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Carcinogenic benzo[a]pyrene diol epoxide (BPDE) is one of the essential materials in tumor pathological research; however, it is expensive and unstable. In addition, its synthetic intermediates are metabolic intermediates of BPDE; thus, there is a need to reduce the handling of these compounds during the synthesis. Accordingly, a precursor of BPDE (i.e., *trans*-7,8-dihydro-7,8-dihydroxybenzo[a]pyrene) was prepared in a multi-gram scale by modified procedures. Efficient work-ups (e.g., simple extraction and precipitation) were also improved, which resulted in a crude product with high target compound content in each step of the synthesis.

Keywords: facile preparation; multi-grams synthesis; BPDE; carcinogen; thermal instability

Benzo[a]pyrene diol epoxide (BPDE) has been known as an ultimate carcinogen.[1-3] Its metabolic precursor is *trans*-7,8-dihydro-7,8-dihydroxybenzo[a]pyrene (**8** in Scheme 1), which is one of the metabolites of benzo[a]pyrene (B[a]P). Even in recent years, DNA adducts coupled with BPDE have been investigated.[4-6] In DNA adductome analysis aimed at identifying carcinogenic agents and environmental factors,[7-9] BPDE is one of the essential materials. It has been shown that BPDE can be synthesized in nine steps using readily available starting materials, such as pyrene and succinic anhydride.[10] However, BPDE is unstable to moisture and its storage is often difficult.[11] Therefore, for the synthesis of DNA adducts, examination of the reactivity to nucleosides, and pathological experiments, BPDE should be freshly prepared. In addition, due to the carcinogenicity of BPDE and its synthetic intermediates,[12] the number of times involved in synthetic handling and purification must be reduced to lower the risk of exposure; thus, we

investigated the multi-gram preparation of **8**.

In multistep synthesis, low-yield steps including recovery of starting materials and generation of byproducts must be avoided. We also intended to avoid purification such as column chromatography or recrystallization. Hence, we prepared a high-purity crude product in each step by simple methods such as liquid extraction or reprecipitation. The crude products can be directly used; thus, this approach is efficient and convenient for multi-step and multi-gram synthesis. In this paper, we report the facile gram-scale preparation of **8** by modified procedure, which improved the reactions conditions and simplified work-ups.

The synthetic route was shown in Scheme 1. In the first step, 10 g of pyrene was used in the Friedel-Crafts reaction with succinic anhydride. Ketocarboxylic acid **1** was precipitated in dilute HCl. A large quantity of the solid was obtained by filtration, which was washed by dispersion in water and collected by filtration. Because of the inconvenience of preparation and disposal of zinc amalgam in the Clemmensen reduction,[10] the Wolff-Kishner reduction was implemented for the reduction of **1**.[13] Along with the removal of water and excess hydrazine, the chosen reaction was monitored by the generation of nitrogen using a bubble counter. The reaction solution was poured into a cold solution of hydrochloric acid to disperse **2**. The collected solid was washed by dispersion in water and filtration to remove diethylene glycol. After thorough drying, the high-purity crude product **2** was obtained in a high yield.

Intramolecular Friedel-Crafts reaction[14] using phosphorus pentachloride and aluminium chloride was carried out for cyclization. The substrate was completely consumed within 30 min of refluxing conditions. After quenching the reaction, insoluble components were removed by filtration, which ensured the good recovery of the product. The filtrate went through a conventional extraction to give the crude product **3** with some impurities. The

reduction of **3** was carried out with $NaBH_4$ under conventional reaction conditions and extraction procedures to obtain the alcohol **4**.

The dehydration of **4** using *p*-TsOH in benzene gave polymerized products. The desired dihydrobenzo[a]pyrene **5** was obtained in a low yield; thus, the reaction conditions were modified using acetic acid with a small amount of concentrated HCl added.[15] The consumption of **4** occurred within 30 min, which was confirmed by TLC. Leaving a black slurry in the flask, the reaction mixture was poured into the water with stirring. A high-purity crude product **5** was successfully obtained and the removal of some impurities in the cyclization reaction of **2** was also accomplished.

Prévost reaction of **5** didn't proceed efficiently in a series of scaled reactions, which gave a mixture of the target compound **6** and the mono benzoyloxy compounds. In this study, this heterogeneous reaction was carried out successfully in 3-gram scale. The benzene suspension was filtered to remove the insoluble components. The filtrate was washed to remove the aqueous byproducts and evaporated to give the crude product of *trans*-**6**[16] in a high yield. Since the styrene moiety is formed by DDQ oxidation of **6** as well as the dehydration of **4**, we monitored carefully the conversion of **6** by the NMR analysis with attention to the potential polymerized byproducts. After quenching the reaction, the insoluble components were filtered off. After careful extraction to avoid emulsion formation due to the dissolved hydroquinone, *trans*-**7** was obtained in a high yield.

We note that *trans*-**8** is thermally instable. It has been reported that the dehydration of **8** to give **9** was enhanced in the presence of tetrabutylammonium hydroxide catalyst[17]; however, we found that the dehydration proceeded partially in a simple solution of **8** in methanol at 40 ºC and completed smoothly at 65 ºC. Therefore, precipitation would be appropriate for the work-up in the hydrolysis. The reaction mixture was concentrated at

<30 ºC. The concentrate was added into dilute HCl to disperse **8**, which was washed with water to remove the remaining organic solvent. Finally, 2 grams of **8** as a fine powder was obtained successfully by reprecipitation using THF and hexane. We also confirmed the stability of **8** for one year in a normal refrigerator.

In summary, we demonstrated a facile multi-gram preparation of *trans*-**8**, which is the synthetic precursor of BPDE. The overall yield was up to 50% by modifying procedures, improving the reaction conditions, and optimizing the work-up processes.

EXPERIMENTAL SECTION

Chemicals and solvents were purchased from Kanto Chemcal Co., Inc., TCI Co., Ltd., and Sigma-Aldrich Co. NMR spectra were recorded on a Bruker AVANCEIII HD400 (400 MHz for ^{1}H-NMR, 100 MHz for ^{13}C-NMR) spectrometer. IR spectra were recorded on Horiba FT-720 spectrometer. Mass spectra were recorded with a Thermo Fischer Scientific Inc. Q exactive. Spectroscopic data of ^{1}H-NMR and ^{13}C-NMR can be found via the section of "Supplementary material" this article's webpage.

4-Oxo-4-(1-pyrenyl)butanoic acid (1)

To a 500-mL round-bottom flask, ground pyrene (10.11 g, 50.05 mmol), ground succinic acid (6.13 g, 61.3 mmol), and dehydrated 1,2-dichloroethane (300 mL) were added. After the addition of ground $AlCl_3$ (16.20 g, 121.5 mmol) at 0 ºC, the reaction mixture was stirred for 2 hrs at 0 ºC, then for 2 hrs at room temperature. The reaction mixture was poured into ice-cold 1N HCl (700 mL) with stirring. The dispersed solid was collected by filtration. Washing of solid involved dispersing and filtering using 1 L of water was performed twice. After drying overnight under reduced pressure, the crude solid **1** was obtained (14.90 g, 49.28 mmol, 98%). Yellow solid. IR (KBr): 3037, 2951, 2873, 1693,

1432, 1275, 1205, 918, 847 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.76 (t, *J* = 6.2 Hz, 2H, CH_2), 3.50 (t, *J* = 6.2 Hz, 2H, CH_2), 8.15 (t, *J* = 7.6 Hz, 1H, Ar), 8.26 (d, *J* = 9.0 Hz, 1H, Ar), 8.329 (d, *J* = 9.4 Hz, 1H, Ar), 8.334 (d, *J* = 9.0 Hz, 1H, Ar), 8.38-8.42 (m, 3H, Ar), 8.58 (d, *J* = 8.0 Hz, 1H, Ar), 8.77 (d, *J* = 8.0 Hz, 1H, Ar), 12.23 (s, 1H, COOH). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 29.0 (CH_2), 37.4 (CH_2), 123.9 (C), 124.4 (C), 124.93 (CH), 124.95 (CH), 126.5 (CH), 126.9 (CH), 127.0 (CH), 127.3 (CH), 127.7 (CH), 128.6 (C), 129.7 (CH), 129.8 (CH), 130.4 (C), 131.1 (C), 132.9 (C), 133.5 (C), 174.5 (C), 203.7 (C) ppm.

4-(1-Pyrenyl)butanoic acid (2)

The crude product **1** (14.76 g, 48.82 mmol) and diethyl glycol (150 mL) were placed in a 500-mL round-bottom flask. Under vigorous stirring, ground KOH (28.04 g, 0.5 mol) and hydrazine monohydrate (26.77g, 0.54 mol) were added. The distillation glassware including an adaptor with a vent was connected to the flask. The reaction mixture was stirred at 120 ºC for 2 hrs, then at 180 ºC for 4 hrs. After the aqueous fraction diminished and nitrogen gas through the vent ceased, the reaction mixture was poured into ice water (600 mL). The resulting mixture was acidified with concentrated HCl and the precipitated solid was collected by filtration. Washing the solid involved dispersing and filtration using water (1 L) performed twice. The wet solid was transferred to a 500-mL round-bottom flask with acetone. After evaporation, the solid was dried under reduced pressure to give the crude product **2** (13.50 g, 47.10 mmol, 96%). Pale yellow solid. IR (KBr): 3037, 2951, 2873, 1894, 1432, 1275, 1205, 918, 847 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.01 (quint, *J* = 7.5 Hz, 2H, CH_2), 2.40 (t, *J* = 7.2 Hz, 2H, CH_2), 2.50 (overlapped with H_2O, 2H, CH_2), 7.94 (d, *J* = 7.8 Hz, 1H, Ar), 8.06 (t, *J* =7.6 Hz, 1H, Ar), 8.13 (d, *J* = 8.8 Hz, 1H, Ar), 8.14 (d, *J* = 9.1 Hz, 1H, Ar), 8.21-8.29 (m, 4H, Ar), 8.40 (d, *J* = 9.3 Hz, 1H, Ar), 12.16 (s, 1H, COOH), ^{13}C NMR (100 MHz, DMSO-d_6): δ = 27.3 (CH_2), 32.5 (CH_2), 33.8 (CH_2), 123.9 (CH), 124.6 (C), 124.7 (C), 125.3 (CH), 125.4 (CH x2), 126.6 (CH), 127.0 (CH), 127.7 (CH), 127.93 (CH), 127.98 (CH), 128.6 (C), 129.8 (C), 130.9 (C), 131.4 (C), 136.8 (C), 174.9 (C) ppm.

7-Oxo-7,8,9,10-tetrahydrobenzo[a]pyrene (3)

To a 500-mL round-bottom flask containing **2** (13.50 g, 47.10 mmol), chlorobenzene (300 mL) was added to form a brown suspension. Ground PCl_5 (14.61 g, 70.16 mmol) was added gradually into the well-stirred suspension. After 15 min, ground $AlCl_3$ (9.50 g, 71.25 mmol) was added to the flask. The resulting dark purple solution was stirred at 120 ºC for 30 min. The full conversion was monitored by TLC. The reaction mixture was then poured into 500 mL of ice water with stirring. The insoluble components were removed by filtration through a celite pad. After the extraction with chlorobenzene, the aqueous layer was extracted with CH_2Cl_2 (120 mL x 3). The organic solvent extracts were dried over $MgSO_4$. After filtration through a celite pad, the volatile components were removed under reduced pressure to give the crude product of **3** (12.24 g, 45.28 mmol, 96%) including some impurities. Light red solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (quint, *J* = 6.4 Hz, 2H, CH_2), 2.88 (t, *J* = 6.6 Hz, 2H, CH_2), 3.63 (t, 2H, CH_2), 7.98-8.19 (m, 6H, Ar), 8.28 (d, *J* = 9.3 Hz, 1H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.1 (CH_2), 26.1 (CH_2), 38.9 (CH_2), 123.13 (CH), 123.19 (CH), 124.3 (C), 125.2 (CH), 125.4 (CH), 127.0 (CH), 127.1 (C), 127.4 (CH), 127.9 (CH), 128.3 (CH), 128.5 (C), 129.4 (C), 129.7 (C), 131.5 (C), 132.0 (C), 137.6 (C), 199.2 (C) ppm.

7-Hydroxy-7,8,9,10-tetrahydrobenzo[a]pyrene (4)

The crude product **3** (12.24 g, 45.28 mmol) was dissolved in THF (150 mL, dehydrated) and CH_3OH (50 mL, dehydrated) in a 500-mL round-bottom flask. $NaBH_4$ (1.71 g, 45.28 mmol) was added over 15 min, and then the reaction mixture was stirred at room temperature for 45 min. After checking the full conversion of **3** by TLC, the reaction was quenched with 1N HCl, and most of the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (250 mL). The solution was washed with water and then dried over $MgSO_4$. The solvent was evaporated under reduced pressure to afford the crude product **4** (11.10 g, 40.76 mmol, 90%). Brown-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.03–2.12 (m, 3H, CH_2 and OH), 2.19–2.29 (m, 2H, CH_2), 3.35 (dt, *J* = 6.5, 17.06 Hz, 1H, ArC*H*H), 3.53 (dt, *J* = 5.8, 17.36 Hz, 1H, ArCH*H*), 5.22 (t, *J* = 4.7 Hz, 1H, C*H*OH), 7.95–8.00 (m, 3H, Ar), 8.09–8.17 (m, 3H, Ar), 8.23 (d, *J* = 9.3 Hz, 1H, Ar), 8.28 (s, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8 (CH_2), 26.3 (CH_2), 32.2 (CH_2), 69.2 (CH), 123.0 (CH), 124.2 (C), 124.6 (C), 124.90 (CH), 124.95 (CH), 125.1 (CH), 125.8 (CH), 126.7 (CH), 127.4 (CH), 127.5 (CH), 128.8 (C), 129.6 (C), 130.8 (C), 130.9 (C), 131.4 (C), 136.7 (C) ppm.

9,10-Dihydrobenzo[a]pyrene (5)

To a 500-mL round-bottom flask containing the crude product **4** (11.10 g, 40.76 mmol), acetic acid (350 mL) was added to form a homogeneous dispersion, followed by the addition of 10 drops of concentrated HCl. The resulting reaction mixture was stirred at 100 ºC for 30 min. The appropriate reaction time was carefully monitored by TLC. Leaving a black slurry in the flask, the mixture was then poured into 1.6 L of cold water with stirring. After the supernatant was decanted, fresh water was added for washing. The resulting mixture was decanted and the solids were collected by filtration. The obtained solids were dried under reduced pressure to give the crude product **5** (9.02 g, 35.46 mmol, 87%). Yellow solid. IR (KBr): 3028, 2924, 2877, 2827, 1597, 1439, 1417, 1298, 1180, 881, 841, 823, 752, 706 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.55–2.61 (m, 2H, CH_2), 3.50 (t, *J* = 8.2 Hz, 2H, $ArCH_2$), 6.26 (dt, *J* = 4.4, 9.5 Hz, 1H, ArCH=C*H*), 6.86 (dt, *J* = 1.8, 9.5 Hz, 1H, ArC*H*=CH), 7.85 (s, 1H, Ar), 7.94 (t, *J* = 7.5 Hz, 1H, Ar), 7.98 (s, 2H, Ar), 8.06 (d, *J* = 9.3 Hz, 1H, Ar), 8.11 (d, *J* = 7.6 Hz, 2H, Ar), 8.26 (d, *J* = 9.3 Hz, 1H, Ar), ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2 (CH_2), 23.3 (CH_2), 123.0 (CH), 123.2 (CH), 124.4 (C), 124.6 (CH), 124.9 (CH), 125.0 (C), 125.6 (CH), 126.6 (CH), 127.37 (CH), 127.43 (CH), 128.0 (C), 128.8 (CH), 129.3 (CH), 129.6 (C), 129.7 (C), 130.7 (C), 131.3 (C), 131.8 (C) ppm. HRMS (ESI): *m/z* calcd for $C_{20}H_{14}$: 254.1096 $[M]^+$; found: 254.1090.

trans-7,8-Dibenzolyoxy-7,8,9,10-tetrahydrobenzo[a]pyrene (6)[16]

To a dispersion of silver benzoate (7.77 g, 26.89 mmol) in benzene (350 mL, dehydrated), iodine (4.30 g, 16.94 mmol) was added. After the purple color disappeared within 20 min, **5** (3.00 g, 11.10 mmol) was added into the dispersion and stirred at 90 ºC for 2 hrs. After the full conversion was confirmed by TLC, the dispersion was filtered through a celite pad. The benzene solution was concentrated to half its volume and washed consecutively with saturated aqueous $Na_2S_2O_3$ (100 mL x 2), aqueous Na_2CO_3 (100 mL x2), water (100 mL x 2), and brine (50 mL x 1). The solution was dried over $MgSO_4$. The benzene was then evaporated to give the crude product *trans*-**6**. (5.41 g, 10.90 mmol, 98%). Beige solid. IR (KBr): 3043, 2960, 2927, 1716, 1600, 1583, 1450, 1315, 1274, 1174, 1108, 1068, 1025, 842, 819, 711 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50‑2.58 (m, 1H, CH*H*), 2.70‑2.78 (m, 1H, C*H*H), 3.75 (m, 2H, $ArCH_2$), 5.79 (m, 1H, BzOCH), 6.99 (d, *J* = 6.1 Hz, 1H, BzOCHAr), 7.35 (t, *J* = 7.7 Hz, 2H, Ar), 7.42 (t, *J* = 7.7 Hz, 2H, Ar), 7.49 (t, *J* = 7.4 Hz,

1H, Ar), 7.55 (t, *J* = 7.4 Hz, 1H, Ar), 7.94–8.03 (m, 5H, Ar), 8.11 (d, *J* = 7.2 Hz, 2H, Ar), 8.16–8.22 (m, 2H, Ar), 8.32 (d, *J* = 9.3 Hz, 1H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.5 (CH_2), 25.1 (CH_2), 71.8 (CH), 72.2 (CH), 122.9 (CH), 124.5 (C), 124.6 (C), 125.2 (CH), 125.3 (CH), 125.5 (CH), 126.2 (CH), 127.2 (CH), 127.5 (CH), 127.9 (CH), 128.4 (CH x2), 128.5 (CH x2), 128.6 (C), 129.7 (CH x2), 129.89 (C x 2), 129.99 (CH x2), 130.02 (C), 130.3 (C), 130.7 (C), 130.9 (C), 131.5 (C), 133.1 (CH), 133.3 (CH), 165.9 (C), 166.3 (C) ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{19}O_2$: 375.1380 $[M–OBz]^+$; found: 375.1379.

trans-7,8-Dibenzolyoxy-7,8-dihydrobenzo[a]pyrene (7)

After purging a benzene solution (250 mL, dehydrated) of the crude product **6** (5.41 g, 10.90 mmol) with nitrogen gas for 10 min, DDQ (3.80 g, 16.74 mmol) was added. The reaction mixture was stirred at 90 ºC for 6 hrs. A 0.5 mL aliquot of the reaction mixture in a test tube was extracted with 5 mL of ethyl acetate and 5 mL of saturated $Na_2S_2O_3$. The ethyl acetate extract was evaporated and the resulting sample was analyzed by NMR to confirm the full conversion of **6**. The reaction mixture cooled and then filtered through a celite pad. The filtrate was concentrated and the residue was extracted with ethyl acetate (200 mL) and saturated $Na_2S_2O_3$ (100 mL). The ethyl acetate extract was washed with aqueous K_2CO_3 (100 mL x3) with gentle shaking to avoid emulsion formation, water (100 mL), and brine (50 mL). The washed extract was dried over $MgSO_4$. After filtration and evaporation of ethyl acetate, the crude product **7** was obtained (5.37 g, 10.86 mmol, 99%). beige solid. IR (KBr): 3033, 1716, 1602, 1585, 1452, 1356, 1338, 1315, 1288, 1265, 1124, 1109, 989, 881, 839, 827, 775, 707, 692, 617 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.22 (ddd, *J* = 1.3, 3.6, 7.2 Hz, 1H, BzOCH), 6.47 (dd, *J* = 3.6, 10.1 Hz, 1H, ArCH=C*H*), 7.07 (d, *J* = 7.5 Hz, 1H, BzOCHAr), 7.37 (t, *J* = 7.7 Hz, 2H, Ar), 7.44 (t, *J* = 7.7 Hz, 2H, Ar), 7.51 (t, *J* = 7.4 Hz, 1H, Ar), 7.57 (t, *J* = 7.4 Hz, 1H, Ar), 7.79 (d, *J* = 9.9 Hz, 1H, ArC*H*=CH), 7.98–8.21 (m, 11H, Ar), 8.41 (d, *J* = 9.9 Hz, 1H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 71.8 (CH), 73.0 (CH), 122.1 (CH), 124.0 (CH), 124.7 (C), 125.1 (C), 125.4 (CH), 125.6 (C), 125.7 (CH), 125.8 (CH), 126.3 (CH x2),127.2 (C), 127.5 (CH), 128.0 (CH), 128.4 (CH x2), 128.46 (CH), 128.52 (CH x2), 129.4 (C), 129.69 (C), 129.71 (C), 129.9 (CH x2), 130.0 (CH x2), 130.8 (C), 131.0 (C), 131.5 (C), 133.2 (CH), 133.4 (CH), 166.04 (C), 166.08 (C) ppm. HRMS (ESI): *m/z* calcd for $C_{27}H_{17}O_2$: 373.1223 $[M–OBz]^+$; found: 373.1224.

trans-7,8-Dihydro-7,8-dihydroxybenzo[a]pyrene (8)

To a THF solution (20 mL, dehydrated) of the crude product **7** (5.13 g, 10.38 mmol) in a 200-mL round-bottom flask, a CH_3OH solution (20 mL, dehydrated) of sodium methoxide (1.68 g, 31.0 mmol) was added. The mixture was stirred at room temperature for 1 h. Most of the solvent was evaporated in a water bath at <30 ºC. The residue was poured into 0.1 M HCl (900 mL), and the resulting supernatant was decanted. The solid was washed by two cycles of dispersion and decantation using 900 mL of water. The solid was then filtered and dried under reduced pressure. The solid was reprecipitated using THF (100 mL) and hexane (900 mL). This was followed by two cycles of dispersion and decantation using 500 mL of hexane. The solid was filtered, and then dried in vacuum to give **8** (2.13g, 7.45 mmol, 72%). Dark green solid. IR (KBr): 3336, 3234, 3041, 2924, 2860, 1597, 1417, 1346, 1306, 1271, 1182, 1161, 1124, 1109, 1088, 899, 840, 831, 777,756, 698, 621 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 4.46 (m, 1H, allylic CH), 4.94 (dd, *J* = 5.7, 10.6 Hz, 1H, benzylic CH), 5.39 (d, *J* = 5.2 Hz, 1H, OH), 5.85 (d, *J* = 5.8 Hz, 1H, OH), 6.24 (dd, *J* = 2.2, 10.1 Hz, 1H, ArCH=CH), 7.55 (dd, *J* = 1.9, 10.2 Hz, 1H, ArCH=CH), 8.04 (t, *J* = 7.6 Hz, 1H, Ar), 8.14–8.20 (m, 3H, Ar), 8.27 (dd, *J* = 2.2, 7.6 Hz, 2H, Ar), 8.46 (s, 1H, Ar), 8.50 (d, *J* = 9.4 Hz, 1H, Ar). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 72.4 (CH), 75.0 (CH), 122.8 (CH), 122.9 (CH), 123.2 (CH), 123.9 (C), 124.6 (C), 125.4 (CH), 125.8 (CH), 126.1 (C), 126.6 (CH), 126.8 (C), 127.6 (CH), 128.09 (CH), 128.11 (CH), 130.3 (C), 130.8 (C), 131.3 (C), 135.3 (CH), 137.4 (C) ppm. HRMS (ESI): *m/z* calcd for $C_{20}H_{13}O$: 269.0961 $[M–OH]^+$; found: 269.0961.

7-Hydoxybenzo[a]pyrene (9)

Dark green solid. ^1H NMR (400 MHz, DMSO-d_6): δ = 7.21 (d, *J* = 7.4 Hz, 1H, Ar), 7.69 (t, *J* = 8.0 Hz, 1H, Ar), 8.01 (d, *J* = 9.1 Hz, 1H, Ar), 8.05 (d, *J* = 7.6 Hz, 1H, Ar), 8.17 (d, *J* = 9.3 Hz, 1H, Ar), 8.19 (d, *J* = 7.4 Hz, 1H, Ar), 8.33 (d, *J* = 7.7 Hz, 1H, Ar), 8.41 (d, *J* = 7.7 Hz, 1H, Ar), 8.62 (d, *J* =8.6 Hz, 1H, Ar), 8.96 (s, 1H, Ar), 9.15 (d, *J* = 9.3 Hz, 1H, Ar), 10.60 (s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 108.8 (CH), 114.2 (CH), 119.7 (CH), 123.1 (C), 123.4 (CH), 123.5 (C), 125.0 (C), 125.2 (CH), 125.8 (CH), 126.9 (CH), 127.0 (C), 127.5 (CH), 127.6 (CH), 127.8 (CH), 128.5 (C), 129.1 (CH), 129.6 (C), 131.4 (C), 131.7 (C), 154.6 (C) ppm. HRMS (ESI): *m/z* calcd for $C_{20}H_{11}O$: 267.0815 $[M–H]^-$; found: 267.0813.

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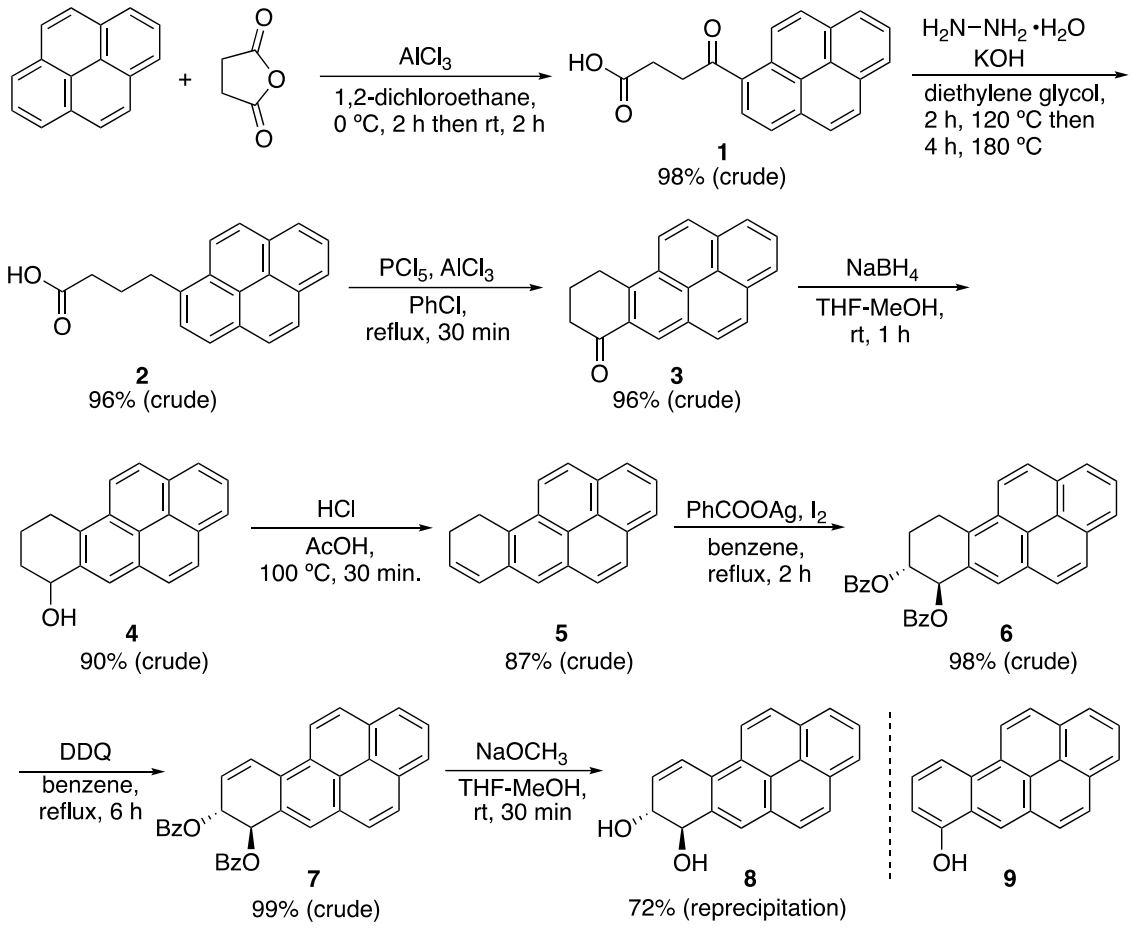
AlCl3
1,2-dichloroethane,
0 °C, 2 h then rt, 2 h
1
98% (crude)
H2N−NH2 •H2O
KOH
diethylene glycol,
2 h, 120 °C then
4 h, 180 °C
2
96% (crude)
PCl5, AlCl3
PhCl,
reflux, 30 min
3
96% (crude)
NaBH4
THF-MeOH,
rt, 1 h
4
90% (crude)
HCl
AcOH,
100 °C, 30 min.
5
87% (crude)
PhCOOAg, I2
benzene,
reflux, 2 h
6
98% (crude)
DDQ
benzene,
reflux, 6 h
7
99% (crude)
NaOCH3
THF-MeOH,
rt, 30 min
8
72% (reprecipitation)
9

Scheme 1.