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RESEARCH ARTICLE

Synthesis of Spirocyclopente-Dione Anthracene Adduct, Precursor of the Cyclopentenone Prostagladins Via Ring-Closing Metathesis Reaction

GEDSIRIN EKSINITKUN[a,b], STEPHEN G. PYNE[b],
WAYA PHUTDHAWONG[a] and WEERACHAI PHUTDHAWONG[c*]

[a]Department of Chemistry, Faculty of Science, Silpakorn University,
Nakhon Pathom-73000, Thailand

[b]School of Chemistry, University of Wollongong, Wollongong, N.S.W-2522, Australia

[c]Department of Chemistry, Faculty of Liberal Arts and Science, Kasetsart University,
Kampeang Sean Campus, Nakhon Pathom-73140, Thailand

faaswcp@ku.ac.th

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Abstract: A synthesis of the spirocyclopente-dione anthracene adduct, a precursor of the cyclopentenone prostaglandins has been reported. The synthesis involved a Diels-Alder reaction of anthracene and dimethyl fumarate to afford **3** followed by reduction, oxidation and esterification reactions to provide methyl ester anthracene adduct **8**, which further converted to the the allylic alcohol (**12**). Then, Ring-Closing Metathesis (RCM) reaction afforded the cyclopentenol anthracene adduct, which after oxidation provided the spirocyclopente-dione anthracene adduct in good yields.

Keywords: Cross-conjugated, Dienone, Ring closing metathesis, Cyclopentenones

Introduction

Functionalized cyclopentenones are considered important precursors in the synthesis of a large number of bioactive natural products such as conjugated dienone prostanoids, clavulone I, clavulone II[1-2] and claviridic acids A-E[3], all exhibiting strong cytotoxicity and anticancer activity. Several synthetic approaches have been proposed to prepare this class of compounds including the Nazarov cyclisation[4], [3+2] annulations[5], metal-catalysed cyclisations[6] and Diels-Alder/retro Diels-Alder reactions using anthracene[7]. In our previous research of stereoselective synthesized cyclopentenone[8], we found the use of sterically crowded anthracene moiety leads to stereocontrol and asymmetric transformations and subsequent retro-Diels-Alder reaction affords alkylidene cyclopentenone A (Figure 1), a precursor of the antitumor alkylidene cyclopentenone prostaglandins (PGs) such as clavulone II[2] and 4-deacetoxyl-12-*O*-deacetylclavulone III[9]. However, the cyclization process using β-allyl ester with an excess of LDA provided cyclopentenone in moderate yields together with the formation of the enaminone[10]. As an extension, we here report a

novel building block for the synthesis of cyclopentenone prostaglandins, in the particular PGA_1 analog clavulones. The synthesis of this key compound, spirocyclopente-dione anthracene adduct, could be envisioned from the cyclopentenol readily obtained from the 1,6-diene using a ring-closing metathesis reaction.

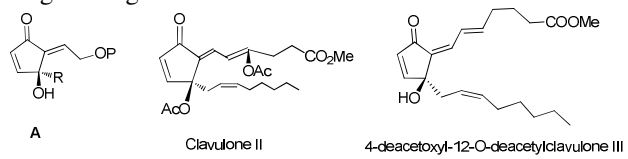


Figure 1

Experimental

Melting points were determined on a Stuart Scientific SMP 2 melting point apparatus and are uncorrected. Infrared spectra were recorded as CH_2Cl_2-films with a Perkin Elmer Spectrum GX FT-IR spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded in (D) chloroform solutions at 300 MHz for ^{1}H and 75 MHz for ^{13}C with a Bruker AVANCE 300 spectrometer. Tetramethylsilane was used as the internal standard. Mass spectra were recorded on a Polaris Q or Hewlett Packard 5973 mass spectrometer.

*9,10-Dihydro-9,10-ethanoanthracene-11,12-dimethyl ester (**3**)*

A mixture of anthracene (2.00 g, 11.22 mmol), dimethyl fumarate (2.05 g, 14.23 mmol) and xylene (15 mL) in a pressured tube with boiling chips was heated at 120 ^{o}C for 48 h. The reaction mixture was cooled to room temperature and the xylene was then removed under *vacuo*. The crude product was purified using column chromatography (silica gel, 30:1 hexane/EtOAc) to afford the adduct **3** (2.82 g, 78%) as a white solid, m.p. 103-105 ^{o}C (lit.[11] 107-108 ^{o}C); IR (CH_2Cl_2) ν_{max} : 1732, 1459, 1435, 1221, 1198, 1018, 760 cm^{-1}; ^{1}H NMR δ 7.28-7.31 (m, 2H, ArH), 7.22-7.25 (m, 2H), 7.07-7.14 (m, 4H), 4.73 (s, 2H), 3.62 (s, 6H), 3.42 (s, 2H); ^{13}C NMR δ 172.8, 142.0, 140.3, 126.4,126.3, 124.6, 123.8, 52.2, 47.8, 46.7.

*9,10-Dihydro-9,10-ethanoanthracene-11,12-dimethyl alcohol (**4**)*

To a solution of **3** (2.75 g, 8.54 mmol) in THF (60 mL) at 0 ^{o}C lithium aluminium hydride (1.94 g, 51.2 mmol) was slowly added. The mixture was stirred at 0 ^{o}C under argon atmosphere for 30 min. The reaction mixture was quenched with sat. $NaHCO_3$ solution and extracted with Et_2O (3x30 mL). The combined organic phase was dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the diol **4** (2.15 g, 98%) as a white solid; m.p. 196-198 ^{o}C; IR (CH_2Cl_2) ν_{max}: 3442, 3054, 2987, 1422, 1022 cm^{-1}; ^{1}H NMR δ 7.38–7.35 (m, 4H), 7.18-7.15 (m, 4H), 4.44 (s, 2H), 3.22-3.17 (m, 2H), 2.89-2.81(m, 2H), 1.38-1.33 (m, 2H); ^{13}C NMR δ 144.5, 141.7, 126.1, 125.8, 123.4, 64.5, 45.9, 45.3; HRESI-MS *m/z* cald for $[M+Na]^+$ $C_{18}H_{18}NaO_2$: 289.1193, found: 289.1182.

*9,10-Dihydro-9,10-ethanoanthracene-11-acetoxy-12-methanol (**5**)*

To a solution of the diol **4** (5.80 g, 21.8 mmol) in DMF (8 mL) at room temperature pyridine (2.11 mL, 26.2 mmol) was added followed by acetic anhydride (2.06 mL, 21.8 mmol). The mixture was stirred at room temperature for 30 min. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (2x20 mL). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 3:1 hexane/ EtOAc) to give the mono-acetate **5** (3.48 g, 52%) as a white solid; m.p. 89-91 ^{o}C; IR (CH_2Cl_2) ν_{max}: 3451, 3054, 2987, 1736, 1422, 1025 cm^{-1}; ^{1}H NMR δ 7.27-7.23 (m, 4H), 7.11-7.07 (m, 4H), 4.32 (d, *J* =1.8 Hz, 1H), 4.21 (d, *J* = 1.8Hz, 1H), 3.81 (dd, *J* =10.6,

5.8 Hz, 1H), 3.51 (dd, *J* = 10.4, 8.7 Hz, 1H), 3.27 (dd, *J* =10.6, 5.8 Hz, 1H), 3.06 (dd, *J* = 10.4, 8.7 Hz, 1H), 2.48 (br. s, 1H), 2.03 (s, 3H), 1.66-1.52 (m, 2H); ^{13}C NMR δ 171.2, 143.5, 143.1, 140.7, 140.4, 126.3, 126.2, 125.9, 125.8, 125.5, 125.4, 123.5*2, 67.1, 65.5, 45.9, 45.7, 45.5, 42.2, 21.0; HRESI-MS *m/z* cald for $[M+Na]^+$ $C_{20}H_{20}NaO_3$: 331.1310, found: 331.1306.

*9,10-Dihydro-9,10-ethanoanthracene-11-acetoxy-12-acetic acid (**6**)*

A solution of alcohol **5** (0.22 g, 0.71 mmol) in acetone (6 mL) was treated with Jones reagent[18] (4 mL) at 0 °C until TLC analysis showed the reaction was complete (*ca.* 1 h). Isopropanol (0.6 mL) was added slowly drop wise to destroy excess reagent and the mixture was stirred for another 5-10 min until the colour of the solution changed from red to green. CH_2Cl_2 (20 mL) and water (20 mL) were added. The aqueous phase was extracted with CH_2Cl_2 (10 mL×3). The combined organic extracts were washed with water (40 mL) and brine (40 mL) and then died (Na_2SO_4), filtered and evaporated *in vacuo* to give compound **6** (0.21 g, 91%) as a yellow oil; IR (CH_2Cl_2) ν_{max}: 3436, 2987, 1737,1708, 1422, 1036 cm^{-1}; ^{1}H NMR δ 7.35-7.28 (m, 4H), 7.18-7.12 (m, 4H), 4.68 (d, *J* = 2.1 Hz, 1H), 4.33 (d, *J* = 2.1 Hz, 1H), 3.89-3.84 (m, 1H), 3.77-3.70 (m, 1H), 2.73-2.65 (m, 1H), 2.42 (dd, *J* = 5.6, 2.3Hz, 1H), 2.60 (s, 3H); ^{13}C NMR δ 178.1, 171.0, 143.3, 141.9, 140.2, 139.9, 126.4*3, 126.1, 125.5, 125.3, 123.6, 123.5, 66.7, 48.2, 46.3, 45.9, 41.7, 20.9; HRESI-MS *m/z* cald for $[M+Na]^+$ $C_{20}H_{18}NaO_4$: 345.1103, found: 345.1089.

*9,10-Dihydro-9,10-ethanoanthracene-11-methanol-12-methyl ester (**7**)*

To a solution of **6** (2.34 g, 7.27 mmol) in methanol (14 mL) was added drop wise conc. H_2SO_4 (1 mL). The mixture was stirred at room temperature for 12 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (3x20 mL). The combined extracts were dried (Na_2SO_4), filtered and concentrated to give **7** (1.82 g, 85%) as a yellow oil; IR (CH_2Cl_2) ν_{max}: 3443, 2987, 1733, 1422, 1023 cm^{-1}; ^{1}H NMR *δ* 9.20 (br. s, 1H), 7.32-7.23 (m, 4H), 7.11-7.05 (m, 4H), 4.62 (d, *J* = 2.1 Hz, 1H), 4.31 (d, *J* = 2.1 Hz, 1H), 3.27 (s, 3H) 3.09-2.96 (m, 2H), 2.58-2.50 (m, 1H), 2.22 (dd, *J* = 5.7, 2.2 Hz, 1H); ^{13}C NMR δ 177.2, 143.6, 142.4, 140.7, 140.2, 126.3, 126.28, 126.25, 126.0, 125.6, 125.5, 123.5, 123.4, 75.8, 58.9, 48.7, 46.1, 45.6, 42.7; HRESI-MS *m/z* cald for $[M+Na]^+$ $C_{19}H_{18}NaO_3$: 317.1154, found: 317.1148.

*11-(tert-Butyl-dimethyl-silanyloxy)methyl-9,10-dihydro-9,10-ethanoanthracene-12-methyl ester (**8**)*

To a solution of alcohol **7** (1.50 g, 5.09 mmol) in dry CH_2Cl_2 (43 mL) under an argon atmosphere imidazole (0.66 g, 10.2 mmol) was added followed by TBDMSCl (0.88 g, 5.61 mmol). The mixture was stirred at room temperature for 15 h. The reaction mixture was quenched with sat. $NaHCO_3$ solution and extracted with CH_2Cl_2 (2×30 mL). The combined extracts were dried (Na_2SO_4), filtered and concentrated. Purification by flash column chromatography (silica gel, 30:1 hexane/ EtOAc) gave silyl ether **8** (1.68 g, 81%) as a white solid, m.p. 81.7-84.8 °C; IR (CH_2Cl_2) ν_{max}: 3445, 2953, 1737, 1470, 1253, 1213, 1094, 837, 746 cm^{-1}; ^{1}H NMR *δ* 7.21-7.13 (m, 4H), 7.03-6.98 (m, 4H), 4.48 (d, *J* = 2.3 Hz, 1H), 4.30 (d, *J* = 2.3 Hz, 1H), 3.20 (s, 3H, OCH_3), 3.12-3.07 (m, 1H), 2.64 (d, *J* = 9.1 Hz, 1H), 2.58-2.52 (m, 1H), 2.06- 2.04 (m, 1H), 0.80 (s, 9H) ,0.08 (s, 3H) , 0.04 (s, 3H); ^{13}C NMR δ 173.5, 144.1, 142.6, 141.1, 140.8, 126.4, 126.2*2, 125.9, 125.8, 125.1, 123.6, 123.5, 65.7, 61.9, 48.0, 46.9, 45.7, 45.6, 26.1; HRESI-MS *m/z* cald for $[M+Na]^+$ $C_{25}H_{32}NaO_3Si$: 431.2018, found: 431.2049.

*11-(tert-Butyl-dimethyl-silanyloxy)methanol-9,10-dihydro-9,10-ethanoanthracene-12,12-dimethylester (**9**)*

To a solution of 2 M lithium diisopropylamide (0.74 mL, 1.47 mmol) in dry THF (2.5 mL) at -78 °C under argon atmosphere a solution of ester **8** (0.50 g, 1.22 mmol) was added in dry

THF (5 mL) and the mixture was allowed to warm to 0 °C for 2 h. Methyl cyanoformate (0.12 mL, 1.47 mmol) was added at -78 °C and the mixture stirred at 0 °C for 2 h. The resulting mixture was quenched with an aqueous saturated $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (2×15 mL) which was washed with water (20 mL) and saturated NaCl (20 mL). The combined extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification of the residue by flash column chromatography (silica gel, 25:1 hexane/ EtOAc) gave **9** (0.41 g, 81%) as a white solid, m.p. 129-131 °C; IR (CH_2Cl_2) ν_{max}: 2952, 1741, 1459, 1220, 1095, 837 cm^{-1}**;** ^{1}H NMR δ 7.44 (d, *J* = 7.3 Hz, 1H), 7.30 (d, *J* = 7.3 Hz,1H), 7.23(d, *J* = 7.1 Hz, 1H), 7.14 (d, *J* = 7.1, 5.5 Hz, 2H), 7.10 (t, *J* = 7.3 Hz, 2H), 7.04 (dd, *J* = 7.5 , 7.3 Hz, 1H), 4.8 (s, 1H), 4.58 (d, *J* = 2.4 Hz, 1H), 3.57 (s, 3H), 3.55 (s, 3H), 3.54-3.51 (m, 1H), 3.30-3.22 (m, 1H), 2.67 (dd, *J* = 10.8, 9.5 Hz, 1H), 0.93 (s, 9H), 0.00 (s, 6H). ^{13}C NMR δ 170.7, 170.1, 143.9, 141.6, 140.5, 140.1, 127.0, 126.9, 126.1, 126.0, 125.9, 125.3, 124.5, 124.4, 62.4, 61.9, 53.1, 52.3, 51.0, 47.1, 45.6, 26.2, -5.16, -5.2. HRESI-MS *m/z* cald for $[M-H]^-$ $C_{27}H_{33}O_5Si$: 465.2097, found: 465.2118.

*11-(tert-Butyl-dimethyl-silanyloxy)methanol-9,10-dihydro-9,10-ethanoanthracene-12,12-dimethanol (**10**)*

To adduct **9** (0.16 g , 0.33 mmol) in Et_2O (2 mL) at 0 ^oC lithium aluminium hydride (53 mg, 1.4 mmol) was slowly added. The mixture was stirred at 0 °C under argon atmosphere for 30 min. The reaction was quenched with saturated $NaHCO_3$ solution and extracted with Et_2O (3x30 mL). The combined extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a diol **10** (74 mg, 61%) as a white solid, m.p. 204-206 °C; IR (CH_2Cl_2) ν_{max}: 3262, 2929, 1466, 1253, 1059, 835 cm^{-1}; ^{1}H NMR δ 7.37-7.34 (m, 1H), 7.28- 7.19 (m, 3H), 7.13-7.08 (m, 4H), 4.35 (s, 1H), 4.06 (d, *J* = 1.78 Hz, 1H), 3.63 (dd, *J* = 10.8, 5.2 Hz, 2H), 3.47 (dd, *J* = 10.6, 1.6 Hz, 1H), 3.35-3.32 (m, 3H), 2.96 (dd, *J* = 10.7, 10.3 Hz, 1H), 2.65 (br.s, 1H), 1.52 (qd, *J* = 5.1, 1.9 Hz, 1H), 0.86 (s, 9H), 0.066 (s, 3H), 0.044 (s, 3H). ^{13}C NMR δ 143.6, 141.8, 141.4, 140.9, 126.3, 126.2*2, 126.0, 125.8, 125.3, 124.9, 123.2, 68.2, 65.3, 65.2, 49.4, 48.5, 48.1, 47.9, 26.0, -5.13, -5.29. HRCI-MS *m/z* cald for $[M+H]^+C_{25}H_{35}O_3Si$: 411.2355, found:411.2361.

*11-(tert-Butyl-dimethyl-silanyloxy)methanol-9,10-dihydro-9,10-ethanoanthracene-12,12-dicarbaldehyde (**11**)*

To a solution of alcohol **10** (0.10 g, 0.24 mmol) in dry CH_2Cl_2 (10 mL) under an argon atmosphere Dess-Martin periodinane (0.36 g, 0.85 mmol) was added. The mixture was stirred at room temperaaature for 2 h. The reaction was quenched with sat. $NaHCO_3$ and $NaS_2O_3.5H_2O$ solution (10 mL) and extracted with CH_2Cl_2 (2×20 mL). The combined extracts were dried (Na_2SO_4), filtered and concentrated to give dialdehyde **11** (94 mg, 95%) as a yellow oil; ^{1}H NMR δ 9.66 (s, 1H), 9.10 (s, 1H), 7.39 (d, *J* = 6.3 Hz, 2H), 7.35 (d, *J* = 7.3 Hz, 1H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.23 (t, *J* = 6.3 Hz, 2H), 7.2-7.12 (m, 2H), 4.82 (s, 1H), 4.38 (s, 1H), 3.76 (dd, *J* = 9.8, 7.3 Hz, 1H), 3.48 (t, *J* = 9.8 Hz,1H,), 2.99 (dd, *J* = 9.3, 7.3 Hz, 1H), 0.85 (s, 9H), 0.05 (s, 3H), 0.01(s, 3H). ^{13}C NMR δ 201.1, 198.4, 143.8, 142.2, 138.4, 138.37, 127.0, 126.9, 126.5, 126.3, 125.3, 125.1, 123.6, 66.5, 62.5, 49.2, 46.8, 46.2, 25.8, -5.5, -5.8.

*11-((tert-Butyl-dimethyl-silanyloxy)methanol-9,10-dihydro-9,10-ethanoanthracene-12,12-diyl)bis(prop-2-en-1-ol) (**12**)*

Vinyl magnesium bromide (1.9 mL, 1.91 mmol) was added drop wise to the solution of the aldehyde **11** (0.15 g, 0.38 mmol) in dry Et_2O (5 mL) at -78 °C under argon atmosphere. The mixture was stirred at -78 °C for 40 min. The reaction was quenched with sat.NH_4Cl

at -78 °C and allowed to warm to room temperature. The mixture was extracted with Et_2O (2×20 mL). The combined organic layers were washed with brine, dried over anhyd. Na_2SO_4, filtered and concentrated. Purification of the residue by flash column chromatography (silica gel, 20:1 hexane/ EtOAc) gave **12** (16 mg g, 8.9%) as a yellow oil; IR (CH_2Cl_2) ν_{max}: 3350, 2929, 1469, 1254, 1086, 836 cm^{-1}; ^1H NMR δ ^1H ; 7.36-7.34 (m, 1H), 7.25-7.22 (m, 2H), 7.10-7.07 (m, 5H), 6.33-6.26 (m, 2H), 6.24-6.18 (m, 2H), 5.22 (dd, *J* = 17.1, 10.4 Hz, 2H), 5.06 (dd, *J* = 17.1, 10.4 Hz, 2H), 4.71 (s, 1H), 4.29 (d, *J* = 1.5 Hz, 1H), 3.79 (d, *J* = 6.5 Hz, 1H), 3.69-3.65 (dd, *J* = 10.7, 7.6 Hz, 1H), 3.50 (dd, *J* = 10.8, 6.9 Hz, 1H), 3.32 (d, *J* = 5.0 Hz, 1H), 1.97 (t, *J* = 7.2 Hz, 1H), 0.92 (s, 9H), 0.096 (s, 3H), 0.065 (s, 3H). ^{13}C NMR δ 143.9, 142.1, 141.9, 141.8, 139.5, 139.4, 126.3, 126.1, 126.0, 125.9, 125.84, 125.82, 125.1, 123.4, 117.1, 114.9, 80.5, 76.9, 65.2, 53.9, 49.3, 48.3, 48.26, 26.1, -5.1, -5.2. HRESI-MS *m/z* cald for [M] $C_{29}H_{38}O_3Si$: 462.2590, found: 462.2613.

*11-((tert-Butyl-dimethyl-silanyloxy)methanol-9,10-dihydrospiro-[9,10-ethanoanthracene -12,1'-cyclopen[3]ene]-2',5'-diol (**13**)*

To a solution of compound **12** (0.11 g, 0.25 mmol) Grubb I catalyst (10 mg, 0.012 mmol) in CH_2Cl_2 (4.3 mL) was added. The reaction was heated at 40 °C under argon atmosphere for 15 h and then concentrated under reduced pressure. The crude product was purified by Flash column chromatography (silica gel, 6:1 hexane/ EtOAc) to give compound **13** (56 mg, 53%) as a yellow oil; ^1H NMR δ 7.39-7.37 (m, 3H), 7.31(d, *J* = 6 Hz, 1H), 7.19-7.11 (m, 4H), 6.01 (d, *J* = 6 Hz, 1H), 5.91-5.90 (m, 1H), 5.08 (s, 1H), 4.59 (s, 1H), 4.53 (s, 1H), 3.83 (s, 1H), 3.54 (dd, *J* = 10.7, 1.2 Hz, 1H), 3.99 (t, *J* = 10.7 Hz, 1H), 1.77 (d, *J* = 9.8 Hz,1H), 0.93 (s, 9H), 0.057 (s, 3H), 0.00 (s, 3H). ^{13}C NMR δ 144.9, 143.4, 142.2, 141.7, 141.3, 131.6, 126.6, 126.59, 126.4, 126.3, 125.9, 124.4, 123.5, 123.45, 85.2, 83.1, 64.9, 58.8, 55.6, 50.8, 46.8, 26.2, -4.9, -5.0. HRESI-MS *m/z* cald for $[M-H]^-$ $C_{27}H_{33}O_3Si$: 433.2199, found: 433.2174.

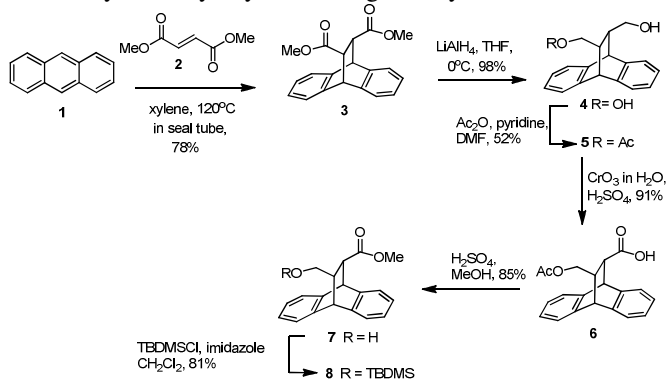
*11-((tert-Butyl-dimethyl-silanyloxy)methanol-9,10-dihydrospiro-[9,10-ethanoanthracene -12,1'-cyclopen[3]ene]-2',5'-dione (**14**)*

To a solution of alcohol **13** (15 mg, 0.035 mmol) in dry CH_2Cl_2 (4 mL) under an argon atmosphere Dess-Martin periodinane (59 mg, 0.14 mmol) was added. The mixture was stirred at room temperature for 2 h. The reaction was quenched with sat. $NaHCO_3$ and $NaS_2O_3.5H_2O$ solution (10 mL) and extracted with CH_2Cl_2 (2×10 mL). The combined extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give dialdehyde **14** (14 mg, 93%) as a yelloe oil; IR (CH_2Cl_2) ν_{max}: 2962, 1704, 1463, 1260 cm^{-1}; ^1H NMR δ 7.33(d, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.26 (s, 1H), 7.20-7.08 (m, 7H), 4.17 (s, 1H), 3.60 (dd, *J* = 9.8, 5.6 Hz, 1H), 3.24 (dd, *J* = 10.8, 9.8 Hz, 1H), 2.55 (dd, *J* = 10.8, 5.6 Hz, 1H), 0.69 (s, 9H), -0.13 (s, 3H), -0.17 (s, 3H). ^{13}C NMR δ 204.4, 201.2, 148.8, 145.4, 144.6, 141.4, 140.1, 138.9, 126.8, 126.6, 126.1, 126.0, 125.7, 125.5, 124.8, 123.0, 63.3, 55.2, 51.5, 51.1, 46.5, 25.8, -5.5, -5.6. HRCI-MS *m/z* cald for $[M+H]^+C_{27}H_{31}O_3Si$: 431.2042, found: 431.2035.

Results and Discussion

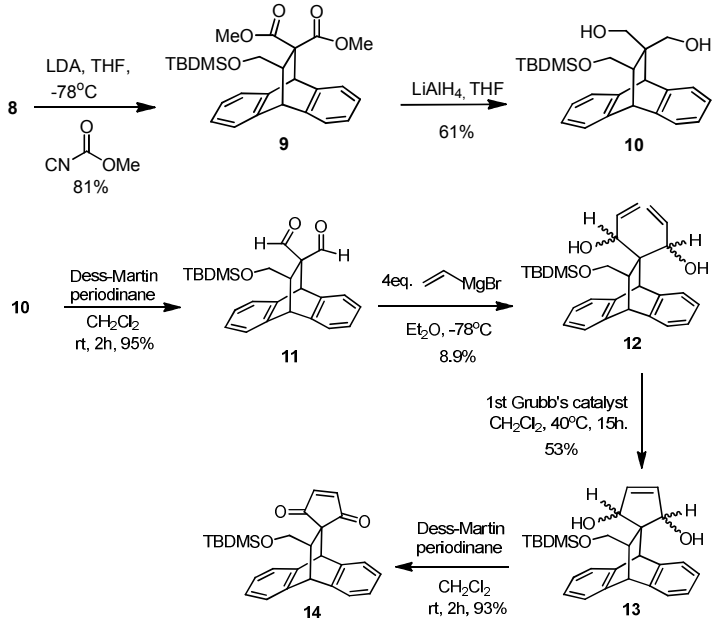
Synthesis of cyclopentenone adduct began from Diels-Alder reaction between the know dimethyl fumarate and anthracene in xylene at 120 °C for 48 h in a sealed tube gave ester **3** in 78% yield (Scheme 1). Reduction of the adduct **3** using $LiAlH_4$ led to the alcohol **4** in quantitative yield. The di-alcohol **4** was protected as its monoacetate adduct **5** and transformed another alcohol group into carboxylic acid **6** by using Jone reagent as high as 91% yield (Scheme 2). Esterification of the carboxylic acid **6** with methanol in the present of

H_2SO_4 into their methyl ester was however, obtained the alcohol **7** as the acetate protecting group was cleaved during this reaction. Thus, re-protected the –OH group of the resulting methyl ester **7** with *t*-butyldimethylsilyl chloride gave silyl adduct **8** in 81%.



Scheme 1. Synthetic route to methylester adduct **8**

Spirocyclopenten-dione **14** required for this synthesis was prepared in a six-steps synthetic route starting with treatment of ester **8** with LDA in THF at -78 °C in the presence of methyl cyanoformate to form dimthylester adduct **9** in 81% yield. This was reacted with $LiAlH_4$ in THF at 0 °C forming the primary alcohol **10** (61%), which was further oxidized to the corresponding dialdehyde **11** by Dess-Martin periodinane, both steps proceeding in excellent yield. Compound **11** was then obtained by addition vinylmagnesium bromide to give secondary alcohol **12** (8.9%) as a mixture of four diastereomer, followed by olefin cross metathesis using Grubb's catalyst to give alkene **13** (53%). Oxidation of di-alcohol **13** with Dess-Martin periodinane gave spirocyclopenten-dione **14** in 93% yield (Scheme 2).



Scheme 2. Synthetic route to Spirocyclopenten-dione **14**

Conclusion

The spirocyclopenten-dione anthracene adduct (**14**), a precursor of the cyclopentenone prostaglandins, has been synthesized in 12 steps. This compound may in the future as a building block to provide an efficient route for the synthesis of prostanoid natural products.

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