



Synthesis of Dimethyl fluorene-9,9-diacetate

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In this work, the synthesis and structural characterization of novel dimethyl fluorene-9,9-diacetate in a 4-step reaction pathway, starting from commercially available fluorene is reported. We envisaged this reagent to be useful in the field of organic semiconductor research.

Key Words: Fluorene, Alkylation, Oxidation, Jones reagent, Steglich esterification.

INTRODUCTION

Fluorene can be easily functionalized by nucleophilic substitution at the 9-position, due to the acidity of the benzylic protons and electrophilic substitution at the 2- and 7-positions due to the reactivity of electrophiles with the electron rich aromatic ring. This ease of synthetic modification has helped fluorene to be a major player in organic semiconductor applications, such as, organic light emitting diodes, organic field effect transistors and organic photovoltaics¹.

We report the convenient synthesis of novel dimethyl fluorene-9,9-diacetate (**4**) in 4 steps, starting from commercially available fluorene. We originally attempted to synthesize the target molecule in one step, using fluorene/*t*-BuOK/methylbromoacetate and in 3 steps starting with fluorene/KOH/bromoethanol (Fig. 1). However, a complex reaction mixture was obtained in both cases, with no observation of the desired molecule. Therefore, an alternative reaction pathway was designed starting from fluorene and allyl bromide (Fig. 2). Fluorene was alkylated at the 9-positions using allylbromide/KOH/KI in DMSO to yield 9,9-diallylfluorene (**1**) in excellent yield (90%). Subsequent cleavage and oxidation of the double bonds, using ruthenium trichloride/sodium periodate in acetonitrile: H₂O (5:1) afforded fluorene 9,9-diacetaldehyde (**2**) (yield = 54%), which was isolated as a complex polymer and not its free-aldehyde. Therefore, no structural characterization was carried out. The di-aldehyde was oxidized by Jones reagent to the corresponding dicarboxylic acid (**3**) in moderate yield (35%). Finally, a steglich esterification² was carried out to afford the desired di-ester (**4**) in good yield (62%).

EXPERIMENTAL

All reagents and solvents were purchased from Sigma-Aldrich®, Alfa-Aesar® and Fisher Scientific and used without

further purification. Column chromatography was performed on silica-gel 60, 0.035-0.070 mm (220-440 mesh). Thin-layer chromatography (TLC) was performed on TLC plates = silica-gel HLF, W/organic binder, W/UV254, 5 × 20 cm, 250 μ (UNIPLATE, ANALTECH), method of visualization = UV lamp (254 nm). ¹H NMR was performed using Varian 400 MHz. ¹³C NMR using Varian 100 MHz mass spectrometry using electrospray (ESI) in positive ionization mode. FTIR using solid-state, Perkin-Elmer spectrum one, golden gate ATR accessory. HPLC using Gilson, 321 pump, UV/VIS-155 and refractive index detector IOTA, column EC 250/4.6 Nucleodur 100-5 normal phase column, length = 250 mm, particle size = 5 μm, internal diameter = 4.6 mm. Solvents used = hexane mixture of isomers (chromasolv for HPLC), DCM (Fisher HPLC grade) and ethyl acetate ((Fisher HPLC grade). Microscope was used for melting point determination, Leica DM2500M POM, with Mettler-Toledo FP90 Central Processor and Mettler-Toledo FP82HT Hot Stage. Calibrated with Mettler-Toledo calibration substances, benzophenone (47.6 + or -0.2 °C) and benzoic acid (122.1 + or -0.2 °C). Melting points of products were conducted at 1 °C/min.

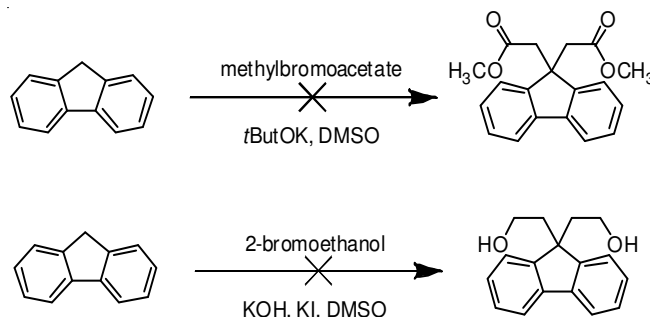


Fig. 1. Initial unsuccessful synthetic route to dimethyl fluorene-9,9-diacetate

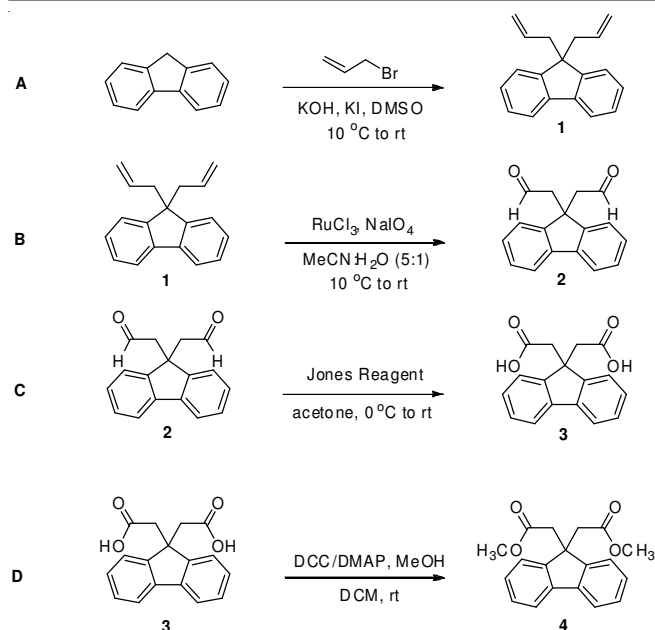


Fig. 2. Synthetic scheme for the 4-step synthesis of dimethyl fluorene-9,9-diacetate

9,9-Diallylfluorene (1): A 250 mL three-necked round-bottomed flask equipped was charged with fluorene (10 g, 60.2 mmol) and DMSO (50 mL) to form a partial solution/suspension. Under a constant atmosphere of nitrogen pulverized potassium hydroxide (20.20 g, 361 mmol) was added and most of the fluorene became dissolved and the reaction mixture became a deep orange-brown colour. After 5 min stirring KI (1.00 g, 6.02 mmol) was added and the resulting mixture was cooled from 20 to 10 °C with the aid of an ice/water bath. When the temperature stabilized allyl bromide (18.20 g, 150 mmol) was slowly added, over a period of 15 min, maintaining the temperature below 20 °C. After the addition the deep orange-brown colour became a light yellow-brown colour and the reaction mixture was stirred for an additional 20 min at 10 °C. After removing the ice/water bath within 15 min the temperature increased to 20 °C and the reaction mixture turned a lime-green colour. The reaction mixture was stirred for a further 95 min and the colour changed to a cloudy light yellow-brown. After TLC analysis confirmed the reaction to be complete, the reaction mixture was added, in one portion, to an ice/water mixture (50 g ice and 100 mL water). The product was extracted into heptane (400 mL) and the aqueous layer washed with additional heptane (2 × 100 mL) and the combined organic extracts washed with brine (2 × 400 mL), water (1 × 400 mL), dried (MgSO₄), filtered and concentrated using a rotary evaporator (55 °C, 75 mmHg) to yield a yellow-brownish crude viscous oil. The crude product was purified by flash column chromatography using 100 % petroleum ether 40/60 to yield a colourless oil (13.3 g, 90 %).

$R_f = 0.35$ (100 % hexane). b.p. = 108-112 °C @ 4 mmHg. ¹H NMR (CDCl₃) ppm, δ : 2.60 (4H, d, $J = 6.8$ Hz), 4.72 (2H, dd, $J = 1.2$ Hz, 10 Hz), 4.82 (2H, d, $J = 16.8$ Hz), 5.20-5.30 (2H, m). ¹³C NMR (CDCl₃) ppm, δ : 43.5, 54.1, 117.5, 119.7, 123.6, 126.9, 127.1, 133.7, 140.7, 149.3. FTIR (cm⁻¹): 3070, 3014, 2978, 2909, 1909, 1834, 1718, 1639, 1477, 1448, 1414, 1318, 1297, 1220, 1155, 1109, 1032, 993, 912, 733. HPLC,

sample dissolved in hexane; t_R (9:1 hexane:dichloromethane) = 5.73 min, 99 %, (7:3 hexane:dichloromethane) = 99.7 %, (1:1 hexane:dichloromethane) = 99.9 %, (8:2 hexane:ethyl acetate) = 100 %.

Fluorene 9,9-diacetaldehyde (2): A 500 mL one-necked flask was charged with 9,9-diallylfluorene (1) (6.00 g, 24.4 mmol), RuCl₃·2H₂O (0.42 g, 1.73 mmol), acetonitrile (200 mL) and water (40 mL). The apparatus was kept under an atmosphere of nitrogen during the course of the reaction. The resulting red-brown solution was cooled with the aid of an ice-water bath to 10 °C and sodium periodate (20.90 g, 97.7 mmol) was added in small portions, over a period of 15 min, using a spatula. The ice/water bath was removed and the reaction mixture was stirred at room temperature for a further 90 min, in which a green precipitate formed. After TLC analysis confirmed the reaction to be complete, 130 mL of saturated sodium thiosulphate solution (30 g of sodium thiosulphate to 150 mL of water) was added in one portion to the reaction flask. A total of 450 mL water was utilized and the organics extracted into 200 mL of EtOAc. The purple aqueous layer was washed with further EtOAc (2 × 100 mL) and the combined organic extracts washed with brine (2 × 200 mL), dried (MgSO₄), filtered and concentrated using a rotary evaporator (55 °C, 75 mmHg). The crude product was dried under high vacuum (4 mmHg) and desiccator to yield a light-yellowish foam-like powder. The crude product was purified by gradient elution flash column chromatography using 100 % dichloromethane to 1:1 (dichloromethane:acetone) to afford a white foam-like solid (3.30 g, 54 %).

$R_f = 0.25$ (3:1, dichloromethane:acetone), m.p. = 149-154 °C.

Fluorene-9,9-diacetic acid (3): A 500 mL three-necked round-bottomed flask was charged with fluorene 9,9-diacetaldehyde (2) (7.5 g, 30 mmol) and acetone (100 mL). The reaction mixture was cooled to 0 °C and when the temperature stabilized Jones reagent (100 mL) was slowly added maintaining the temperature below 10 °C (0.5 h). The reaction was stirred at room temperature for 24 h under a nitrogen atmosphere. After TLC analysis confirmed the reaction to be complete, propan-2-ol (50 mL) was added dropwise and after the addition the volatiles were removed using a rotary evaporator. Water (300 mL) was added and the product was extracted using diethyl ether (350 mL). The ether layer was washed again with water (1 × 300 mL) and base extraction (2 × 100 mL) using an aqueous saturated sodium bicarbonate solution (50 g NaHCO₃ in 200 mL water) and as a result an aqueous sodium di-carboxylate salt is formed. The aqueous layer was acidified with concentrated hydrochloric acid until pH 1 (litmus paper) and the product extracted into diethyl ether (2 × 200 mL) and washed with water (3 × 300 mL). The ethereal extracts were dried (MgSO₄), filtered and concentrated using a rotary evaporator (55 °C, 75 mmHg) to yield a viscous glassy type solid. The crude product was purified by gravity column chromatography using 3:1 (dichloromethane:acetone) to yield a sticky light-yellow amorphous solid (3.00 g, 35 %).

$R_f = 0.21$ (3:1, dichloromethane:acetone). m.p. = 149-154 °C. ¹H NMR (CDCl₃) ppm, δ : 3.14 (4H, s), 7.34-7.42 (4H, m), 7.64 (2H, d, $J = 7.6$ Hz), 7.74 (2H, d, $J = 7.6$ Hz). ¹H NMR [(CD₃)₂SO] ppm, δ : 2.97 (4H, s), 7.26-7.32 (4H, m),

7.58 (2H, d, $J = 7.2$ Hz), 7.78 (2H, d, $J = 7.2$ Hz), 11.85 (2H, br, -COOH). ^{13}C NMR [$(\text{CD}_3)_2\text{SO}$] ppm, δ : 42.2, 49.8, 120.2, 120.5, 124, 124.3, 127.4, 127.6, 127.7, 128, 140.2, 149.7, 172. FTIR (cm^{-1}): 3014 (very br.), 1714, 1665, 1477, 1447, 1412, 1332, 1289, 1264, 1236, 1213, 1190, 1164, 1099, 1016, 985, 931, 877, 760, 734, 620. ES-MS, 305 ($M + \text{Na}$ 23).

Dimethyl fluorene-9,9-diacetate (4): A one-necked 250 mL round bottomed flask was charged with fluorene 9,9-diacetic acid (**3**) (5.00 g, 17.7 mmol), 4-(dimethylamino)pyridine (8.65 g, 70.9 mmol), dichloromethane (120 mL) and methanol (5.67 g, 177 mmol). The reaction mixture was stirred at room temperature for 5 min and *N,N'*-dicyclohexylcarbodiimide (14.60 g, 70.9 mmol) added using a spatula. The reaction mixture was stirred at room temperature, under a nitrogen atmosphere, for 24 h. After TLC analysis confirmed the reaction to be complete, the one-necked flask was stoppered and placed in the freezer for 0.5 h. The dicyclohexylurea was filtered and the dichloromethane solution was washed with 1N hydrochloric acid (100 mL) and dichloromethane (100 mL). The organic layer was washed with water (2×200 mL), aided with brine (2×200 mL), dried (MgSO_4), filtered and concentrated using a rotary evaporator (55°C , 75 mmHg). When only 50 mL remained in the flask 10 g of silica gel was added and the crude product adsorbed on silica. The crude product was purified by gravity column chromatography using 10 % ethylacetate/hexane to yield a white powder (2.80 g, 62 %).

$R_f = 0.15$ (10 % ethylacetate/hexane). m.p. = $87.0\text{--}91.5^\circ\text{C}$. ^1H NMR (CDCl_3) ppm, δ : 3.07 (4H, s), 3.51 (6H, s), 7.27-7.39 (4H, m), 7.53 (2H, d, $J = 7.6$ Hz), 7.72 (2H, d, $J = 7.6$ Hz). ^{13}C NMR (CDCl_3) ppm, δ : 41.3, 49.5, 51.3, 120.1, 123.7, 127.4, 127.9, 139.9, 148.7, 171.4. FTIR (cm^{-1}): 3459, 3061, 2954, 2855,

1927, 1736, 1698, 1477, 1441, 1404, 1380, 1365, 1295, 1261, 1197, 1178, 1160, 1150, 1137, 1039, 1030, 995, 892, 810, 767, 735, 702. ES-MS, 333 ($M + \text{Na}$ 23). HPLC; sample dissolved in hexane (9:1 hexane:ethylacetate) = > 99 %.

RESULTS AND DISCUSSION

Dimethyl fluorene-9,9-diacetate is synthesized successfully in four-steps from fluorene, which is commercially available and low cost. The final material has been fully characterized by ^1H NMR, ^{13}C NMR, FTIR, ES-MS and purity determined to be greater than 99 % by HPLC analysis. Due to the importance of the aromatic fluorene core in organic semiconductor applications, it is believed that this material would be very useful and important to the organic chemistry and applied chemistry research fields.

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