

Polystyrene-supported *N*-Methylthiourea: A Convenient New Reagent for the Hydrogenolysis of Bicyclic Endoperoxides

Alan C. Spivey, Carles Giró Mañas, Inderjit Mann

Supporting Information

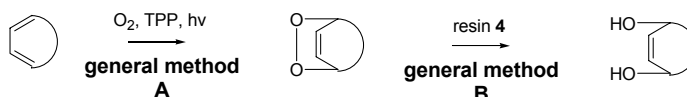
Experimental:

General Directions: All reactions were performed under anhydrous conditions and an atmosphere of nitrogen in flame-dried glassware. Yields refer to chromatographically and spectroscopically (^1H NMR) homogenous materials, unless otherwise indicated.

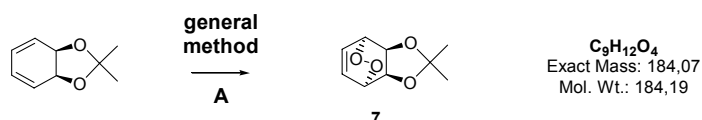
Solvents and reagents: All solvents were distilled before use. 'Petrol' refers to the fraction of light petroleum-ether boiling between 40 – 60°C. Commercial grade solvents used for flash chromatography were distilled before use. Anhydrous solvents were obtained as follows: CH_2Cl_2 and Et_2O were distilled from sodium/benzophenone ketyl under nitrogen immediately prior to use. All chemicals were handled in accordance with COSHH regulations. All reagents were used as commercially supplied. Ac_2O was shaken with P_2O_5 , separated and fractionally distilled from K_2CO_3 . Et_3N was stirred over CaH_2 under nitrogen for 24h, then distilled and stored over molecular sieves (4 Å) under nitrogen. **Chromatography:** Flash chromatography (FC) was carried out using Merck Kiesegel 60 F₂₅₄ (230-400 mesh) silica gel. Thin layer chromatography (TLC) was performed on Merck aluminium-backed plates pre-coated with silica (0.2 mm, 60 F₂₅₄) which were visualised either by quenching of ultraviolet fluorescence ($\lambda_{\text{max}} = 254$ and 366 nm) or by charring with 10% KMnO_4 in 1M H_2SO_4 . **Infra red spectra:** These were recorded as KBr discs on a Perkin-Elmer Paragon 1000 Fourier transform spectrometer. Only selected absorbances (ν_{max}) are reported. **^1H NMR spectra:** These were recorded at either 270, 300 or 400 MHz on Jeol 270GSX, Bruker DRX-300, or Bruker AMX-400 instruments respectively. Chemical shifts (δH) are quoted in parts per million (ppm), referenced to the appropriate residual solvent peak. Coupling constants (J) are reported to the nearest 0.5 Hz. The abbreviation *app* = 'apparent'. **^{13}C NMR spectra:** These were recorded at 100 MHz on a Bruker AMX-400 instrument. Chemical shifts (δC) are quoted in ppm, referenced to the appropriate solvent peak. **Mass spectra:** Low resolution mass spectra (m/z) were recorded on either a VG platform II or VG AutoSpec spectrometers, with only molecular ions (M^+ , MH^+ , MNH_4^+) and major peaks being reported with intensities quoted as percentages of the

base peak. High Resolution Mass Spectrometry (HRMS) measurements are valid to ± 5 ppm. Microanalysis performed by Warwick Analytical Services Ltd., Coventry.

Experimental Procedures: The following general methods were applied

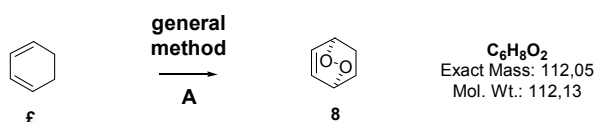


4,4-Dimethyl-3,5,8,9-tetraoxatricyclo[5.2.2.0^{2,6}]undec-10-ene (7)¹



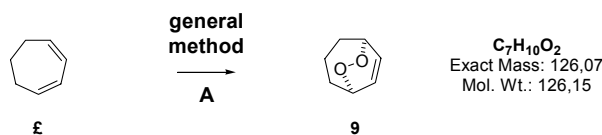
General Method A: To a stirred solution of *cis*-2,2-dimethyl-3a,7a-dihydrobenzo[1,3]dioxole² (0.30 g, 1.97 mmol) in CCl₄ (15 mL) was added tetraphenylporphyrin (TPP) (55 mg, 1.07 mmol) in CHCl₃ (5 mL). The resulting solution was irradiated with a 300 W tungsten filament lamp while bubbling oxygen through at 0 °C until all the diene had been consumed (by TLC, 2.5 h in this case). The reaction mixture was then concentrated *in vacuo* at RT, the resulting green residue dissolved in ice-cold hexane (5 mL), and activated charcoal (1.5 g) was added. The resulting black suspension was stirred for 10 min at 0 °C, filtered through a pad of CeliteTM and the CeliteTM washed with a further portion of ice-cold hexane (50 mL). The filtrate was concentrated *in vacuo* to give endoperoxide **7** as light brown needles (0.32 g, 88%). R_f 0.25 (Et₂O/pentane, 1:2); δ_H (CDCl₃, 300 MHz) 1.36 (3H, s, CH₃), 1.38 (3H, s, CH₃), 4.69 (2H, br s, H-2 and H-3), 4.81 (2H, br s, H-1 and H-4), 6.55 (2H, d, *J* 10.0, H-5 and H-6); *m/z* (Cl⁺) 202 (MNH₄⁺, 100%).

2,3-Dioxabicyclo[2.2.2]oct-5-ene (8)³



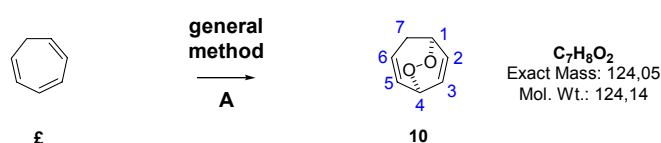
Using **general method A**, 1,3-cyclohexadiene (0.25 g, 3.12 mmol) and TPP (6 mg) after 2 h gave off-white crystals of endoperoxide **8** (238 mg, 68 %). R_f 0.3 (Et₂O/pentane, 3:7); δ_H (CDCl₃, 300 MHz) 1.46 (2H, d, *J* 10.0, CH₂), 2.27 (2H, d, *J* 10.0, CH₂), 4.63 (2H, br s, 2 × CHO), 6.70 (2H, dd, *J* 3.0, 3.0, CH=CH); *m/z* (Cl⁺) 130 (MNH₄⁺, 100%).

6,7-Dioxabicyclo[3.2.2]non-8-ene (9)⁴



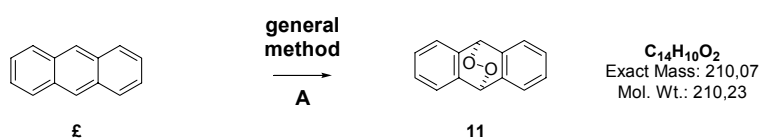
Using **general method A**, cycloheptadiene (0.25 g, 2.66 mmol) and TPP (6 mg) after 3 h gave endoperoxide **9** as a white solid (230 mg, 62%). R_f 0.35 (Et₂O/petrol, 3:7); δ_H (CDCl₃, 300 MHz) 1.23-1.42 (1H, CHH), 1.44-1.73 (1H, CHH), 1.87-2.06 (4H, 2 × CH₂), 4.62-4.81 (2H, 2 × CHO), 6.21-6.41 (2H, CH=CH); m/z (CI⁺) 127 (MH⁺, 19%), 144 (MNH₄⁺, 100%).

6,7-Dioxabicyclo[3.2.2]nona-2,8-diene (**10**)⁵



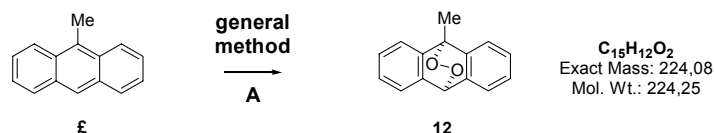
Using **general method A**, cycloheptatriene (1.00 g, 2.72 mmol) and TPP (66 mg) after 7 h and purification by FC (CH₂Cl₂/pentane, 1:1) at -50 °C gave the endoperoxide **10** as a white solid (543 mg, 45%). R_f 0.75 (CH₂Cl₂); δ_H (CDCl₃, 300 MHz); 2.39 (1H, *app* dq, *J* 20.0, 2.0, H-7), 2.92 (1H, *app* dddd, *J* 20.0, 3.5, 3.0, 2.5, H-7), 4.67 (1H, *app* tq, *J* 7.0, 2.0, H-4), 4.78 (1H, *app* tquin, *J* 5.0, 1.5, H-1), 5.69 (1H, *app* tt, *J* 3.5, 1.5, H-5), 6.05 (1H, *app* dt, *J* 9.0, 2.0, H-6), 5.32 (1H, *app* dd, *J* 7.5, 1.0, H-3), 6.75 (1H, *app* t, *J* 8.5, H-2); m/z (CI⁺) 125 (MH⁺, 58%), 142 (MNH₄⁺, 100%).

9,10-Dioxatricyclo[6.6.2.0^{2,7}]anthracene (**11**)⁶



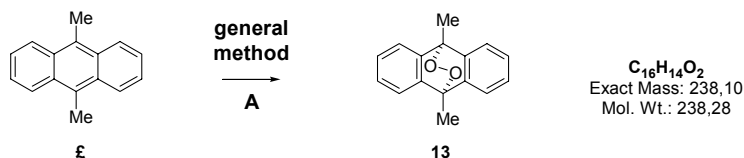
Using **general method A** (but omitting the decolourisation with activated charcoal and instead filtering through a plug of silica gel with pentane), anthracene (0.25 g, 1.40 mmol) and TPP (6 mg, 1 mol%) after 3 h gave endoperoxide **11** as a dark brown powder (280 mg, 92 %). R_f 0.2 (pentane); δ_H (CDCl₃, 300 MHz) 5.98 (2H, br s, 2 × CHO), 7.21-7.35 (4H, ArCHs), 7.39-7.41 (4H, ArCHs); m/z (CI⁺) 211 (MH⁺, 56%), 228 (MNH₄⁺, 100%).

9-Methyl-9,10-dioxatricyclo[6.6.2.0^{2,7}]anthracene (**12**)⁷



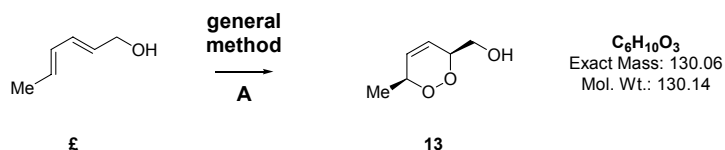
Using **general method A** (but omitting the decolourisation with activated charcoal and instead filtering through a plug of silica gel with pentane), 9-methyl anthracene (1.00 g, 5.20 mmol) and TPP (32 mg, 1 mol%) after 3.5 h gave endoperoxide **12** as a white crystalline solid (1.13 g, 95%). R_f 0.3 (pentane); δ_H (CDCl_3 , 270 MHz) 2.14 (3H, s, CH_3), 5.97 (1H, s, CH), 7.33-7.38 (4H, ArCHs), 7.42-7.51 (4H, ArCHs); m/z (CI^+) 225 (MH^+ , 56 %).

9,10-Dimethyl-9,10-dioxatricyclo[6.6.2.0^{2,7}]anthracene (**13**)⁸



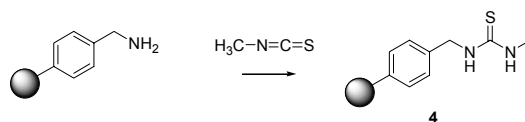
Using **general method A** (but omitting the decolourisation with activated charcoal and instead filtering through a plug of silica gel with pentane), 9,10-dimethyl anthracene (0.60 g, 2.90 mmol) and TPP (9 mg, 1 mol%) after 2.5 h gave endoperoxide **13** as a white crystalline solid (690 mg, 99 %). R_f 0.3 (pentane); δ_H (CDCl_3 , 300 MHz) 2.23 (6H, s, $2 \times \text{CH}_3$), 7.33-7.38 (4H, ArCHs), 7.41-7.45 (4H, ArCHs); m/z (CI^+) 239 (MH^+ , 100%).

cis-(6-Methyl-3,6-dihydro-[1,2]dioxin-3-yl)methanol (**14**)⁹



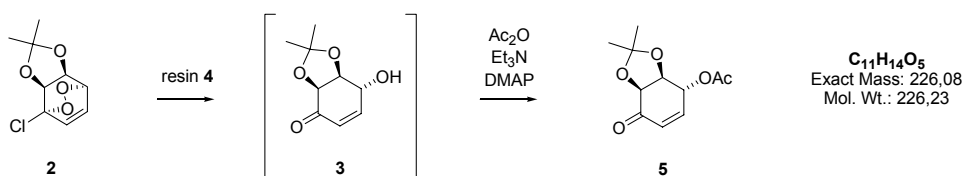
Using **general method A**, sorbic alcohol (0.50 g, 5.10 mmol) and TPP (10 mg, 1 mol%) after 4 h and purification by FC (Pet. $\text{Et}_2\text{O}/\text{Et}_2\text{O}$, 2:1) gave endoperoxide **14** as a light brown mobile oil (185 mg, 30%). R_f 0.35 (Et_2O); δ_H (CDCl_3 , 300 MHz) 1.13 (3H, d, J 7.0, CH_3), 3.17 (1H, br s, OH), 3.61 (1H, m, CHH), 3.78 (1H, t, J 9.0, CHH), 4.38 (1H, m, CHO), 4.72 (1H, m, CHCH_3), 5.80 (1H, ddd, J 10.0, 3.5, 2.0, $\text{CH}=\text{CH}$), 5.89 (1H, dt, J 10.0, 2.0, $\text{CH}=\text{CH}$); m/z (CI^+) 148 (MNH_4^+ , 100%).

Polystyrene-bound thiourea (**4**)



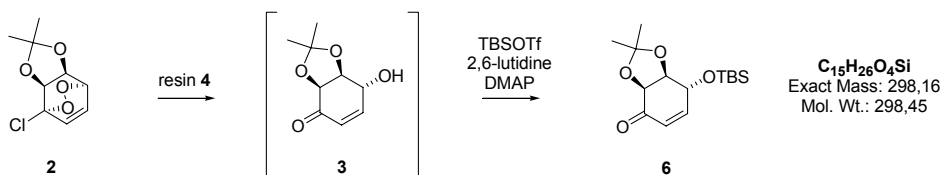
Aminomethylated polystyrene (5.00 g, 5.50 mmol, 1.1 g mol⁻¹) was added to Et₂O (30 mL) and allowed to swell for 20 min with vigorous stirring. Methylisothiocyanate (0.44 g, 5.60 mmol) was then added and the reaction mixture was refluxed for 4 h. After cooling to RT, the resin was filtered off, washed with Et₂O (3 × 100 mL) and dried *in vacuo* for 2 d to give a free flowing pale yellow resin **4** (5.32g, 94%, 1.1 g mol⁻¹). ν_{\max} (KBr) 3463.6, 3249.5, 3.164.3, 1537.6, 1522.1, 1289.5 (C=S), 1045.2; Microanalysis: N, 2.9; S, 3.3 %.

(4*R*,5*S*,6*R*)-4-*O*-Acetoxy-5,6-di-*O*-isopropylidencyclohex-2-ene-1-one (5)¹⁰



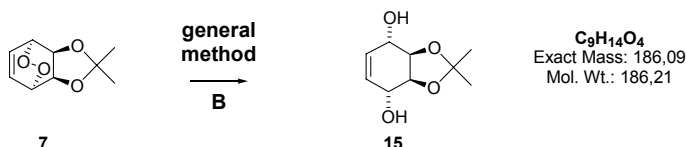
To a suspension of resin **4** (1.03 g, 1.03 mmol) in CH₂Cl₂ (15 mL) at 0 °C was added a solution of 1-chloro-4-methyl-3,5,8,9-tetraoxa-tricyclo[5.2.2.0]undec-10-ene **2**¹¹ (0.15 g, 0.69 mmol) in CH₂Cl₂ (5 mL) *via* a cannula. After stirring for 30 min the resin was filtered off and washed with CH₂Cl₂ (3 × 30 mL). The filtrate was concentrated *in vacuo* to a volume of ~10 mL and a mixture of DMAP (8 mg, 0.07 mmol), Et₃N (144 μL, 1.03 mmol) and Ac₂O (97 μL, 0.96 mmol) in CH₂Cl₂ (3 mL) was added at RT. After stirring for a further 20 min, the reaction mixture was quenched with NaHCO₃ (sat. aq., 5 mL). The organic layer was separated, washed with H₂O (4 × 30 mL), dried over Na₂SO₄ and concentrated *in vacuo* to give a yellow solid. Purification by FC (Et₂O/pentane, 1:1) gave acetoxyenone **5** as light yellow oil (135 mg, 85 %). *R_f* 0.75 (Et₂O/pentane, 9:1); δ_{H} (CDCl₃, 300 MHz) 1.41 (6H, s, 2 × CH₃), 2.15 (3H, s, OCH₃), 4.47 (1H, d, *J* 5.5, H-5), 4.54 (1H, dd, *J* 5.5, 3.5, H-4), 5.61 (1H, m, H-4), 6.21 (1H, d, *J* 10.5, H-2), 6.81 (1H, dd, *J* 10.5, 3.5, H-3); *m/z* (CI⁺) 227 (MH⁺, 35%), 244 (MNH₄⁺, 100%).

(4*R*,5*S*,6*R*)-4-*O*-(*tert*-Butyldimethylsilyl) -5,6-di-*O*-isopropylidencyclohex-2-ene-1-one (6)¹²



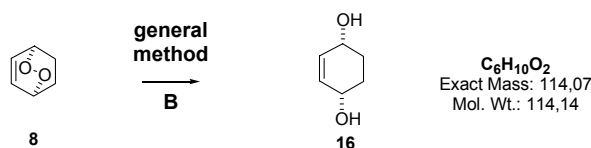
To a suspension of resin **4** (1.10 g, 1.10 mmol) in CH_2Cl_2 (15 mL) at 0 °C was added a solution of 1-chloro-4-methyl-3,5,8,9-tetraoxa-tricyclo[5.2.2.0]undec-10-ene **2**¹¹ (0.16 g, 0.73 mmol) in CH_2Cl_2 (5 mL) *via* a cannula. After stirring for 30 min the resin was filtered off and washed with CH_2Cl_2 (3 × 20 mL). The filtrate was concentrated *in vacuo* to a volume of ~5 mL and a mixture of DMAP (12 mg, 0.07 mmol), 2,6-lutidine (109 μL , 1.03 mmol) and TBSOTf (184 μL , 0.81 mmol) in CH_2Cl_2 (3 mL) was added at RT. After stirring for a further 20 min, the reaction mixture was quenched with NaHCO_3 (sat. aq. 5 mL). The organic layer was separated, washed with H_2O (4 × 30 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give a yellow solid. Purification by FC (EtOAc/hexane, 3:7) gave silyl ether **6** as a viscous colourless oil, which solidified upon refrigeration (176 mg, 81 %). R_f 0.7 (EtOAc/hexane, 2:1); δ_{H} (CDCl_3 , 300 MHz) 0.15 (3H, s, SiCH_3), 0.18 (3H, s, SiCH_3), 0.94 [9H, s, $\text{Si}(\text{CH}_3)_3$], 1.40 (3H, s, CH_3), 1.41 (3H, s, CH_3), 4.47 (2H, m, H-5 and H-6), 4.56 (1H, m, H-4), 6.09 (1H, dd, J 10.0, 1.0, H-2), 6.90 (1H, ddd, J 10.0, 4.0, 1.0, H-3); m/z (Cl^+) 299 (MH^+ , 12%), 316 (MNH_4^+ , 100%).

***cis*-2,2-Dimethyl-3a,4,7,7a-tetrahydrobenzo[1,3]dioxole-4,7-diol (**15**)**¹³



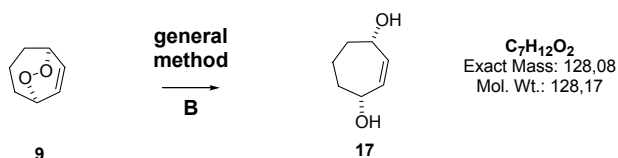
General Method B: To a suspension of resin **4** (0.814 g, 0.814 mmol) in CH_2Cl_2 (15 mL) at 0 °C was added a solution of endoperoxide **7** (0.10 g, 0.54 mmol) in CH_2Cl_2 (5 mL) *via* a cannula. The reaction mixture was then stirred at RT until all the endoperoxide had been consumed (by TLC, 2.5 h in this case) and then the resin was filtered off and washed with CH_2Cl_2 (3 × 20 mL). The filtrate was concentrated *in vacuo* to give diol **15** as light brown needles (98 mg, 98 %). R_f 0.35 (Et₂O/pentane, 9:1); δ_{H} (CDCl_3 , 300 MHz) 1.37 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.79-2.98 (2H, br s, 2 × OH), 4.18 (4H, s, 2 × CHOH and 2 × CHO), 5.81 (2H, s, $\text{CH}=\text{CH}$); m/z (Cl^+) 187 (MH^+ , 100%), 204 (MNH_4^+ , 63%).

***cis*-1,4-Dihydroxycyclohex-2-ene (16)³**



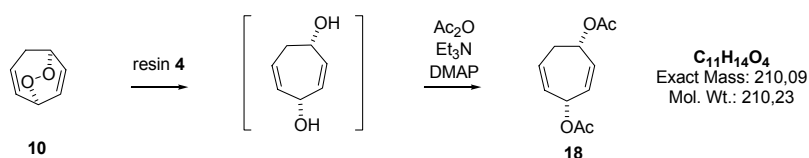
Using **general method B**, endoperoxide **8** (0.05 g, 0.446 mmol) and resin **4** (0.67 g, 0.67 mmol) after 96 h gave diol **16** as a white amorphous solid (51 mg, 99 %). R_f 0.10 (heptane/Et₂O, 7:3); δ_H (CDCl₃, 300 MHz) 1.88 (4H, br s, 2 × CH₂), 3.31 (2H, br s, 2 × OH), 4.16 (2H, br s, 2 × CHOH), 5.87 (2H, br s, CH=CH); m/z (CI⁺) 132 (MNH₄⁺, 100%).

***cis*-Cyclohept-2-ene-1,4-diol (17)⁴**



Using **general method B**, endoperoxide **9** (0.05 g, 0.39 mmol) and resin **4** (0.59 g, 0.59 mmol) after 70 h gave diol **17** as a white powder (43 mg, 85 %). R_f 0.5 (Et₂O); δ_H (CDCl₃, 300 MHz) 1.43-1.89 (4H, 2 × CH₂), 2.02-2.15 (2H, CH₂), 4.29 (2H, d, J 9.0, 2 × CHOH), 5.76 (2H, s, CH=CH), 2 × OH (absent); m/z (CI⁺) 129 (MH⁺, 37%), 146 (MNH₄⁺, 98%).

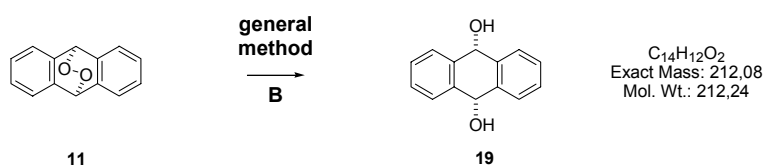
***cis*-1,4-Diacetoxycyclohepta-2,5-diene (18)**



To a suspension of resin **4** (0.610 g, 0.610 mmol) in CH₂Cl₂ (15 mL) at 0 °C was added a solution of endoperoxide **10** (0.05 g, 0.40 mmol) in CH₂Cl₂ (5 mL) *via* a cannula. After stirring for 120 h the resin was filtered off and washed with CH₂Cl₂ (3 × 30 mL). The filtrate was concentrated *in vacuo* to a volume of ~10 mL and a mixture of DMAP (5 mg, 0.04 mmol), Et₃N (85 μL, 1.20 mmol) and Ac₂O (49 μL, 1.04 mmol) in CH₂Cl₂ (3 mL) was added at RT. After stirring for a further 20 min, the reaction mixture was quenched with NaHCO₃ (sat. aq., 5 mL). The organic layer was separated, washed with H₂O (4 × 30 mL), dried over Na₂SO₄ and concentrated *in vacuo* to give a brown oil.

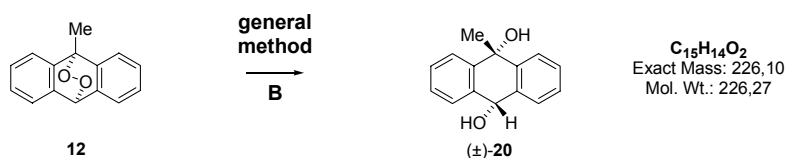
Purification by FC (CH₂Cl₂, 2:1) gave diacetate **18** as light brown oil (66 mg, 77 %). *R_f* 0.8 (petrol/EtOAc, 1:2); δ_H (CDCl₃, 400 MHz) 2.05 (3H, s, CH₃), 2.09 (3H, s, CH₃), 2.47 (2H, br s, CH₂), 5.52-5.76 (5H, 2 × CH=CH and CHO), 6.14 (1H, br s, CHO); δ_C (CDCl₃, 100 MHz) 21.2 (q), 21.3 (q), 31.4 (t), 68.7 (*d*), 71.8 (*d*), 126.3 (*d*), 130.8 (*d*), 131.2 (*d*), 131.6 (*d*); *m/z* (CI⁺) 228 (MNH₄⁺, 92%). Found: *m/z* MNH₄⁺ 228.12226, C₁₁H₁₈NO₄ requires 228.12223 (Δ = + 0.3 ppm).

***cis*-9,10-Dihydroanthracene-9,10-diol (**19**)**¹⁴



Using **general method B**, endoperoxide **11** (0.05 g, 0.238 mmol) and resin **4** (0.357 g, 0.357 mmol) after 3 h gave diol **19** as a white solid (50.5 mg, 85 %). Recrystallisation from hot toluene gave a fluffy white solid (45.7 mg, 77%). *R_f* 0.3 (Et₂O); δ_H (*d*₆-DMSO, 300 MHz) 5.38 (2H, br d, *J* 7.5, 2 × CHO), 7.21-7.35 (4H, ArCHs), 7.39-7.41 (4H, ArCHs); *m/z* (CI⁺) 213 (MH⁺, 43%) 230 (MNH₄⁺, 100%).

(±)-*cis*-9-Methyl-9,10-dihydroanthracene-9,10-diol (20**)**⁷



Using **general method B**, endoperoxide **12** (0.05 g, 0.222 mmol) and resin **4** (0.334 g, 0.334 mmol) after 5.5 h gave diol (±)-**20** as a white needles (50.2 mg, 99 %). *R_f* 0.5 (Et₂O); δ_H (CDCl₃, 270 MHz) 1.49 (3H, s, CH₃), 2.26 (2H, s, 2 × OH), 5.46 (1H, d, *J* 9.0, CHOH), 7.33-7.40 (4H, ArCHs), 7.70-7.77 (4H, ArCHs); *m/z* (CI⁺) 209 (MH⁺-H₂O, 100%), 226 (MNH₄⁺-H₂O, 23%).

References:

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