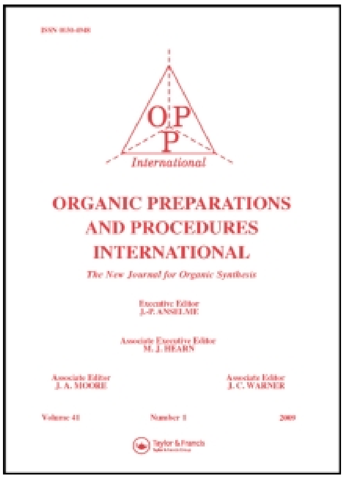


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

AN IMPROVED SYNTHESIS OF 2-METHYLBENZ[a]ANTHRACENE

Lorraine M. Deck[a]; Guido H. Daub[a]; Alberto A. Leon[ab]
[a] Department of Chemistry, University of New Mexico, Albuquerque, NM [b] Department of Radiology, University of New Mexico, Albuquerque, NM

To cite this Article Deck, Lorraine M. , Daub, Guido H. and Leon, Alberto A.(1987) 'AN IMPROVED SYNTHESIS OF 2-METHYLBENZ[a]ANTHRACENE', Organic Preparations and Procedures International, 19: 4, 277 — 282

To link to this Article: DOI: 10.1080/00304948709356199

URL: http://dx.doi.org/10.1080/00304948709356199

ORGANIC PREPARATIONS AND PROCEDURES INT. 19(4-5), 277-282 (1987)

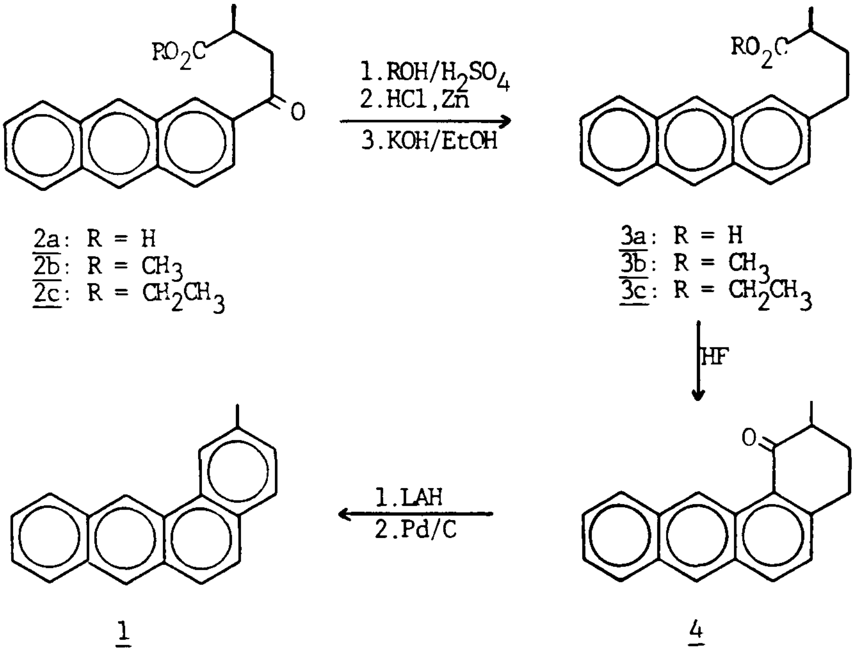
AN IMPROVED SYNTHESIS OF 2-METHYLBENZ[a]ANTHRACENE

Lorraine M. Deck, Guido H. Daub,† and Alberto A. Leon*††

Department of Chemistry, University of New Mexico,
Albuquerque, NM 87131

As part of a program designed to prepare multigram quantities of monomethylbenz[a]anthracenes, the synthesis of 2-methylbenz[a]anthracene (1) was undertaken. Prior syntheses[1-3] were relatively complex and suffered from low yields. This paper reports the synthesis of 1 in 6 steps from anthracene in 6% overall yield.

Treatment of anthracene with methylsuccinic anhydride in the presence of aluminum chloride afforded the ketoacid 2a in 20% yield. Although the yield of 2a is low, anthracene is inexpensive, and the product obtained is analytically pure. Clemmensen reduction of 2a furnished the corresponding



carboxylic acid 3a. NMR analysis showed the formation of side-products including a lactone. This problem was partially circumvented by esterification of the ketoacid to the methyl or ethyl esters 2b and 2c which underwent reduction to the corresponding esters 3b and 3c in 47% and 42% yield, respectively. Saponification of esters 3b and 3c gave the free acid 3a in 90% and 96% yield. Cyclization of 3a in anhydrous hydrogen fluoride provided the ketone 4 in 70% yield. Reduction of 4 with lithium aluminum hydride gave the alcohol (100% yield) which was dehydrogenated to the desired hydrocarbon 1 in 65% yield using 10% Pd/C. The alcohol was used directly because noticeable dehydration occurred upon acidic work as evidenced by C-13 NMR.

EXPERIMENTAL SECTION

Melting points were obtained with a Thomas-Hoover capillary melting point apparatus and are uncorrected as are reported boiling points. Elemental analyses were performed by Mrs. Ruby Ju, Department of Chemistry, UNM. IR measurements were obtained on a Perkin-Elmer Model 337 spectrophotometer. ^{1}H NMR spectra and ^{13}C NMR were recorded on a Varian FT-80 instrument at ambient temperature and are referenced to tetramethylsilane as an internal standard.

2-Methyl-3-(2-anthroyl)propionic Acid (2a).- To a cooled solution (10°) of 57 g (0.50 mol) of methylsuccinic anhydride, 89 g (0.50 mol) of anthracene and 500 mL of dry nitrobenzene was added 133 g (1.0 mol) of aluminum chloride at such a rate that the temperature remained below 15°. After stirring for 7 hrs at room temperature, the reaction was hydrolyzed by the addition of 1 L of ice water containing 20 mL of conc HCl and steam distilled to remove the nitrobenzene. The resulting solid was dissolved in 4 L of hot 1 N NH_4OH solution and filtered through a hot funnel containing a celite pad. Solid NaCl was added to the hot filtrate to precipitate the sodium salt which was filtered and dissolved in hot water. Acidification with conc HCl afforded a crude acid, mp. 196-205°, which was triturated with warm benzene, filtered, and then extracted with ethyl acetate for 24 hrs using a Soxhlet thimble. Concentration of the ethyl acetate afforded 29 g (20%) of 2a, mp. 208.5-209.5°.

Anal. Calcd. for $C_{19}H_{16}O_3$: C, 78.06; H, 5.52

Found: C, 77.97; H, 5.42

IR: 1675 (C=O, ketone), 1700 (C=O, acid) cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.47 -8.87(m,9H), 2.95-3.50(m,3H), 1.13-1.25(d,3H).

Methyl-2-methyl-3-(2-anthroyl)propionate (2b).- A mixture of 1.1 g (3.6 mmol) of 2a, 1 mL of conc sulfuric acid, 5 g (16 mmol) of methanol and 100 mL of benzene was heated to reflux for 24 hrs using a Dean-Stark water trap. After cooling, the reaction mixture was washed with water, 5% aq $NaHCO_3$, and satd NaCl. After the organic layer was dried ($MgSO_4$), the solvent was removed to give a yellow solid which was crystallized from methanol to give 0.95 g (86%) of yellow crystals, mp. 135-136°.

Anal. Calcd for $C_{20}H_{18}O_3$: C, 78.39; H, 5.93

Found: C, 78.22; H, 5.71

IR: 1670 (C=O, ketone), 1730 (C=O, ester) cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.20 -8.65(m, 9H), 3.65-3.75(d, 2H), 3.70(s,3H), 2.95-3.55(m, 1H), 1.25-1.40 (d,3H).

Ethyl-2-methyl-3-(2-anthroyl)propionate (2c).- As described for the synthesis of 2b, a solution of 1.10 g (3.76 mmol) of 2a, conc sulfuric acid, ethanol, and benzene was heated under reflux for 24 hrs. Similar workup afforded a solid which was crystallized from ethanol to give 1.05 g (88%) of yellow crystals, mp. 120-121°.

Anal. Calcd for $C_{21}H_{20}O_3$: C, 78.71; H, 6.30

Found: C, 78.57; H, 6.24

IR: 1680 (C=O, ketone), 1725 (C=O, ester) cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.35-8.45

(m, 9H), 4.15-4.35(q, 2H), 3.50-3.60(d, 2H), 2.90-3.50(m, 1H), 1.30-1.40 (d, 3H), 1.15-1.35(t, 3H).

Methyl 4-(2-anthryl)-2-methylbutanoate (3b).- A mixture of 2b (1.8 g, 5.9 mmol) in 100 mL of toluene, 24 mL of conc HCl, 10 mL of H_2O, and 18 g of mossy zinc (amalgamated) was stirred under reflux for 24 hrs. After cooling, the organic layer was washed with H_2O, satd NaCl and dried ($MgSO_4$). Removal of the toluene afforded a pale yellow solid which was chromatographed over neutral alumina using benzene to give 0.80 g (47%) of a white solid. Recrystallization from methanol afforded white crystals, mp. 116-117°.

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.15; H, 6.89
Found: C, 82.12; H, 6.69

IR: 1730 (C=O, ester) cm^{-1}. ^1H ($CDCl_3$): δ 7.15-8.35(m, 9H), 3.65(s, 3H), 2.65-2.85(t, 2H), 2.40-2.65(q, 2H), 1.70-2.20(m, 1H), 1.15-1.25(d, 3H).

Ethyl 4-(2-anthryl)-2-methylbutanoate (3c).- As described for the synthesis of 3b, a solution of 2c (0.90 g, 2.8 mmol) in 70 mL of toluene was stirred under reflux with 9 g of amalgamated Zn, 15 mL of conc HCl and 15 mL of HOAc for 28 hrs. Similar workup afforded 0.36 g (42%) of a pale yellow solid. An analytical sample was obtained by recrystallization from ethanol to give white crystals, mp. 114-115°.

Anal. Calcd for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24
Found: C, 82.38; H, 7.23

IR: 1725 (C=O, ester) cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.25-8.30(m, 9H), 3.95-4.30(q, 2H), 2.70-2.90(t, 2H), 2.45-2.70(q, 2H), 1.75-2.25(m, 1H), 1.15-1.35(t, 3H), 1.15-1.25(d, 3H).

4-(2-Anthryl)-2-methylbutanoic Acid (3a).- a) A mixture of 1.0 g (15 mmol) of KOH (85%), 0.75 g (2.5 mmol) of 3c and 70 mL of 95% of EtOH was refluxed for 4 hrs. The ethanol was removed and water was added to dissolve the residue. The aqueous solution was extracted with ether and then acidified with conc HCl to give a white precipitate. Recrystallization from ethyl acetate afforded 0.65 g (96%) of white crystals, mp. 192-193°.

Anal. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52

Found: C, 81.90; H, 6.31

IR: 1719 (C=O, acid) cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.30-8.50(m, 9H), 2.65 -2.95(t, 2H), 2.25-2.60(q, 2H), 1.60-2.15(m, 1H), 1.15-1.25(d, 3H).

b) As described for the synthesis of 3a, a mixture of 1.5 g of KOH (85%), 1.1 g (3.7 mmol) of 3b and 80 mL of methanol was refluxed for 3 hrs. Similar workup afforded 0.93 g (90%) of a white solid, mp. 189-190°.

c) As described for the synthesis of 3b, 6.0 g of amalgamated Zn was stirred under reflux with 4 mL of H_2O, 8 mL of conc HCl and a solution of 2 (2.0 g, 6.8 mmol) in 200 mL of toluene for 48 hrs. Four 2-mL aliquots of conc HCl were added at intervals. Similar workup afforded 1.2 g (63%) of a tan solid, mp. 180-185°.

3,4-Dihydro-2-methyl-1,2,3,4-tetrahydrobenz[a]anthracene-1(2H)-one (4).- Ten mL of anhydrous HF was added to 3a (0.93 g, 3.3 mmol) in a polyethylene beaker. After evaporation of the HF, the residual solid was stirred with 5% aq. $NaHCO_3$ and benzene. The benzene layer was separated, washed with water and satd NaCl, and dried ($MgSO_4$). Evaporation of the benzene gave a residue which was chromatographed over Woelm neutral alumina using benzene to yield a yellow solid which was recrystallized from methanol to give yellow needles, 0.60 g (70%), mp. 91.5-92.5.

Anal. Calcd for $C_{19}H_{16}O$: C, 87.66; H, 6.19

Found: C, 87.89; H, 6.05

IR: 1655 (C=O, ketone) cm^{-1}. ^1H NMR ($CDCl_3$): δ 6.80-8.25(m, 8H), 2.70 -2.90(t, 2H), 2.40-2.70(q, 2H), 1.70-2.20(m, 1H), 1.30-1.40(d, 3H).

2-Methylbenz[a]anthracene (1).- To a solution of 4.0 g (15 mmol) of 4 in 200 mL of anhydrous ether was slowly added 1.3 g (34 mmol) of lithium aluminum hydride. The mixture was refluxed for 23 hrs and after cooling 5% sulfuric acid was added dropwise. The organic layer was separated, washed, and removal of the solvent afforded 4.0 g (100%) of a yellow solid. The solid was dehydrogenated over 10% Pd/C (0.4 g) at 250° for 30 min and then at 300° for 4 hrs. The residue was dissolved in benzene and filtered. Removal of the benzene afforded 3.8 g of a solid which was chromatographed over neutral alumina using benzene. Evaporation of the eluents gave 2.4 g (65%) of a white solid, mp. 148-150°. Recrystallization from cyclohexane gave white needles, mp. 150-151°, lit.[2,3] mp. 150-151.7°; picrate, mp. 184-185°, lit.[3] mp. 179-180°.

^{1}H NMR ($CDCl_3$): δ 7.40-8.85(m, 11H), 2.60(s, 3H).

Acknowledgement.- This work was supported in part by Contract No. FDA 67-42. The authors acknowledge the help provided by Charles M. Miller.

REFERENCES

† Deceased, June 4, 1984

†† Present Address: Department of Radiology, University of New Mexico, Albuquerque, NM 87131.

1. J. W. Cook, J. Chem. Soc., 456 (1932).

2. W. E. Bachmann and G. D. Cortes, J. Am. Chem. Soc., 65, 1329 (1943).

3. M. S. Newman and R. Gaertner, ibid., 72, 264 (1950).

(Received May 5, 1986; in revised form November 11, 1986)