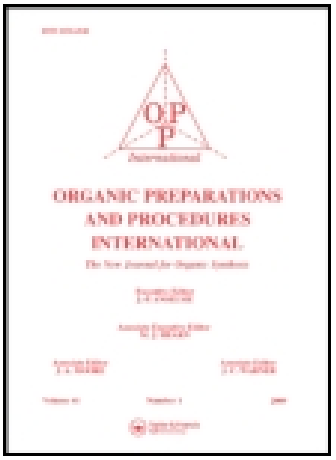

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10-Alkyl-2,7-dinitro-9(10H)-acridinones by Tandem S_NAr Reactions

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10-Alkyl-2,7-dinitro-9(10*H*)-acridinones by Tandem S_NAr Reactions

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Our recent work has described several approaches to the synthesis of heterocyclic systems using tandem reaction processes terminated by a nucleophilic aromatic substitution (S_NAr) reaction.[1–8] With this background, we were interested in the feasibility of preparing substituted 9(10*H*)-acridinones in a single laboratory operation *via* two sequential S_NAr reactions. Based on our previous work, these structures would be expected from 2,2′-difluorobenzophenone derivatives bearing strategically positioned electron-withdrawing groups to activate the aromatic rings toward addition by nucleophilic amines. While 2,2′-difluorobenzophenone could potentially undergo such a reaction, it was expected that further activation would be necessary. The easiest activating group to introduce to this system is the nitro function. This could be added by electrophilic aromatic substitution and would be expected to add *para* to the fluoro substituents.[9]

Numerous studies have demonstrated that nitroacridinones possess significant biological activity. To date, these compounds have attracted attention as antibiotic,[10] antiparasitic,[11–13] antifungal[12] and antiviral agents.[12,14] Furthermore, several derivatives have displayed potent anticancer properties[10,15–18] and may have use in the treatment of neurodegenerative diseases such as multiple sclerosis.[19] Thus, nitroacridinones are worthy targets for organic synthesis.

The syntheses of several potential cyclization substrates are illustrated in *Scheme 1*. The synthesis begins with 2-bromofluorobenzene (**1**). Lithium-bromine exchange on **1** was carried out in THF by addition of *n*-butyllithium at −78°C, followed by warming to −30°C. The resulting solution of 2-fluorophenyllithium (**2**) was cooled to −78°C and reacted with 0.5 equivalents of ethyl formate to give 2,2′-difluorobenzhydrol (**3**) in 89% yield. Oxidation of **3** with chromic acid[20] in aqueous acetone then afforded 2,2′-difluorobenzophenone (**4**) in 90% yield.[21] Double nitration of **4** was accomplished by treatment with 2.2 equivalents of sodium nitrate in concentrated sulfuric acid at 0–5°C to afford 2,2′-difluoro-5,5′-dinitrobenzophenone (**5**) in 66% yield.[22]

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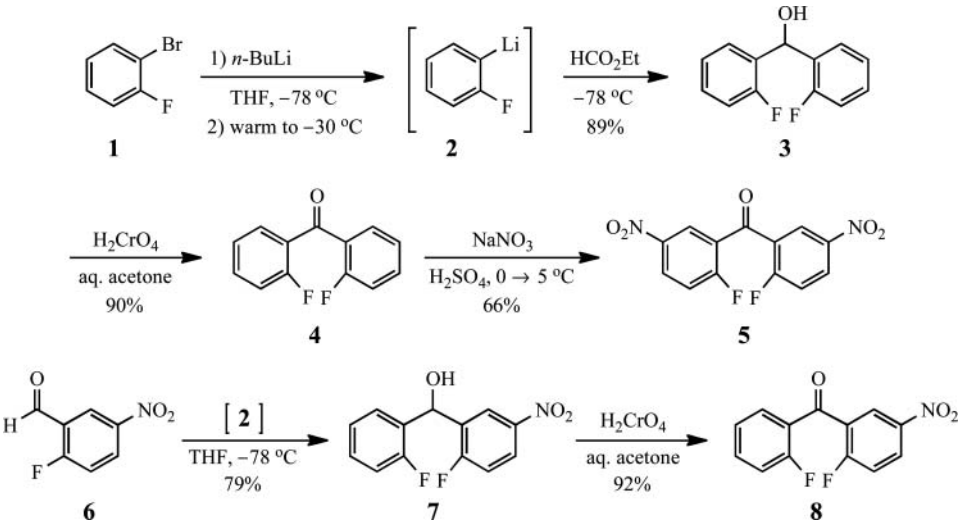


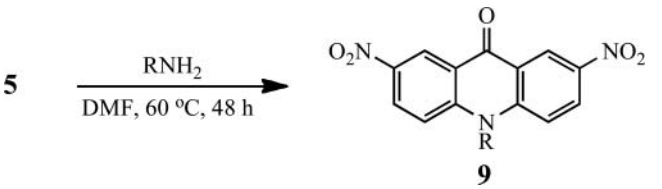
Scheme 1
Synthesis of Substrates **4**, **5** and **8**

To further explore the requirements of the proposed cyclization reaction, an unsymmetrical benzophenone derivative incorporating one single- and one double-activated aromatic ring was also prepared by modification of the above synthesis. Treatment of **2** with 2-fluoro-5-nitrobenzaldehyde (**6**)[22] at −78°C yielded benzhydrol **7** in 79% yield.[23] Chromic acid oxidation as above then furnished 2,2′-difluoro-5-nitrobenzophenone in 92% yield. Thus, benzophenone derivatives with two single-activated and two double-activated rings (*i. e*. **4** and **5**, respectively) as well as a substrate with one single-activated and one double-activated ring (*i.e*. **8**) were available for the current study.

Substrate **5** (both rings double-activated) offered the best chance for success and, thus, was the first case studied. A solution of 1.0 mmol of **5** in DMF was heated to 60°C and 1.1 mmole of benzylamine was added. The reaction immediately turned from tan to dark yellow and the reaction was heated at 60°C for 48 h. Aqueous workup afforded a sparingly soluble yellow solid, which was triturated with boiling 1:1 chloroform:ethanol to afford 10-benzyl-2,7-dinitro-9(10*H*)-acridinone (**9a**) in 82% yield. A total of 7 other amines were reacted with **5** and the results are summarized in *Table 1*. Since the nitrogen must add twice to form the central ring, primary amines were necessary and unhindered cases afforded the best yields.[24]

Our results for the attempted cyclization with substrate **8** (one ring double-activated) with three different amines are given in *Table 2*. In this case, addition occurred only to the double-activated ring to give a near-quantitative yield of the hydrogen-bond-stabilized products **10**. The desired cyclization products were totally absent from the reaction mixture. Attempts to cyclize adducts **10** under more forcing conditions (100°C in DMF for 48 h) were unsuccessful. Cyclizations using substrate **4** (both rings single-activated) also proved unsatisfactory. Reaction of **4** with benzylamine at 100°C for 48 h resulted in only 8% of the acridinone product.[25]

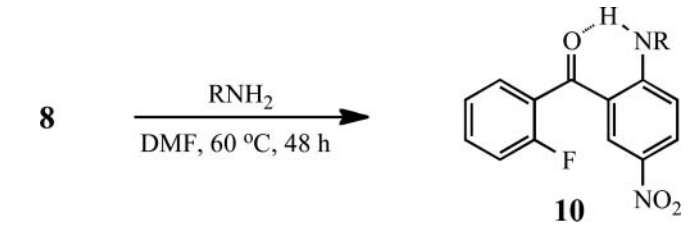
Table 1
Summary of Cyclization Results for **5**



	R	Product	Yield (%)
a	$PhCH_2-$	**9a**	82
b	$4\text{-}CH_3OPhCH_2-$	**9b**	79
c	$4\text{-}ClPhCH_2-$	**9c**	78
d	$4\text{-}CF_3PhCH_2-$	**9d**	81
e	$PhCH_2CH_2-$	**9e**	62
f	$n\text{-}C_6H_{13}-$	**9f**	77
g	$i\text{-}C_4H_9-$	**9g**	76
h	$i\text{-}PrOCH_2CH_2CH_2-$	**9h**	73

In summary, we have successfully developed a tandem S_NAr reaction for the synthesis of 10-alkyl-2,7-dinitro-9(10*H*)-acridinones. The reaction is successful when both aromatic rings are double-activated, but fails in substrates having fewer electron-withdrawing groups. The current reaction demonstrates the feasibility of this strategy for preparing selected acridinones. While the products of the current reaction have potential use as precursors to pharmaceutical agents, additional methodology would be necessary to expand the reaction to structures with more diverse functionality.

Table 2
Summary of Reaction Results for **8**



	R	Product	Yield (%)
a	$PhCH_2-$	**10a**	95
f	$n\text{-}C_6H_{13}-$	**10f**	96
g	$i\text{-}C_4H_9-$	**10g**	92

Experimental Section

Unless otherwise indicated, all reactions were run under dry nitrogen in oven-dried glassware. Commercial anhydrous *N,N*-dimethylformamide (DMF) was stored under nitrogen and transferred by syringe into reactions where it was used. Tetrahydrofuran (THF) was dried over potassium hydroxide pellets and distilled from lithium aluminum hydride under nitrogen. Other reagents and solvents were used as received. Reactions were monitored by thin layer chromatography (TLC) on silica gel GF plates (Analtech No. 21521). Preparative separations were performed using flash column chromatography[26] on silica gel (Grade 62, 60–200 mesh) mixed with UV-active phosphor (Sorbent Technologies No. UV-5); band elution was monitored using a hand-held UV lamp. Melting points were uncorrected. IR spectra were run as thin films on sodium chloride disks. ^{1}H and ^{13}C NMR spectra were measured at 300 MHz and 75 MHz, respectively, and were referenced to internal tetramethylsilane; coupling constants (J) are reported in Hz. Low-resolution mass spectra (EI/DP) were run at 30 eV.

2,2′-Difluorobenzhydrol (3)

The general procedure of Herold and co-workers[21] was modified. A 250-mL, three-necked, round-bottomed flask, equipped with a rubber septum, a magnetic stirrer and an argon atmosphere, was charged with a solution of 4.40 g (25.0 mmol) of 1-bromo-2-fluorobenzene (**1**) in 50 mL of dry THF and the flask was cooled to −78°C. Once cooled, 10.0 mL (25.0 mmol) of 2.5 *M n*-butyllithium in hexanes was added dropwise to the mixture over a period of 30 min. The reaction turned light brown during the addition. The reaction mixture was stirred for 10 min at −78°C, warmed to −30°C over 1 h, recooled to −78°C and 0.92 g (1.0 mL, 12.5 mmol) of freshly distilled ethyl formate in 5 mL of THF was added dropwise. The reaction was stirred for 15 min at −78°C, then slowly warmed to −30°C and quenched with 10 mL of saturated aqueous ammonium chloride. The mixture was transferred to a separatory funnel containing 100 mL of saturated aqueous ammonium chloride and extracted with ether (3 × 100 mL). The combined ether extracts were washed once with water and saturated aqueous sodium chloride, then dried ($MgSO_4$) and concentrated under vacuum to give crude **3** as a yellow oil. A small amount of 5-nonanol present in this product was removed by warming to 60°C at 1 mmHg. This yielded 2.43 g (89%) of **3**, which was used without further purification. IR: 3350, 1225 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.43 (t, J = 7.7 Hz, 2 H), 7.26 (m, 2 H), 7.13 (t, J = 7.7 Hz, 2 H), 7.02 (t, J = 8.8 Hz, 2 H), 6.40 (d, J = 3.3 Hz, 1 H), 2.53 (br s, 1 H); ^{13}C NMR ($CDCl_3$): δ 160.0 (d, J = 246.8 Hz), 129.4 (2 d, $J \approx$ 8.3 and 3.0 Hz), 128.0 (d, J = 2.7 Hz), 124.2, 115.4 (d, J = 21.8 Hz), 64.5; ms: *m/z* 220 (M^+).

Anal. Calcd for $C_{13}H_{10}F_2O$: C, 70.90; H, 4.55. Found: C, 71.04; H, 4.61.

2,2′-Difluorobenzophenone (4)

The general procedure of Danishefsky and co-workers[23] was used. A 100-mL, one-necked, round-bottomed flask, equipped with a magnetic stirrer and an addition funnel, was charged with a solution of 1.92 g (8.75 mmol) of **3** in 40 mL of acetone. The solution was stirred and 4.45 mL of freshly prepared Jones reagent (*ca* 2.95 *M*, 13.1 mmol, 1.5 equiv)[20] was slowly

added dropwise over a period of 45 min. The reaction mixture was stirred for an additional 15 min and then quenched with 20 mL of ice water followed by 3.75 mL of saturated aqueous sodium bisulfite. The resulting mixture was saturated with sodium chloride and extracted with ether (4 × 50 mL). The combined extracts were washed three times with water and once with saturated sodium bicarbonate and saturated aqueous sodium chloride, then dried ($MgSO_4$) and concentrated under vacuum. The resulting yellow oil was distilled *in vacuo* to give 1.72 g (90%) of **4** as a colorless oil, bp 118–120°C at 1.5 mmHg (*lit.*[21] bp 119°C at 1.5 mmHg). IR: 1667 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.71 (td, $J = 7.7$, 1.6 Hz, 2 H), 7.54 (m, 2 H); 7.26 (t, $J = 7.7$ Hz, 2 H), 7.11 (dd, $J = 10.4$, 9.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$): δ 189.7, 161.0 (d, $J = 254.8$ Hz), 134.2 (d, $J = 9.4$ Hz), 130.8, 127.5 (d, $J = 13.0$ Hz), 124.3, 116.2 (d, $J = 22.3$ Hz); ms: *m/z* 218 (M^+).

Anal. Calcd for $C_{13}H_8F_2O$: C, 71.56; H, 3.67. Found: C, 71.53; H, 3.68.

2,2′-Difluoro-5,5′-dinitrobenzophenone (5)

The 2,2′-difluorobenzophenone prepared above was nitrated using the general procedure of Gale and Wilshire,[22] adjusted to give double nitration. A solution of 1.46 g (17.2 mmol) of finely ground sodium nitrate in 20 mL of concentrated sulfuric acid was prepared at room temperature in a 100-mL, three-necked, round-bottomed flask, equipped with an addition funnel and a magnetic stirrer. This solution was cooled to 0°C (ice-salt bath) and 1.70 g (7.80 mmol) of **4** was slowly added over a period of 30 min. The reaction mixture was stirred at 0°C for 1 h, the solution was poured onto 100 g of crushed ice and the mixture was extracted with 1:1 benzene:ether (3 × 50 mL). The combined organic layers were washed once with water and saturated aqueous sodium chloride, then dried ($MgSO_4$) and concentrated under vacuum. The resulting light brown solid was recrystallized from ethanol to give 1.58 g (66%) of **5** as pale yellow crystals, mp 136–137°C. IR: 1677, 1534, 1352 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.70 (dd, $J = 6.0$, 2.7 Hz, 2 H), 8.51 (ddd, $J = 9.3$, 3.8, 2.7 Hz, 2 H), 7.37 (t, $J = 9.3$ Hz, 2 H); ^{13}C NMR ($CDCl_3$): δ 184.7, 164.0 (d, $J = 265.1$ Hz), 144.6, 130.0 (d, $J = 11.5$ Hz), 130.0, 127.0 (t, $J = 2.1$ Hz), 117.8 (d, $J = 25.4$ Hz); ms: *m/z* 308 (M^+).

Anal. Calcd for $C_{13}H_6F_2N_2O_5$: C, 50.65; H, 1.95; N, 9.09. Found: C, 50.68; H, 1.97; N, 9.05.

2,2′-Difluoro-5-nitrobenzhydrol (7)

In a 250-mL three-necked, round-bottomed flask, equipped with a rubber septum, a magnetic stirrer and an argon atmosphere, 4.40 g (25.0 mmol) of **1** was subjected to lithium-bromine exchange as described for the preparation of **3**. To the resulting solution of **2** at −78°C was slowly added a solution of 4.22 g (25.0 mmol) of 2-fluoro-5-nitrobenzaldehyde (**6**)[22] in dry THF. The reaction mixture was stirred for 30 min with warming to −50°C and then quenched with 10 mL of saturated aqueous ammonium chloride. The mixture was transferred to a separatory funnel containing 100 mL of saturated aqueous ammonium chloride and extracted with ether (3 × 100 mL). The combined ether extracts were washed once with water and saturated aqueous sodium chloride, then dried ($MgSO_4$) and concentrated under vacuum to give 5.23 g (79%) of **7** an orange oil, which was carried on without

further purification. IR: 3422, 1530, 1352, 1227 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.51 (dd, J = 6.0, 2.7 Hz, 1 H), 8.20 (ddd, J = 8.8, 4.4, 2.7 Hz, 1 H), 7.41 (td, J = 7.7, 1.6 Hz, 1 H), 7.32 (m, 1 H), 7.16 (apparent t, $J \approx 8.0$ Hz, 2 H), 7.06 (t, J = 9.3 Hz, 1 H), 6.42 (d, J = 3.3 Hz, 1 H), 2.75 and 2.69 (2 s, 1 H); ^{13}C NMR ($CDCl_3$): δ 163.0 (d, J = 258.8 Hz), 159.8 (d, J = 247.6 Hz), 144.4, 131.6 (d, J = 15.5 Hz), 130.2 (d, J = 8.3 Hz), 128.3 (d, J = 12.9 Hz), 127.9 (d, J = 3.4 Hz), 125.2 (d, J = 10.3 Hz), 124.6, (d, J = 3.7 Hz), 124.1 (d, J = 6.3 Hz), 116.5 (d, J = 24.0 Hz), 115.7 (d, J = 21.2 Hz), 63.8; ms (30 eV): *m/z* 265 (M^+).

Anal. Calcd for $C_{13}H_9F_2NO_3$: C, 58.87; H, 3.40; N, 5.28. Found: C, 58.98; H, 3.49; N, 5.19.

2,2′-Difluoro-5-nitrobenzophenone (8)

By using the procedure outlined for the preparation of **4**, 5.20 g (19.6 mmol), benzhydrol **7** was oxidized using 1.5 equivalents of chromic acid to give a brown oil. Purification by flash chromatography using increasing concentrations (10% to 40%) of ether in hexanes gave 4.73 g (92%) of **8** as an orange oil, which crystallized on standing to a yellow-orange solid, mp 68–70°C. IR: 1670, 1533, 1354 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.59 (dd, J = 6.0, 2.7 Hz, 1 H), 8.44 (ddd, J = 9.3, 4.4, 3.3 Hz, 1 H), 7.82 (td, J = 7.7, 2.2 Hz, 1 H), 7.63 (m, 1 H), 7.33 (2 t, $J \approx 7.7$ Hz, 2 H), 7.15 (dd, J = 10.9, 9.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$): δ 187.0, 163.8 (d, J = 264.8 Hz), 161.3 (d, J = 255.8 Hz), 144.2, 135.5 (d, J = 8.9 Hz), 131.0, 128.9 (d, J = 10.6 Hz), 128.8 (obscured d), 126.6 (d, J = 4.6 Hz), 125.9 (d, J = 12.3 Hz), 124.8 (d, J = 3.4 Hz), 117.5 (d, J = 24.6 Hz), 116.4 (d, J = 22.0 Hz); ms: *m/z* 263 (M^+).

Anal. Calcd for $C_{13}H_7F_2NO_3$: C, 59.32; H, 2.66; N, 5.32. Found: C, 59.35; H, 2.70; N, 5.24.

Representative Procedure for the Cyclization of Dinitroacridinones: 10-Benzyl-2,7-dinitro-9(10H)-acridinone (9a)

A 50-mL, one-necked, round-bottomed flask, equipped with a magnetic stirrer and a condenser, was charged with 77 mg (0.25 mmol) of **5** and 2.5 mL of anhydrous DMF. The mixture was heated with stirring to 60°C and 29.4 mg (0.030 mL, 0.28 mmol) of benzylamine was added. The mixture was stirred at 60°C for 48 h, then cooled and added to 50 mL of saturated aqueous sodium chloride. The mixture was extracted with dichloromethane (3 × 25 mL) and the combined organic layers dried ($MgSO_4$) and concentrated under vacuum. Further concentration at 1 mmHg removed the DMF. The resulting solid was triturated with ether and collected to give 77 mg (82%) of **9a** as a yellow solid, which was spectroscopically pure. An analytical sample could be obtained by trituration of the solid in boiling 1:1 chloroform:ethanol followed by filtration, mp 282–284°C. IR: 1652, 1522, 1329 cm^{-1}; ^1H NMR (DMSO-d_6): δ 8.97 (d, J = 2.7 Hz, 2 H), 8.54 (dd, J = 9.3, 2.7 Hz, 2 H), 7.90 (d, J = 9.9 Hz, 2 H), 7.35 (m, 3 H), 7.26 (d, J = 6.6 Hz, 2 H), 5.96 (s, 2 H); ^{13}C NMR[27] (DMSO-d_6): δ 175.8, 145.7, 142.1, 134.7, 129.0, 128.8, 127.7, 125.8, 122.7, 121.3, 118.9, 50.5; ms: *m/z* 375.

Anal. Calcd for $C_{20}H_{13}N_3O_5$: C, 64.00; H, 3.47; N, 11.20. Found: C, 64.05; H, 3.51; N, 11.12.

10-(4-Methoxybenzyl)-2,7-dinitro-9(10H)-acridinone (9b)

This compound was prepared from 77 mg (0.25 mmol) of **5** and 38 mg (0.036 mL, 0.28 mmol) of 4-methoxybenzylamine to give 80 mg (79%) of **9b** as a yellow powder, mp 264–266°C. IR: 2837, 1664, 1513, 1333 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.00 (d, $J = 2.7$ Hz, 2 H), 8.54 (dd, $J = 9.3$, 2.7 Hz, 2 H), 7.91 (d, $J = 9.3$ Hz, 2 H), 7.18 (d, $J = 8.8$ Hz, 2 H), 6.92 ($J = 8.8$ Hz, 2 H), 5.88 (s, 2 H), 3.71 (s, 3 H); ^{13}C NMR (DMSO-d_6): δ 175.9, 158.8, 145.7, 142.1, 128.0, 127.1, 126.3, 122.7, 121.3, 118.9, 114.3, 55.1, 50.1; ms: *m/z* 405 (M^+).

Anal. Calcd for $C_{21}H_{15}N_3O_6$: C, 62.22; H, 3.70; N, 10.37. Found: C, 62.29; H, 3.75; N, 10.28.

10-(4-Chlorobenzyl)-2,7-dinitro-9(10H)-acridinone (9c)

This compound was prepared from 77 mg (0.25 mmol) of **5** and 39 mg (0.034 mL, 0.28 mmol) of 4-chlorobenzylamine to give 80 mg (78%) of **9c** as yellow crystals, mp 300–302°C. IR: 1648, 1522, 1327 cm^{-1}; ^1H NMR (DMSO-d_6): δ 8.96 (d, $J = 2.7$ Hz, 2 H), 8.53 (dd, $J = 9.3$, 2.7 Hz, 2 H), 7.88 (d, $J = 9.9$ Hz, 2 H), 7.44 (d, $J = 8.2$ Hz, 2 H), 7.29 (d, $J = 8.2$ Hz, 2 H), 5.95 (s, 2 H); ^{13}C NMR (DMSO-d_6): δ 175.8, 145.6, 142.1, 133.7, 132.3, 128.9, 128.8, 127.8, 122.6, 121.4, 118.8, 50.0; ms: *m/z* 409/411 (*ca* 3:1, M^+).

Anal. Calcd for $C_{20}H_{12}ClN_3O_5$: C, 58.61; H, 2.93; N, 10.26. Found: C, 58.67; H, 2.94; N, 10.19.

10-(4-Trifluoromethylbenzyl)-2,7-dinitro-9(10H)-acridinone (9d)

This compound was prepared from 77 mg (0.25 mmol) of **5** and 48 mg (0.039 mL, 0.28 mmol) of 4-(trifluoromethyl)benzylamine to give 90 mg (81%) of **9d** as yellow crystals, mp 282–284°C. IR: 1655, 1524, 1323 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.01 (d, $J =$ 2.7 Hz, 2 H), 8.54 (dd, $J = 9.3$, 2.7 Hz, 2 H), 7.90 (d, $J = 9.3$ Hz, 2 H), 7.75 (d, $J = 8.2$ Hz, 2 H), 7.50 (d, $J = 8.2$ Hz, 2 H), 6.08 (s, 2 H); ^{13}C NMR (DMSO-d_6): δ 175.9, 145.7, 142.2, 139.7, 128.9, 126.8, 125.9, 125.8 (q, $J = 3.0$ Hz), 124.6 (q, $J = 260.3$ Hz), 122.7, 121.5, 118.8, 50.3; ms: *m/z* 443 (M^+).

Anal. Calcd for $C_{21}H_{12}F_3N_3O_5$: C, 56.88; H, 2.71; N, 9.48. Found: C, 56.95; H, 2.74; N, 9.43.

10-(2-Phenylethyl)-2,7-dinitro-9(10H)-acridinone (9e)

This compound was prepared from 77 mg (0.25 mmol) of **5** and 33 mg (0.035 mL, 0.28 mmol) of 2-phenylethylamine to give 60 mg (62%) of **9e** as a yellow powder, mp 316–318°C. IR: 1649, 1534, 1327 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.01 (d, $J = 2.7$ Hz, 2 H), 8.58 (dd, $J = 9.3$, 2.7 Hz, 2 H), 8.16 (d, $J = 9.3$ Hz, 2 H), 7.42 (d, $J = 7.1$ Hz, 2 H), 7.31 (t, $J = 7.1$ Hz, 2 H), 7.26 (t, $J = 7.1$ Hz, 1 H), 4.87 (t, $J = 7.7$ Hz, 2 H), 3.16 (t, $J = 7.7$ Hz, 2 H); ^{13}C NMR (DMSO-d_6); δ 175.6, 145.0, 141.9, 137.0, 129.1, 128.6, 128.5, 126.8, 122.8, 121.1, 118.9, 47.7, 32.5; ms: *m/z* 298 (M^+-C_7H_7).

Anal. Calcd for $C_{21}H_{15}N_3O_5$: C, 64.78; H, 3.86; N, 10.80. Found: C, 64.84; H, 3.88; N, 10.69.

10-Hexyl-2,7-dinitro-9(10H)-acridinone (9f)

This compound was prepared from 77 mg (0.25 mmol) of **5** and 28 mg (0.036 mL, 0.28 mmol) of hexylamine to give 71 mg (77%) of **9f** as a yellow powder, mp 216.5–218.5°C. IR: 1655, 1528, 1330 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.32 (d, $J = 2.7$ Hz, 2 H), 8.57 (dd, $J = 9.3$, 2.7 Hz, 2 H), 7.65 (d, $J = 9.3$ Hz, 2 H), 4.44 (t, $J = 8.2$ Hz, 2 H), 2.01 (quintet, $J = 8.2$, Hz, 2 H), 1.64 (quintet, $J = 7.1$ Hz, 2 H), 1.46 (m, 4 H), 0.97 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (DMSO-d_6): δ 175.3, 144.8, 141.7, 128.6, 122.6, 120.8, 118.7, 47.0, 31.1, 26.7, 25.5, 22.1, 13.9; ms: *m/z* 369 (M^+).

Anal. Calcd for $C_{19}H_{19}N_3O_5$: C, 61.79; H, 5.15; N, 11.38. Found: C, 61.87; H, 5.19; N, 11.31.

10-Isobutyl-2,7-dinitro-9(10H)-acridinone (9g)

This compound was prepared from 77 mg (0.25 mmol) of **5** and 20 mg (0.027 mL, 0.28 mmol) of isobutylamine to give 65 mg (76%) of **9g** as a yellow powder, mp 284–285°C. IR: 1652, 1530, 1330 cm^{-1}; ^1H NMR (DMSO-d_6): δ 8.99 (d, $J = 2.7$ Hz, 2 H), 8.55 (dd, $J = 9.3$, 2.7 Hz, 2 H), 8.24 (d, $J = 9.3$ Hz, 2 H), 4.56 (d, $J = 7.7$ Hz, 2 H), 2.27 (nonet, $J = 6.6$ Hz, 1 H), 0.99 (d, $J = 6.6$ Hz, 6 H); ^{13}C NMR (DMSO-d_6): δ 175.8, 145.6, 141.8, 128.3, 122.8, 121.1, 119.6, 52.1, 27.3, 19.5; ms: *m/z* 341 (M^+).

Anal. Calcd for $C_{17}H_{15}N_3O_5$: C, 59.82; H, 4.40; N, 12.32. Found: C, 59.90; H, 4.42; N, 12.27.

10-(3-Isopropoxypropyl)-2,7-dinitro-9(10H)-acridinone (9h)

This compound was prepared from 77 mg (0.25 mmol) of **5** and 32 mg (0.038 mL, 0.28 mmol) of 3-isopropoxypropylamine to give 71 mg (74%) of **9h** as a yellow powder, mp 200–202°C. IR: 1655, 1524, 1331 cm^{-1}; ^1H NMR (DMSO-d_6): δ 8.87 (d, J = 2.7 Hz, 2 H), 8.49 (dd, J = 9.3, 2.7 Hz, 2 H), 8.06 (d, J = 9.9 Hz, 2 H), 4.56 (t, J = 7.1 Hz, 2 H), 3.56 (m, 3 H), 2.05 (m, 2 H), 1.14 (d, J = 6.0 Hz, 6 H); ^{13}C NMR (DMSO-d_6): δ 175.2, 145.0, 141.6, 128.4, 122.5, 120.8, 118.5, 71.0, 64.0, 44.5, 27.4, 21.9; ms: *m/z* 385 (M^+).

Anal. Calcd for $C_{19}H_{19}N_3O_6$: C, 59.22; H, 4.94; N, 10.91. Found: C, 59.33; H, 4.97; N, 10.79.

Representative Reaction with 2,2′-Difluoro-5-nitrobenzophenone (8): 2-(Benzylamino)-5-nitro-2′-fluorobenzophenone (10a)

This compound was prepared as described for **9a** from 66 mg (0.25 mmol) of **8** and 29.4 mg (0.030 mL, 0.28 mmol) of benzylamine to give 83 mg (95%) of **10a** as a yellow powder, mp 166–168°C. IR: 3288, 1634, 1535, 1330 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.96 (br s, 1 H), 8.38 (t, $J = 2.7$ Hz, 1 H), 8.19 (dd, $J = 9.3$, 2.7 Hz, 1 H), 7.55 (m, 1 H), 7.45 (td, $J = 7.7$, 1.6 Hz, 1 H), 7.40–7.33 (complex, 5 H), 7.32 (t, $J = 7.7$ Hz, 1 H), 7.21 (t, $J = 9.3$ Hz, 1 H), 6.78 (d, $J = 9.3$ Hz, 1 H), 4.62 (d, $J = 5.5$ Hz, 2 H); ^{13}C NMR ($CDCl_3$): δ 195.1, 159.0 (d, $J = 250.8$ Hz), 154.9, 136.4, 136.0, 132.9 (d, $J = 8.3$ Hz), 132.3, 130.4, 129.8 (d, $J = 2.9$ Hz), 129.0, 127.9, 127.1, 127.1 (obscured d), 124.6 (d, $J = 3.4$ Hz), 116.4 (d, $J = 21.5$ Hz), 116.2, 112.1, 47.2; ms: *m/z* 350 (M^+).

Anal. Calcd for $C_{20}H_{15}FN_2O_3$: C, 68.57; H, 4.29; N, 8.00. Found: C, 68.61; H, 4.31; N, 7.96.

2-(Hexylamino)-5-nitro-2′-fluorobenzophenone (10f)

This compound was prepared from 66 mg (0.25 mmol) of **8** and 28 mg (0.036 mL, 0.28 mmol) of hexylamine to give 83 mg (96%) of **10f** as a yellow powder, mp 59–60°C. IR: 3289, 1631, 1534, 1327 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.62 (br s, 1 H), 8.35 (t, $J = 2.7$ Hz, 1 H), 8.23 (dd, $J = 9.3$, 2.7 Hz, 1 H), 7.54 (m, 1 H), 7.43 (td, $J = 7.1$, 1.6 Hz, 1 H), 7.30 (t, $J = 7.1$ Hz, 1 H), 7.21 (t, $J = 9.3$ Hz, 1 H), 6.79 (d, $J = 9.9$ Hz, 1 H), 3.38 (q, $J =$ 6.6 Hz, 2 H), 1.78 (quintet, $J = 7.1$ Hz, 2 H), 1.58–1.28 (complex, 6 H), 0.91 (distorted t, $J = 7.1$ Hz, 3 H); ^{13}C NMR ($CDCl_3$): δ 195.0, 159.0 (d, $J = 250.5$ Hz), 155.1, 135.4, 132.8, (d, $J = 8.3$ Hz), 132.6, 130.4, 129.7 (d, $J = 2.9$ Hz), 127.2 (d, $J = 16.5$ Hz), 124.6 (d, $J = 3.4$ Hz), 116.4 (d, $J = 21.5$ Hz), 115.7 111.6, 43.2, 31.4, 28.7, 26.7, 22.5, 14.0; ms: *m/z* 344 (M^+).

Anal. Calcd for $C_{19}H_{21}FN_2O_3$: C, 66.28; H, 6.10; N, 8.14. Found: C, 66.23; H, 6.13; N, 8.11.

2-(Isobutylamino)-5-nitro-2′-fluorobenzophenone (10g)

This compound was prepared from 66 mg (0.25 mmol) of **8** and 20 mg (0.027 mL, 0.28 mmol) of isobutylamine to give 73 mg (92%) of **10g** as a yellow powder, mp 85–86°C. IR: 3287, 1629, 1583, 1327 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.73 (br s, 1 H), 8.36 (t, $J = 2.7$ Hz, 1 H), 8.22 (dd. $J = 9.3$, 2.7 Hz, 1 H), 7.55 (m, 1 H), 7.44 (td, $J = 7.7$, 1.6 Hz, 1 H), 7.30 (t, $J = 7.7$ Hz, 1 H), 7.21 (t, $J = 9.3$ Hz, 1 H), 6.79 (d, $J = 9.9$ Hz, 1 H), 3.21 (dd, $J =$ 6.6, 5.5 Hz, 2 H), 2.07 (nonet, $J = 6.6$ Hz, 2 H), 1.09 (d, $J = 6.6$ Hz, 6 H); ^{13}C NMR ($CDCl_3$): δ 195.0, 159.0 (d, $J = 250.5$ Hz), 155.2, 135.3, 132.8 (d, $J = 8.0$ Hz), 132.6, 130.4, 129.8 (d, $J = 2.9$ Hz), 127.1 (d, $J = 16.3$ Hz), 124.6 (d, $J = 3.4$ Hz), 116.4 (d, $J =$ 21.5 Hz), 115.6, 111.6, 50.8, 28.0, 20.4; ms: *m/z* 316 (M^+).

Anal. Calcd for $C_{17}H_{17}FN_2O_3$: C, 64.56; H, 5.38; N, 8.86. Found: C, 64.72; H, 5.43; N, 8.77.

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