mg, 28.7 mmol) and dichloromethyl methyl ether (5 μL, 57.4 μmol) in 1 mL of dichloromethane at 0 °C. The instantly black mixture was stirred at 0 °C for 15 min (TLC, ethyl acetate–hexane, 1:1; R_f 0.32, ortho isomer; R_f 0.17, **20**), and 1 M aqueous hydrochloric acid (1 mL) was added. After being stirred for 15 min, the mixture was extracted with dichloromethane (4 × 5 mL), and the extracts were dried ($MgSO_4$) and concentrated under reduced pressure to a yellow solid. Flash chromatography on a 1 × 12 cm column using 5% ethyl acetate in dichloromethane gave 0.5 mg (4%) of the ortho isomer, followed by 5.8 mg (51%) of the desired para isomer **21**.

Ortho isomer: ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.05 (s, 3 H), 4.15 (s, 3 H), 4.17 (s, 3 H), 5.50 (d, 1 H, J = 10.6 Hz), 6.00 (d, 1 H, J = 17.5 Hz), 6.83 (dd, 1 H, J = 17.5, 10.6 Hz), 7.42 (br s, 1 H), 8.00 (d, 1 H, J = 9.0 Hz), 8.21 (d, 1 H, J = 1.1 Hz), 8.45 (d, 1 H, J = 9.0 Hz), 8.57 (s, 1 H), 10.63 (s, 1 H).

21: mp 195–200 °C dec; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.03 (s, 3 H), 4.04 (s, 3 H), 4.13 (s, 3 H), 5.47 (d, 1 H, J = 11.0 Hz), 5.96 (d, 1 H, J = 17.7 Hz), 6.79 (dd, 1 H, J = 17.7, 11.0 Hz), 6.98 (d, 1 H, J = 8.6 Hz), 7.35 (d, 1 H, J = 1.6 Hz), 8.10 (d, 1 H, J = 8.6 Hz), 8.11 (d, 1 H, J = 1.6 Hz), 8.50 (s, 1 H), 11.15 (s, 1 H); NOE difference spectrum, irradiation of the δ 4.03 methyl signal showed a 5.9% enhancement of the doublet at δ 6.98; IR ($CHCl_3$) 1730, 1675, 1605, 1585, 1140 cm^{-1}; MS, m/e (%) 390 (M^+, 100.0), 362 (15.3), 203 (24.5).

Acknowledgment. This research was supported by PHS Grant AI 16943. An American Cancer Society Fellowship (Grant PF 2764) to A.D.P. and a Merck Postdoctoral Fellowship to N.H.N. are gratefully acknowledged. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale University, which was supported by NSF Chemistry Division Grant CHE7916210. We also thank Dr. L. McGee of Du Pont for an authentic sample of defucogilvocarcin V and for apprising us of their total synthesis.

Registry No. 1, 80155-95-9; 7, 5293-42-5; 8, 110582-82-6; 8 (acid chloride), 112374-25-1; 10, 112374-26-2; 11, 112374-27-3; 13, 112374-28-4; 14, 112374-29-5; 16, 112374-30-8; 17, 112374-31-9; 18, 112374-32-0; 19, 112374-33-1; 21 (*ortho*-formyl), 112374-34-2; 21 (*para*-formyl), 112374-35-3; $Ph_3MeP^+ \cdot Br^-$, 1779-49-3; $H_2NC(CH_3)_2CH_2OH$, 124-68-5; 3-bromo-4,5-dimethoxybenzaldehyde, 6948-30-7; 2-bromojuglone, 69008-03-3.

Oxidation of Polynuclear Aromatic Hydrocarbons with Ceric Ammonium Sulfate: Preparation of Quinones and Lactones[1,2]

George Balanikas, Nalband Hussain, Shantu Amin,* and Stephen S. Hecht

Division of Chemical Carcinogenesis, Naylor Dana Institute for Disease Prevention, American Health Foundation, Valhalla, New York 10595

Received June 6, 1987

The oxidation of polynuclear aromatic hydrocarbons with ceric ammonium sulfate (CAS) in sulfuric acid was investigated. Oxidation of benzo[*k*]fluoranthene (**1**) gave a mixture of the 7,12- and 2,3-diones **3** and **4**. The 2,3-dione (**4**) was used as the starting material for a facile synthesis of 2,3-dihydro-2,3-dihydroxybenzo[*k*]fluoranthene (**5**) and the corresponding diol epoxide **6**, which are potentially important metabolites of benzo[*k*]fluoranthene. In a similar manner, 2,3-dihydro-2,3-dihydroxyfluoranthene (**7**) and its diol epoxide **8** were prepared from fluoranthene. Oxidation of benzo[*b*]fluoranthene (**2**) with CAS did not yield quinones, but instead gave benzo[*d*]fluoreno[2,1-*b*]pyran-5,13-dione (**9**), which was identified by its spectral properties and by reduction with $LiAlH_4$. The lactone **9** formed via initial *K*-region oxidation of **2**. It was not formed from 1-hydroxybenzo[*b*]fluoranthene (**12**), which gave benzo[*b*]fluoranthene-1,2-dione (**13**) upon CAS oxidation. CAS oxidation of benzo[*a*]pyrene (**14**) gave a mixture of the 1,6- and 3,6-quinones **17** and **18**. Treatment of benz[*a*]anthracene (**15**) with CAS yielded 7-oxo-12-hydroxy-7,12-dihydrobenz[*a*]anthracene (**19**) and the 7,12-quinone **20**. Oxidation of chrysene (**16**) with CAS gave 6*H*-benzo[*d*]naphtho[1,2-*b*]pyran-6-one (**21**) and the 5,6-quinone **22**. The results of this study demonstrate that CAS oxidation is useful for the synthesis of certain PAH quinones or lactones, from polynuclear aromatic hydrocarbons, depending on the ring system.

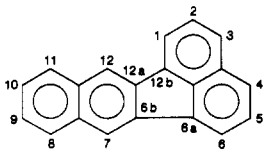
Polynuclear aromatic hydrocarbons (PAH) are an important class of environmental carcinogens. Their carcinogenic properties are due in part to an initial interaction of specific metabolites with DNA. Although diol epoxides are believed to be key metabolites involved in DNA binding, other pathways of metabolic activation may also play a role, and consequently it is essential that PAH metabolites be thoroughly characterized.[3,4] Extensive synthetic methods have been developed for the preparation of PAH metabolites.[5] In some cases, multistep syntheses are required. We are interested in new methods that might yield key metabolites of PAH efficiently and inexpensively. Therefore, we have investigated the reaction of ceric ammonium sulfate (CAS) with several PAH. In previous studies, CAS has been shown to oxidize naphthalene, phenanthrene, anthracene, fluoranthene, and some substituted naphthalenes to quinones in good yield but the application of the method to higher PAH has not been reported.[6-9] Ceric ammonium nitrate has also been used to oxidize substituted aromatic systems.[10-13]

(1) Paper 109 in the series "A Study of Chemical Carcinogenesis".
(2) Supported by Contract N01 CP 61041 from the National Cancer Institute. We thank Dr. Bijaya Misra for obtaining NMR spectra.
(3) Dipple, A.; Moschel, R. C.; Bigger, C. A. H. In *Chemical Carcinogens*; Searle, C. E., Ed.; American Chemical Society: Washington, DC, 1984; pp 41–163.
(4) *International Agency for Research on Cancer Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*; International Agency for Research on Cancer: Lyon, France, 1983; Vol. 32, pp 33–91.
(5) Harvey, R. G. *Synthesis* **1986**, 605.
(6) Periasamy, M.; Bhatt, M. V. *Synthesis* **1977**, 330.
(7) Periasamy, M.; Bhatt, M. V. *Tetrahedron Lett.* **1977**, 2357.
(8) Skarzewski, J. *Tetrahedron* **1984**, *40*, 4997.
(9) Beletskaya, I. P.; Makhonkov, D. I. *Russ. Chem. Rev.* (*Engl. Transl.*) **1981**, *50*, 534.
(10) Ho, T.-L. *Synthesis* **1973**, 347.
(11) Farina, F.; Torres, T. *J. Chem. Res. Synop.* **1985**, 202.

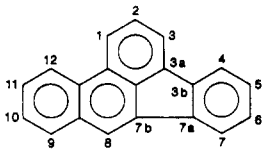
0022-3263/88/1953-1007$01.50/0

Results and Discussion

Since we are interested in mechanisms of activation of nonalternant PAH, and the CAS oxidation of fluoranthene had been shown to proceed in good yield, our initial studies focused on benzo[*k*]fluoranthene (**1**) and benzo[*b*]-fluoranthene (**2**). Oxidation of **1** with CAS gave a mixture

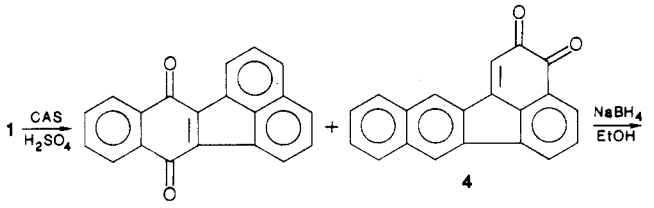


1

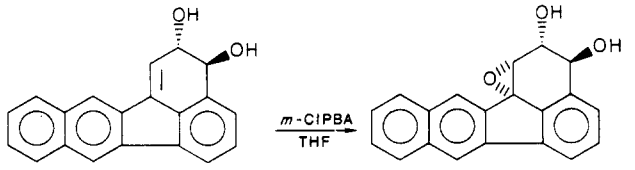


2

of the 7,12-dione **3** (28%) and the 2,3-dione **4** (10%). They were separated by column chromatography and identified by their MS and NMR. The dione **4** provided the starting material for preparation of dihydrodiol **5** by reduction with $NaBH_4$. This two-step procedure for synthesis of **5**, which



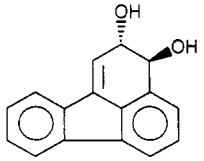
3 **4**



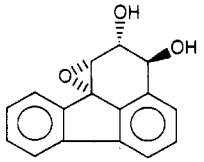
5 **6**

may be a key metabolite of **1**, avoids the lengthy procedures potentially involved in preparation of 3-oxo-1,2,3,12b-tetrahydrobenzo[*k*]fluoranthene, which is an alternate precursor to **5**. The diol epoxide **6**, a potential ultimate carcinogen of **1**, was prepared from **5**.

The CAS method was also applied to the synthesis of the fluoranthene dihydrodiol **7** and the corresponding diol epoxide **8**, which has been implicated in macromolecular binding of fluoranthene.[14] For this synthesis, fluoranthene-2,3-dione was prepared by CAS oxidation of fluoranthene, as previously described.[6] Conversion to **7** and **8** proceeded in 21% and 55% yields, respectively. Although the overall yield of **8** from fluoranthene was 8%, the synthesis required only three steps. Previously reported syntheses of dihydrodiol **7** proceeded in overall yields of 4–12% from fluorene-9-carboxylic acid, in eight steps.[15,16]

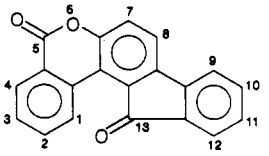


7

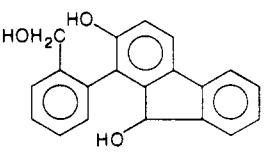


8

We expected that oxidation of benzo[*b*]fluoranthene (**2**) would provide the corresponding 1,2-dione, by analogy to the results with fluoranthene. However, the major product from this reaction, isolated in 53% yield, had a molecular composition of $C_{20}H_{10}O_3$. Its IR spectrum had bands at 1700, 1725, and 1730 cm^{-1}. These data indicated that the product was a lactone. The structure was determined to be benzo[*d*]fluoreno[2,1-*b*]pyran-5,13-dione (**9**), from the 300-MHz proton NMR spectrum. The couplings of the assigned protons were confirmed by the COSY spectrum. Further evidence for the structure was obtained from the ^{13}C NMR spectrum which showed resonances at 192.0 ppm, corresponding to the carbonyl of the five-membered ring, 174.0 ppm, corresponding to the lactone carbonyl, and 160.0 and 152.3 ppm, corresponding to the carbons adjacent to the oxygen and carbonyl of the lactone, respectively. Reduction of **9** with $LiAlH_4$ gave predominantly the triol **10**, consistent with the assigned structure.

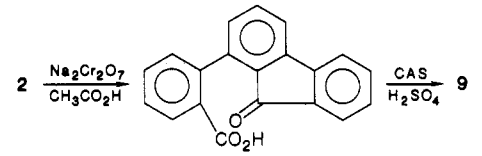


9



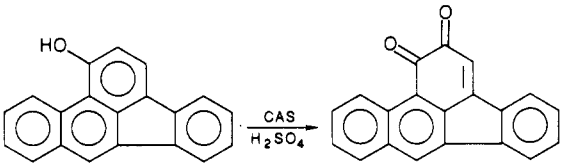
10

A plausible mechanism for formation of **9** is through the keto acid **11**. Earlier studies had shown that **11** is the major product of sodium dichromate oxidation of **2**.[17]



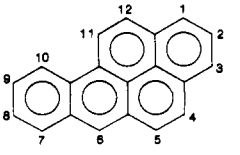
11

Preparation of **11** and reaction with CAS gave **9** in 40% yield, confirming this pathway. It also seemed possible that **9** could have formed from 1-hydroxybenzo[*b*]-fluoranthene (**12**), which might have been the initial product of CAS oxidation of **2**. To test this hypothesis, **12** was subjected to CAS oxidation. The lactone **9** was not obtained. Instead the product was the 1,2-dione **13**, which was formed rapidly in 30% yield. This observation suggests that CAS oxidation may be useful for the preparation of diones from PAH phenols.

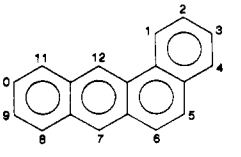


12 **13**

Investigation of the CAS reaction was then extended to three of the most commonly studied alternant PAH, benzo[*a*]pyrene (**14**), benz[*a*]anthracene (**15**), and chrysene (**16**), since formation of the appropriate quinones might

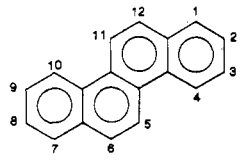


14



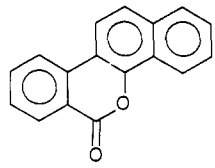
15

(12) Syper, L. *Tetrahedron Lett.* **1966**, 4493.
(13) Chorn, T. A.; Giles, R. G. F.; Mitchell, P. R. K.; Green, I. R. *J. Chem. Soc. Chem. Commun.* **1981**, 534.
(14) Babson, J. R.; Russo-Rodriguez, S. E.; Rastetter, H.; Wogan, G. N. *Carcinogenesis* **1986**, *7*, 859.
(15) Rastetter, W. H.; Nachbar, R. B., Jr.; Russo-Rodriguez, S.; Wattley, R. V.; Thilly, W. G.; Andon, B. M.; Jorgensen, W. L.; Ibrahim, M. *J. Org. Chem.* **1982**, *47*, 4873.
(16) Rice, J. E.; LaVoie, E. J.; Hoffmann, D. *J. Org. Chem.* **1983**, *48*, 2360.
(17) Clar, E. *Polycyclic Hydrocarbons*; Academic: New York, 1964; Vol. 2, p 311.



16

lead to improved dihydrodiol syntheses. Oxidation of **14** gave a 43% yield of a mixture of the 1,6- and 3,6-quinones **17** and **18**. Oxidation of **15** produced 7-oxo-12-hydroxy-7,12-dihydrobenz[a]anthracene (**19**) (8%) and the 7,12-quinone (**20**) in 23% yield. CAS oxidation of **16** yielded 6*H*-benzo[*d*]naphtho[1,2-*b*]pyran-6-one (**21**) (8%) and the 5,6-quinone **22** (23%). The structure of **21** was confirmed by its proton NMR spectrum and MS.



21

The results of this study demonstrate that CAS oxidation followed by reduction is useful for the synthesis of the 2,3-dihydrodiols of fluoranthene and benzo[*k*]fluoranthene. However, this approach is not appropriate for the preparation of dihydrodiols of **2** and **14–16**. The CAS oxidation appears to have promise for the synthesis of certain lactones, as well as for the preparation of quinones from PAH phenols.

Experimental Section

Infrared spectra were run on a Perkin-Elmer Model 267 grating infrared spectrophotometer in CH_2Cl_2. NMR spectra were determined in $CDCl_3$ with a Jeol Model FX90Q spectrometer, a Jeol Model JNM-GX 400 FT-NMR, Hunter College, City University of New York, a Bruker AM300 spectrometer, Bruker Instruments, Billerica, MA, and a Bruker AM360 spectrometer. UV spectra were taken on a Cary Model 118 instrument. HPLC was carried out with a Waters Associates Model ALC/GPC-204 high-speed liquid chromatograph equipped with a Model 660 solvent programmer, a Model LC-25 UV–vis detector, and a 4.0 × 250 mm Lichrosorb RP-18 10-μm column (EM Reagents, Cincinnati, OH). MS were run with a Hewlett-Packard Model 5988A instrument. High-resolution MS were determined on a VG 70-250 double-focusing magnetic sector instrument, at the Rockefeller University Mass Spectrometric Biotechnology Resource. All starting materials were obtained from Aldrich Chemical Co., Milwaukee, WI, unless otherwise stated. Reference standard quinoines of benzo[*a*]pyrene were obtained from the National Cancer Institute Chemical Carcinogen Repository, a function of the Division of Cancer Etiology, NCI.

Oxidation of Benzo[*k*]fluoranthene (1) with CAS. A solution of ceric ammonium sulfate (5.4 g, 0.01 mol) in 500 mL of 4N H_2SO_4 was added to a stirred suspension of benzo[*k*]-fluoranthene (**1**) (1.26 g, 0.005 mol) in 500 mL of acetonitrile/4 N H_2SO_4 (50:50) at room temperature. The reaction slowly turned red and then deep red after 3 h of stirring. After 5 h, the reaction mixture was filtered, and the filtrate was diluted with cold H_2O and extracted with EtOAc (3 × 200 mL). The EtOAc extracts were washed with H_2O and brine and dried ($MgSO_4$). Removal of the solvent afforded a mixture of crude quinones **3** and **4**. The quinones were purified by chromatography on silica gel. Elution by hexane afforded unreacted benzo[*k*]fluoranthene. Elution with CH_2Cl_2/hexane (50:50) afforded the quinone **3** (0.3 g, 28%), mp 214–216 °C. Elution with CH_2Cl_2 gave pure **4**, mp 286–288 °C (0.14 g, 10%).

Spectral properties of **3**: NMR δ 7.4–7.85 (m, 4, H_2, H_5, H_9, and H_{10}), 8.07 (d, 2, H_3 and H_4, $J_{2,3} = J_{4,5}$ = 8.1 Hz), 8.2–8.9 (m, 2, H_8 and H_{11}), 8.65 (d, 2, H_1 and H_6, $J_{1,2} = J_{5,6}$ = 8.1 Hz); UV λ_{max} (ε) 307 (18 310), 296 (16 200), 266 (33 800), 247 (41 200); MS, *m/e* (relative intensity) 282 (M^+, 100), 254 (64.7), 226 (47.9); HRMS, calcd for $C_{20}H_{10}O_2$, MH^+ 283.0759, found 283.0699.

Spectral properties of **4**: NMR δ 7.04 (s, 1, H_1), 7.35–7.48 (m, 2, H_9 and H_{10}), 7.50 (t, 1, H_5, $J_{4,5} = J_{5,6}$ = 8.1 Hz), 7.59 (dd, 1, H_6, $J_{5,6}$ = 8.1 Hz, $J_{4,6}$ = 1.5 Hz), 7.81 (br d, 2, H_8 and H_{11}, $J_{8,9}$ = 8.1 Hz), 8.13 (dd, 1, H_4, $J_{4,5}$ = 8.1 Hz, $J_{4,6}$ = 1.5 Hz), 8.23 (s, 1, H_7), 8.50 (s, 1, H_{12}), UV λ_{max} (ε) 309 (59 260), 296 (60 000), 276 (52 590), 242 (50 370); MS *m/e* (relative intensity) 282 (M^+, 45), 254 (100); HRMS calcd MH^+ 283.0759, found 283.0763.

***trans*-2,3-Dihydro-2,3-dihydroxybenzo[*k*]fluoranthene (5).** $NaBH_4$ (0.5 g) was added to a stirred suspension of the quinone **4** (57 mg, 0.2 mmol) in 100 mL of ethanol. The reaction mixture was stirred for 1 h, and the resulting light yellow solution was poured into H_2O and extracted with EtOAc. The organic phase was washed with H_2O, dried ($MgSO_4$), and evaporated to dryness. The crude product was purified by chromatography on Florisil with elution by CH_2Cl_2 and CH_2Cl_2/EtOAc (80:20) to give the pure *trans*-dihydrodiol **5** (35 mg, 62%), mp 225–227 °C. Spectral properties: NMR δ 4.60–4.75 (m, 1, H_2), 4.8–4.87 (dd, 1, H_3, $J_{2,3}$ = 6.1 Hz, J_{8,OH_3} = 6.62 Hz), 5.46 (d, 1, OH_2, J_{2,OH_2} = 6.6 Hz), 5.57 (d, 1, OH_3, J_{3,OH_3} = 6.25 Hz), 6.75 (d, 1, H_1, $J_{1,2}$ = 3.3 Hz), 7.3–7.6 (m, 4, H_5, H_6, H_9, and H_{10}), 7.81 (dd, 1, H_4, $J_{4,5}$ = 5.5 Hz, $J_{4,6}$ = 2.58 Hz), 7.98 (dd, 2 H, H_8 and H_{11}, $J_{8,9}$ = 5.88 Hz, $J_{8,10}$ = 2.2 Hz), 8.3 (s, 1, H_{12}), 8.37 (s, 1, H_7); MS, *m/e* (relative intensity) 286 (M^+, 10.5), 268 (100); UV λ_{max} (ε) 338 (8180), 300 (33 640), 284 (54 090), 271 (51 360), 258 (74 550); HRMS calcd for $C_{20}H_{14}O_2$ (M − H) 286.0992, found 286.1009.

***anti*-2,3-Dihydroxy-1,12b-epoxy-1,2,3,12b-tetrahydrobenzo[*k*]fluoranthene (6).** A mixture of 14 mg (0.05 mmol) of dihydrodiol **5**, 100 mg of *m*-chloroperbenzoic acid, and 10 mL of dry THF was stirred under N_2 for 1 h at 0 °C and then at room temperature for 1 h. The reaction mixture was diluted with 50 mL of ether, washed with 1% ice-cold aqueous NaOH (3 × 20 mL) and H_2O, and dried (K_2CO_3). Evaporation of the solvent gave a light yellow solid (**6**), which was recrystallized from ether/CH_2Cl_2, mp 128 °C dec (9 mg, 56%). Spectral properties: NMR δ 3.8 (dd, 1, H_2, $J_{2,3}$ = 9.0 Hz, J_{2,OH_2} = 4.5 Hz), 4.5 (s, 1, H_1), 4.6 (m, 1, H_3), 5.7 (br s, 2, OH_2 and OH_3), 7.4–7.7 (m, 4, H_5, H_6, H_9, and H_{10}), 7.8–8.1 (m + s, 4, H_4, H_7, H_8, and H_{11}), 8.35 (s, 1, H_{12}); HRMS calcd for $C_{20}H_{14}O_3$ (M − H) 302.0942, found 302.0938.

***trans*-2,3-Dihydro-2,3-dihydroxyfluoranthene (7).** A suspension of fluoranthene-2,3-dione (1.1 g, 0.005 mol) and $NaBH_4$ (1.85 g, 0.005 mol) in 500 mL of ethanol was stirred for 8 h while O_2 was bubbled into the solution. Stirring was then continued for 48 h without bubbling O_2. The reaction mixture was partitioned between EtOAc and H_2O and worked up conventionally to afford the crude dihydrodiol **7** (1.2 g). Chromatography on Florisil and elution with CH_2Cl_2 gave unreacted dione. Further elution with CH_2Cl_2/EtOAc (90:10) gave pure **7** (250 mg, 21%), mp 167–168 °C (lit.[15] mp 167–168 °C). Spectral properties: NMR δ 4.65–4.7 (m, 1, H_2), 4.8 (d, 1, H_3, $J_{2,3}$ = 6.9 Hz), 5.45 (br s, 1, OH_2), 5.55 (br s, 1, OH_2), 6.7 (d, 1, H_1, $J_{1,2}$ = 4.3 Hz), 7.3–7.45 (m, 4, H_4, H_5, H_8, H_9), 7.6–7.7 (m, 1, H_{10}), 7.8–7.9 (m, 2, H_6 and H_7); MS, *m/e* (relative intensity) 236 (M^+, 29.8), 218 (100).

***anti*-2,3-Dihydroxy-1,10b-epoxy-1,2,3,10b-tetrahydrofluoranthene (8).** A solution of **7** (0.12 g, 0.5 mmol) in 20 mL of anhydrous THF was stirred with *m*-chloroperbenzoic acid (0.85 g, 0.005 mol) for 3 h under N_2. The solution was diluted with 100 mL of ether and washed with ice-cold 2 N NaOH and then ice–water. The solvent was removed under reduced pressure at room temperature. The solid residue (100 mg) was triturated with dry Et_2O to yield **8** (70 mg, 55%), mp 127–128 °C (lit.[15] mp 126–129 °C). Spectral properties: NMR δ 3.82 (dd, 1, H_2), 4.3 (d, 1, H_1), 4.8–5.05 (m, 3, OH_1, OH_2, and H_3), 7.2–7.8 (m, 7); HRMS, calcd for $C_{16}H_{12}O_3$ (M–H) 251.0721, found 251.0708.

Oxidation of Benzo[*b*]fluoranthene (2) with CAS. The conversion of **2** (1.25 g, 0.001 mol) to the lactone **9** was carried out as described for preparation of **3**. The crude product was purified by chromatography on silica gel. Elution by hexane afforded unreacted **2** and further elution with CH_2Cl_2/hexane (80:20) afforded the lactone **9** (0.16 g, 53%), mp 240–241 °C. Spectral properties: IR, 1700, 1725, 1735 cm^{-1}; NMR δ 7.3–7.34 (m, 1, H_{11}), 7.5–7.53 (m, 3, H_7, H_9, and H_{10}), 7.64 (d, 1, H_8, $J_{7,8}$ = 8.2 Hz), 7.66–7.72 (m, 2, H_3, and H_{12}), 7.92 (dd, 1, H_2, $J_{1,2} = J_{2,3}$ = 8.2 Hz, $J_{2,4}$ = 1.5 Hz), 8.46 (dd, 1, H_4, $J_{3,4}$ = 8.0 Hz, $J_{2,4}$ =

1.5 Hz), 9.76 (d, 1, H_1, $J_{1,2}$ = 8.2 Hz); MS, *m/e* (relative intensity) 298 (M^+, 100), 270 (14.3); HRMS, calcd for $C_{20}H_{10}O_3$ 298.0629, found 298.0622.

Reduction of Lactone 9 with $LiAlH_4$. The lactone **9** (10 mg) in 20 mL of THF was added at room temperature for 5 min to a stirred suspension of 10 mg of $LiAlH_4$ in 20 mL of THF. After stirring 1 h at room temperature, conventional workup gave 10 mg of crude product, which was purified by chromatography on Florisil. Elution by CH_2Cl_2/hexane (80:20) and CH_2Cl_2/EtOAc (95:5) gave **10** (6 mg) as a thick oil. Spectral properties: NMR δ 2.75 (br s, 1, OH), 4.45 (s, 2, CH_2OH), 5.1 (s, 1, CHOH), 5.6 (s, 1, OH), 7.0 (d, 1, H ortho to OH, *J* = 10.5 Hz), 7.15-7.8 (m, 9 H); MS, *m/e* (relative intensity) 304 (M^+, 24.8), 286 (100).

Oxidation of Benzo[*a*]pyrene (14) with CAS. Benzo[*a*]pyrene (**14**) (0.12 g, 0.5 mmol) was allowed to react with CAS (0.54 g, 1.0 mmol) under the conditions used for oxidation of **1**. The crude product was purified by chromatography on silica gel. Elution by hexane afforded the unreacted hydrocarbon. Further elution with CH_2Cl_2/hexane (80:20) afforded a mixture of the 1,6- and 3,6-quinones **17** and **18** (60 mg, 43%): MS, *m/e* (relative intensity) 282 (M^+, 100), 258 (37.7). These two diones were separated by HPLC, using a linear gradient from 40-100% CH_3OH in H_2O at 2 mL/min. Their retention volumes (71 mL, **18**, and 68.8 mL, **17**) and UV were identical with those of reference samples.

Oxidation of Benzo[*a*]anthracene (15) by CAS. Benz[*a*]anthracene (**15**) (0.11 g, 0.5 mmol) on oxidation with CAS (0.54 g, 1 mmol) as described for **1** gave a crude product, which was purified by chromatography on silica gel. Elution by hexane afforded the unreacted hydrocarbon. Elution with CH_2Cl_2/hexane (30:70) gave 7-oxo-12-hydroxy-7,12-dihydrobenz[*a*]anthracene (**19**, 10 mg, 8%), mp 181-183 °C (lit.[18] mp 186 °C). Spectral properties: IR 1652 cm^{-1}; NMR δ 7.4-8.0 (m, 7), 8.1-8.4 (m, 2), 8.5-8.7 (m, 1, H_1); MS, *m/e* (relative intensity) 260 (M^+, 100), 231 (63.6). Further elution by CH_2Cl_2 gave benz[*a*]anthracene-7,12-dione (**20**, 30 mg, 23%), mp 166-167 °C (lit.[19] mp 170-171 °C). Spectral properties: NMR δ 7.6-8.0 (m, 5, H_2, H_3, H_4, H_9, and H_{10}), 8.1-8.5 (m, 4, H_5, H_6, H_8, and H_{11}), 9.65 (dd, 1, H_1); MS, *m/e* (relative intensity) 258 (M^+, 100), 230 (41.3).

Oxidation of Chrysene (16) by CAS. Chrysene (**16**) (0.11 g, 0.5 mmol) on oxidation with CAS (0.54 g, 1 mmol) as described for **1** gave a crude product, which was purified by chromatography on silica gel. Elution by hexane afforded unreacted chrysene. Further elution with CH_2Cl_2/hexane (30:70) gave the lactone **21** (10 mg, 8%), mp 179-180 °C (lit.[19] mp 188-189 °C). Spectral properties: IR, 1730, 1735 cm^{-1}; NMR δ 7.58-7.68 (m, 3, H_2, H_3, and H_8), 7.78 (d, 1, H_{12}, $J_{11,12}$ = 9.1 Hz), 7.55-7.92 (m, 2, H_1, H_9), 8.08 (d, 1, H_{11}, $J_{11,12}$ = 9.0 Hz), 8.2 (d, 1, H_{10}, $J_{9,10}$ = 9.0 Hz), 8.48 (d, 1, H_7, $J_{7,8}$ = 9.1 Hz), 8.6 (d, 1, H_4, $J_{3,4}$ = 9.0 Hz); MS, *m/e* (relative intensity) 246 (M^+, 100), 218 (25.2); HRMS calcd for $C_{16}H_{10}O_2$ (M - H) 245.060, found, 245.062. Further elution by CH_2Cl_2 gave chrysene-5,6-dione (**22**, 30 mg, 23%), mp 239-240 °C (lit.[19] mp 240-241 °C). Spectral properties: NMR δ 7.4-7.95 (m, 6, H_1, H_2, H_3, H_8, H_9, and H_{12}), 8.0-8.3 (m, 3, H_7, H_{10}, and H_{11}), 9.4 (dd, 1, H_4); MS, *m/e* (relative intensity) 258 (M^+, 12.1), 230 (100).

(18) Boyland, E.; Sims, P. *Biochem. J.* **1964**, *94*, 493.
(19) Copeland, P. G.; Dean, R. E.; McNeil, D. *J. Chem. Soc.* **1961**, 1232.

Stereochemistry of Addition of Allyl Grignard Reagents to (*R*)-(+)-Pulegone and Other α,β-Ethylenic Ketones

Mostafa El Idrissi and Maurice Santelli*

Unité Associée au CNRS No. 109, Centre de St-Jérôme, Avenue Esc. Normandie-Niemen, 13397, Marseille Cedex 13, France

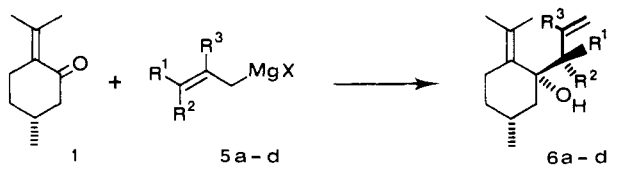
Received May 21, 1987

The 1,2-addition of allyl, crotyl, and 2-methyl-2-butenyl Grignard reagents to (*R*)-(+)-pulegone is regio- and stereoselective. In contrast, 3-penten-2-yl and 3-methyl-2-butenyl Grignard reagents undergo 1,2- and 1,4-additions. A "compact approach" stabilized by orbital interaction is the proposed mechanism. A further confirmation was obtained with acyclic enones.

Carbonyl alkylation has long been studied and constitutes one of the largest collections of fundamental bond construction reactions in organic synthesis. A great deal of work has been devoted to the stereochemistry of addition of Grignard reagents to cycloalkanones.[1] These reactions proceed via attack predominantly at the less hindered side of the carbonyl, i.e., generally equatorial attack.[1a,b]

The addition reactions of allyl Grignard compounds to cycloalkanones exhibit low selectivity and are, therefore, of little preparative interest.[2,3] Stereochemical and relative-rates studies suggest that carbonyl compounds react with allyl Grignard reagents via a noncyclic, bimolecular, electrophilic substitution mechanism (S_E2')[4] (substitution anti).[5] On the other hand, allylmagnesium derivatives

Scheme I[a]



[a] **a**, $R^1 = R^2 = R^3 = H$, X = Cl; **b**, $R^1 = CH_3$, $R^2 = R^3 = H$, X = Cl; **c**, $R^1 = R^2 = H$, $R^3 = CH_3$, X = Cl; **d**, $R^1 = R^3 = CH_3$, $R^2 = H$, X = Br.

(1) (a) Ashby, E. C.; Laemme, J. T. *Chem. Rev.* **1975**, *75*, 521. (b) Ashby, E. C.; Chao, C. L.; Laemme, J. T. *J. Org. Chem.* **1974**, *39*, 3258. (c) Reetz, M. T.; Steinbach, J.; Westermann, J.; Peter, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1011. (d) Perry, M.; Maroni-Barnaud, Y. *Bull. Soc. Chim. Fr.* **1969**, 3574.
(2) (a) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, 2205. (b) Abenhaim, D.; Henry-Basch, E.; Feron, P. *Bull. Soc. Chim. Fr.* **1969**, 4038.
(3) In contrast, the relative insensitivity of the allyl Grignard toward steric crowding about the carbonyl has obvious synthetic utility.
(4) (a) Felkin, H.; Gault, Y.; Roussi, G. *Tetrahedron* **1970**, *26*, 3761. (b) Cherest, M.; Felkin, H.; Frajerman, C. *Tetrahedron Lett.* **1971**, 379. (c) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1971**, 383. (d) Felkin, H.; Frajerman, C.; Roussi, G. *Ann. Chim. (Paris)* **1971**, *6*, 17.

0022-3263/88/1953-1010$01.50/0