Synthesis of Aminochrysenes by the Oxidative Photocyclization of Acetylaminostilbenes

Yoshinori TOMINAGA,*[,a] Raymond N. CASTLE,[b] and Milton L. LEE[c]

Faculty of Pharmaceutical Sciences, Nagasaki University,[a] 1–14, Bunkyo-machi, Nagasaki 852, Japan, Department of Chemistry, University of South Florida,[b] Tampa, Florida 33620, U.S.A. and Department of Chemistry, Brigham Young University,[c] Provo, Utah 84602, U.S.A. Received March 4, 1993

Aminochrysene derivatives were synthesized by the oxidative photocyclization of acetylaminostilbenes in the presence of iodine and air, followed by hydrolysis.

Keywords aminochrysene; oxidative photocyclization; acetylaminostilbene; polycyclic aromatic amine; Wadsworth–Emmons reaction

Many polycyclic aromatic amines have been detected in coal liquids, shale oils and coal derived products.[1] Some of these polycyclic aromatic amines, such as 2-naphthylamine, are carcinogens. Others have mutagenic activity and thus may be carcinogenic.[2] In this paper we described the synthesis of aminochrysenes, which occur or are suspected of occurring in coal liquids, shale oils and coal-derived products.[3] (Their mutagenicity and their presence in coal liquids will be described elsewhere.) The key step in this synthesis is the oxidative photocyclization of aminostyrylnaphthalenes. The stilbenes have been widely utilized as versatile intermediate reagents for the synthesis of polycyclic hydrocarbon derivatives in photocyclization reactions.[4] The photochemical cyclization of stilbene and its derivatives has received considerable attention, but the photochemistry of amino or nitrostilbenes has not been as thoroughly investigated.

The Wadsworth–Emmons reaction[5] of diethyl 1-naphthylmethylphosphonate (**1**) with *o*-nitrobenzaldehyde (**2a**), *m*-nitrobenzaldehyde (**2b**) or *p*-nitrobenzaldehyde (**2c**) gave respectively, 1-(*o*-nitrostyryl)naphthalene (**3a**) (83% yield), 1-(*p*-nitrostyryl)naphthalene (**3b**) (81% yield) or 1-(*m*-nitrostyryl)naphthalene (**3c**) (87% yield). Reduction of **3a—c** with hydrazine gave respectively, 1-(*o*-aminostyryl)-naphthalene (**4a**) (67%), 1-(*m*-aminostyryl)naphthalene (**4b**) (70% yield) or 1-(*p*-aminostyryl)naphthalene (**4c**) (67% yield). Photocyclization of the amines could not be accomplished, so **4a—c** were acetylated with acetic anhydride to give 1-(*o*-acetylaminostyryl)naphthalene (**5a**) (94% yield), 1-(*m*-acetylaminostyryl)naphthalene (**5b**) (90% yield) or 1-(*p*-acetylaminostyryl)naphthalene (**5c**) (92% yield). Photocyclization of the acetylaminostyrylnaphthalenes (**5a—c**) was accomplished by irradiation in dry benzene solution using a 450 W Hanovia medium-pressure mercury lamp with air and iodine as the oxidants. Thus, photocyclization of **5a** gave 1-acetylaminochrysene (**6a**) in 67% yield, and photocyclization of **5c** gave 3-acetylaminochrysene (**6c**) in 70% yield. However, photocyclization of **5b** gave a mixture of **6b** and **6d** in 62% combined yield. Hydrolysis of **6a** or **6c** with concentrated hydrochloric acid–absolute ethanol (1 : 1) gave 1-aminochrysene (**7a**) (83% yield) or 3-aminochrysene (**7c**) (85% yield), respectively. When the mixture of compounds **6b** and **6d** was hydrolyzed, it gave a separable mixture of **7b** and **7d**. 4-Aminochrysene (**7d**) was eluted first (30% yield) on a silica gel column using hexane–benzene as the eluent. The second fraction contained of pure 2-aminochrysene (**7b**) (32% yield). These transformations are outlined in Chart 1. Compounds **7b** and **7d** have previously been obtained *via* a different approach.[6]

This photocyclization of acetylaminostilbenes is the first example of photocyclization of stilbenes to polycyclic hydrocarbons. In conclusion, the present synthetic method of aminochrysenes by the oxidative photocyclization of acetylaminostilbenes should be convenient and useful for the synthesis of various other polycyclic aromatic amine

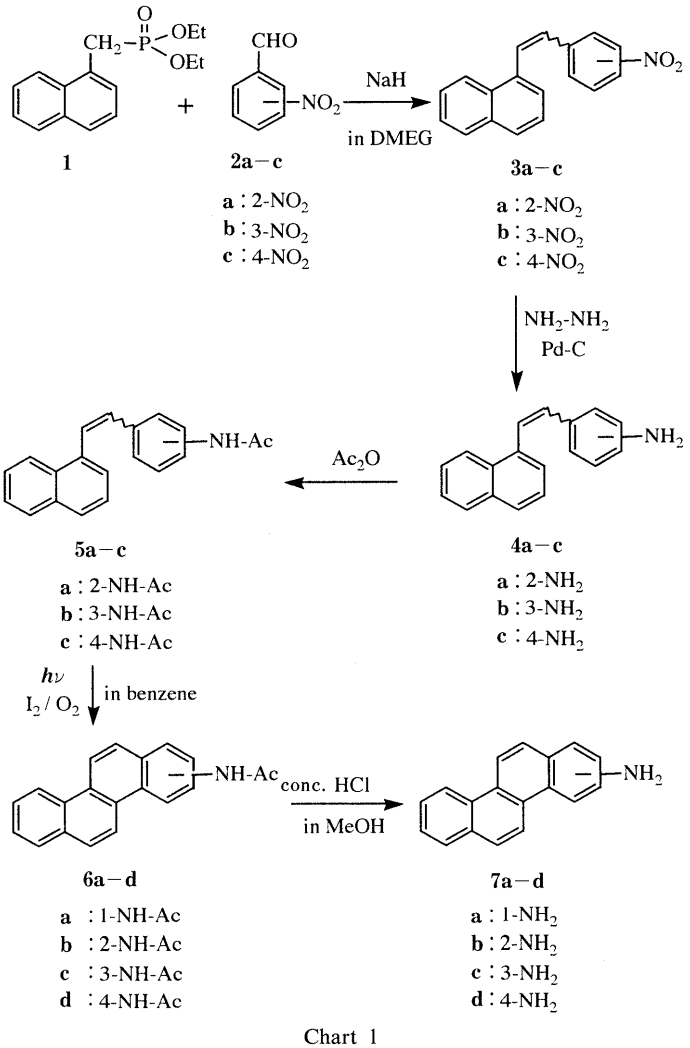

Chart 1

compounds.

Experimental

Melting points were determined in open capillary tubes on a Thomas–Hoover capillary melting point apparatus without correction. The infrared (IR) spectra were obtained on a Beckman Acculab 2 spectrometer. The IR spectral data are given in reciprocal centimeters (cm^{-1}). The proton magnetic resonance spectra (^{1}H-NMR) of all compounds were obtained on a Varian EM-360-A spectrometer or a JEOL FX-90Q spectrometer in the solvents indicated. Chemical shifts are reported in ppm from tetramethylsilane (TMS) as an internal standard and are given in δ units. Mass spectra (MS) were determined on a Hewelett–Packard model 5980A mass spectrometer electron impactionization mode. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona.

1-(*o*-Nitrostyryl)naphthalene (3a) Sodium hydride (50% dispersion in mineral oil, 0.6 g, 0.013 mol) was placed in dry 1,2-dimethoxyethane (50 ml) and used after being washed twice with hexane (60 ml). The slurry was cooled to 20 °C and diethyl naphthylmethylphosphonate (**1**)[5c] (2.78 g, 0.01 mol) was added with stirring under a stream of nitrogen. After the addition, the solution was stirred at room temperature for 15 min. *o*-Nitrobenzaldehyde (**2a**) (1.51 g, 0.01 mol) was added at a rate such that the temperature did not exceed 25 °C. The solution was stirred at room temperature for 2 h and then poured into a large excess of ice-water under nitrogen. The resulting precipitate was collected by filtration and recrystallized from benzene, giving pale yellow needles in 83% yield, mp 121—122 °C. IR ν^{KBr} cm^{-1}: 2923, 1514, 1345, 787, 777. ^{1}H-NMR ($CDCl_3$) δ: 7.12—8.29 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 277 (M^+ + 2, 3), 276 (M^+ + 1, 22), 275 (M^+, 100), 229 (45), 226 (39). *Anal.* Calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.60; H, 4.88; N, 5.04.

1-(*m*-Nitrostyryl)naphthalene (3b) This compound was prepared from **2b** in a manner similar to that described for the synthesis of **3a**. Pale yellow needles were obtained in 87% yield, mp 101–103 °C. IR ν^{KBr} cm^{-1}: 1525, 1347, 771, 730. ^{1}H-NMR ($CDCl_3$) δ: 7.10—8.38 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 277 (M^+ + 2, 2), 276 (M^+ + 1, 20), 275 (M^+, 100), 228 (79), 227 (45), 226 (46). *Anal.* Calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.68; H, 4.81; N, 5.14.

1-(*p*-Nitrostyryl)naphthalene (3c) This compound was prepared from **2c** in a manner similar to that described for the synthesis of **3a**. Pale yellow needles were obtained in 81% yield, mp 187—188 °C. IR ν^{KBr} cm^{-1}: 1589, 1499, 1332, 769, 746. ^{1}H-NMR ($CDCl_3$) δ: 7.02—8.31 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 277 (M^+ + 2, 2), 276 (M^+ + 1, 20), 275 (M^+, 100), 229 (43), 228 (69), 226 (39). *Anal.* Calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.80; H, 4.86; N, 5.24.

1-(*o*-Aminostyryl)naphthalene (4a) A 10% solution of hydrazine in absolute ethanol (6 ml) was added to a mixture of compound **3a** (0.5 g, 0.0018 mol), 5% Pd/C (0.3 g) and absolute ethanol (400 ml) at 60 °C. After the addition, the mixture was refluxed for 30 min. The Pd/C was removed by filtration and the ethanol was evaporated *in vacuo*, affording pale yellow needles in 67% yield, mp 89—90 °C. IR ν^{KBr} cm^{-1}: 3428, 3353 (NH_2), 1628, 1509, 1489, 1453, 797, 771, 748. ^{1}H-NMR ($CDCl_3$) δ: 3.75 (2H, br s, NH_2), 6.51—8.30 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 247 (M^+ + 2, 2), 276 (M^+ + 1, 19), 245 (M^+, 100), 244 (83). *Anal.* Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.27; H, 6.16; N, 5.59.

1-(*m*-Aminostyryl)naphthalene (4b) This compound was prepared from compound **3b** in a manner similar to that described for the synthesis of **4a**. Pale yellow needles were obtained in 70% yield, mp 66—67 °C. IR ν^{KBr} cm^{-1}: 3417, 3327 (NH_2), 1599, 1581, 954, 795, 774, 694. ^{1}H-NMR ($CDCl_3$) δ: 3.39 (2H, br s, NH_2), 6.31—8.29 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 247 (M^+ + 2, 2), 246 (M^+ + 1, 18), 245 (M^+, 100), 244 (79). *Anal.* Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.35; H, 6.13; N, 5.87.

1-(*p*-Aminostyryl)naphthalene (4c) This compound was prepared from compound **3c** in a manner similar to that described for the synthesis of **4a**. Pale yellow needles were obtained in 81% yield, mp 112—113 °C. IR ν^{KBr} cm^{-1}: 3440, 3374 (NH_2), 1615, 1514, 797, 771. ^{1}H-NMR ($CDCl_3$) δ: 3.47 (2H, br s, NH_2), 6.56—8.32 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 247 (M^+ + 2, 2), 246 (M^+ + 1, 19), 245 (M^+, 100), 244 (83). *Anal.* Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.27; H, 6.16; N, 5.59.

1-(*o*-Acetylaminostyryl)naphthalene (5a) A mixture of **4a** (1.23 g, 0.005 mol) and acetic anhydride (2 ml) was stirred at 50 °C for 1 h. The reaction mixture was poured into 50 ml of water and stirred for 2 h. The precipitate was collected by filtration and recrystallized from methanol, affording colorless needles in 94% yield, mp 164—165 °C. IR ν^{KBr} cm^{-1}: 3289 (NH), 1653 (C=O), 1532, 789, 771, 753. ^{1}H-NMR ($CDCl_3$) δ: 2.19 (3H, s, CH_3), 6.67—8.12 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 289 (M^+ + 2, 1), 288 (M^+ + 1, 8), 287 (M^+, 94), 244 (100). *Anal.* Calcd for $C_{20}H_{17}NO$: C, 83.60; H, 5.96; N, 4.87. Found: C, 83.58; H, 5.87; N, 4.85.

1-(*m*-Acetylaminostyryl)naphthalene (5b) This compound was prepared from compound **4b** in a manner similar to that described for the synthesis of **5a**. Pale yellow needles were obtained in 95% yield, mp 133—134 °C. IR ν^{KBr} cm^{-1}: 3219 (NH), 1640 (C=O), 1535, 1424, 949, 797, 771. ^{1}H-NMR ($CDCl_3$) δ: 2.16 (2H, br s, NH_2), 6.73—8.13 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 289 (M^+ + 2, 2), 288 (M^+ + 1, 16), 287 (M^+, 67), 286 (6), 244 (100). *Anal.* Calcd for $C_{20}H_{17}NO$: C, 83.60; H, 5.96; N, 4.87. Found: C, 83.33; H, 5.85; N, 4.91.

1-(*p*-Acetylaminostyryl)naphthalene (5c) This compound was prepared from compound **4c** in a manner similar to that described for synthesis of **5a** and pale yellow needles were obtained in 92% yield, mp 225—226 °C. IR ν^{KBr} cm^{-1}: 3235 (NH), 1661 (C=O), 1597, 1540, 1507, 1411, 1507, 1322, 967, 820, 795, 777. ^{1}H-NMR ($CDCl_3$) δ: 2.14 (2H, br s, NH_2), 6.81—7.99 (13H, m, 2 × ethylene-H and aromatic-H). MS *m/z* (%): 289 (M^+ + 2, 2), 288 (M^+ + 1, 12), 287 (M^+, 52), 243 (100), 215 (32). *Anal.* Calcd for $C_{20}H_{17}NO$: C, 83.60; H, 5.96; N, 4.87. Found: C, 83.42; H, 5.91; N, 4.91.

1-Acetylaminochrysene (6a) A solution of compound **5a** (0.9 g, 0.0031 mol) and iodine (0.05 g) in dry benzene (360 ml) was irradiated for 4 h with a 450 W Hanovia mercury lamp. During the course of the reaction a slow stream of air, the solvent was evaporated *in vacuo* and finally the residue was washed with ethanol, giving colorless needles, mp 229—231 °C, in 67% yield. An analytical samples was recrystallized from methanol to give colorless leaflets, mp 236—237 °C. IR ν^{KBr} cm^{-1}: 3260 (NH), 1648 (C=O), 1540, 1275, 800, 769. ^{1}H-NMR ($CDCl_3$) δ: 2.23 (3H, s, CH_3), 7.41—8.28 (7H, m, 2-H, 3-H, 6-H, 7-H, 8-H, 9-H, 12-H), 8.70—9.16 (4H, m, 4-H, 5-H, 10-H, 11-H), 10.12 (1H, br s, NH). MS *m/z* (%): 286 (M^+ + 1, 9), 285 (M^+, 45), 243 (100), 215 (34). *Anal.* Calcd for $C_{20}H_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 84.37; H, 5.32; N, 4.86.

3-Acetylaminochrysene (6c) This compound was prepared by photocyclization of compound **5b** in a manner similar to that described for the synthesis of **6a**. Yellow needles were obtained in 70% yield, mp 265—266 °C. IR ν^{KBr} cm^{-1}: 3273 (NH), 1661 (C=O), 1518, 1491, 838, 753, 746. ^{1}H-NMR ($CDCl_3$) δ: 2.21 (3H, s, CH_3), 7.50—8.12 (7H, m, 1-H, 2-H, 6-H, 7-H, 8-H, 9-H, 12-H), 8.40—9.04 (3H, m, 5-H, 10-H, 11-H), 9.24 (1H, s, 4-H), 10.13 (1H, br s, NH). MS *m/z* (%): 287 (M^+ + 2, 2), 286 (M^+ + 1, 11), 285 (M^+, 52), 243 (100), 215 (32). *Anal.* Calcd for $C_{20}H_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 84.37; H, 5.32; N, 4.86.

2-Acetylaminochrysene (6b) and 4-Acetylaminochrysene (6d) The mixture of compounds **6b** and **6d** was prepared by the photocyclization of **5b** in a manner similar to that described for the synthesis of **6a**. Colorless needles were obtained, mp 295—305 °C. MS of the mixture *m/z* (%): 286 (M^+ + 1, 12), 285 (M^+, 56), 249 (100), 244 (23), 215 (32). This mixture was used for the next step without separation or purification.

1-Aminochrysene (7a) A mixture of compound **6a** (0.4 g, 0.0014 mol), concentrated hydrochloric acid (5 ml) and ethanol (30 ml) was refluxed for 10 h. After cooling of the mixture, ammonium hydroxide (20 ml) was added and the whole was stirred for 2 h at room temperature. The tan solid was collected by filtration and recrystallized from methanol to give tan leaflets, mp 289—290 °C, in 85% yield. IR ν^{KBr} cm^{-1}: 3395, 3307 (NH_2), 1640, 1591, 1278, 800, 766. ^{1}H-NMR ($CDCl_3$) δ: 4.02 (2H, br s, NH_2), 6.72—6.99 (1H, m, 2-H), 7.22—8.40 (6H, m, 3-H, 6-H, 8-H, 9-H, 12-H), 8.59—9.11 (4H, m, 4-H, 5-H, 10-H, 11-H). MS *m/z* (%): 245 (M^+ + 2, 2), 244 (M^+ + 1, 19), 243 (M^+, 100), 215 (23). *Anal.* Calcd for $C_{18}H_{13}N$: C, 88.86; H, 5.39; N, 5.76. Found: C, 89.04; H, 5.51; N, 5.77.

3-Aminochrysene (7c) This compound was synthesized from **6c** in a manner similar to that described for synthesis of **7a**. Tan needles were obtained in 85% yield, mp 237—238 °C. IR ν^{KBr} cm^{-1}: 3433, 3353 (NH_2), 1625 (C=O), 1239, 1229, 833, 825, 746. ^{1}H-NMR ($CDCl_3$) δ: 4.00 (2H, br s, NH_2), 7.00 (1H, dd, J=2.0, 8.0 Hz, 2-H), 7.39—8.11 (6H, m, 1-H, 6-H, 7-H, 8-H, 9-H, 12-H), 8.30—8.94 (4H, 4-H, 5-H, 10-H, 11-H). MS *m/z* (%): 244 (M^+ + 1, 18), 243 (M^+, 100). *Anal.* Calcd for $C_{18}H_{13}N$: C, 88.86; H, 5.39; N, 5.76. Found: C, 88.79; H, 5.43; N, 5.69.

2-Aminochrysene (7b) and 4-Aminochrysene (7d) Compounds **7b** and **7d** were prepared from a mixture of **6b** and **6d** in a manner similar to that described for the synthesis of **7a**. The crude mixture was chromatographed on a silica gel column using hexane–benzene (4 : 1) as the eluent to afford from the first fraction pure **7d** in 30% yield followed by pure **7b** in 32% yield.

Compound 7b This compound eluted last and was obtained as tan leaflets, mp 221—222 °C (mp 205—206 °C,[6a] 223—224 °C[6b]). IR ν^{KBr} cm^{-1}: 3386, 3317 (NH_2), 1628, 1522, 861, 856, 810, 746. ^{1}H-NMR ($CDCl_3$) δ: 3.90 (2H, br s, NH_2), 7.03 (1H, s, 1-H), 7.09 (1H, dd, J=2.0, 8.0 Hz, 3-H), 7.40—8.14 (5H, m, 6-H, 7-H, 8-H, 9-H, 12-H), 8.48—8.83 (4H, m, 4-H, 5-H, 10-H, 11-H), MS m/z (%): 245 (M^++2, 2), 244 (M^++1, 20), 243 (M^+, 100), 215 (19).

Compound 7d This compound eluted first and was obtained as pale yellow leaflets, mp 158—159 °C (mp 159 °C[6c]). IR ν^{KBr} cm^{-1}: 3420, 3350, 1622, 1520, 1435, 831, 746. ^{1}H-NMR ($CDCl_3$) δ: 4.32 (2H, br s, NH_2), 6.82—7.11 (1H, m, 3-H), 7.30—8.14 (7H, m, 1-H, 2-H, 6-H, 7-H, 8-H, 9-H, 12-H), 8.49—8.91 (2H, m, 10-H, 11-H), 9.30 (1H, d, J=8.0 Hz, 5-H). MS m/z (%): 245 (M^++2, 2), 244 (M^++1, 18), 243 (M^+, 100).

Acknowledgement This study was supported by the U.S. Department of Energy, Office of Health and Environmental Research, Contract No. DEAC0279EV10237.

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