Asian Journal of Chemistry; Vol. 25, No. 11 (2013), 5968-5970

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2013.14207

# An Expeditious Assembly of 3,4-Benzannulated-8-oxabicyclo[3:2:1]octane Systems

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(*Received*: 18 June 2012; *Accepted*: 22 April 2013) AJC-13379

Substituted diarylmethylidenefluorene derivatives are generally synthesized by addition of fluorenylidene anions to benzophenone and subsequent dehydration and very recently using Peterson olefination.

**Key Words: Diarylmethylidenefluorenes, Benzophenone, Wittig olefination, $Hg(OAc)_2$.**

## INTRODUCTION

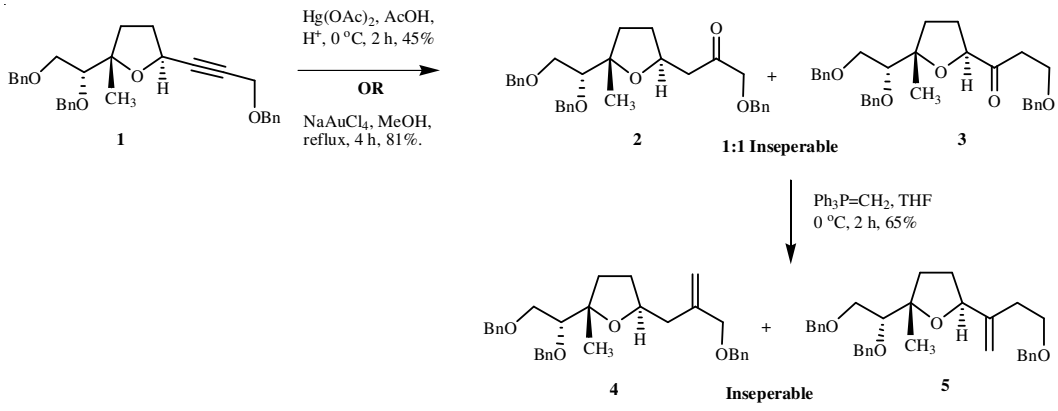
There is great interest in the chemistry of fluorenes and their polymers as electroluminescent compositions and the alkylidene fluorene liquid crystalline semiconducting polymers organic field effect transistor devices[1,2]. Diary lmethylidenefluorenes in general and the dications or radical anions derived from them in particular, are subjects of extensive physical studies. The studies are related to antiarornaticity or electron-spin distribution/conformation and are evaluated by means of either magnetic criteria focusing on the consequences of the existence of a ring current or ESR and ENDOR spectra. While there appears to be a great deal of discussion about the derived transient intermediates by theoretical and experimental calculations, little has focused on the synthesis of these diary lmethylidenefluorene derivatives[3,4].

Substituted diarylmethylidenefluorene derivatives are generally synthesized by addition of fluorenylidene anions to benzophenone and subsequent dehydration and recently using Peterson olefination. There are a few reports in which the addition of diazofluorene to a thioketone, Wittig olefination[5], [2+2] addition of fluorenylidene stannene to a benzophenone and subsequent [2+2] decomposition have been described. In many of these approaches, the use of strong bases to generate the requisite benzylic anion and strong acids to dehydrate the intermediate alcohol limits the variation of the substituents on aromatic rings, especially the lack of a protocol compatible with base- sensitive groups[6,7]. We introduce a facile synthesis of diarylmethylidenefluorenes by means of Suzuki coupling of dibromomethylidenefluorene with arylboronic acids.

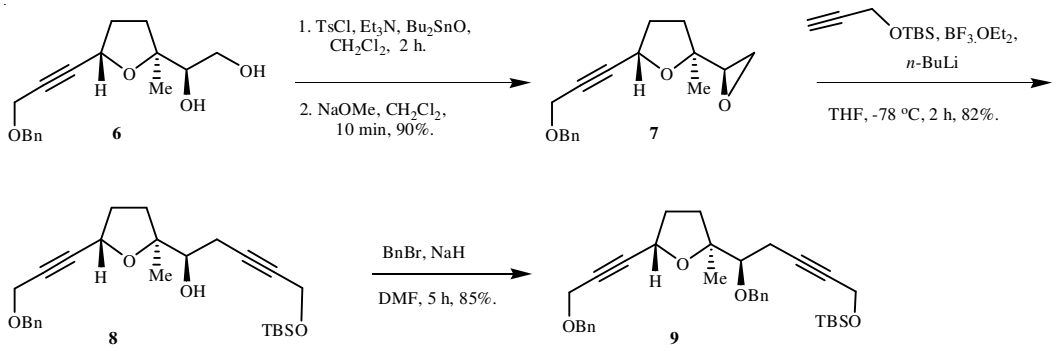
## EXPERIMENTAL

**Synthesis of (2S,5S)-5-(3-(benzyloxy)prop-1-ynyl)-2-((R)-1,2-*bis*(benzyloxy)ethyl)-2methyl tetrahydrofuran[8] (1):** To a solution of acetonide 224 (100 mg, 0.30 mmol) in methanol (5 mL) was added PTSA (21 mg, 0.12 mmol) and the mixture was stirred at room temperature for 3 h. Added trithylamine (2 mL) and stirred for another 0.5 h. Methanol was removed *in vacuo* and the residue obtained was purified by column chromatography (1:1 petroleum ether/ethyl acetate) gave diol 225 (71 mg, 81 %) as colourless oil. To a solution of diol (70 mg, 0.24 mmol) in dry DMF (2 mL) was added NaH (28 mg of 60 % dispersed in mineral oil, 0.72 mmol) at ice-cold temperature. The mixture was stirred for 10 min and to the dark brown solution was added benzyl bromide (0.06 mL, 0.50 mmol) slowly dropwise and the mixture was stirred at r.t. 4 h. The mixture was quenched with ice and diluted with ethyl acetate (5 mL). The organic phase was separated and washed with water (3 mL × 3 mL), brine (3 mL), dried over $Na_2SO_4$, filtered and concentrated. The residue was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give tribenzyl derivative 226 (98 mg, 85 %) as colourless oil. m.f.: $C_{31}H_{34}O_4$, $[\alpha]_D$: -9.17 (c 2.5, $CHCl_3$), IR (Neat, $\nu_{max}$, $cm^{-1}$): 2926, 2855, 1956, 1453, $^1H$ NMR ($CDCl_3$, 200 MHz): δ 1.27 (s, 3H), 1.71-1.81 (m, 1H), 1.97-2.24 (m, 3H), 3.48-3.62 (m, 2H), 3.78 (dd, *J* = 9.8, 1.7 Hz, 1H), 4.19 (d, *J* = 1.4 Hz, 2H), 4.51 (s, 2H), 4.57 (s, 2H), 4.62-4.68 (m, 1H), 4.66 (d, *J* = 11.7 Hz, 1H), 4.83 (d, *J* = 11.7 Hz, 1H), 7.23-7.35 (m, 15H) ppm. $^{13}C$ NMR ($CDCl_3$, 50 MHz): δ 23.68 (q), 33.51 (t), 34.42 (t), 57.18 (t), 68.34 (d), 71.16 (t), 71.80 (t), 73.21 (t), 73.58 (t), 80.13 (s), 83.14 (d), 85.07 (s), 86.78 (s), 127.17 (d), 127.30 (d), 127.57 (d), 127.78 (d), 127.99 (d), 128.13 (d), 137.31 (s), 138.15 (s), 138.78 (s) ppm. Elemental analysis calcd. (%): C, 79.12; H, 7.28. Found (%): C, 79.08; H, 7.10.

**1-(Benzyloxy)-3-((2S,5S)-5-((R)-1,2-*bis*(benzyloxy) ethyl)-5-methyl tetrahydrofuran-2-yl)propan-2-one (2):** To a mixture of alkyne **1** (100 mg, 0.212 mmol) and acetic acid




**Scheme-I**




**Scheme-II**

(2 mL) a drop of sulfuric acid at 0 ºC was added and the mixture was stirred for 3 h. The mixture was diluted with water (3 mL) and acids were quenched with solid $NaHCO_3$. The mixture was extracted with ethyl acetate (2 mL × 10 mL), washed with brine (5 mL), dried over $NaSO_4$, filtered and concentrated. Column purification (7:3 petroleum ether/ethyl acetate) of crude residue gave inseparable mixture of keto compounds **2/3** (47 mg, 45 %) as colourless oil. m.f.: $C_{31}H_{36}O_5$, IR ($CHCl_3$, $\nu_{max}$, $cm^{-1}$): 3031, 1726, 1453. $^1H$ NMR ($CDCl_3$, 200 MHz): δ 1.11, 1.13 (2s, 3H), 1.50-1.67 (m, 2H), 1.99-2.17 (m, 2H), 2.40-2.81 (m, 2H), 3.41-3.63 (m, 2H), 3.71-3.79 (m, 1H), 4.00 (d, *J* = 3.6 Hz, 1H), 4.08 (s, 1H), 4.23-4.38 (m, 1H), 4.50-4.58 (m, 4H), 4.63-4.87 (m, 2H), 7.27-7.35 (m, 15H) ppm. $^{13}C$ NMR ($CDCl_3$, 50 MHz): δ 22.70 (q), 23.92 (q), 31.92 (t), 31.98 (t), 34.77 (t), 34.98 (t), 45.49 (t), 45.76 (t), 72.06 (t), 72.17 (t), 73.20 (t), 73.24 (t), 73.39 (t), 73.70 (t), 73.82 (t), 74.48 (d), 75.31 (t), 75.50 (t), 75.54 (d), 83.49 (d), 83.65 (d), 84.42 (s), 84.45 (s), 126.91 (d), 127.32 (d), 127.49 (d), 127.67 (d), 127.84 (d), 127.89 (d), 127.94 (d), 128.17 (d), 128.32 (d), 128.46 (d), 137.27 (s), 138.42 (s), 139.07 (s), 206.55 (s), 206.57 (s) ppm. Elemental analysis calcd. (%): C, 76.20; H, 7.43, found (%): C, 76.11; H, 7.30.

**(2S,5S)-5-(2-(Benzyloxymethyl)allyl)-2-((R)-1,2-*bis*(benzyloxy)ethyl)-2-methyl tetrahydrofuran (4):** A solution of mixture of keto compounds **2/3** (40 mg, 0.082 mmol) in dry THF (4 mL) was treated with freshly prepared triphenyl phosphonium methylide (using 146 mg of $PPh_3^+CH_3Br^-$ 0.41 mmol and 0.2 mL of 1.6 M *n*-BuLi 0.33 mmol in 4 mL of THF) at 0 ºC and stirred for 2 h. Added a solution of sat. aq. $NH_4Cl$ (3 mL) and the mixture was diluted with ethyl acetate (5 mL). The organic phase was separated and the aq. phase was washed with ethyl acetate (2 mL × 5 mL). The combined organic extracts were dried over $Na_2SO_4$, filtered and concentrated. The residue was purified by column chromatography (1:9 petroleum ether/ethyl acetate) to give inseparable mixture of exo-methylene compounds **4/5** (25 mg, 63 %) as colourless oil. m.f.: $C_{32}H_{38}O_4$. $^1H$ NMR ($CDCl_3$, 500 MHz): δ 1.14, 1.15 (2s, 3H), 1.50-1.66 (m, 2H), 1.90-1.98 (m, 1H), 2.05-2.13 (m, 1H), 2.17-2.24 (m, 1H), 2.32-2.39 (m, 1H), 3.48-3.56 (m, 1H), 3.58-3.64 (m, 1H), 3.79-3.86 (m, 1H), 3.92-3.99 (m, 2H), 4.07-4.14 (m, 1H), 4.47 (s, 2H), 4.52 (s, 2H), 4.68 (d, *J* = 11.7 Hz, 1H), 4.87 (dd, *J* = 11.7, 7.8 Hz, 1H), 4.97 (d, *J* = 15.7 Hz, 1H), 5.10 (d, *J* = 7.9 Hz, 1H), 7.25-7.35 (m, 15H) ppm. $^{13}C$ NMR ($CDCl_3$, 125 MHz): δ 22.59 (q), 23.90 (q), 31.70 (t), 31.83 (t), 35.07 (t), 35.41 (t), 40.14 (t), 40.24 (t), 71.93 (t), 71.96 (t), 72.38 (t), 72.50 (t), 73.26 (t), 73.42 (t), 73.82 (t), 77.42 (d), 78.49 (d), 83.77 (d), 83.84 (d), 84.08 (s), 84.15 (s), 113.39 (t), 113.58 (t), 127.29 (d), 127.51 (d), 127.63 (d), 127.75 (d), 128.16 (d), 128.33 (d), 138.45 (s), 138.53 (s), 138.58 (s), 139.26 (s), 143.38 (s), 143.45 (s) ppm. Elemental analysis calcd. (%): C, 78.98; H, 7.87, found (%): C, 78.85; H, 7.62.

**(2S,5S)-5-(3-(Benzyloxy)prop-1-ynyl)-2-methyl-2-((R)-oxiran-2-yl)tetrahydrofuran (7):** To a solution of diol **6** (4 g, 13.77 mmol) in dry DCM (40 mL) was added tosyl chloride (2.63 g, 13.77 mmol), dibutyltin oxide (68 mg, 0.28 mmol) followed by triethylamine (3.8 mL, 27.54 mmol) and stirred at r.t. for 6 h. DCM was removed under reduced pressure and the crude reaction mixture was taken in methanol (40 mL), added potassium carbonate (3.8 mg, 27.54 mmol) and stirred at r.t. for 0.5 h. Methanol was concentrated *in vacuo* and the crude product was diluted by adding water (50 mL) and ethyl

acetate (75 mL). Organic phase was separated and aq. phase was washed with ethyl acetate (2 mL × 50 mL). The combined organic extracts were dried over $Na_2SO_4$, filtered, concentrated and the residue was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give epoxide **8** (3.75 g, 90 %) as colourless oil. m.f.: $C_{17}H_{20}O_3$, $[\alpha]_D$: -8.7 (c 1.0, $CHCl_3$). IR (Neat, $\nu_{max}$, $cm^{-1}$): 2978, 2118, 1956, 1453. $^1H$ NMR ($CDCl_3$, 500 MHz): δ 1.35 (s, 3H), 1.72 (ddd, *J* = 12.5, 8.0, 6.6 Hz, 1H), 1.81 (ddd, *J* = 12.5, 8.0, 7.0 Hz, 1H), 2.01-2.08 (m, 1H), 2.20-2.26 (m, 1H), 2.50 (dd, *J* = 4.7, 2.7 Hz, 1H), 2.70 (t, *J* = 4.7 Hz, 1H), 2.97 (dd, *J* = 4.0, 2.7 Hz, 1H), 4.19 (d, *J* = 1.3 Hz, 2H), 4.57 (s, 2H), 4.67-4.71 (m, 1H), 7.26-7.34 (m, 5H) ppm. $^{13}C$ NMR ($CDCl_3$, 125 MHz): δ 24.36 (q), 32.00 (t), 33.74 (t), 43.54 (t), 56.50 (d), 57.37 (t), 68.54 (d), 71.43 (t), 80.56 (s), 82.48 (s), 86.51 (s), 127.78 (d), 128.01 (d) 2C, 128.38 (d) 2C, 137.47 (s) ppm. ESI-MS (m/z): 295.1 $[M + Na]^+$. Elemental analysis calcd. (%): C, 74.97; H, 7.40. Found (%): C, 74.88; H, 7.26.

**(R)-1-((2S,5S)-5-(3-(Benzyloxy)prop-1-ynyl)-2-methyltetrahydrofuran-2-yl)-5-(*tert*-butyldimethylsilyloxy) pent-3-yn-1-ol (8):** To a solution of propargyl TBS ether (1.74 g, 10.2 mmol) in dry THF (10 mL) was added *n*-BuLi (6 mL of 1.6 M in hexanes, 9.54 mmol) at -78 ºC. The mixture was stirred for 0.5 h and added a solution of epoxide **7** (927 mg, 3.4 mmol) slowly dropwise followed by $BF_3$:$OEt_2$ (0.86 mL, 6.8 mmol). After stirring the mixture for 2 h at -78 ºC, the mixture was quenched with sat. aq. $NH_4Cl$ solution (5 mL) carefully and the temperature was raised to r.t. slowly. The mixture was diluted with ethyl acetate (10 mL). The organic phase was separated and the aq. phase was washed with ethyl acetate (2 mL × 10 mL). The combined organic extracts were dried over $Na_2SO_4$, filtered and concentrated. The residue was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give alcohol **8** (1.23 g, 82 %) as colourless oil. m.f.: $C_{26}H_{38}O_4Si$, $[\alpha]_D$: -9.87 (c 1.0, $CHCl_3$). IR ($CHCl_3$, $\nu_{max}$, $cm^{-1}$): 3444, 2972, 2118, 1453. $^1H$ NMR ($CDCl_3$, 200 MHz): δ 0.11 (s, 6H), 0.90 (s, 9H), 1.29 (s, 3H), 1.74-1.82 (m, 1H), 2.04-2.37 (m, 4H), 2.46-2.57 (m, 1H), 3.63 (dd, *J* = 8.7, 3.5 Hz, 1H), 4.19 (s, 2H), 4.29 (q, *J* = 1.8 Hz, 2H), 4.57 (s, 2H), 4.64-4.70 (m, 1H), 7.27-7.35 (m, 5H) ppm. $^{13}C$ NMR ($CDCl_3$, 50 MHz): δ -5.08 (q) 2C, 18.35 (s), 22.72 (t), 23.06 (q), 25.89 (q) 3C, 32.96 (t), 33.77 (t), 51.88 (t), 57.39 (t), 68.78 (d), 71.50 (t), 74.80 (d), 80.67 (s), 80.90 (s), 82.03 (s), 85.99 (s), 86.71 (s), 127.82 (d), 128.03 (d) 2C, 128.40 (d) 2C, 137.43 (s) ppm. ESI-MS (m/z): 443.3 $[M + 1]^+$, 465.3 $[M + Na]^+$. Elemental analysis calcd. (%): C, 70.55; H, 8.65. Found (%): C, 70.39; H, 8.41.

**((R)-5-(Benzyloxy)-5-((2S,5S)-5-(3-(benzyloxy)prop-1-ynyl)-2-methyltetrahydrofuran-2-yl)pent-2-ynyloxy)(*tert*-butyl)dimethylsilane (9):** To a solution of alcohol **8** (530 mg, 1.2 mmol) in dry DMF (5 mL) was added NaH (58 mg of 60 % in mineral oil, 1.44 mmol) at ice-cold temperature. The mixture was stirred for 10 min and to the dark brown solution was added benzyl bromide (0.285 mL, 2.4 mmol) slowly dropwise and the mixture was stirred at r.t. 5 h. The mixture was quenched with ice and diluted with ethyl acetate (15 mL). The organic phase was separated and washed with water (3 mL × 10 mL), brine (10 mL), dried over $Na_2SO_4$, filtered and concentrated. Chromatographic purification of residue (9:1 petroleum ether/ethyl acetate) gave benzyl derivative **9** (504 mg, 79 %) as colourless oil. m.f.: $C_{33}H_{44}O_4Si$, $[\alpha]_D$: -10.7 (c 3.3, $CHCl_3$). IR ($CHCl_3$, $\nu_{max}$, $cm^{-1}$): 3012, 2953, 2234, 1216. $^1H$ NMR ($CDCl_3$, 200 MHz): δ 0.10 (s, 6H), 0.90 (s, 9H), 1.29 (s, 3H), 1.71-1.85 (m, 1H), 1.98-2.22 (m, 3H), 2.29-2.43 (m, 1H), 2.54-2.66 (m, 1H), 3.49 (dd, *J* = 7.8, 3.5 Hz, 1H), 4.19 (d, *J* = 1.2 Hz, 2H), 4.29 (t, *J* = 1.8 Hz, 2H), 4.57 (s, 2H), 4.59-4.67 (m, 1H), 4.67 (d, *J* = 11.4 Hz, 1H), 4.87 (d, *J* = 11.4 Hz, 1H), 7.23-7.35 (m, 10H) ppm. $^{13}C$ NMR ($CDCl_3$, 50 MHz): δ -5.07 (q) 2C, 18.38 (s), 21.52 (t), 23.71 (q), 25.92 (q) 3C, 29.75 (t), 33.86 (t), 51.97 (t), 57.46 (t), 68.63 (d), 71.49 (t), 74.08 (t), 80.03 (s), 80.38 (s), 82.95 (d), 83.19 (s), 86.20 (s), 86.82 (s), 127.52 (d), 127.82 (d), 127.89 (d) 2C, 128.05 (d) 2C, 128.25 (d) 2C, 128.40 (d) 2C, 137.48 (s), 138.65 (s) ppm. ESI-MS (m/z): 555.6 $[M + Na]^+$. Elemental analysis calcd. (%): C, 74.39; H, 8.32. Found (%): C, 74.22; H, 8.41.

## RESULTS AND DISCUSSION

The tribenzyl derivative (**1**) was subjected to hydration reaction under standard reaction condition by using $Hg(OAc)_2$ in acetic acid with catalytic sulfuric acid[9] unfortunately resulted in 1:1 mixture of inseparable regiomeric ketones **2** and **3** in 45 % yield, which were fully confirmed by their spectral and analytical data. The C-5 methyl was observed as two singlets at δ 1.11 and 1.13 with equal intensity. $^{13}C$ NMR further confirmed the equal ratio of regiomers. Even the gold mediated hydration by using $NaAuCl_4$ in refluxing methanol resulted in same ratio of regiomers. The mixture of regiomeric ketones (**2/3**) were subjected to one carbon Wittig homologation by insitu generated ylide of methyl triphenylphosphonium bromide again gave the inseparable mixture of regio-exo methylene compounds (**4/5**) (**Scheme-I**). The exo-methylene protons were observed at δ 4.97 and 5.10 in the $^1H$ NMR spectrum of the mixture. $^{13}C$ NMR spectrum further confirmed the regiomeric mixture.

## ACKNOWLEDGEMENTS

The author thanks to DST-PURSE PROGRAMME for providing financial assistance. (Proceedings No. SVU/DST-PURSE/ST-A, 2011-12, Dated 01-11-2011).

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