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Palladium-catalysed amination of bromofluorans and an investigation of their thermochromic behaviour

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ABSTRACT

The palladium-catalysed amination of readily accessible bromofluorans and bromobenzo[*a*]fluorans has been accomplished with a series of anilines and morpholine. The resulting aminofluorans generated intense black shades upon formulation in methyl stearate containing bisphenol A. The route provides an alternative approach to various amino substituted fluorans without the need of a series of individual diphenylamine intermediates.

1. Introduction

Interest in functional dye systems continues at a pace as a consequence of technological developments and more widespread applications [1–3] particularly in the areas of sensors and probes for a variety of organic and inorganic analytes [4] and dyes for solar cell applications [5]. The (thio)xanthene unit [6] forms the core of many functional dyes including rhodamines [7], rosamines [8], thiofluoresceins [9] and fluorans [10].

Transition metal-catalysed arylation [11] and amination reactions [12] have been widely employed in organic syntheses to facilitate efficient transformations that would otherwise necessitate many sequential steps. However, such transition metal-catalysed techniques have only very recently been applied to the preparation of functional dye systems such as rhodols and rosamines. In the former, a methoxymethyl (MOM) protected fluorescein monotriflate was successfully aminated at the 3′-position with a variety of amines under $Pd(OAc)_2$–BINAP catalysis (Scheme 1) [13] and in the latter an aryl moiety was introduced into the 9-position of a xanthene unit through $PdCl_2(PPh_3)_2$-mediated coupling of a triarylboroxin to a 9-trifloxyxanthene (Scheme 2) [14]. We now describe our preliminary results on the application of the Pd-catalysed amination reaction for the direct amination of bromo-substituted fluorans and benzo[*a*]fluorans.

2. Experimental

2.1. Equipment

Unless otherwise stated, reagents were used as supplied. 2′-Bromo-6′-di(*n*-butylamino)-3′-methylfluoran (Vermillion DCF) was obtained from Sun Chemical (France) Ltd. NMR spectra were recorded on a Bruker Avance 400 MHz instrument (^{1}H NMR 400 MHz, ^{13}C NMR 100 MHz) for sample solutions in $CDCl_3$ with tetramethylsilane as an internal reference unless indicated otherwise. All compounds were homogeneous by TLC, Merck TLC aluminium sheets either silica gel 60 F_{254} (cat. No 105554) or neutral aluminium oxide 60 F_{254} (cat. No 105550), using a range of eluent systems of differing polarity. Flash column chromatography was performed on chromatography silica gel (Fluorochem, 35–70 μm particle size distribution). All percentage yields are unoptimised. Reflectance spectra of the new thermochromic compounds in methyl stearate containing bisphenol A [ratio of fluoran:bisphenol A:methyl stearate = 5:1:15] as a thin film sandwiched between two glass microscope slides were recorded using a Datacolor Spectraflash 500 (Xe flash simulating natural daylight, diffuse illumination, collected at 8° to normal), with

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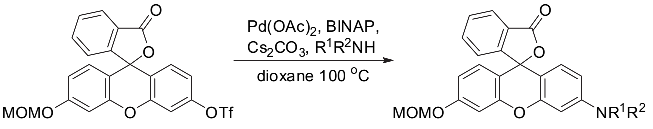


Scheme 1. Pd-Catalysed amination of a protected fluorescein.

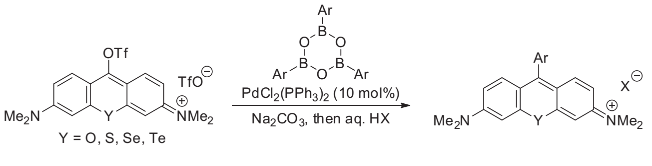
specular excluded, UV 100%, small aperture setting, four flashes and a single measurement. FTIR spectra were recorded using a Perkin Elmer Spectrum One spectrophotometer equipped with a diamond probe ATR attachment (neat sample). Mass spectra were recorded at the National EPSRC Mass Spectrometry Service Centre, Swansea.

2.2. Synthesis of 9′-diethylamino-3′-bromobenzo[a]fluoran **2**

2′-[4-(Diethylamino)-2-hydroxybenzoyl]benzoic acid **1** (5 g; 16 mmol) and 6-bromo-2-naphthol (3.57 g; 16 mmol) were heated at 120–125 °C in sulphuric acid (85%, 25 g) for 4 h. The reaction mixture was poured into ice water (75 mL) and a green/purple solid was precipitated by adding NaOH (2 M, aq, ~15 mL). The precipitate was collected by vacuum filtration and washed with water (3 × 50 mL). The precipitate was suspended in a mixture of water (25 mL), sodium hydroxide (1.25 g; 52 mmol) and toluene (75 mL) and heated under reflux for 0.5 h. The toluene layer was separated, washed with sodium hydroxide solution (3.5%, aq, 2 × 25 mL) and water (2 × 25 mL), and reduced in volume to ~25 mL. The precipitate formed on cooling was collected by vacuum filtration and washed with a small amount of cold toluene (10 mL) to afford the product as pale pink microcrystals in 27% yield, m.p. 227–230 °C, $\nu_{\max}$ (cm^{-1}) 1754.7, 1351.7, 1198.2, 665.3, δ_{H} 1.05 (6H, t, J = 7.2, $(\mathrm{C\underline{H}_3CH_2})_2\mathrm{N}$), 3.33 (4H, q, J = 7.2, $(\mathrm{CH_3C\underline{H}_2})_2\mathrm{N}$), 6.36 (1H, dd, J = 8.8 and 2.4, 10′-H), 6.43 (1H, d, J = 2.7, 8′-H), 6.50 (1H, d, J = 8.8, 11′-H), 6.92 (1H, dd, J = 8.8 and 2.4, 6′-H), 7.09 (1H, d, J = 7.2, 7-H), 7.21 (1H, dd, J = 8.8 and 2.4, 2′-H), 7.45 (1H, d, J = 8.8, 1′-H), 7.58 (2H, m, 5-H and 6-H), 7.79 (1H, d, J = 8.8, 5′-H), 7.92 (1H, d, J = 2.4, 4′-H), 8.12 (1H, d, J = 7.2, 4-H), δ_{C} 12.50, 44.46, 84.22, 96.90, 105.86, 109.00, 109.05, 117.95, 119.64, 123.50, 125.25, 125.46, 136.90, 128.21, 129.45, 130.13, 130.31, 131.03, 131.48, 132.47, 135.27, 149.11, 150.65, 151.35, 155.27, 170.01, found $[\mathrm{M}+\mathrm{H}]^+$ = 500.0850 $\mathrm{C_{28}H_{22}BrNO_3}$ requires $[\mathrm{M}+\mathrm{H}]^+$ = 500.0856.

2.3. Synthesis of 2′-bromo-6′-diethylaminofluoran **4**

4-Bromoanisole (2.99 g; 16 mmol) was added to a solution of 2′-[4-(diethylamino)-2-hydroxybenzoyl]benzoic acid **1** (5 g; 16 mmol) in sulphuric acid (98%, 40 g) and the mixture was stirred at 10–20 °C for 5 h. The reaction mixture was then poured into ice water (150 mL) and a purple solid was precipitated by adding NaOH (10%, aq, 20 mL). The precipitate was collected by vacuum filtration and washed with water (3 × 25 mL). The solid was suspended in sodium hydroxide (10%, aq, 30 mL) and toluene (60 mL), and heated under reflux for 2 h, and then allowed to cool. The toluene layer was then separated, washed with sodium hydroxide (3.5%, aq, 2 × 25 mL) and water (2 × 25 mL), and evaporated to ~25 mL. The precipitate formed on cooling was then collected by vacuum filtration and washed with a small amount of cold toluene (10 mL) to afford the title compound as pale pink crystals in 70% yield, m.p. 173–175 °C, $\nu_{\max}$ (cm^{-1}) 1749.4, 1348.9, 1194.5, 664.8, δ_{H} 1.17 (6H, t, J = 7.2, $(\mathrm{C\underline{H}_3CH_2})_2\mathrm{N}$), 3.36 (4H, q, J = 7.2, $(\mathrm{CH_3C\underline{H}_2})_2\mathrm{N}$), 6.36 (1H, dd, J = 8.8 and 2.5, 7′-H), 6.44 (1H, d, J = 2.5, 5′-H), 6.55 (1H, d, J = 8.8, 8′-H), 6.86 (1H, d, J = 2.4, 1′-H), 7.27 (2H, m, 4′-H and 7-H), 7.45 (1H, dd, J = 8.8 and 2.4, 3′-H), 7.66 (2H, m, 5-H and 6-H), 8.04 (1H, d, J = 7.2, 4-H), found $[\mathrm{M}+\mathrm{H}]^+$ = 450.0701 $\mathrm{C_{24}H_{20}BrNO_3}$ requires $[\mathrm{M}+\mathrm{H}]^+$ = 450.0705.



Scheme 2. Pd-Catalysed arylation of 9-trifloxyxanthenes.

2.4. 9′-Diethylaminobenzo[a]fluoran **3**

2′-[(4-Diethylamino)-2-hydroxybenzoyl]benzoic acid **1** (1 g; 3.2 mmol) and 2-naphthol (0.42 g; 2.9 mmol) were added portionwise to methanesulfonic acid (98%, 6 mL), ensuring the temperature did not exceed 25 °C. The reaction mixture was then stirred at 20–25 °C for 24 h, with monitoring by TLC (silica/70% ethyl acetate in hexane). The reaction mixture was poured into ice water (20 mL) and neutralised. The precipitate was collected by vacuum filtration and washed with water (3 × 25 mL). The solid intermediate was then added to sodium hydroxide (1%, aq, 5 mL) and heated to 75–80 °C for 4 h. Vacuum filtration of the solution afforded pink crystals, which were washed with hexane containing a little diethyl ether to afford the title compound as off-white microcrystals in 67% yield, m.p. 218–220 °C (Lit. m.p. 215–217 °C [15]), $\nu_{\max}$ (cm^{-1}) 1754.3, 1352.8, 1197.1, δ_{H} 1.16 (6H, t, J = 7.2, $(\mathrm{C\underline{H}_3CH_2})_2\mathrm{N}$), 3.34 (4H, q, J = 7.2, $(\mathrm{CH_3C\underline{H}_2})_2\mathrm{N}$), 6.49 (1H, dd, J = 8.8 and 2.4, 10′-H), 6.59 (2H, m, 8′-H and 11′-H), 7.00 (1H, d, J = 8.8, 1′-H), 7.21 (2H, dd, J = 8.8 and 2.4, 2′-H and 3′-H), 7.43 (1H, d, J = 7.6, 6′-H), 7.61 (2H, d, J = 7.6, 5′-H and 7-H), 7.78 (2H, m, 5-H and 6-H), 8.04 (1H, dd, J = 8.8 and 2.4, 4′-H), 8.22 (1H, d, J = 7.6, 4-H).

2.5. 3′-Diethylaminofluoran **5**

2′-[4-(Diethylamino)-2-hydroxybenzoyl]benzoic acid **1** (5 g; 16 mmol) was added to sulphuric acid (98%, 40 g) at room temperature and dissolved. Phenol (1.49 g; 16 mmol) was then added to the foregoing cooled solution and the mixture was stirred at 10–20 °C for 5 h. The reaction mixture was then poured into ice water (150 mL) and a purple solid was precipitated by adding NaOH (10%, aq). This was collected by vacuum filtration and washed with water. The precipitate was then suspended in sodium hydroxide (10%, aq, 30 mL) and toluene (60 mL), and was heated by reflux for 2 h. The cold toluene layer was then separated, washed with sodium hydroxide (3.5%, aq, 2 × 15 mL) and water (2 × 15 mL), and evaporated to ~25 mL. The precipitate formed on cooling was then collected by vacuum filtration and washed with a small amount of cold toluene (10 mL) to afford the title compound as pale pink crystals in 62% yield, m.p. 128–130 °C, $\nu_{\max}$ (cm^{-1}) 1748.0, 1351.2, 1196.5, δ_{H} 1.16 (6H, t, J = 7.2, $(\mathrm{C\underline{H}_3CH_2})_2\mathrm{N}$), 3.38 (4H, q, J = 7.2, $(\mathrm{CH_3C\underline{H}_2})_2\mathrm{N}$), 6.37 (1H, dd, J = 9.0 and 2.8, 7′-H), 6.41 (1H, d, J = 2.8, 5′-H), 6.75 (1H, d, J = 8.8, 8′-H), 6.96 (1H, d, J = 2.4, 1′-H), 7.20 (2H, m, 4′-H and 7-H), 7.51 (2H, dd, J = 9 and 2.4, 2′-H and 3′-H), 7.66 (2H, m, 5-H and 6-H), 8.04 (1H, d, J = 7.2, 4-H), found $[\mathrm{M}+\mathrm{H}]^+$ = 372.1590 $\mathrm{C_{24}H_{21}NO_3}$ requires $[\mathrm{M}+\mathrm{H}]^+$ = 372.1594.

2.6. General method for the Pd-catalysed amination of bromofluorans

Sodium *t*-butoxide (6 mmol), the bromofluoran (2 mmol), the appropriate amine (3 mmol), tri-(*t*-butyl)phosphonium tetrafluoroborate (4 mol%) and $\mathrm{Pd_2(dba)_3}$ (5 mol%) were placed in a 100 mL round bottomed flask under N$_2$. Anhydrous toluene (25 mL), previously bubbled N$_2$ for 15 min, was added via a transfer needle and the mixture was heated to 70 °C until TLC examination revealed that no further reaction had occurred. The reaction mixture was poured into cold, dilute HCl (0.01 M, aq, 200 mL) and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were washed with dilute NaOH (0.1 M, aq, 50 mL) and water (2 × 50 mL), dried over sodium sulphate and evaporated to afford the crude product which was purified by column chromatography (30% ethyl acetate in toluene) and recrystallisation (ethyl acetate in hexane). The following compounds were obtained by this protocol:

2.6.1. 3′-Anilino-9′-diethylaminobenzo[a]fluoran

7a from **2** and aniline after column chromatography and recrystallisation as pink microcrystals in 19% yield, m.p. 200–204 °C [16], ν_{max} (cm^{-1}) 3378.4, 1740.3, 1236.1, δ_H 1.15 (6H, t, $J = 7.2$, $(C\underline{H}_3CH_2)_2N$), 3.33 (4H, q, $J = 7.2$, $(CH_3C\underline{H}_2)_2N$), 5.90 (1H, s, NH), 6.35 (1H, dd, $J = 8.8$ and 2.4, 10′-H), 6.43 (1H, d, $J = 2.8$, 8′-H), 6.51 (1H, d, $J = 8.8$, 11′-H), 6.85 (1H, dd, $J = 8.8$ and 2.4, 2′-H), 6.92 (3H, m, Ar-H, 1′-H), 7.06 (4H, m, Ar-H, 7-H), 7.13 (1H, d, $J = 2.4$, 4′-H), 7.28 (1H, d, $J = 9.0$, 6′-H), 7.55 (2H, m, 5-H and 6-H), 7.65 (1H, d, $J = 9.0$, 5′-H), 8.11 (1H, m, 4-H), δ_C 12.52, 44.42, 84.82, 96.90, 106.05, 108.71, 108.75, 113.20, 118.11, 118.76, 120.34, 121.21, 123.56, 124.90, 125.13, 126.15, 126.95, 128.26, 129.29, 131.21, 132.51, 135.14, 138.11, 139.39, 142.58, 149.02, 149.60, 150.85, 155.65, 170.38, found $[M + H]^+ = 513.2169$ $C_{34}H_{28}N_2O_3$ requires $[M + H]^+ = 513.2178$.

2.6.2. 9′-Diethylamino-3′-(4-methoxyanilino)benzo[a]fluoran

7b from **2** and *p*-anisidine after column chromatography as pale pink microcrystals in 58% yield, m.p. 150–154 °C, ν_{max} (cm^{-1}) 3374.7, 1736.9, 1237.0, δ_H 1.15 (6H, t, $J = 7.2$, $(C\underline{H}_3CH_2)_2N$), 3.33 (4H, q, $J = 7.2$, $(CH_3C\underline{H}_2)_2N$), 3.84 (3H, s, OCH_3), 5.51 (1H, s, NH), 6.35 (1H, dd, $J = 8.8$ and 2.4, 10′-H), 6.43 (1H, d, $J = 2.8$, 8′-H), 6.51 (1H, d, $J = 8.8$, 11′-H), 6.75 (1H, dd, $J = 9.2$ and 2.4, 2′-H), 6.85 (2H, m, Ar-H), 6.92 (1H, d, $J = 9.2$, 1′-H), 7.05 (2H, m, Ar-H), 7.13 (1H, m, 7-H), 7.16 (1H, d, $J = 2.4$, 4′-H), 7.32 (1H, d, $J = 9.2$, 6′-H), 7.55 (2H, m, 5-H and 6-H), 7.65 (1H, d, $J = 9.2$, 5′-H), 8.11 (1H, m, 4-H), δ_C 12.52, 21.07, 44.42, 60.42, 84.82, 96.90, 106.06, 108.74, 113.22, 118.09, 118.72, 120.37, 121.24, 123.58, 124.87, 125.09, 126.18, 126.99, 128.23, 129.31, 131.19, 132.52, 135.16, 138.08, 139.41, 142.60, 148.99, 149.59, 150.90, 155.60, 170.35, found $[M + H]^+ = 543.2274$ $C_{35}H_{30}N_2O_4$ requires $[M + H]^+ = 543.2278$.

2.6.3. 9′-Diethylamino-3′-(4-trifluoromethylanilino)benzo[a]fluoran

7c from **2** and 4-trifluoromethylaniline after column chromatography as pale yellow microcrystals in 86% yield, m.p. 137–140 °C, ν_{max} (cm^{-1}) 3368.2, 1740.0, 1235.3, 1096.8, δ_H 1.16 (6H, t, $J = 7.2$, $(C\underline{H}_3CH_2)_2N$), 3.35 (4H, q, $J = 7.2$, $(CH_3C\underline{H}_2)_2N$), 5.95 (1H, s, NH), 6.38 (1H, dd, $J = 8.8$ and 2.4, 10′-H), 6.43 (1H, d, $J = 2.8$, 8′-H), 6.51 (1H, d, $J = 8.8$, 11′-H), 6.92 (1H, dd, $J = 8.8$ and 2.4, 2′-H), 7.02 (3H, m, Ar-H, 1′-H), 7.13 (1H, m, 7-H), 7.41 (1H, d, $J = 9.0$, 6′-H), 7.47 (3H, m, Ar-H, 4′-H), 7.58 (2H, m, 5-H and 6-H), 7.75 (1H, d, $J = 9.0$, 5′-H), 8.10 (1H, d, $J = 7.2$, 4-H), δ_C 12.51, 78.12, 44.44, 84.78, 96.90, 105.93, 108.86, 114.22, 115.55, 116.25, 119.00, 121.44, 121.80, 123.58, 124.99, 125.30, 125.92, 126.56, 126.93, 127.23, 128.23, 129.04, 129.36, 131.38, 132.25, 135.24, 137.41, 146.33, 149.08, 150.83, 155.51, 170.33, found $[M + H]^+ = 581.2030$ $C_{35}H_{27}N_2O_3F_3$ requires $[M + H]^+ = 581.2047$.

2.6.4. 9′-Diethylamino-3′-(4-ethoxycarbonylanilino)benzo[a]fluoran

7d from **2** and ethyl 4-aminobenzoate after column chromatography and recrystallisation as fawn microcrystals in 53% yield, m.p. 99–102 °C, ν_{max} (cm^{-1}) 3349.7, 1737.6, 1686.0, 1595.2, 1280.3, 1172.8, δ_H 1.15 (6H, t, $J = 7.2$, $(C\underline{H}_3CH_2)_2N$), 1.36 (3H, t, $J = 7.2$, $OCH_2C\underline{H}_3$), 3.34 (4H, q, $J = 7.2$, $(CH_3C\underline{H}_2)_2N$), 4.32 (2H, q, $J = 7.2$, $OC\underline{H}_2CH_3$), 6.37 (1H, dd, $J = 8.8$ and 2.4, 10′-H), 6.41 (1H, d, $J = 2.4$, 8′-H), 6.45 (1H, bs, NH), 6.52 (1H, d, $J = 8.8$, 11′-H), 6.95 (4H, m, Ar-H, 1′-H, 2′-H), 7.10 (1H, m, 7-H), 7.36 (1H, d, $J = 8.9$, 6′-H), 7.45 (1H, d, $J = 2.3$, 4′-H), 7.58 (2H, m, 5-H and 6-H), 7.69 (1H, d, $J = 8.9$, 6′-H), 7.85 (2H, m, Ar-H), 8.12 (1H, m, 4-H), δ_C 11.49, 13.40, 20.04, 27.93, 37.79, 43.28, 43.41, 59.24, 59.36, 83.27, 83.75, 95.88, 104.93, 107.88, 112.74, 113.74, 117.35, 117.86, 120.56, 122.76, 123.04, 123.80, 126.17, 127.21, 128.33, 130.46, 131.51, 134.22, 146.59, 148.02, 149.81, 154.51, 165.71, 169.29, 170.17, found $[M + H]^+ = 585.2384$ $C_{37}H_{32}N_2O_5$ requires $[M + H]^+ = 585.2389$.

2.6.5. 9′-Diethylamino-3′-morpholinobenzo[a]fluoran

7e from **2** and morpholine after column chromatography as pale beige microcrystals in 57% yield, m.p. 140–144 °C, ν_{max} (cm^{-1}) 1750.0, 1306.9, 1227.0, δ_H (DMSO-d_6) 1.16 (6H, t, $J = 7.2$, $(C\underline{H}_3CH_2)_2N$), 3.14 (4H, m, $-CH_2NCH_2-$), 3.34 (4H, q, $J = 7.2$, $(CH_3C\underline{H}_2)_2N$), 3.83 (4H, m, $-CH_2OCH_2-$), 6.36 (1H, dd, $J = 8.8$ and 2.4, 10′-H), 6.44 (1H, d, $J = 2.4$, 8′-H), 6.54 (1H, d, $J = 8.8$, 11′-H), 6.90 (1H, dd, $J = 8.8$ and 2.4, 2′-H), 6.99 (1H, d, $J = 8.8$, 1′-H), 7.06 (1H, d, $J = 2.4$, 4′-H), 7.10 (1H, m, 7-H), 7.36 (1H, d, $J = 9.0$, 6′-H), 7.57 (2H, m, 5-H and 6-H), 7.78 (1H, d, $J = 9.0$, 5′-H), 8.12 (1H, m, 4-H), δ_C (DMSO-d_6) 12.94, 21.88, 29.45, 44.85, 49.65, 67.23, 85.17, 94.13, 97.33, 106.49, 109.15, 112.04, 119.58, 124.01, 125.14, 125.70, 126.14, 127.47, 128.66, 129.61, 131.85, 132.85, 135.51, 138.29, 147.72, 149.42, 150.05, 151.35, 156.05, 170.72, found $[M + H]^+ = 507.2265$ $C_{32}H_{30}N_2O_4$ requires $[M + H]^+ = 507.2278$.

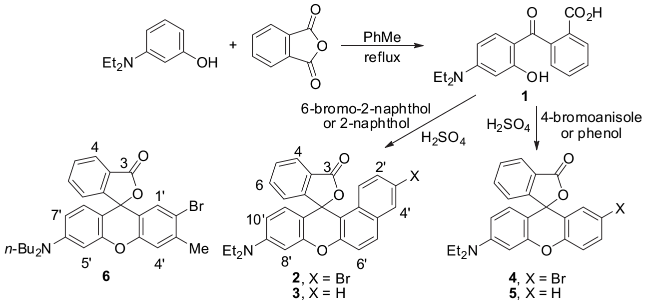
2.6.6. 6′-Di-n-butylamino-2′-(4-methoxyanilino)-3′-methylfluoran

7g from **6** and *p*-anisidine after column chromatography as very pale red–purple microcrystals in 68% yield, m.p. 142–145 °C, ν_{max} (cm^{-1}) 3394.1, 1746.8, 1240.4, δ_H 0.95 (6H, t, $J = 7.2$, $(C\underline{H}_3CH_2CH_2CH_2)_2N$), 1.33 (4H, sextet, $J = 7.2$, $(CH_3C\underline{H}_2CH_2CH_2)_2N$), 1.56 (4H, quintet, $J = 7.2$, $(CH_3CH_2C\underline{H}_2CH_2)_2N$), 2.40 (3H, s, CH_3), 3.26 (4H, t, $J = 7.6$, $(CH_3CH_2CH_2C\underline{H}_2)_2N$), 3.42 (1H, bs, NH), 3.74 (3H, s, OCH_3), 6.32 (1H, dd, $J = 8.8$ and 2.4, 7′-H), 6.38 (1H, d, $J = 2.4$, 5′-H), 6.52 (1H, d, $J = 8.8$, 8′-H), 6.65 (2H, m, Ar-H), 6.74 (2H, m, Ar-H), 6.88 (1H, s, 1′-H), 7.16 (1H, s, 4′-H), 7.18 (1H, dd, $J = 7.2$ and 1.2, 7-H), 7.65 (2H, m, 5-H and 6-H), 8.02 (1H, dd, $J = 7.2$ and 1.2, 4-H), δ_C 13.98, 20.28, 23.00, 29.26, 50.79, 55.72, 83.39, 97.51, 104.46, 108.57, 114.78, 116.42, 118.09, 118.86, 118.90, 124.00, 125.04, 126.99, 128.74, 129.72, 131.12, 134.98, 139.90, 140.47, 150.81, 152.57, 152.71, 152.78, 157.96, 169.44 found $[M + H]^+ = 563.2906$ $C_{36}H_{38}N_2O_4$ requires $[M + H]^+ = 563.2910$.

3. Discussion

In order to assess the versatility of the palladium-catalysed coupling reaction three bromo-substituted fluorans were examined as substrates, 3′-bromo-9′-diethylaminobenzo[*a*]fluoran **2**, 2′-bromo-6′-diethylaminofluoran **4** and a commercial sample of 2′-bromo-6′-di(*n*-butylamino)-3′-methylfluoran **6** [17]. Fluorans **2** and **4** were derived from the common ketoacid **1** which was readily available from the Friedel–Crafts reaction between 3-diethylaminophenol and phthalic anhydride in toluene [18]. Heating **1** with either 6-bromo-2-naphthol or 4-bromoanisole in 85% sulphuric acid gave, after basification and purification, the requisite bromofluorans **2** and **4** in moderate yield (Scheme 3). As a consequence of reported instances where debromination had occurred during the attempted preparation of bromofluorans via this general method [19] careful structural characterisation of **2** and **4** was undertaken.

The key ^1H NMR signals employed for the characterisation of **2** were the *ortho*-coupled doublet at δ 7.45 ($J = 9.2$ Hz, 1′-H), a double doublet at δ 7.21 ($J = 9.2$ and 2.4 Hz, 2′-H) and the *meta*-coupled doublet at δ 7.92 ($J = 2.4$ Hz, 4′-H) which confirmed the position of the bromine atom. A group of mutually coupled signals resonating upfield of these signals assigned to the bromonaphthalene unit were assigned to 11′-H (δ 6.50, d, $J = 8.8$ Hz), 10′-H (δ 6.37, dd, $J = 8.8$ and



Scheme 3. Preparation of fluorans and bromofluorans.

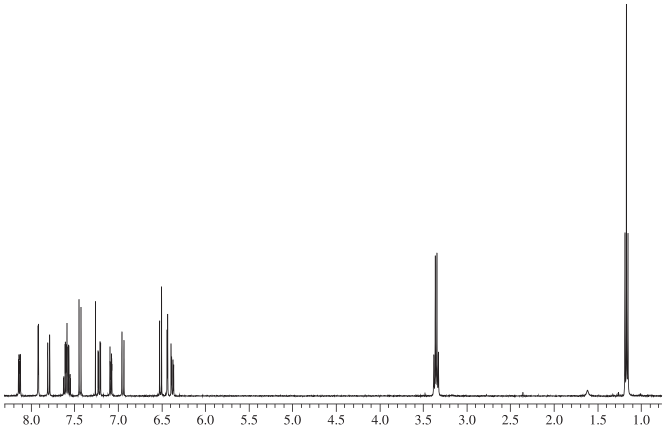


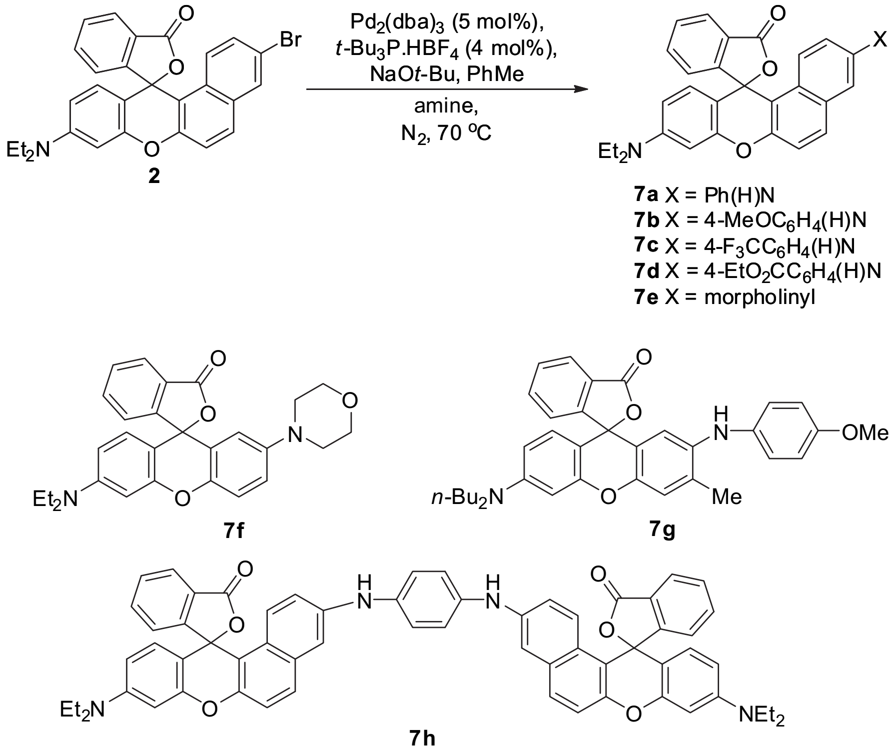
Fig. 1. ^{1}H NMR spectrum of 9′-diethylamino-3′-bromobenzo[*a*]fluoran **2**.

2.6 Hz) and 8′-H (δ 6.43, d, $J = 2.6$ Hz) which confirmed the location of the diethylamino group on the xanthene core (Fig. 1). The presence of the lactone carbonyl was confirmed by ^{13}C NMR spectroscopy with a signal at δ 170.0 [20] and also by a C=O stretch at 1754 cm^{-1} in the infrared spectrum. Mass spectrometry gave the expected molecular ions $M + H^+ = 500.2$ and 502.2 in a ca. 1:1 ratio (Br^{79} and Br^{81}) which confirmed the incorporation of the bromine atom.

The ^{1}H NMR spectrum of **4** displayed a similar grouping of signals at ca. δ 6.4 assigned to the Et$_2$N substituted xanthene unit and the protons of the furanone moiety were assigned to signals at δ 7.27 (multiplet including 4′-H), δ 7.66 (m) and δ 8.04 (d, $J = 7.2$ Hz) for 7-H, 5-H and 6-H, and 4-H respectively. The incorporation of the bromine atom was confirmed by mass spectrometry with $M + H^+ = 450.2$ and 452.2 and the lactone carbonyl stretching band appeared at 1749 cm^{-1} in the infrared spectrum.

With the required bromofluorans to hand examination of their Pd-catalysed amination reaction was next explored (Scheme 2). In 1994 Buchwald et al. and Hartwig et al. independently published work on the coupling of aryl halides with amines using palladium catalysis in the presence of a base [21]. Since then, palladium-catalysed aminations have been widely investigated and have featured in reviews which highlight the apparent ease with which this amination occurs [12]. From the considerable body of work undertaken in this area it is apparent that an exceptionally wide range of aryl halides and amines can be coupled together and that an extensive range of catalysts, ligands and solvents have been employed.

The Pd source employed throughout this study was Pd$_2$(dba)$_3$ since this has been widely employed in Pd-catalysed aminations [22]. The ligand employed was tris(*t*-butyl)phosphine, used as the more convenient tris(*t*-butyl)phosphonium fluoroborate salt with the free phosphine liberated *in situ* using an additional equivalent of sodium *tert*-butoxide. Thus heating a solution of **2** in anhydrous toluene (previously bubbled with nitrogen for 15 min) containing 1 eq. of the aniline, 2 eq. of *t*-BuONa, *t*-Bu$_3$P·HBF$_4$ (4 mol%) and Pd$_2$(dba)$_3$ (5 mol%) gave, after 24 h at 70 °C, a reaction mixture



Scheme 4. Pd-catalysed amination reactions of bromofluorans.

containing none of the original bromofluoran **2** and two new components which, although poorly resolved on TLC, were separated by column chromatography. The faster running red colouring component was identified as the benzo[*a*]fluoran **3** (10%) by comparison of physical and spectroscopic data with an independently synthesised sample. The debromination of aromatic bromides in Pd-catalysed reactions is a frequently encountered problem [23].

The more polar purple–black colouring compound was characterised as the target 3′-anilinofluoran **7a** albeit in a disappointingly low isolated yield of 19% (Scheme 4), in spite of the relatively high conversion indicated by TLC analysis of the reaction mixture. It is likely that the low isolated yield of pure **7a** is in part attributed to a combination of the poor resolution between the two products and the chromatographic purification process which results in some ring-opening of the fluorans on the chromatography silica. The ^{1}H NMR spectrum for **7a** displayed a singlet for the NH group at δ 5.90 confirming the success of the coupling process. The naphthalene ring protons in close proximity to the 3′-aniline group gave rise to signals at δ 6.85 (dd, $J = 8.8$ and 2.4 Hz, 2′-H), δ 6.92 (m, 1′-H) and δ 7.13 (d, $J = 2.4$ Hz, 4′-H). The expected signals for the diethylamino-substituted xanthene unit appeared at δ 6.43 (8′-H), δ 6.35 (10′-H) and δ 6.51 (11′-H). The robustness of the lactone ring towards the amination conditions was confirmed by the presence of a low field multiplet at δ 8.11 assigned to 4-H, a low field signal at δ 170.4 in the ^{13}C NMR spectrum for the C=O group and a stretching bond at 1740 cm^{-1} (C=O) in the infrared spectrum. Additional confirmation of the amination of **2** came from the infrared stretching band for the NH group, which appeared in the expected region at 3378 cm^{-1}. There are only a very limited number of examples of 3′-anilino substituted benzo[*a*]fluorans described in the patent literature and these have been obtained by a more traditional and lengthy strategy involving the preparation of 6-anilino-2-methoxynaphthalene by an Ullmann reaction [24] and its subsequent reaction with a ketoacid [16].

Repeating the amination of **2** with a series of electron rich and electron deficient anilines gave the 3′-anilinobenzo[*a*]fluorans **7b–d** in 53–86% yield and amination of **2** with morpholine gave a respectable yield of **7e** (57%). The structure of each of the new amino substituted benzo[*a*]fluorans **7b–7e** was confirmed by NMR spectroscopy which indicated an upfield shift of the naphthalene ring protons adjacent to the new amine function and the aniline NH (**7b–d**) appeared as a slightly broadened signal between δ 5.5 and δ 6.5. In the ^{13}C NMR spectrum the lactone C=O group resonated at ca. δ 170, typical for the fluoran unit [20].

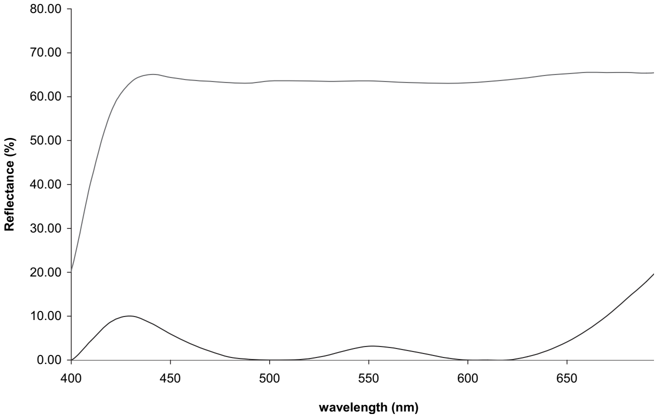


Fig. 2. Reflectance spectra of **7b** in methyl stearate containing bisphenol A at rt (lower line) and at ca. 50 °C (upper line).

Amination of bromofluoran **4** with morpholine resulted in a complex reaction product from which unrecovered **4** (17%) and debrominated fluoran **5** (35%) could be isolated but the known red-developing (TLC) diaminofluoran **7f** [25] remained impure. However, treatment of **6** with *p*-anisidine proceeded smoothly under identical conditions to afford **7g** in 68% yield in spite of the sterically important proximal methyl group. Attempts to accomplish a double amination with 1,4-diaminobenzene, thereby linking two molecules of **2** together, to afford **7h** gave a complex reaction product by TLC which indicated a new purple–black colouring species had formed but which could not be resolved by chromatography. Further investigations of Pd-catalysed aminations with other secondary amines and diamines are in hand.

The colour forming properties of the new fluorans in methyl stearate containing bisphenol A as the acidic developer were next examined. At room temperature each of the new aminofluoran formulations appeared intensely coloured with **7b** appearing blue–black, **7c–e** purple–black and **7g** a green–black in agreement with established colour–structure trends [19]. Upon warming to ca. 50 °C each of the foregoing formulations faded to near colourless with **7b** and **7c** displaying very weak residual pale yellow and pale pink shades, respectively. Selected reflectance spectra recorded at room temperature (rt) and at ca. 50 °C are presented in Figs. 2–4 and illustrate the significant contrast between the ring-opened coloured and ring-closed colourless forms and the broad absorption over the full range of the visible spectrum confirming the near

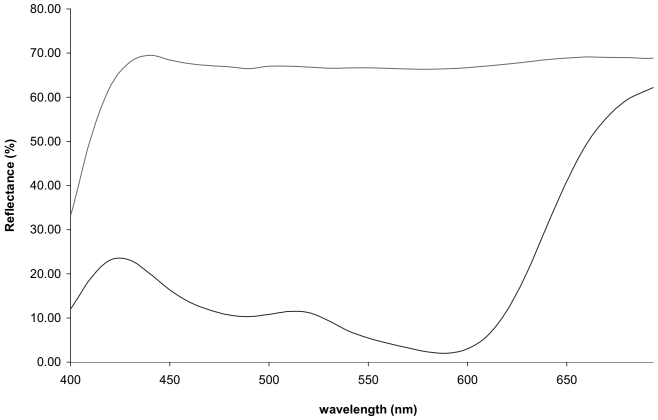


Fig. 3. Reflectance spectra of **7c** in methyl stearate containing bisphenol A at rt (lower line) and at ca. 50 °C (upper line).

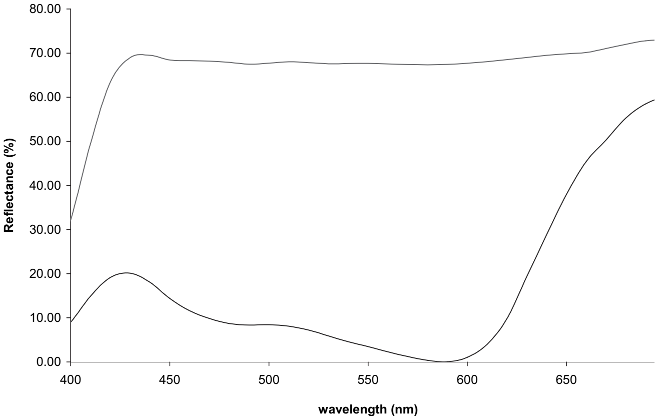
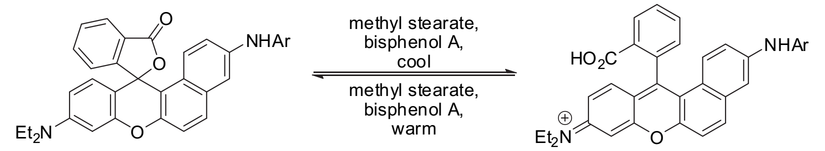


Fig. 4. Reflectance spectra of **7e** in methyl stearate containing bisphenol A at rt (lower line) and at ca. 50 °C (upper line).



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Scheme 5. Reversible colour forming process of benzo[*a*]fluorans **7** in methyl stearate containing bisphenol A.

black shades (Scheme 5). The interactions leading to colour development between colour forming fluorans and acidic developers such as bisphenol A are well established [26].

4. Conclusions

The amination of bromo-fluorans and benzo[*a*]fluorans was accomplished employing $Pd_2(dba)_3$ and tris(*t*-Bu)$_3$P as the catalyst–ligand combination. Electronically rich and electronically deficient anilines coupled in moderate to good yield to 3′-bromo-9′-diethylaminobenzo[*a*]fluoran to afford a series of 3′-anilino derivatives which performed as efficient colour formers, developing near black shades on formulation with bisphenol A in methyl stearate. Using an identical method amination of 2′-bromo-6′-di(*n*-butylamino)-3′-methylfluoran with *p*-anisidine proceeded efficiently in spite of the proximal methyl substituent. Amination of 3′-bromo-9′-diethylaminobenzo[*a*]fluoran and 2′-bromo-6′-diethylaminofluoran with morpholine gave contrasting results with the former proceeding efficiently and the latter suffering from extensive debromination of the substrate.

This preliminary study has illustrated that a series of desirable black colouring fluorans can be readily obtained by a simple amination protocol applied to common, readily available bromo-substituted precursors thus obviating the need to access a wide variety of diarylamine intermediates which require delicate handling when preparing fluorans by the traditional acid-mediated process. Catalyst optimisation studies to enhance conversion and minimize complicating debromination reactions are ongoing.

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