**Synthesis of Alkylated Aminofluorenes by Palladium-Catalyzed Substitution at
Halofluorenes**

Ginagunta Saroja, Zhang Pingzhu, Nikolaus P. Ernsting, Jürgen Liebscher*

*Department of Chemistry, Humboldt-University, Brook Taylor-Str. 2,
12489 Berlin, Germany*

liebscher@chemie.hu-berlin.de

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General Experimental: Chemicals including 2-nitrofluorene, 2-bromofluorene **5d**, 2,7-dinitrofluorene and 2-formylfluorene were purchased. 2-Iodo-7-nitro-9*H*-fluorene **5a**,¹ and 2,7-dibromofluorene **5e**² were prepared according to the literature. 2-Cyanofluorene and 2-amino-7-nitrofluorene are known but more efficient preparations were developed (see supporting information). TLC analysis was performed on silica gel 60F₂₅₄ plates and visualized with UV illumination and charring with phosphomolybdic acid in EtOH (5%, v/v) or 0.3% ninhydrine in EtOH. Column chromatography was conducted with silica gel 60 (400-639 mesh). Melting points were determined on a hot-stage apparatus and are reported uncorrected. ¹H NMR and ¹³C NMR spectra were recorded at 300 and 75.5 MHz, respectively in CDCl₃ with TMS as internal standard. Mass spectra were measured at 70 eV.

9H-Fluorene-2-carbonitrile: To the solution of 9*H*-fluorene-2-carbaldehyde (3 g, 0.015 mol) in N-methylpyrrolidone (23 mL), H₂NOH · HCl (1.25 g, 0.018 mol) was added. After heating to 115 °C for 5-6 h, the reaction mixture was poured into cold water. The light brownish precipitate formed was collected by filtration; it was subjected to recrystallisation from ethanol, water mixture to yield 2.7 g (94% yield). mp 87 °C, ¹H NMR (300 MHz, CDCl₃): δ 7.82 (s, 1H, CH), 7.79 (s, 1H, CH), 7.66-7.63 (dm, 1H, CH), 7.59-7.56 (dm, 1H, CH), 7.42-7.38 (m, 2H, CH), 3.91 (s, 2H, CH₂). ¹³C NMR (300 MHz, CDCl₃): δ 146.2, 143.8, 139.8, 131.1, 128.6, 127.2, 125.3, 120.9, 120.4, 119.6, 109.6, 36.7. Anal calc for C₁₄H₉N: C, 87.93; H, 4.74; N, 7.32. Found: C, 87.14; H, 5.02; N, 7.51.

¹ Marhevko, V. C.; Ebner, N. A.; Sehorn, R. D; Hanna, P. E. *J. Med. Chem.* **1985**, 28, 18.

² Kelley, Charles J.; Ghiorghis, Alem; Kauffman, Joel M. *J.Chem.Res.(Miniprint)* **1997**, 12, 2701.

2,7-Dinitro-9H-fluorene (1): Fuming HNO₃ (90 mL) was slowly added to mixture of 2-nitrofluorene (9 g, 0.043 mol) and acetic acid (90 mL) under vigorous stirring and careful cooling with an ice bath. After stirring for 5 h at room temperature, the yellow product

separated. It was filtered off,, washed with water and dried to yield crude **1** (6.93 g, 62% yield). mp 295-298 °C, Anal calc for C₁₃H₈N₂O₂: C, 60.93; H, 3.31; N, 10.94. Found: C, 61.29; H, 3.28; N, 10.68.

2-Bromo-7-nitro-9H-fluorene (5b): To a stirred solution of 2-nitrofluorene (8 g, 0.038 mol) in dry CH₂Cl₂ (40 mL) was added Br₂ (0.076 mol). The HBr, which soon evolved from solution was guided through a trap to a scrubbing solution of NaOH. The mixture was stirred for 5-6 h. A yellow precipitate appeared, which was filtered off, washed with 5% NaHSO₃ and water and dried with MgSO₄. The crude yellowish product was purified from recrystallisation from a mixture of DMF and water to yield light yellow material **5b** (7.7 g, 70% yield). M. p. 235-237 °C, ¹H NMR (300 MHz, DMF-*d*6): δ 8.50 (s, 1H), 8.33 (dd, 1H), 8.22 (d, 1H), 8.09 (dd, 1H), 7.94 (s, 1H), 7.69 (dd, 1H), 4.18 (s, 2H). Anal Calcd for C₁₃H₈BrNO₂: C, 53.82; H, 2.78; N, 4.83. Found: C, 53.72; H, 2.83; N, 4.90..

7-Bromo-9H-fluorene-2-carbonitrile (5c): To a stirred solution of 9H-fluorene-2-carbonitrile (500 mg, 2.6 mmol) in dry CH₂Cl₂ (6 mL) was added Br₂ (10.5 mmol). The HBr evolved from solution was guided through a trap to a scrubbing solution of NaOH. The mixture was stirring for 5-6 h. The yellow precipitate was filtered off, washed with 5% NaHSO₃ and water and was dried. The crude yellowish solid was purified by recrystallisation from DMF/water mixture to yield yellow product **5c** (380 mg, 70% yield). M.p. 172°C Anal calc for C₁₄H₈BrN: C, 62.25; H, 2.99; N, 5.19. Found: C, 62.31; H, 3.12; N, 5.38. ¹H (300MHz CDCl₃): δ 3.90 (s, 2H, CH₂), 7.79 (d, *J* = 7.5 Hz, 2H, CH), 7.54 (dd, *J* = 8.3 Hz, 1H, CH), 7.65 (d, *J* = 8.3 Hz, 2H, CH), 7.7 (s, 1H, CH). ¹³C NMR (300MHz CDCl₃): δ 36.55 (CH₂), 110.11 (C), 119.41 (C), 120.44 (CH), 122.13 (CH), 122.63 (C), 128.55 (CH), 130.53 (CH), 131.33 (CH), 138.81 (C), 143.20 (C), 145.08 (C), 145.70 (C). Anal. Calcd for C₁₄H₈BrN: C, 62.25; H, 2.99; N, 5.19. Found: C, 62.31; H, 3.12; N, 5.38.

9,9-Dialkyl-9H-fluorenes 7, General Procedure: A mixture of the fluorene **5** (1 mmol), alkyl halide (2.5 mmol, MeI or EtI or PrBr), KI (0.12 mmol) and DMSO 82.2 mL) was stirred at room temperature under argon and powdered KOH or t-BuOK (4.5 mmol) was slowly

added. The color of the mixture turned from orange-red to dark green or purple. After stirring for 3-5 h, the reaction mixture was poured into water (150 mL). The product was filtered off and dried.

2-Iodo-7-nitro-9,9-dipropyl-9H-fluorene (7a): Yield 96%, dark yellow powder, mp 105-110°C ¹H (300MHz CDCl₃): δ 0.68 (m, 10H, CH₂, CH₃), 1.99 (m, 4H, CH₂), 7.52 (d, *J* = 7.9 Hz, 1H, CH), 7.75 (t, *J* = 8.7 Hz, 3H, CH), 8.20 (d, *J* = 1.9 Hz, 1H, CH), 8.25 (dd, *J* = 8.7 Hz, 1H, CH). ¹³C NMR (300MHz CDCl₃): δ 14.2 (CH₃), 17.1 (CH₂), 42.2 (CH₂), 56.1 (C), 95.5 (C), 118.3 (CH), 120.0 (CH), 122.7 (CH), 123.4 (CH), 132.5 (CH), 136.6 (CH), 146.5 (C), 147.5 (C), 151.4 (C), 154.4 (C). Anal. calc for C₁₉H₂₀INO₂: C, 54.17; H, 4.79; I, 30.12; N, 3.32; O, 7.60. Found: C, 54.33; H, 4.19; N, 3.55.

2-Bromo-7-nitro-9,9-dipropyl-9H-fluorene (7b): yield 79% (using Pr-Br), light brown solid, mp 109 -115°C, ¹H (300MHz CDCl₃): δ 0.61 (m, 10H, CH₂, CH₃), 1.92 (m, 4H, CH₂), 7.46 (m, 2H, CH), 7.57 (d, *J* = 7.5 Hz, 1H, CH), 7.69 (d, *J* = 8.3 Hz, 1H, CH), 8.12 (d, *J* = 1.9 Hz, 1H, CH), 8.18 (dd, *J* = 8.3 Hz, 1H, CH). ¹³C NMR (300MHz CDCl₃): δ 14.2 (CH₃), 17.1 (CH₂), 42.2 (CH₂), 56.1 (C), 118.3 (CH), 119.9 (CH), 122.4 (CH), 123.4 (CH), 123.69 (C), 126.6 (CH), 130.7 (CH), 137.7 (C), 146.4 (C), 147.4 (C), 151.6 (C), 154.4 (C). Anal. Calcd for C₁₉H₂₀BrNO₂: C, 60.97; H, 5.39; Br, 21.35; N, 3.74; O, 8.55. Found: C, 60.87; H, 5.50; Br, 20.47; N, 3.89.

2-Bromo-9,9-dimethyl-7-nitro-9H-fluorene (7c): Yield 91%, yellowish solid, mp 225-242°C; ¹H (300MHz CDCl₃): δ 1.53 (s, 6H, CH₃), 7.54 (dd, *J* = 8.3 Hz, 1H, CH), 7.63 (d, *J* = 1.5 Hz, 1H, CH), 7.66 (d, *J* = 8.3 Hz, 1H, CH), 7.79 (dd, *J* = 8.3 Hz, 1H, CH), 8.26 (m, 2H, CH); ¹³C NMR (300MHz, CDCl₃): δ 26.6 (CH₃), 47.6 (C), 118.4 (CH), 120.3 (CH), 122.8 (CH), 123.5 (CH), 126.6 (CH), 130.9 (CH), 135.8 (C), 144.6 (C), 147.4 (C), 154.2 (C), 156.9 (C). Anal. Calcd for C₁₅H₁₂BrNO₂: C, 56.62; H, 3.80; Br, 25.11; N, 4.40; O, 10.06. Found: C, 56.62; H, 3.87; N, 4.48.

2-Bromo-7-cyano-9,9-dimethyl-9H-fluorene (7d): Yield : 78%, colorless crystals, mp 180-190°C; ¹H (300MHz CDCl₃): δ 1.49 (s, 6H, CH₃), 7.52 (d, *J* = 8.3 Hz, 1H, CH), 7.62 (d, 2H, *J* = 8.3 Hz, 2H, CH), 7.67 (d, *J* = 8.3 Hz, 2H, CH), 7.75 (d, *J* = 7.9 Hz, 1H, CH); ¹³C NMR

(300MHz CDCl₃): δ 26.7 (CH₃), 47.4 (C), 110.6 (C), 119.5 (C), 120.6 (CH), 122.4 (CH), 123.2 (C), 126.5 (CH), 130.7 (C), 131.6 (CH), 136.2 (C), 142.7 (C), 153.7 (C), 156.1 (C); Anal. Calcd for C₁₆H₁₂BrN: C, 64.45; H, 4.06; Br, 26.80; N, 4.70. Found: C, 64.24; H, 4.31; N, 4.80.

2-Bromo-9,9-diethyl-9H-fluorene (7e): Yield: 86%, orange solid, mp 40-42°C; ¹H (300MHz CDCl₃): δ 0.31 (t, J = 7.5 Hz, 6H, CH₃), 2.00 (q, J = 7.5Hz, 4H, CH₂), 7.31 (m, 3H, CH), 7.45 (dd, J = 6.4 Hz, 2H, CH), 7.56 (dd, J = 6.4 Hz, 1H, CH), 7.66 (m, J = 3.4 Hz, 1H, CH); ¹³C NMR (300MHz CDCl₃): δ 8.4 (CH₃), 32.7 (CH₂), 56.0 (C), 119.7 (CH), 121.0 (CH), 122.9 (CH), 126.2 (CH), 127.0 (CH), 127.5 (CH), 129.9 (CH), 140.4 (C), 140.5 (C), 149.4 (C), 152.1 (C); Anal. Calcd for C₁₇H₁₇Br: C, 67.78; H, 5.69; Br, 26.53. Found: C, 67.02; H, 5.87.

2,7-Dibromo-9,9-diethyl-9H-fluorene (7f): Yield 97%, colorless crystals 164-170°C; ¹H (300MHz CDCl₃): δ 1.44 (s, 6H, CH₃), 7.44 (dd, J = 8.3 Hz, 2H, CH), 7.53 (d, J = 8.7 Hz, 4H, CH); ¹³C NMR (300MHz CDCl₃): δ 26.8 (CH₃), 47.3 (C), 121.4 (CH), 126.2 (CH), 130.3 (CH), 137.1 (C), 155.2 (C); Anal. Calcd for C₁₅H₁₂Br₂: C, 51.17; H, 3.44; Br, 45.39. Found: C, 50.94; H, 3.70.