A New and General Synthesis of Substituted 2-Azafluorenones

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Abstract: A short high yield synthesis of polysubstituted 2-azafluorenones from 1,2,4-triazines using the metalation and intramolecular Diels–Alder reaction is described.

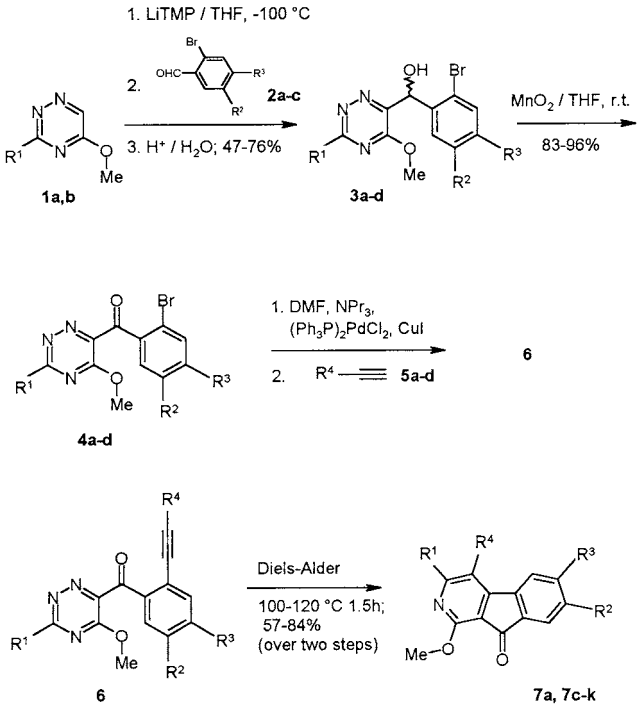
Key words: 1,2,4-triazines, 2-azafluorenones, metalations, Sonogashira reaction, Diels–Alder reaction

Fluorenones and their derivatives are known to be good antiviral[1] and antibacterial[2] agents, aldose reductase inhibitors[3] and anticancer agents (such as TAS-103).[4] Therefore azafluorenone derivatives may also have interesting biological properties. This led to an increasing interest in the chemistry of azafluorenones over the last 20 years. Recently,[5] we developed a flexible and quite a general approach to 1-azafluorenones using metalation, Sonogashira coupling and intramolecular inverse Diels–Alder reactions of 1,2,4-triazines. Here we report a high yield synthesis of 2-azafluorenones using the same strategy.

A survey of the methods known for the preparation of 2-azafluorenones indicated only a few routes: preparation from 4-arylpyridine derivatives,[6] via photochemical Pschorr cyclization of 3-(2-aminoaryl)pyridine ketones,[7] from indenacetamides[8] and cyclization of 2-arylphenylcarbenes.[9] Most of these methods provided only a limited choice of exocyclic functional groups.

The general approach of our work is outlined in Scheme 1, Table 1. The starting 5-methoxy-1,2,4-triazines **1a**,**b** were obtained by methylation of the corresponding 1,2,4-triazin-5-ones.[10] Standard lithiation[11] of **1a**,**b** with LiTMP at –100 °C, followed (after 1 h of accumulation) by addition of the corresponding 2-bromobenzaldehydes **2a**–**c**, afforded the alcohols **3a**–**d** (47–76%). Oxidation of **3a**–**d** to **4a**–**d** using MnO_2 in THF proceeded in yields greater than 80%. Treatment of the 2-bromoaryl ketones **4a**–**d** with alkynes **5a**–**d** under Sonogashira coupling[12] conditions [$PdCl_2(Ph_3P)_2$/CuI catalysis] led to **6** which under the reaction conditions underwent an intramolecular Diels–Alder reaction affording the 1-methoxy-2-azafluorenones **7a**, **7c**–**k** in good yields (57–84%).

It is necessary to note that only in the reaction of **4a** with **5a** the corresponding 2-benzoylacetylene **6a** could be isolated. In the reactions of the alkynes **5b**–**d** with the 2-bromoaryl ketones **4a**–**d** no changes could be observed by



Scheme 1 Substituents for compounds **1a**,**b**; **2a**–**c**; **3a**–**d**; **4a**–**d**; **5a**–**d**; **6**; **7a**–**k**, see Table 1

TLC under mild reaction conditions (r.t. to 50 °C). Only by heating the reaction mixture at 70–80 °C formation of reaction products could be observed by TLC and the 2-azafluorenones **7c**–**k** were the only isolable reaction products. It is known that Sonogashira coupling of alkynes with electron-donating substituents requires harder reaction conditions.[13] On the other hand the π-deficient nature of the 1,2,4-triazine and the electron-rich alkyne moiety in **6** facilitates the inverse intramolecular Diels–Alder reaction. Therefore, both Sonogashira coupling and Diels–Alder reaction proceed at similar reaction conditions.

In view of these results, we decided to use the one-pot method for the synthesis of target compounds **7**. Thus, the 6-(2-bromobenzoyl)-5-methoxy-1,2,4-triazines **4a**–**d** were treated with **5b**–**d** in dimethylformamide in the presence of a Pd/Cu catalyst and tripropylamine. After 1–1.5 hours of heating at 100–120 °C, the expected 2-azafluorenones **7c**–**k** were isolated in good to high yields (57–84%).

Desilylation of **7a** with concentrated HCl resulted in the 2-azafluorenone **7b** in quantitative yield (Scheme 2), in contrast to the previously described 4-trimethylsilyl-1-azafluorenones,[5] which are less active toward similar

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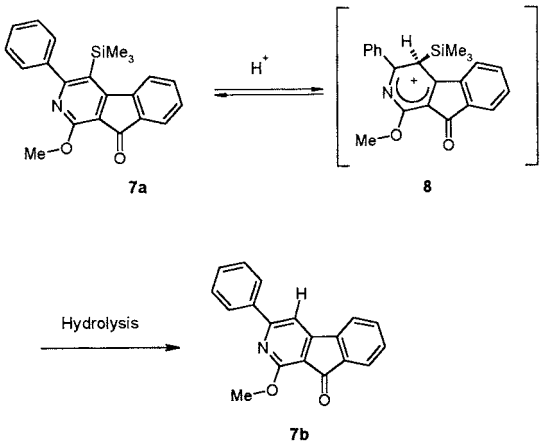
Table 1 Substituents for Compounds **1**–**7**

Compound	R^1	R^2	R^3	R^4
1a	Ph	–	–	–
1b	4-$MeOC_6H_4$	–	–	–
2a	–	H	H	–
2b	–	OMe	OMe	–
2c	–	OCH_2O		–
3a	Ph	H	H	–
3b	Ph	OMe	OMe	–
3c	Ph	OCH_2O		–
3d	4-$MeOC_6H_4$	OMe	OMe	–
4a	Ph	H	H	–
4b	Ph	OMe	OMe	–
4c	Ph	OCH_2O		–
4d	4-$MeOC_6H_4$	OMe	OMe	–
5a	–	–		$SiMe_3$
5b	–	–		CH_2OH
5c	–	–		CH_2NMe_2
5d	–	–		$(CH_2)_3Me$
6a	Ph	H	H	$SiMe_3$
7a	Ph	H	H	$SiMe_3$
7b	Ph	H	H	H
7c	Ph	H	H	CH_2OH
7d	Ph	H	H	CH_2NMe_2
7e	Ph	H	H	$(CH_2)_3Me$
7f	Ph	OMe	OMe	CH_2NMe_2
7g	Ph	OMe	OMe	$(CH_2)_3Me$
7h	Ph	OCH_2O		CH_2NMe_2
7i	Ph	OCH_2O		$(CH_2)_3Me$
7k	4-$MeOC_6H_4$	OMe	OMe	CH_2NMe_2

transformation and could be desilylated only with TBAF, and not with HCl. The different behaviour of 1- and 2-azafluorenone derivatives in these reactions can be explained in terms of more effective delocalization of charge in the transition state **8** in the case of the 2-azafluorenone.

In summary, it has been shown that the 1,2,4-triazines are suitable precursors for the formation of 2-azafluorenone ring. Moreover, the method allows widely varying substituents in the pyridine and benzene moiety. Finally, 2-azafluorenones **7** were prepared in excellent overall yields of 27–61% from readily available starting materials.



Scheme 2

Therefore this new and efficient synthetic route to 2-azafluorenones may complement and (or) supersede the previous reported procedures.[6–9]

Metalation experiments were carried out under Ar in THF, which was freshly distilled from sodium benzophenone ketyl under Ar prior to use. Solvents used in all other experiments (oxidation, Sonogashira coupling, Diels–Alder reaction, desilylation) were dried over molecular sieves. IR spectra were obtained on a Nicolet impact 400 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-300 or ARX-300 spectrometer using TMS as an internal standard. MS were determined on a Varian 212 instrument at 70 eV. Elemental analyses were obtained on a Perkin-Elmer CHN 240 A or 240 B.

3-Substituted 6-(2-Bromo-α-hydroxybenzyl)-5-methoxy-1,2,4-triazines 3a–d; General Procedure

To cold (–60 °C) THF (40 mL) were added 2,2,6,6-tetramethylpiperidine (TMPH, 1.6 mL, 9.4 mmol) and 2.5 M solution of BuLi in hexanes (3.2 mL, 8.0 mmol). The mixture was allowed to warm to r.t., stirred for 30 min and cooled to –100 °C. The 1,2,4-triazine **1a**,**b** (2.0 mmol) in THF (10 mL) was added in portions while keeping the internal temperature < –95 °C. After 60 min (accumulation time), the corresponding 2-bromobenzaldehyde **2a–c** (8.0 mmol) was added and the solution was stirred for 60 min (< –95 °C). The mixture was treated with conc. HCl–MeOH–THF (1:1:4, 4.5 mL), and was allowed to warm to r.t. Then, aq sat. $NaHCO_3$ solution was added until pH 8, the organic solvent was removed under vacuum (40 °C), and the remaining solution was extracted with CH_2Cl_2 (3 × 30 mL). The organic layer was dried ($MgSO_4$), the solvent was removed under vacuum and the crude residue was purified by column chromatography with cyclohexane–EtOAc (2:1) as the eluent.

6-(2-Bromo-α-hydroxybenzyl)-5-methoxy-3-phenyl-1,2,4-triazine (3a)

From **1a** (374 mg) and **2a** (1.48 g); yield: 566 mg (76%); light yellow crystals; mp 171–172 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.44 (2 H, m, ArH), 7.48 (5 H, m, ArH), 7.18 (1 H, m, ArH), 7.09 (1 H, m, ArH), 6.50 (1 H, s, C*H*OH), 4.76 (1 H, s, OH), 4.03 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 163.1, 160.8, 149.6, 139.4, 134.4, 133.2, 131.9, 129.8, 129.3, 128.9, 128.4, 127.8, 124.1, 70.0, 54.2.

Anal. Calcd for $C_{17}H_{14}BrN_3O_2$: C, 54.86; H, 3.79; N, 11.29. Found: C, 55.08; H, 3.83; N, 11.25.

6-(2-Bromo-3,4-dimethoxy-α-hydroxybenzyl)-5-methoxy-3-phenyl-1,2,4-triazine (3b)
From **1a** (374 mg) and **2b** (1.96 g); yield: 572 mg (66%); light yellow crystals; mp 154–155 °C.

IR (KBr): 3533, 3065, 2947, 1591, 1510, 1453, 1400, 1367, 775, 709 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.42 (2 H, m, ArH), 7.59 (3 H, m, ArH), 7.41 (1 H, s, ArH), 7.10 (1 H, s, ArH), 6.53 (1 H, d, *J* = 6.05 Hz, C*H*OH), 6.24 (1 H, d, *J* = 6.05 Hz, C*H*OH), 4.19 (3 H, s, OCH_3), 3.82 (3 H, s, OCH_3), 3.79 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 161.8, 161.1, 151.2, 148.7, 147.9, 134.3, 132.5, 131.7, 128.9, 127.7, 115.1, 112.3, 111.1, 68.3, 55.9, 55.6, 54.2.

Anal. Calcd for $C_{19}H_{18}BrN_3O_4$: C, 52.79; H, 4.20; N, 9.72. Found: C, 52.50; H, 4.32; N, 10.04.

6-(2-Bromo-α-hydroxy-4,5-methylenedioxybenzyl)-5-methoxy-3-phenyl-1,2,4-triazine (3c)
From **1a** (374 mg) and **2c** (1.832 g); yield: 516 mg (62%); light yellow crystals; mp 135–137 °C.

IR (KBr): 3342, 3039, 2854, 1552, 1459, 1380, 1038, 900, 168, 703 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.42 (2 H, m, ArH), 7.60 (3 H, m, ArH), 7.31 (1 H, s, ArH), 7.18 (1 H, s, ArH), 6.52 (1 H, d, *J* = 6.05 Hz, C*H*OH), 6.23 (1 H, d, *J* = 6.05 Hz, C*H*OH), 6.10 (2 H, d, *J* = 6.15 Hz, CH_2), 4.20 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 161.2, 160.7, 151.1, 147.4, 147.0, 134.3, 134.2, 131.7, 128.9, 127.7, 111.8, 111.5, 109.1, 101.9, 68.2, 54.3.

Anal. Calcd for $C_{18}H_{14}BrN_3O_4$: C, 51.94; H, 3.39; N, 10.10. Found: C, 52.08; H, 3.32; N, 10.24.

6-(2-Bromo-3,4-dimethoxy-α-hydroxybenzyl)-5-methoxy-3-(4-methoxyphenyl)-1,2,4-triazine (3d)
From **1b** (434 mg) and **2b** (1.96 g); yield: 434 mg (47%); light yellow crystals; mp 168–170 °C.

IR (KBr): 3508, 3060, 2897, 1584, 1500, 1453, 1390, 709 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.35 (2 H, d, *J* = 8.2 Hz, ArH), 7.39 (1 H, s, ArH), 7.11 (2 H, d, *J* = 8.2 Hz, ArH), 7.08 (1 H, s, ArH), 6.42 (1 H, d, *J* = 5.85 Hz, C*H*OH), 6.21 (1 H, d, *J* = 5.85 Hz, C*H*OH), 4.16 (3 H, s, OCH_3), 3.85 (3 H, s, OCH_3), 3.80 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 162.1, 161.0, 160.5, 150.5, 148.7, 148.0, 132.7, 129.5, 126.6, 115.2, 114.3, 112.5, 111.1, 68.3, 55.9, 55.6, 55.3, 54.0.

Anal. Calcd for $C_{20}H_{20}BrN_3O_5$: C, 51.96; H, 4.36; N, 9.09. Found: C, 51.66; H, 4.34; N, 8.87.

6-(2-Bromobenzoyl)-5-methoxy-1,2,4-triazines 4a–d; General Procedure
To a solution of **3a–d** (0.5 mmol) in THF (20 mL) was added MnO_2 (0.87 g, 10.0 mmol), and this suspension was stirred at r.t. for 5 h. The mixture was filtered, the solvent evaporated under vacuum, and the crude residue was purified by column chromatography with cyclohexane–EtOAc (1:1) as the eluent.

6-(2-Bromobenzoyl)-5-methoxy-3-phenyl-1,2,4-triazine (4a)
From **3a** (186 mg); yield: 178 mg (96%); light yellow crystals; mp 135–136 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.52 (2 H, m, ArH), 7.44 (7 H, m, ArH), 4.22 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 190.6, 162.4, 160.5, 144.7, 138.5, 133.0, 132.3, 131.7, 131.6, 129.9, 128.0, 127.9, 126.5, 119.7, 53.6.

Anal. Calcd for $C_{17}H_{12}BrN_3O_2$: C, 55.16; H, 3.27; N, 11.35. Found: C, 55.00; H, 3.49; N, 11.49.

6-(2-Bromo-3,4-dimethoxybenzoyl)-5-methoxy-3-phenyl-1,2,4-triazine (4b)
From **3b** (216 mg); yield: 196 mg (91%); light yellow crystals; mp 168–169 °C.

IR (KBr): 2947, 1690, 1604, 1519, 1446, 1387, 1367, 1216, 985, 775 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.50 (2 H, m, C_6H_5), 7.62 (3 H, m, C_6H_5), 7.37 (1 H, s, ArH), 7.30 (1 H, s, ArH), 4.21 (3 H, s, OCH_3), 3.90 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 189.5, 162.3, 160.9, 152.7, 148.0, 147.0, 133.8, 132.5, 129.7, 129.0, 128.4, 116.3, 114.1, 113.2, 56.3, 55.9, 54.6.

Anal. Calcd for $C_{19}H_{16}BrN_3O_4$: C, 53.04; H, 3.75; N, 9.77. Found: C, 52.76; H, 3.75; N, 9.42.

6-(2-Bromo-3,4-methylenedioxybenzoyl)-5-methoxy-3-phenyl-1,2,4-triazine (4c)
From **3c** (208 mg); yield: 174 mg (84%); light yellow crystals; mp 138–140 °C.

IR (KBr): 2927, 1677, 1552, 1525, 1486, 1374, 1255, 985, cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.52 (2 H, m, ArH), 7.67 (3 H, m, ArH), 7.39 (1 H, s, ArH), 7.36 (1 H, s, ArH), 6.10 (2 H, s, CH_2), 4.20 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 189.4, 170.0, 162.4, 151.3, 147.3, 146.4, 133.7, 132.5, 131.4, 129.0, 128.4, 113.5, 113.4, 111.0, 103.0, 54.6.

Anal. Calcd for $C_{18}H_{12}BrN_3O_4$: C, 52.19; H, 2.92; N, 10.14. Found: C, 51.86; H, 2.89; N, 10.12.

6-(2-Bromo-3,4-dimethoxybenzoyl)-5-methoxy-3-(4-methoxyphenyl)-1,2,4-triazine (4d)
From **3d** (231 mg); 191 mg (83%); light yellow crystals; mp 182–183 °C.

IR (KBr): 3007, 2941, 2839, 1683, 1607, 1510, 1459, 1362, 1265, 1164, 1031, 853, cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.46 (2 H, d, *J* = 8.2 Hz, ArH), 7.33 (1 H, s, ArH), 7.27 (1 H, s, ArH), 7.17 (2 H, d, *J* = 8.2 Hz, ArH), 4.18 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.79 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 191.5, 164.6, 163.9, 162.5, 154.3, 149.8, 147.8, 132.1, 131.9, 127.8, 118.1, 116.3, 115.9, 114.7, 58.0, 57.7, 57.2, 56.1.

Anal. Calcd for $C_{20}H_{18}BrN_3O_5$: C, 52.19; H, 3.94; N, 9.13. Found: C, 52.30; H, 3.80; N, 9.24.

5-Methoxy-6-[2-(trimethylsilylethynyl)benzoyl]-3-phenyl-1,2,4-triazine (6a)
To a solution of **4a** (0.35 mmol, 130 mg) in DMF (2.0 mL) and Et_3N (2.0 mL) was added CuI (3.0 mg, 16 μmol) and $PdCl_2(Ph_3P)_2$ (10 mg, 14 μmol). The mixture was stirred at r.t. for 20 min. Then trimethylsilylacetylene (**5a**; 0.1 mL, 0.79 mmol) was added, and the mixture stirred at r.t. for 3 h. H_2O (10 mL) and Et_2O (10 mL) were added, and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were separated, dried ($MgSO_4$) and purified by column chromatography (cyclohexane–EtOAc, 1:1); yield: 123 mg (91%); light yellow crystals; mp 113–114 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.60 (2 H, d, *J* = 8.1, ArH), 7.89

(1 H, m, ArH), 7.55 (6 H, m, ArH), 4.23 (3 H, s, OCH_3), –0.08 [9 H, s, $Si(CH_3)_3$].

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 191.6, 163.0, 161.2, 147.3, 144.3, 139.4, 134.2, 134.1, 132.3, 132.2, 129.7, 128.9, 128.8, 123.4, 102.8, 102.2, 54.3, 0.1.

Anal. Calcd for $C_{22}H_{21}N_3O_2Si$: C, 68.19; H, 5.46; N, 10.84. Found: C, 68.31; H, 5.35; N, 11.02.

1-Methoxy-4-(trimethylsilyl)-3-phenyl-2-azafluorenone (7a)
The alkyne **6a** (97 mg, 0.25 mmol) in triisopropylbenzene (TIPB, 5 mL) was heated to 120 °C for 1 h. The mixture was cooled, the solvent removed under high vacuum (0.1 mbar) and the crude residue was purified by column chromatography (cyclohexane–EtOAc, 1:1); yield: 79 mg (88%); yellow crystals; mp 247–248 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.67 (2 H, m, ArH), 7.55 (2 H, m, ArH), 7.42 (5 H, m, ArH), 4.09 (3 H, s, OCH_3), 0.05 [9 H, s, $Si(CH_3)_3$].

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 191.5, 172.0, 165.1, 159.9, 143.9, 143.2, 135.2, 133.1, 130.6, 129.8, 129.6, 128.3, 125.8, 123.8, 121.8, 112.1, 53.9, 2.2.

EIMS: *m*/*z* (%) = 359 (M^+, 38), 344 (100), 314 (20), 73 (18).

Anal. Calcd for $C_{22}H_{21}NO_2Si$: C, 73.50; H, 5.89; N, 3.90. Found: C, 73.19; H, 5.94; N, 3.83.

1-Methoxy-3-phenyl-2-azafluorenone (7b)
To a solution of **7a** (24 mg, 67 μmol) in MeOH–CH_2Cl_2 (1:1, 20 mL) was added conc. HCl (0.5 mL). The solution was stirred at r.t. for 24 h. Aq sat. $NaHCO_3$ (10 mL) was then added and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed under vacuum. The crude product was purified by column chromatography (cyclohexane–EtOAc, 1:1); yield: 18 mg (98%); yellow crystals; mp 208 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.09 (2 H, m, ArH), 7.48 (8 H, m, ArH), 4.17 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 189.6, 163.5, 161.2, 157.2, 140.9, 138.1, 133.8, 131.2, 130.5, 128.9, 128.8, 127.5, 124.1, 121.2, 120.2, 105.8, 54.0.

EIMS: *m*/*z* (%) = 287 (M^+, 100), 257 (35), 228 (14), 149 (16).

Anal. Calcd for $C_{19}H_{13}NO_2$: C, 79.43; H, 4.56; N, 4.87. Found: C, 79.16; H, 4.53; N, 4.82.

1-Methoxy-2-azafluorenones 7c–k; General Procedure
To **4a–d** (0.25 mmol) in DMF (2.0 mL) and tripropylamine (2.0 mL) was added CuI (2.0 mg, 11 μmol) and $PdCl_2(Ph_3P)_2$ (7.0 mg, 10 μmol). The solution was stirred at r.t. for 20 min. Then the corresponding acetylene **5b–d** (0.50 mmol) was added, and the mixture was stirred under Ar at 100–120 °C for 1–1.5 h (TLC control). The solvent was removed under vacuum and the crude product was purified by column chromatography with cyclohexane–EtOAc (2:1) (for **7e**, cyclohexane–EtOAc, 3:1) as the eluent.

4-Hydroxymethyl-1-methoxy-3-phenyl-2-azafluorenone (7c)
From **4a** (92 mg) and **5b** (28 mg); yield: 66 mg (84%); yellow crystals; mp 215–217 °C.

IR (KBr): 3531, 3091, 2961, 2912, 1694, 1607, 1566, 1383, 1321, 1235, 1081, 975, 756, 700 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.07 (1 H, d, *J* = 7.8 Hz, H-9), 7.82 (2 H, m, ArH), 7.70 (2 H, m, ArH), 7.54 (4 H, m, ArH), 5.55 (1 H, t, *J* = 3.9 Hz, OH), 4.65 (2 H, d, *J* = 3.9 Hz, C*H*$_2$OH), 4.02 (3 H, s, OCH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 190.9, 164.3, 158.0, 156.8, 140.3, 138.5, 134.5, 133.8, 131.1, 129.3, 129.2, 128.1, 125.8, 123.1, 122.8, 111.4, 57.0, 53.5.

EIMS: *m*/*z* (%) = 317 (M^+, 100), 302 (13), 257 (21), 227 (21), 115 (17), 28 (60).

Anal. Calcd for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N, 4.41. Found: C, 75.69; H, 4.90; N, 4.31.

1-Methoxy-4-[(dimethylamino)methyl]-3-phenyl-2-azafluorenone (7d)
From **4a** (92 mg) and **5c** (42 mg); yield: 65 mg (76%); yellow crystals; mp 212–214 °C.

IR (KBr): 2961, 2863, 1719, 1564, 1466, 1396, 1354, 1319, 996, 772 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.85 (1 H, d, *J* = 7.58 Hz, H-9), 7.69 (2 H, m, ArH), 7.54 (6 H, m, ArH), 3.99 (3 H, s, OCH_3), 3.69 (2 H, s, C*H*$_2$NMe$_2$), 1.97 [6 H, s, $CH_2N(CH_3)_2$].

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 190.1, 165.7, 157.8, 156.3, 140.8, 139.4, 134.3, 133.7, 130.8, 129.3, 128.5, 127.8, 126.8, 122.8, 122.0, 111.8, 55.1, 53.4, 44.4.

EIMS: *m*/*z* (%) = 344 (M^+, 34), 329 (25), 300 (95), 285 (38), 264 (25), 239 (22), 227 (16), 166 (10), 148 (25), 126 (6), 84 (7), 58 (100).

Anal. Calcd for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.13. Found: C, 76.77; H, 5.81; N, 8.40.

4-Butyl-1-methoxy-3-phenyl-2-azafluorenone (7e)
From **4a** (92 mg) and **5d** (41 mg); yield: 68 mg (79%); yellow crystals; mp 141–143 °C.

IR (KBr): 3046, 2953, 2868, 1710, 1597, 1571, 1469, 1394, 1005, 894, 749, 705 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.70 (1 H, dd, *J* = 7.5, 0.73 Hz, H-9), 7.59 (1 H, d, *J* = 7.55 Hz, ArH), 7.43 (7 H, m, ArH), 4.03 (3 H, s, OCH_3), 2.83 (2 H, m, ArC*H*$_2$), 1.49 (2 H, m, $ArCH_2CH_2$), 1.23 (2 H, m, $ArCH_2CH_2CH_2CH_3$), 0.76 (3 H, t, J = 7.3 Hz, CH_2CH_3).

^{13}C NMR (75.4 MHz,$CDCl_3$): δ = 186.2, 160.0, 152.8, 149.2, 136.4, 134.8, 129.6, 128.7, 125.1, 123.5, 123.2, 122.9, 120.4, 118.9, 118.8, 107.2, 48.8, 27.1, 23.1, 17.4, 8.4.

EIMS: *m*/*z* (%) = 343 (M^+, 97), 314 (11), 300 (100), 285 (37), 270 (5), 239 (10), 86 (14), 71 (5), 57 (18).

Anal. Calcd for $C_{23}H_{21}NO_2$: C, 80.44; H, 6.16; N, 4.08. Found: C, 80.22; H, 6.18; N, 4.02.

1,6,7-Trimethoxy-4-[dimethylamino)methyl]-3-phenyl-2-azafluorenone (7f)
From **4b** (107 mg) and **5c** (42 mg); yield: 65 mg (64%); light orange crystals; mp 174–176 °C.

IR (KBr): 2947, 2868, 2782, 1716, 1578, 1499, 1466, 1387, 1288, 1216, 1025, 782, 716 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.48 (5 H, m, C_6H_5), 7.46 (1 H, s, ArH), 7.20 (1 H, s, ArH), 3.94 (3 H, s, OCH_3), 3.93 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.66 (2 H, s, C*H*$_2$NMe$_2$), 2.00 [6 H, s, $CH_2N(CH_3)_2$].

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 189.4, 165.4, 157.1, 156.3, 153.0, 150.5, 139.6, 135.0, 129.2, 128.4, 127.9, 126.8, 121.0, 111.8, 110.5, 105.9, 55.8, 55.2, 53.3, 44.4.

EIMS: *m*/*z* (%) = 404 (M^+, 35), 389 (29), 360 (100), 330 (9), 302 (8), 202 (9), 58 (38).

Anal. Calcd for $C_{24}H_{24}N_2O_4$: C, 71.27; H, 5.98; N, 6.93. Found: C, 71.03; H, 5.71; N, 6.58.

4-Butyl-1,6,7-trimethoxy-3-phenyl-2-azafluorenone (7g)
From **4b** (107 mg) and **5d** (41 mg); yield: 78 mg (78%); light orange crystals; mp 178–179 °C.

IR (KBr): 3006, 2954, 2881, 1710, 1578, 1499, 1400, 1295, 1229, 1018, 795, 716 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.52 (5 H, m, C_6H_5), 7.23 (1 H, s, ArH), 7.21 (1 H, s, ArH), 3.93 (6 H, s, 2 OCH_3), 3.89 (3 H, s, OCH_3), 2.81 (2 H, m, $ArCH_2$), 1.44 (2 H, m, $ArCH_2CH_2$), 1.28 (2 H, m, $ArCH_2CH_2CH_2CH_3$), 0.70 (3 H, t, *J* = 7.3 Hz, CH_2CH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 189.5, 164.9, 157.6, 153.8, 153.3, 150.5, 139.5, 134.8, 128.4, 128.2, 128.1, 127.4, 124.4, 111.9, 107.9, 106.5, 55.9, 55.8, 53.2, 31.8, 27.5, 22.1, 13.5.

EIMS: *m*/*z* (%) = 403 (M^+, 100), 388 (7), 360 (40), 344 (10), 302 (7).

Anal. Calcd for $C_{25}H_{25}NO_4$: C, 74.42; H, 6.25; N, 3.47. Found: C, 74.43; H, 6.22; N, 3.30.

4-[(Dimethylamino)methyl]-1-methoxy-6,7-methylenedioxy-3-phenyl-2-azafluorenone (7h)
From **4c** (103 mg) and **5c** (42 mg); yield: 55 mg (57%); light orange crystals; mp 174–176 °C.

IR (KBr): 2940, 2874, 2776, 1710, 1585, 1486, 1394, 1295, 1038, 1012, 801, 709 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.50 (5 H, m, C_6H_5), 7.29 (1 H, s, ArH), 7.15 (1 H, s, ArH), 6.21 (2 H, s, CH_2), 3.94 (3 H, s, OCH_3), 3.60 (2 H, s, CH_2NMe_2), 1.95 [6 H, s, $CH_2N(CH_3)_2$].

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 189.6, 165.7, 157.7, 156.5, 153.1, 149.2, 139.5, 137.1, 129.2, 128.8, 128.5, 127.9, 121.1, 112.1, 107.9, 103.5, 102.7, 55.0, 53.3, 44.3.

EIMS: *m*/*z* (%) = 388 (M^+, 47), 373 (26), 344 (100), 329 (20), 309 (9), 58 (66).

Anal. Calcd for $C_{23}H_{20}N_2O_4$: C, 71.12; H, 5.19; N, 7.21. Found: C, 71.03; H, 5.31; N, 7.08.

4-Butyl-1-methoxy-6,7-methylenedioxy-3-phenyl-2-azafluorenone (7i)
From **4c** (103 mg) and **5d** (41 mg); yield: 76 mg (79%); light orange crystals; mp 204–205 °C.

IR (KBr): 3085, 2954, 2927, 2868, 1716, 1578, 1486, 1387, 1288, 1038, 999, 709 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.50 (5 H, m, C_6H_5), 7.25 (1 H, s, ArH), 7.18 (1 H, s, ArH), 6.22 (2 H, s, OCH_2O), 3.91 (3 H, s, 2 OCH_3), 2.80 (2 H, m, $ArCH_2$), 1.44 (2 H, m, $ArCH_2CH_2$), 1.22 (2 H, m, $ArCH_2CH_2CH_2CH_3$), 0.72 (3 H, t, *J* = 7.3 Hz, CH_2CH_3).

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 189.1, 165.3, 157.2, 154.0, 153.7, 149.7, 139.6, 136.6, 128.9, 128.5, 128.2, 128.0, 124.5, 111.8, 105.5, 104.1, 53.3, 31.7, 21.9, 21.6, 22.1, 13.3.

EIMS: *m*/*z* (%) = 387 (M^+, 100), 358 (9), 344 (73), 329 (21).

Anal. Calcd for $C_{24}H_{21}NO_4$: C, 74.40; H, 5.46; N, 3.62. Found: C, 74.23; H, 5.55; N, 3.31.

1,6,7-Trimethoxy-4-[(dimethylamino)methyl]-3-(4-methoxyphenyl)-2-azafluorenone (7k)
From **4d** (115 mg) and **5c** (42 mg); yield: 74 mg (68%); orange crystals; mp 250 °C.

IR (KBr): 3073, 3022, 2976, 2951, 2844, 2778, 1703, 1576, 1495, 1454, 1388, 1291, 1250, 1174, 1026, 1016, 838, 777 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.45 (3 H, m, ArH), 7.17 (1 H, s, ArH), 7.05 (2 H, d, *J* = 8.73 Hz, ArH), 3.94 (3 H, s, OCH_3), 3.93 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 3.84 (3 H, s, OCH_3) 3.70 (2 H, s, CH_2NMe_2), 2.00 [6 H, s, $CH_2N(CH_3)_2$].

^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 189.5, 165.2, 159.5, 157.1, 156.2, 152.9, 150.5, 135.1, 131.8, 130.8, 126.9, 121.0, 113.3, 111.4, 110.6, 105.9, 55.8, 55.3, 55.1, 53.1, 44.3.

EIMS: *m*/*z* (%) = 434 (M^+, 38), 419 (21), 390 (100), 374 (9), 58 (66).

Anal. Calcd for $C_{25}H_{26}N_2O_5$: C, 69.11; H, 6.03; N, 6.45. Found: C, 68.95; H, 5.96; N, 6.33.

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