard Varian pulse sequences. Infrared spectra were measured on a Perkin-Elmer Model 1600 FT-IR instrument. Combustion analyses were performed by Atlantic Microlabs, Inc., Norcross, GA. High resolution mass spectral analyses were performed at the Center for Advanced Food Technology, Cook College, Rutgers–The State University of New Jersey.

Phenyl 2-(4-Fluorophenyl)-1-naphthoate (4). A solution of phenyl 2-methoxy-1-naphthoate (2.5 g, 9.0 mmol) in 80 mL of 1:1 ether/benzene was added to (4-fluorophenyl)magnesium bromide (10 mL of a 1 M solution in THF) at room temperature. Following the addition, the solution was heated at reflux for 12 h. An additional portion of the Grignard reagent (6 mL) was added, and refluxing was continued for 12 h more. The solution was cooled and poured into a mixture of ice and saturated NH_4Cl solution and extracted three times with benzene. The combined organic extracts were washed with water and then brine, dried over Na_2SO_4, and evaporated under reduced pressure. Flash chromatography on silica gel (230–400 mesh), eluting with 20% CH_2Cl_2/hexanes, afforded 2.37 g (77%) of **4** as a white solid, mp 163–163.5 °C: IR (Nujol) 1748, 1559, 1210, 1123, 995 cm^{-1}; ^1H NMR δ 8.17 (m, 1), 8.04 (d, 1, J = 8.4 Hz), 7.97 (m, 1), 7.70–7.52 (m, 5), 7.40–7.31 (m, 2), 7.26–7.16 (m, 3), 6.85–6.79 (m, 2); ^{13}C NMR δ 168.36, 163.29 (d, J = 246.5 Hz), 151.02, 137.91, 137.44 (d, J = 3.4 Hz), 132.93, 131.22 (d, J = 8.2 Hz), 130.95, 130.47, 130.24, 130.02, 128.87, 128.56, 127.86, 127.17, 126.65, 125.35, 121.83, 116.10 (d, J = 21.5 Hz). Anal. Calcd for $C_{23}H_{15}FO_2$: C, 80.70; H, 4.39. Found: C, 80.53; H, 4.44.

9-Fluoro-11*H*-benzo[*a*]fluoren-11-one (5). A solution of **4** (600 mg, 1.75 mmol) in 20 mL of methanesulfonic acid was stirred at room temperature under N_2 for 12 h. The dark red solution was poured into 300 mL of ice–water, which was then extracted twice with EtOAc. The combined extracts were washed with saturated Na_2CO_3, water, and then brine and dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a red solid, which was crystallized from 1:1 ether/hexanes to give 205 mg (47% yield) of **5** as red needles. The mother liquor was concentrated and purified by flash chromatography on silica gel, eluting with 20% ether/hexanes to give an additional 52 mg of **5**. The total yield was 59%. An analytical sample was recrystallized from MeOH–EtOAc to give red needles, mp 175.5–176.5 °C: IR (CCl_4) 3054, 1710, 1585, 1479, 1446, 1267, 1245, 1212, 1161 cm^{-1}; ^1H NMR δ 8.89 (d, H_1, $J_{1,2}$ = 8.4 Hz), 7.98 (d, H_5, $J_{5,6}$ = 8.4 Hz), 7.77 (d, H_4, $J_{3,4}$ = 8.1 Hz), 7.63–7.54 (m, $H_{2,6}$), 7.47–7.38 (m, $H_{3,7}$), 7.28 (dd, H_{10}, $J_{9F,10}$ = 7.2 Hz, $J_{8,10}$ = 2.4 Hz), 7.08 (m, H_8); ^{13}C NMR δ 194.44, 164.48 (d, J = 249.10 Hz), 146.37, 137.48, 136.89, 134.58, 130.73, 130.20, 129.10, 127.55, 126.99, 124.63, 121.60 (d, J = 7.8 Hz), 120.39 (d, J = 23.3 Hz), 118.38, 112.40 (d, J = 24.1 Hz). Anal. Calcd for $C_{17}H_9FO$: C, 82.26; H, 3.63. Found: C, 82.05; H, 3.69.

2-(2-[9-Fluoro-11-hydroxybenzo[*a*]fluoren-11-yl]ethyl)-1,3-dioxane (6). Magnesium turnings (125 mg, 5.1 mmol) were covered with THF (12 mL) under a nitrogen atmosphere and treated at room temperature with ethylene dibromide (146 μL, 1.7 mmol) and freshly distilled 2-(2-bromoethyl)-1,3-dioxane (466 μL, 3.4 mmol). The mixture was warmed in an oil bath at 55 °C for 4 h and then **5** (850 mg, 3.4 mmol) in 40 mL of THF was added dropwise to the warm solution, which was maintained at 55 °C overnight. TLC of the reaction mixture indicated that a considerable amount of **5** remained unreacted. An additional portion (5.1 mmol) of Grignard reagent was prepared in a separate flask and added to the reaction mixture. After being stirred at 60 °C for 1 h, the reaction was judged to be complete by TLC (silica gel, 1:1 ether/hexanes) and was allowed to cool to room temperature. The mixture was poured into cold saturated NH_4Cl and extracted with EtOAc. The organic layer was separated and the aqueous layer extracted with an additional portion of EtOAc. The combined EtOAc extracts were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. Flash chromatography on silica gel eluting with 20% EtOAc/hexanes afforded 1.23 g (98% yield) of **6** as a colorless oil: IR (neat) 3397, 3053, 2961, 2854, 1481, 1257, 1144, 816, 736 cm^{-1}; ^1H NMR δ 8.36 (m, 1, H_1, J = 8.3 Hz), 7.86 (d, 1, J = 7.3 Hz), 7.81 (d, 1, J = 6.1 Hz), 7.64 (d, 1, J = 8.3 Hz), 7.57–7.40 (m, 3), 7.22 (dd, H_{10}, $J_{10,F}$ = 8.4 Hz, $J_{8,10}$ = 2.4 Hz), 7.04 (m, H_8, $J_{8,F}$ = 9.1 Hz, $J_{7,8}$ 8.3 Hz), 4.17 (t, $CHOR_2$, J = 5.6 Hz), 3.95 (m, 2, CH_2O), 3.50 (m, 2, CH_2O), 2.53 (t, CH_2COH, J = 8.0 Hz), 2.05–1.80 (m, 1), 1.30–0.90 (m, 3); ^{13}C NMR δ 163.61 (d, J = 245.9 Hz), 152.74 (d, J = 7.2 Hz), 142.70 (d, J = 2.6 Hz), 136.78, 136.22, 134.17, 130.71, 130.20, 129.62, 127.26, 125.90, 124.63, 121.16 (d, J = 8.4 Hz), 118.44, 116.04 (d, J = 23.0 Hz), 111.52 (d, J = 23.2 Hz), 102.12, 84.39, 66.97, 34.18, 29.94, 25.79; high resolution mass spectrum, exact mass calcd for $C_{23}H_{21}FO_3$ 364.147530, obsd 364.147470.

(8) Brown, S. P.; Bal, B. S.; Pinnick, H. W. *Tetrahedron Lett.* **1981**, 22, 4891.

4-Fluorobenzo[j]fluoranthene (2). A solution of **6** (23 mg, 0.064 mmol) in $CHCl_3$ (2 mL) was added dropwise with stirring to polyphosphoric acid (2 mL) at 60 °C under a nitrogen atmosphere. The $CHCl_3$ evaporated, leaving a homogeneous solution of **6** in PPA. Stirring was continued at 60 °C for 12 h, whereupon the reaction mixture was poured into cold water. The solution was extracted twice with EtOAc and the combined organic layer was then washed with water, saturated aqueous $NaHCO_3$, and brine and dried over Na_2SO_4. Following solvent removal, the residue was purified by flash chromatography on silica, eluting with hexanes giving 6.1 mg (35% yield) of **2** as a yellow solid. Recrystallization from EtOH afforded **2** as yellow needles, mp 185 °C: ^1H NMR δ 8.67 (d, H_{12}, $J_{11,12}$ = 8.4 Hz), 8.47 (d, H_1, $J_{1,2}$ = 7.3 Hz), 8.04 (d, H_3, $J_{2,3}$ = 8.4 Hz), 8.00 (d, H_8, $J_{7,8}$ = 8.4 Hz), 7.93 (m, H_9), 7.86 (d, H_6), 7.85 (d, H_7), 7.74 (dd, H_2), 7.63 (m, H_{11}), 7.49 (m, H_{10}), 7.23 (m, H_5); ^{13}C NMR δ 160.63 (d, J = 257.2 Hz), 138.06, 137.83, 134.65 (d, J = 2.6 Hz), 134.20, 133.91 (d, J = 9.0 Hz), 133.72, 131.16, 129.91, 129.30, 128.97, 127.68, 125.78, 125.30, 124.53, 121.82 (d, J = 8.2 Hz), 121.21, 120.91 (d, J = 19.3 Hz), 120.07, 112.21 (d, J = 21.5 Hz). Anal. Calcd for $C_{20}H_{11}F$: C, 88.89; H, 4.07. Found: C, 88.75; H, 4.13.

1-Bromoacenaphthylene (7). A solution of 1,2-dibromoacenaphthene[9] (8.28 g, 26.5 mmol) and potassium hydroxide (8 g, 0.14 mol) in EtOH (200 mL) was stirred at reflux for 48 h. After being cooled to room temperature, the solution was poured into water and extracted with EtOAc. The organic layer was washed with water and then brine, dried over Na_2SO_4, and evaporated to a dark-colored oil. Kugelrohr distillation (0.3 mmHg, pot temperature 126–140 °C) afforded 5.82 g of **7** as a yellow oil (95% yield): ^1H NMR δ 7.89–7.48 (m, 6), 7.17 (s, H_1); ^{13}C NMR δ 138.79, 138.56, 129.50, 129.35, 129.06, 128.50, 128.19, 128.04, 127.61, 124.21, 124.02, 121.29.

1-(4-Fluorophenyl)acenaphthylene (8). A suspension of dichloro[1,2-bis(diphenylphosphino)ethane]nickel(II) (27 mg, 0.05 mmol) in 30 mL of ether was stirred at 0 °C under nitrogen as **7** (1.135 g, 4.9 mmol) in 30 mL of ether was added. To this cold solution was added (4-fluorophenyl)magnesium bromide (6.3 mL of a 1 M solution in ether). After the addition, the solution was allowed to warm to room temperature, stirred for 30 min, and then heated at reflux overnight. After cooling to room temperature, 1 N HCl was added (5 mL), and the ether layer was separated and was washed with saturated aqueous $NaHCO_3$, water, and brine. Ether was removed in vacuo and the residue purified by flash chromatography on silica, eluting with hexanes. The pure product **8** was isolated as orange-yellow crystals, 860 mg (71% yield), mp 62–63 °C: ^1H NMR δ 7.96–7.58 (m, 8), 7.28–7.20 (m, 2), 7.16 (s, H_1); ^{13}C NMR δ 163.20 (d, J = 246.5 Hz), 142.97, 139.62, 139.15, 132.89 (d, J = 3.6 Hz), 130.06 (d, J = 8.0 Hz), 129.85, 129.03, 128.64, 128.32, 128.12, 127.70, 126.05, 124.86, 124.56, 116.31 (d, J = 21.5 Hz). Anal. Calcd for $C_{18}H_{11}F$: C, 87.81; H, 4.47. Found: C, 87.68; H, 4.53.

Products from the Reaction of Ethyl Diazoacetate with 8. A mixture of **8** (738 mg, 3 mmol) and copper bronze (64 mg, 1 mmol) was heated in an oil bath at 100 °C. To this melt was added ethyl diazoacetate (0.315 mL, 3 mmol). When the bubbling subsided, an additional 0.315 mL of ethyl diazoacetate was added followed immediately by 64 mg of copper bronze. This was repeated until a total of 18 mmol of ethyl diazoacetate and 6 mmol of copper bronze was added. After the final addition, the flask was heated at 100 °C for 1 h and then cooled to room temperature. The mixture was filtered, rinsing the filter with CH_2Cl_2, and the filtrate was evaporated. Kugelrohr distillation (0.3 mmHg, pot temperature 40–50 °C) removed a mixture of diethyl fumarate and diethyl maleate. The residue was purified by flash chromatography on silica, eluting first with hexane to removed unreacted **8** (38 mg). The eluting solvent was changed to 20% EtOAc/hexanes to elute anti cyclopropyl ester **9**, 235 mg (34% yield): IR (CCl_4) 3051, 2983, 2925, 1731, 1549, 1515, 1198 cm^{-1}; ^1H NMR δ 7.71–7.65 (m, 2), 7.57–7.46 (m, 4), 7.44–7.37 (m, 1), 7.23–7.08 (m, 3), 4.08–3.97 (m, 3, CH_2OR and $CHAr$), 2.22 (d, $CHCO_2R$, J = 3.3 Hz), 1.10 (t, CH_3, J = 7.0 Hz); ^{13}C NMR δ 169.56, 162.92 (d, J = 245.2 Hz), 146.82, 142.93, 136.00, 132.18, 132.17 (d, J = 8.2 Hz), 128.24, 128.11, 124.70, 124.36, 120.99, 120.75, 116.03 (d, J = 21.3 Hz), 61.03, 47.07, 45.09, 36.12, 14.29; high resolution mass spectrum, exact mass calcd for $C_{22}H_{17}FO_2$ 332.121310, obsd 332.121255. Syn cyclopropyl ester **10** eluted second and was obtained in 15% yield (153 mg): IR (CCl_4) 3046, 2982, 2930, 1741, 1550, 1514, 1234, 1224, 1157 cm^{-1}; ^1H NMR δ 7.73–7.60 (m, 2), 7.55–7.40 (m, 5), 7.20–7.05 (m, 3), 3.67 (q, CH_2O, J = 7.6 Hz), 3.57 (d, $CHAr$, J = 9.0), 3.06 (d, $CHCO_2R$), 0.68 (t, CH_3); ^{13}C NMR δ 168.67, 162.83 (d, J = 245.7 Hz), 144.05, 140.50, 137.93, 135.72 (d, J = 3.4 Hz), 131.55 (d, J = 8.1 Hz), 131.24, 128.19, 128.14, 124.68, 124.25, 122.32, 122.00, 116.07 (d, J = 21.4 Hz), 60.47, 45.76, 39.84, 38.25, 13.78; high resolution mass spectrum, exact mass calcd for $C_{22}H_{17}FO_2$ 332.121310, obsd 332.121255.

Ethyl [2-(4′-Fluorophenyl)acenaphthylen-1-yl]acetate (11). A solution of a mixture of **9** and **10** (35 mg, 0.105 mmol) in dry CH_2Cl_2 (5 mL, distilled from P_2O_5) was stirred under nitrogen as iodotrimethylsilane (0.060 mL, 0.44 mmol) was added by syringe. Stirring at room temperature was continued for 90 min. The reaction mixture was then poured onto a short column of silica gel and eluted with 10% EtOAc/hexanes to give **11** as a yellow oil, 29.9 mg, 85% yield: IR (CCl_4) 3065, 3048, 2982, 1738, 1503, 1227, 1159, 1034 cm^{-1}; ^1H NMR δ 7.86–7.79 (m, 3), 7.69–7.54 (m, 5), 7.27–7.19 (m, 2), 4.21 (q, CH_2O, J = 7.0 Hz), 3.84 (s, CH_2CO_2R), 1.28 (t, CH_3); ^{13}C NMR δ 172.01, 163.09 (d, J = 246.5 Hz), 140.34, 140.24, 140.12, 131.81, (d, J = 8.0 Hz), 131.15, 131.09, 128.71, 128.44, 128.16, 127.87, 127.82, 123.99, 123.51, 116.14 (d, J = 21.2 Hz), 61.48, 33.13, 14.39; high resolution mass spectrum, exact mass calcd for $C_{22}H_{17}FO_2$ 332.121310, obsd 332.121255.

Preparation of *anti*-Cyclopropanecarboxaldehyde 13. A solution of **9** (133 mg, 0.40 mmol) in 10 mL of toluene (freshly distilled from CaH_2) was cooled to −60 °C under nitrogen and treated with 1 mL of a 1 M solution of diisobutylaluminum hydride in toluene. The temperature was allowed to warm to 20 °C and stirring was continued for 2.5 h. Excess DIBAL-H was destroyed by treatment with 1 mL of methanol, and the solution was diluted with ether (70 mL), washed with water and brine, and dried over Na_2SO_4. Evaporation of the solvents under reduced pressure afforded the carbinol as a yellow oil, 138 mg: IR (CCl_4) 3387, 3045, 2929, 1608, 1513, 1490, 1222, 1022, 906, 782, 726 cm^{-1}; ^1H NMR δ 7.70–7.08 (m, 10), 3.53 (d, CH_2OH, J = 7.0 Hz), 3.23 (d, $CHAr$, J = 3.5 Hz), 1.68 (m, $CHCH_2OH$). The crude carbinol was dissolved in CH_2Cl_2 and added to a stirred suspension of pyridinium chlorochromate (95 mg, 0.44 mmol) in CH_2Cl_2 (5 mL). Stirring at room temperature was continued for 90 min, and the reaction mixture was added directly to the top of a column of silica gel and flash chromatographed, eluting with 20% EtOAc/hexanes. Aldehyde **11** was obtained as a yellow solid, 83 mg, 72% yield. Recrystallization from ether–hexanes afforded **13** as yellow prisms, mp 132 °C: IR (CCl_4) 3044, 2963, 2923, 2823, 2732, 1708, 1547, 1512, 1235, 1220, 1004, 973 cm^{-1}; ^1H NMR δ 9.07 (d, CHO, J = 6.0 Hz), 7.74–7.65 (m, 2), 7.58–7.38 (m, 5), 7.21–7.08 (m, 3), 4.09 (d, $CHAr$, J = 3.2 Hz), 2.30 (dd, $CHCHO$); ^{13}C NMR δ 197.24, 163.04 (d, J = 246.6 Hz), 146.26, 141.93, 135.62, 132.55 (d, J = 8.3 Hz), 132.15, 131.36 (d, J = 3.1 Hz), 128.31, 128.22, 125.10, 124.72, 121.26, 120.95, 116.55 (d, J = 21.7 Hz). 53.44, 48.31, 36.33. Anal. Calcd for $C_{20}H_{13}FO$: C, 83.33; H, 4.51: Found: C, 83.08, H, 4.59.

Preparation of *syn*-Cyclopropanecarboxaldehyde 14. This compound was prepared as described above for **13**, giving the aldehyde **12** in 57% yield. The product was recrystallized from ether–hexanes as yellow needles, mp 130 °C: IR (CCl_4) 3045, 2962, 2931, 2850, 1705, 1549, 1253, 1238, 1222, 1004, 978 cm^{-1}; ^1H NMR δ 8.16 (d, CHO, J = 6.6 Hz), 7.76–7.68 (m, 2), 7.58–7.41 (m, 5), 7.26–7.06 (m, 3), 3.77 (d, $CHAr$, J = 8.3 Hz), 2.78 (dd, $CHCHO$); ^{13}C NMR δ 201.93, 162.96 (d, J = 246.5 Hz), 142.92, 139.10, 137.53, 134.76 (d, J = 3.1 Hz), 131.42 (d, J = 8.2 Hz), 131.27, 128.77, 125.26, 124.86, 122.74, 122.37, 116.20 (d, J = 21.2 Hz), 48.08, 44.35, 40.25. Anal. Calcd for $C_{20}H_{13}FO$: C, 83.33; H, 4.51: Found: C, 83.23; H, 4.55.

10-Fluorobenzo[j]fluoranthene (3). A solution of **13** (22 mg, 0.076 mmol) in a small amount of CH_2Cl_2 was added slowly to polyphosphoric acid (10 mL) at 100 °C. The reaction mixture was stirred at this temperature for 20 h, was then allowed to cool slightly, and was poured into water. The mixture was extracted with ether and the organic layer was washed with water and then brine and dried over Na_2SO_4. Flash chromatography on silica gel, eluting with hexanes, gave 11 mg (53%) of **3** as a yellow solid.

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Recrystallization from MeOH afforded **3** as yellow needles; mp 183.5 °C: ^{1}H NMR δ 8.67 (dd, H_{12}, $J_{11,12}$ = 9.3 Hz, $J_{10F,12}$ = 5.4 Hz), 8.37 (d, H_1, $J_{1,2}$ = 7.1 Hz), 8.04 (d, H_8, $J_{7,8}$ = 8.4 Hz), 7.98 (d, H_6, $J_{5,6}$ = 6.8 Hz), 7.88 (d, H_4, $J_{4,5}$ = 8.3 Hz), 7.86 (d, H_3, $J_{2,3}$ = 8.2 Hz), 7.77 (d, H_7), 7.74-7.60 (m, $H_{2,5}$), 7.53 (dd, H_9, $J_{9,10F}$ = 9.9 Hz, $J_{9,11}$ = 2.6 Hz), 7.38 (m, H_{11}); ^{13}C NMR δ 160.77 (d, J = 245.4 Hz), 137.94, 137.59, 137.54, 137.47, 135.52, 135.34, 132.35, 130.16, 128.64, 128.46, 128.03, 127.90, 127.74, 127.04 (d, J = 8.7 Hz), 124.59, 121.42, 121.37, 117.65 (d, J = 25.0 Hz), 112.75 (d, J = 20.2 Hz); high resolution mass spectrum, exact mass calcd for $C_{20}H_{11}F$ 270.084530, obsd 270.084475.

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Improved Correlation of ^{33}S Chemical Shifts with pK_a's of Arenesulfonic Acids: Use of ^{33}S NMR for pK_a Determination

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Reported here is an improved linear correlation between ^{33}S chemical shifts and the pK_a's of arenesulfonic acids **1**, **2**, and **8-10**, previously determined by UV spectroscopy. Using that linear correlation, we determined the following previously unreported pK_a's (±0.04) from ^{33}S chemical shifts: *p*-aminobenzenesulfonic (-6.47), *p*-(dimethylamino)benzenesulfonic (-6.43), *p*-(dimethylammonio)benzenesulfonic (-7.18), *p*-chlorobenzenesulfonic (-6.88), *p*-acetylbenzenesulfonic (-6.96), *p*-nitrobenzenesulfonic (-7.23), *m*-(trifluoromethyl)benzenesulfonic (-7.04), and *m*-nitrobenzenesulfonic (-7.25) acids. Also, ^{33}S NMR provides an improved value for the second pK_a of *m*-benzenedisulfonic acid (-7.00); the second pK_a of *p*-benzenedisulfonic acid (-6.99) is, within experimental error, identical with that of the meta compound.

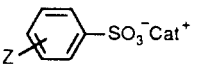
Introduction

Previous studies of substituent effects on the acidities of arenesulfonic acids, including **1**, **2**, and **8-10**, and the first pK_a's of **3** and **13**, have been conducted by measuring their degrees of ionization in solutions of varying Hammett acidity (H_0) with UV or ^{1}H NMR methods.[1] It has been necessary to carry out these pK_a determinations in concentrated sulfuric acid solution, where significant amounts of the free sulfonic acid and its conjugate base are both present. Experimental difficulties limited these methods to sulfonic acids showing an isolated B band in the UV and to the determination of first ionizations of disulfonic acids only. Therefore, the pK_a's of **4**, **5**, **15**, and 3,5-bis(trifluoromethyl)benzenesulfonic acid have previously been calculated from a Hammett plot of pK_a vs σ, with use of the experimentally determined pK_a's of **1**, **2**, **8**, **10**, and the first ionization of **3**.[2]

The field of ^{33}S NMR has grown rapidly, and a good review of the subject has appeared.[3] Hinton found a linear relationship between the ^{33}S chemical shifts of arenesulfonic acids **1**, **8**, **11**, and **15** and Hammett σ constants.[4] Crumrine et al. reported a linear correlation between the ^{33}S NMR chemical shifts of sulfonic acids **1**, **2**, **4**, **5**, **8**, **10**, **15**, and their pK_a's.[5] The ^{33}S NMR spectra in both of these studies were recorded on low-field spectrometers, with aqueous solutions of rather high concentration.

With higher applied magnetic field strength, the receptivity of the nucleus and spectral resolution are both enhanced. Recently, we reported that, in a given solvent, line widths were narrowest at low concentration where ion-ion contributions to nuclear relaxation were minimized.[6] It is well-known that narrower spectral lines are obtained at higher temperatures than at lower ones.[7] By these principles, more accurate ^{33}S chemical shifts were obtained in this investigation. Also, it was possible to record the ^{33}S spectra of several compounds with limited solubility. Subsequently, we found ^{33}S NMR to be an accurate and facile experimental method for determining the pK_a's of arenesulfonic acids, which circumvented the experimental difficulties of earlier methods.

The ^{33}S NMR spectra of arenesulfonates ($ZC_6H_4SO_3^-Cat^+$) **1-15** were recorded in 0.046-0.13 M aqueous solutions, where the sulfonates are almost completely ionized.[8] Consequently, the ^{33}S chemical shifts were not affected by the counterion.[9]



1, Z = H	**6**, Z = *p*-N(CH$_3$)$_2$	**11**, Z = *p*-Cl
2, Z = *m*-CH$_3$	**7**, Z = *p*-NH$_2$	**12**, Z = *p*-COCH$_3$
3, Z = *m*-SO$_3^-$	**8**, Z = *p*-CH$_3$	**13**, Z = *p*-SO$_3^-$
4, Z = *m*-CF$_3$	**9**, Z = *p*-NH$_3^+$	**14**, Z = *p*-NH(CH$_3$)$_2^+$
5, Z = *m*-NO$_2$	**10**, Z = *p*-Br	**15**, Z = *p*-NO$_2$

Results and Discussion

Table I shows the ^{33}S chemical shifts and line widths of the arenesulfonates ($ZC_6H_4SO_3^-Cat^+$) at 20 and 39 °C. Errors in the chemical shift values are ca. ±0.3 ppm for

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