Synthesis of 10-Aryl- and 10-(Arylmethyl)acridin-9(10*H*)-ones *via* the Reaction of (2-Fluorophenyl)(2-halophenyl)methanones with Benzenamines and Arylmethanamines

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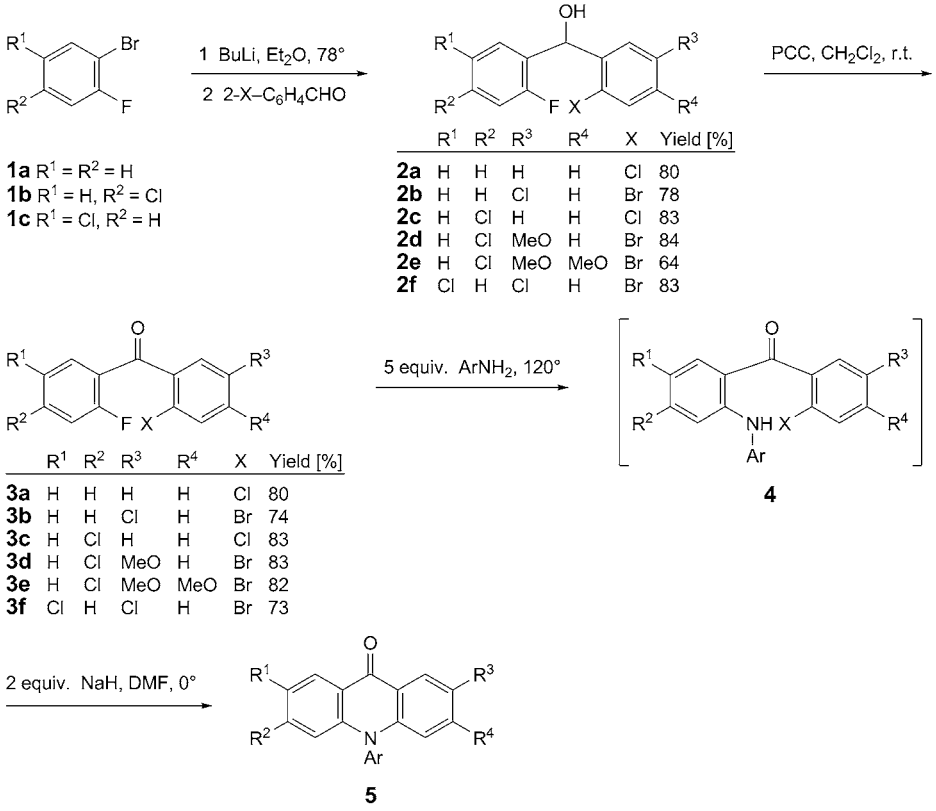
The reaction of 1-fluoro-2-lithiobenzenes, generated from 1-bromo-2-fluorobenzenes **1** and BuLi, with 2-halobenzaldehydes and subsequent oxidation of the resulting alcohols **2** afforded (2-fluorophenyl)(2-halophenyl)methanones **3**, which, on treatment with benzenamines or arylmethanamines, followed by NaH, gave rise efficiently to 10-aryl- or 10-(arylmethyl)acridin-9(10*H*)-ones (**5** or **7**), respectively.

Introduction. – Acridin-9(10*H*)-one derivatives have attracted much attention of not only medicinal but also synthetic chemists, because a number of molecules with this heterocyclic skeleton have been reported to exhibit a variety of biological activities [1][2], and some have been isolated from nature [3]. The acridin-9(10*H*)-one structure has been constructed by intramolecular *Friedel–Crafts* acylation of 2-(arylamino)benzoic acids with appropriate acid catalysts under harsh conditions [2][4], while several direct methods for the synthesis of 10-substituted acridin-9(10*H*)-ones have recently reported by several groups [5]. In this article, we describe a new method for the preparation of 10-substituted acridin-9(10*H*)-ones starting with 1-bromo-2-fluorobenzenes **1** and 2-halobenzaldehydes. We found that 10-aryl- and 10-(arylmethyl)acridin-9(10*H*)-ones, **5** and **7**, respectively, which are rather difficult to prepare by previously described methods [2][4][5], can be obtained by the substitution reaction of (2-fluorophenyl)(2-halophenyl)methanones **3**, derived by an easy two-step sequence from these starting materials, with benzenamines and arylmethanamines, followed by cyclization of the resulting intermediates **4** and **6**, respectively, by treatment with NaH. After completion of this work, a similar approach, which allows the synthesis of fluorinated acridin-9(10*H*)-ones by the reaction of highly fluorinated benzophenones with primary amines under heating, has been reported as a special case [5d].

Results and Discussion. – The key precursors, (2-fluorophenyl)(2-halophenyl)methanones **3**, were prepared as outlined in *Scheme 1*. 1-Bromo-2-fluorobenzenes **1** were treated with BuLi in Et_2O at $-78°$ to generate 1-fluoro-2-lithiobenzenes, which were allowed to react with 2-halobenzaldehydes to give (2-fluorophenyl)(2-halophenyl)methanols **2**. These were oxidized with pyridinium chlorochomates (PCC) in CH_2Cl_2 at room temperature to give **3** in satisfactory yields.

Scheme 1



1a $R^1 = R^2 = H$
1b $R^1 = H$, $R^2 = Cl$
1c $R^1 = Cl$, $R^2 = H$

	R^1	R^2	R^3	R^4	X	Yield [%]
2a	H	H	H	H	Cl	80
2b	H	H	Cl	H	Br	78
2c	H	Cl	H	H	Cl	83
2d	H	Cl	MeO	H	Br	84
2e	H	Cl	MeO	MeO	Br	64
2f	Cl	H	Cl	H	Br	83

	R^1	R^2	R^3	R^4	X	Yield [%]
3a	H	H	H	H	Cl	80
3b	H	H	Cl	H	Br	74
3c	H	Cl	H	H	Cl	83
3d	H	Cl	MeO	H	Br	83
3e	H	Cl	MeO	MeO	Br	82
3f	Cl	H	Cl	H	Br	73

4

5

With these ketones **3** in hand, we tried to prepare 10-arylacridin-9(10*H*)-ones **5** in a one-pot reaction from **3** and benzenamines. As indicated in *Scheme 1*, compounds **3** were heated with excess benzenamines at 120°. The substitution reaction proceeded slowly, and it took *ca.* 10 h, until TLC analyses (silica gel) revealed disappearance of **3**. The cooled mixtures including the resulting substitution products **4** were dissolved in DMF, and 2 equiv. of NaH were added at 0°. At this temperature, cyclization proceeded rapidly to give, after aqueous workup and subsequent recrystallization of the resulting precipitate, the desired products **5** in good yields, as compiled in *Table 1*.

Subsequently, the preparation of 10-(arylmethyl)acridin-9(10*H*)-ones **7** was achieved by a similar one-pot reaction as described above for the preparation of **5** (*Scheme 2*). Thus, heating of mixtures of **3** and arylmethanamines proceeded more smoothly even at lower temperature (100°) than that of the reaction of **3** with benzenamines to form (arylmethyl)amino-substituted intermediates **6** more cleanly than the intermediates **4** (TLC on silica gel). Cyclization of the adducts **6** with NaH required room temperature, and it proceeded slowly to give, after aqueous workup and subsequent recrystallization of the resulting precipitate, the desired products **7** in fair-to-good yields, as collected in *Table 2*.

Table 1. *Preparation of 10-Arylacridin-9(10*H*)-ones* **5**

Entry	**3**	Ar	**5**	Yield[a]) [%]
1	**3a** $R^1 = R^2 = R^3 = R^4 = H$, X = Cl	Ph	**5a**	85
2	**3b** $R^1 = R^2 = R^4 = H$, R^3 = Cl, X = Br	4-MeO–C_6H_4	**5b**	76
3	**3c** $R^1 = R^3 = R^4 = H$, R^2 = X = Cl	3-Cl–C_6H_4	**5c**	77
4	**3c**	4-Cl–C_6H_4	**5d**	86
5	**3c**	4-MeO–C_6H_4	**5e**	79
6	**3d** $R^1 = R^4 = H$, R^2 = Cl, R^3 = MeO, X = Br	4-Me–C_6H_4	**5f**	79
7	**3e** $R^1 = H$, R^2 = Cl, $R^3 = R^4$ = MeO, X = Br	Ph	**5g**	84
8	**3f** $R^1 = R^3$ = Cl, $R^2 = R^4 = H$, X = Br	Ph	**5h**	81
9	**3f**	4-Me–C_6H_4	**5i**	86

[a]) Yields of the isolated products.

Scheme 2

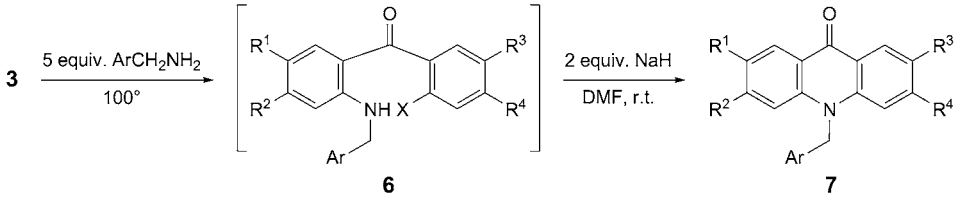


Table 2. *Preparation of 10-(Arylmethyl)acridin-9(10*H*)-ones* **7**

Entry	**3**	Ar	**7**	Yield[a]) [%]
1	**3a** $R^1 = R^2 = R^3 = R^4 = H$, X = Cl	Ph	**7a**	80
2	**3b** $R^1 = R^2 = R^4 = H$, R^3 = Cl, X = Br	Ph	**7b**	74
3	**3b**	4-Cl–C_6H_4	**7c**	67
4	**3b**	4-MeO–C_6H_4	**7d**	82
5	**3c** $R^1 = R^3 = R^4 = H$, R^2 = X = Cl	4-Me–C_6H_4	**7e**	80
6	**3c**	4-MeO–C_6H_4	**7f**	71
7	**3d** $R^1 = R^4 = H$, R^2 = Cl, R^3 = MeO, X = Br	4-MeO–C_6H_4	**7g**	68
8	**3f** $R^1 = R^3$ = Cl, $R^2 = R^4 = H$, X = Br	Ph	**7h**	81
9	**3f**	4-MeO–C_6H_4	**7i**	69

[a]) Yields of the isolated products.

In conclusion, we have shown that 10-substituted acridin-9(10*H*)-ones can be prepared *via* the one-pot reaction of (2-fluorophenyl)(2-halophenyl)methanones, derived by an easy two-step sequence starting from readily available 1-bromo-2-fluorobenzenes and 2-halobenzaldehydes, with benzenamines and arylmethanamines, respectively. Further synthetic applications of the present methodology are currently being explored to develop methods for preparing related heterocycles.

Experimental Part

General. All of the org. solvents used in this study were dried over appropriate drying agents and distilled prior to use. BuLi was supplied by *Asia Lithium Corporation*. All other chemicals were commercially available. TLC: *Merck* silica gel *60 PF_{254}*. Column chromatography (CC): *Wako Gel C-200E*.M.p.: *Laboratory Devices MEL-TEMP II* melting-point apparatus; uncorrected. IR Spectra: *Perkin–Elmer Spectrum65* FT-IR spectrophotometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H-NMR Spectra: *JEOL ECP500* FT NMR spectrometer at 500 MHz or *JEOL LA400* FT NMR spectrometer at 400 MHz; in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, J in Hz. ^{13}C-NMR Spectra: *JEOL ECP500* FT NMR spectrometer at 125 MHz; in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard. EI-MS (70 eV): *JEOL JMS AX505 HA* spectrometer; in *m/z* (rel. %).

(2-Chlorophenyl)(2-fluorophenyl)methanol (**2a**). *Representative Procedure.* To a stirred soln. of *1-bromo-2-fluorobenzene* (**1a**; 0.90 g, 5.0 mmol) in Et_2O (20 ml) at $-78°$ were added successively BuLi (1.6M soln. in hexane; 5.0 mmol) and 2-chlorobenzaldehyde (0.70 g, 5.0 mmol). After 10 min, sat. aq. NH_4Cl soln. (50 ml) was added. The mixture was warmed to r.t., and the mixture was extracted with AcOEt (3×25 ml). The combined extracts were washed with brine (30 ml), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by CC (SiO_2; AcOEt/hexane 1:8) to give **2a** (0.94 g, 80%). Colorless oil. R_f 0.32. IR (neat): 3334, 1615. ^{1}H-NMR (500 MHz): 2.45 (*s*, 1 H); 6.48 (*s*, 1 H); 7.05 (*ddd*, $J = 9.2, 7.4, 2.3$, 1 H); 7.10 (*td*, $J = 7.4, 2.3$, 1 H); 7.22–7.34 (*m*, 4 H); 7.35 (*dd*, $J = 8.0, 2.3$, 1 H); 7.55 (*dd*, $J = 8.0, 1.7$, 1 H). Anal. calc. for $C_{13}H_{10}ClFO$ (236.67): C 65.97, H 4.26; found: C 65.96, H 4.25.

(2-Bromo-5-chlorophenyl)(2-fluorophenyl)methanol (**2b**). Colorless oil. R_f (AcOEt/hexane 1:20) 0.36. IR (neat): 3311, 1615. ^{1}H-NMR (500 MHz): 2.47 (*d*, $J = 4.6$, 1 H); 6.38 (*d*, $J = 4.6$, 1 H); 7.06–7.22 (*m*, 3 H); 7.29–7.40 (*m*, 2 H); 7.47 (*d*, $J = 8.6$, 1 H); 7.61 (*d*, $J = 2.3$, 1 H). Anal. calc. for $C_{13}H_9BrClFO$ (315.57): C 49.48, H 2.87; found: C 49.45, H 2.94.

(4-Chloro-2-fluorophenyl)(2-chlorophenyl)methanol (**2c**). Colorless oil. R_f (THF/hexane 1:5) 0.39. IR (KBr): 3305, 1610. ^{1}H-NMR (400 MHz): 2.47 (*d*, $J = 3.9$, 1 H); 6.44 (*d*, $J = 3.9$, 1 H); 7.08–7.13 (*m*, 2 H); 7.23 (*d*, $J = 7.8$, 1 H); 7.27–7.38 (*m*, 3 H); 7.53 (*dd*, $J = 7.8, 2.0$, 1 H). Anal. calc. for $C_{13}H_9Cl_2FO$ (271.11): C 57.59, H 3.35; found: C 57.50, H 3.45.

(2-Bromo-5-methoxyphenyl)(4-chloro-2-fluorophenyl)methanol (**2d**). Pale-yellow oil. R_f (THF/hexane 1:5) 0.25. IR (neat): 3371, 1611. ^{1}H-NMR (400 MHz): 2.47 (*d*, $J = 3.9$, 1 H); 3.82 (*s*, 3 H); 6.33 (*d*, $J = 3.9$, 1 H); 6.75 (*dd*, $J = 8.8, 2.9$, 1 H); 7.09–7.11 (*m*, 3 H); 7.18 (*t*, $J = 7.8$, 1 H); 7.43 (*d*, $J = 8.8$, 1 H). Anal. calc. for $C_{14}H_{11}BrClFO_2$ (345.59): C 48.66, H 3.21; found: C 48.57, H 3.48.

(2-Bromo-4,5-dimethoxyphenyl)(4-chloro-2-fluorophenyl)methanol (**2e**). Colorless oil. R_f (THF/hexane 1:5) 0.23. IR (neat): 3448, 1605. ^{1}H-NMR (500 MHz): 2.44 (*d*, $J = 3.7$, 1 H); 3.85 (*s*, 3 H); 3.88 (*s*, 3 H); 6.32 (*d*, $J = 3.7$, 1 H); 7.01 (*s*, 1 H); 7.05 (*s*, 1 H); 7.09–7.12 (*m*, 2 H); 7.20 (*dd*, $J = 8.7, 7.8$, 1 H). Anal. calc. for $C_{15}H_{13}BrClFO_3$ (375.62): C 47.96, H 3.49; found: C 47.90, H 3.50.

(2-Bromo-5-chlorophenyl)(5-chloro-2-fluorophenyl)methanol (**2f**). White solid. M.p. 82–84° (hexane/THF). IR (KBr): 3234. ^{1}H-NMR (400 MHz): 2.49 (*d*, $J = 3.9$, 1 H); 6.33 (*d*, $J = 3.9$, 1 H); 7.02 (*dd*, $J = 9.8, 8.8$, 1 H); 7.19 (*dd*, $J = 8.8, 2.9$, 1 H); 7.23 (*dd*, $J = 4.9, 2.9$, 1 H); 7.25–7.30 (*m*, 1 H); 7.49 (*d*, $J = 8.8$, 1 H); 7.54 (*d*, $J = 2.0$, 1 H). Anal. calc. for $C_{13}H_8BrCl_2FO$ (350.01): C 44.61, H 2.30; found: C 44.50, H 2.29.

Diarylmethanones **3**. These compounds were prepared by the oxidation of **2** with PCC under the conditions reported previously by us in [6].

(2-Chlorophenyl)(2-fluorophenyl)methanone (**3a**). Colorless oil. R_f (AcOEt/hexane 1:16) 0.39. IR (neat): 1673, 1609. ^{1}H-NMR (500 MHz): 7.10 (*dd*, $J = 9.7, 8.7$, 1 H); 7.26 (*ddd*, $J = 7.8, 7.3, 1.0$, 1 H); 7.34–7.48 (*m*, 4 H); 7.53–7.59 (*m*, 1 H); 7.76 (*td*, $J = 7.8, 2.0$, 1 H). Anal. calc. for $C_{13}H_8ClFO$ (234.65): C 66.54, H 3.44; found: C 66.61, H 3.51.

(2-Bromo-5-chlorophenyl)(2-fluorophenyl)methanone (**3b**). White solid. M.p. 110–112° (hexane/Et_2O). IR (KBr): 1662, 1607. ^{1}H-NMR (400 MHz): 7.12 (*dd*, $J = 9.9, 9.2$, 1 H); 7.27–7.35 (*m*, 2 H); 7.38 (*d*, $J = 2.3$, 1 H); 7.55 (*d*, $J = 9.2$, 1 H); 7.58–7.65 (*m*, 1 H); 7.79 (*td*, $J = 7.6, 2.3$, 1 H). Anal. calc. for $C_{13}H_7BrClFO$ (313.55): C 49.80, H 2.25; found: C 49.70, H 2.29.

(4-Chloro-2-fluorophenyl)(2-chlorophenyl)methanone (**3c**). White solid. M.p. 62–64° (hexane/Et_2O). IR (KBr): 1664, 1601. ^{1}H-NMR (400 MHz): 7.15 (*dd*, *J* = 10.7, 2.0, 1 H); 7.27 (*dd*, *J* = 7.8, 2.0, 1 H); 7.38 (*ddd*, *J* = 8.8, 7.8, 2.0, 1 H); 7.42–7.48 (*m*, 3 H); 7.73 (*t*, *J* = 7.8, 1 H). Anal. calc. for $C_{13}H_7Cl_2FO$ (269.10): C 58.02, H 2.62; found: C 57.95, H 2.85.

(2-Bromo-5-methoxyphenyl)(4-chloro-2-fluorophenyl)methanone (**3d**). White solid. M.p. 123–125° (hexane/AcOEt). IR (KBr): 1656. ^{1}H-NMR (400 MHz): 3.82 (*s*, 3 H); 6.90–6.93 (*m*, 2 H); 7.15 (*dd*, *J* = 10.7, 2.9, 1 H); 7.26 (*dd*, *J* = 8.8, 2.0, 1 H); 7.49 (*d*, *J* = 8.8, 1 H); 7.72 (*dd*, *J* = 8.8, 7.8, 1 H). Anal. calc. for $C_{14}H_9BrClFO_2$ (343.58): C 48.94, H 2.64; found: C 48.70, H 2.62.

(2-Bromo-4,5-dimethoxyphenyl)(4-chloro-2-fluorophenyl)methanone (**3e**). Colorless oil. R_f (THF/hexane 1: 4) 0.32. IR (KBr): 1667. ^{1}H-NMR (500 MHz): 3.88 (*s*, 3 H); 3.94 (*s*, 3 H); 7.01 (*s*, 1 H); 7.05 (*s*, 1 H); 7.15 (*dd*, *J* = 8.2, 1.8, 1 H); 7.25 (*dd*, *J* = 8.2, 1.4, 1 H); 7.65 (*dd*, *J* = 8.2, 7.8, 1 H). Anal. calc. for $C_{15}H_{11}BrClFO_3$ (373.60): C 48.22, H 2.97; found: C 48.06, H 2.83.

(2-Bromo-5-chlorophenyl)(5-chloro-2-fluorophenyl)methanone (**3f**). White solid. M.p. 106–108° (hexane/AcOEt). IR (KBr): 1655, 1602. ^{1}H-NMR (500 MHz): 7.08 (*dd*, *J* = 9.7, 9.2, 1 H); 7.35 (*dd*, *J* = 8.6, 2.3, 1 H); 7.39 (*d*, *J* = 2.3, 1 H); 7.52–7.57 (*m*, 2 H); 7.77 (*dd*, *J* = 6.3, 2.3, 1 H). Anal. calc. for $C_{13}H_6BrCl_2FO$ (347.99): C 44.87, H 1.74; found: C 44.62, H 1.85.

*10-Phenylacridin-9(10*H*)-one* (**5a**) [7]. *Representative Procedure.* A mixture of **3a** (0.23 g, 1.0 mmol) and $PhNH_2$ (0.46 g, 5.0 mmol) was heated at 120° until consumption of **3a** had been confirmed by TLC (SiO_2; AcOEt/hexane 1 : 5; *ca.* 10 h). The cooled mixture was dissolved in DMF (6 ml), and NaH (60 % in mineral oil; 80 mg, 2.0 mmol) was added to the stirred soln. at 0°. Stirring was continued at the same temp. for 20 min before H_2O (30 ml) and sat. aq. NH_4Cl soln. (5 ml) were added. The precipitate was collected by filtration and recrystallized from hexane/CH_2Cl_2 to give **5a** (0.23 g, 85%). White solid. M.p. 274–277° ([7]: 276°). IR (KBr): 1634. ^{1}H-NMR (500 MHz): 6.75 (*d*, *J* = 9.2, 2 H); 7.28 (*dd*, *J* = 7.6, 6.9, 2 H); 7.38 (*d*, *J* = 7.6, 2 H); 7.50 (*td*, *J* = 7.6, 1.5, 2 H); 7.65 (*t*, *J* = 7.6, 1 H); 7.72 (*t*, *J* = 7.6, 2 H); 8.59 (*d*, *J* = 6.9, 2 H).

*2-Chloro-10-(4-methoxyphenyl)acridin-9(10*H*)-one* (**5b**). Pale-yellow solid. M.p. 228–230° (hexane/CH_2Cl_2). IR (KBr): 1635. ^{1}H-NMR (500 MHz): 3.96 (*s*, 3 H); 6.78 (*d*, *J* = 9.2, 1 H); 6.82 (*d*, *J* = 8.6, 1 H); 7.20 (*d*, *J* = 9.2, 2 H); 7.26 (*d*, *J* = 9.2, 2 H); 7.29 (*d*, *J* = 7.4, 1 H); 7.42 (*dd*, *J* = 9.2, 2.3, 1 H); 7.52 (*ddd*, *J* = 8.6, 6.9, 1.7, 1 H); 8.53 (*d*, *J* = 2.3, 1 H); 8.55 (*dd*, *J* = 8.0, 1.7, 1 H). ^{13}C-NMR: 55.64; 116.25; 116.96; 118.70; 121.69; 121.79; 122.56; 126.30; 127.24; 127.42; 130.81; 130.97; 133.32; 133.51; 141.87; 143.35; 160.28; 177.06. MS: 335 (100, M^+). Anal. calc. for $C_{20}H_{14}ClNO_2$ (335.78): C 71.54, H 4.20, N 4.17; found: C 71.49, H 4.38, N 4.06.

*3-Chloro-10-(3-chlorophenyl)acridin-9(10*H*)-one* (**5c**). White solid. M.p. 250–253° (hexane/CH_2Cl_2). IR (KBr): 1638, 1609. ^{1}H-NMR (500 MHz): 6.71–6.73 (*m*, 2 H); 7.25 (*dd*, *J* = 8.6, 1.7, 1 H); 7.30–7.34 (*m*, 2 H); 7.41 (*s*, 1 H); 7.55 (*ddd*, *J* = 8.0, 6.9, 1.1, 1 H); 7.69–7.71 (*m*, 2 H); 8.51 (*d*, *J* = 8.6, 1 H); 8.56 (*dd*, *J* = 8.0, 1.1, 1 H). ^{13}C-NMR: 116.00; 116.63; 120.19; 121.92; 122.34; 122.56; 127.41; 128.31; 129.19; 130.30; 130.46; 132.32; 133.75; 136.88; 139.48; 139.94; 142.81; 143.38; 177.31. MS: 339 (100, M^+). Anal. calc. for $C_{19}H_{11}Cl_2NO$ (340.20): C 67.08, H 3.26, N 4.12; found: C 66.86, H 3.32, N 3.85.

*3-Chloro-10-(4-chlorophenyl)acridin-9(10*H*)-one* (**5d**). White solid. M.p. 266–268° (hexane/CH_2Cl_2). IR (KBr): 1639, 1610. ^{1}H-NMR (500 MHz): 6.71–6.73 (*m*, 2 H); 7.25 (*dd*, *J* = 8.6, 1.7, 1 H); 7.30–7.34 (*m*, 3 H); 7.53 (*ddd*, *J* = 8.0, 6.9, 1.1, 1 H); 7.72 (*d*, *J* = 8.6, 2 H); 8.51 (*d*, *J* = 8.6, 1 H); 8.56 (*dd*, *J* = 8.0, 1.1, 1 H). ^{13}C-NMR: 116.00; 116.63; 120.23; 121.95; 122.27; 122.49; 127.41; 129.29; 131.36; 131.72; 133.71; 136.08; 136.80; 139.91; 142.94; 143.51; 177.33. MS: 339 (100, M^+). Anal. calc. for $C_{19}H_{11}Cl_2NO$ (340.21): C 67.08, H 3.26, N 4.12; found: C 66.85, H 3.50, N 3.96.

*3-Chloro-10-(4-methoxyphenyl)acridin-9(10*H*)-one* (**5e**). White solid. M.p. 210–212° (hexane/CH_2Cl_2). IR (KBr): 1637, 1607. ^{1}H-NMR (500 MHz): 3.96 (*s*, 3 H); 6.78–6.79 (*m*, 2 H); 7.20–7.30 (*m*, 6 H); 7.52 (*dd*, *J* = 7.5, 6.9, 1 H); 8.48–8.56 (*m*, 2 H). ^{13}C-NMR: 55.67; 116.36 (two overlapped C-atoms); 117.00; 120.23; 121.96; 122.17; 127.21; 129.02; 130.71; 130.81 (two overlapped C-atoms); 133.50; 139.67; 143.52; 144.10; 160.32; 177.47. MS: 335 (100, M^+). Anal. calc. for $C_{20}H_{14}ClNO_2$ (335.78): C 71.54, H 4.20, N 4.17; found: C 71.38, H 4.29, N 4.16.

*6-Chloro-2-methoxy-10-(4-methylphenyl)acridin-9(10*H*)-one* (**5f**). Pale-yellow solid. M.p. 240–242° (hexane/CH_2Cl_2). IR (KBr): 1638, 1616, 1597. ^{1}H-NMR (500 MHz): 2.55 (*s*, 3 H); 3.94 (*s*, 3 H); 6.74 (*d*, *J* = 9.2, 1 H); 6.78 (*s*, 1 H); 7.15 (*dd*, *J* = 9.2, 2.3, 1 H); 7.20–7.23 (*m*, 3 H); 7.50 (*d*, *J* = 8.0, 2 H); 7.94 (*d*,

$J = 2.3$, 1 H); 8.52 (*d*, $J = 8.6$, 1 H). ^{13}C-NMR: 21.42; 61.99; 105.91; 116.14; 118.85; 121.94; 124.21; 124.28; 126.99; 128.97; 129.47; 131.86; 135.76; 139.40; 139.98; 143.32; 146.57; 154.96; 177.18. MS: 349 (100, M^+). Anal. calc. for $C_{21}H_{16}ClNO_2$ (349.81): C 72.10, H 4.61, N 4.00; found: C 72.12, H 4.64, N 4.03.

*6-Chloro-2,3-dimethoxy-10-phenylacridin-9(10*H*)-one* (**5g**). White solid. M.p. 251–253° (hexane/$CHCl_3$). IR (KBr): 1617, 1595. ^{1}H-NMR (500 MHz): 3.64 (*s*, 3 H); 4.02 (*s*, 3 H); 6.07 (*s*, 1 H); 6.72 (*d*, $J =$ 1.7, 1 H); 7.22 (*dd*, $J = 8.6$, 1.7, 1 H); 7.38 (*dd*, $J = 8.6$, 1.1, 2 H); 7.69 (*t*, $J = 7.4$, 1 H); 7.74 (*dd*, $J = 8.6$, 7.4, 2 H); 7.93 (*s*, 1 H); 8.52 (*d*, $J = 8.6$, 1 H). ^{13}C-NMR: 55.75; 56.25; 98.42; 106.36; 115.75; 116.05; 119.78; 122.08; 128.83; 129.81; 130.04; 131.27; 138.54; 138.81; 139.42; 143.18; 145.92; 154.56; 175.88. MS: 365 (100, M^+). Anal. calc. for $C_{21}H_{16}ClNO_3$ (365.81): C 68.95, H 4.41, N 3.83; found: C 68.90, H 4.48, N 3.70.

*2,7-Dichloro-10-phenylacridin-9(10*H*)-one* (**5h**). White solid. M.p. 271–273° (hexane/CH_2Cl_2). IR (KBr): 1639. ^{1}H-NMR (500 MHz): 6.71 (*d*, $J = 8.0$, 2 H); 7.36 (*d*, $J = 8.0$, 2 H); 7.43 (*dd*, $J = 8.0$, 2.9, 2 H); 7.68 (*t*, $J = 7.4$, 1 H); 7.73 (*dd*, $J = 8.0$, 7.4, 2 H); 8.50 (*d*, $J = 2.9$, 2 H). ^{13}C-NMR: 118.69; 122.34; 126.35; 127.93; 129.72; 130.08; 131.36; 133.71; 138.31; 141.35; 175.91. MS: 339 (100, M^+). Anal. calc. for $C_{19}H_{11}Cl_2NO$ (340.20): C 67.08, H 3.26, N 4.12; found: C 67.06, H 3.29, N 4.08.

*2,7-Dichloro-10-(4-methylphenyl)acridin-9(10*H*)-one* (**5i**). White solid. M.p. 329–331° (hexane/CH_2Cl_2). IR (KBr): 1637, 1621, 1609. ^{1}H-NMR (500 MHz): 2.55 (*s*, 3 H); 6.75 (*d*, $J = 9.2$, 2 H); 7.22 (*d*, $J = 8.0$, 2 H); 7.42 (*dd*, $J = 8.0$, 2.9, 2 H); 7.51 (*d*, $J = 8.0$, 2 H); 8.49 (*d*, $J = 2.9$, 2 H). ^{13}C-NMR: 21.36; 118.82; 122.42; 126.35; 126.37; 127.89; 131.94; 133.69; 135.58; 140.31; 141.51; 176.03. MS: 353 (100, M^+). Anal. calc. for $C_{20}H_{13}Cl_2NO$ (354.23): C 67.81, H 3.70, N 3.95; found: C 67.72, H 3.82, N 4.05.

*10-(Phenylmethyl)acridin-9(10*H*)-one* (**7a**) [8]. *Representative Procedure.* A mixture of **3a** (0.23 g, 1.0 mmol) and $BnNH_2$ (0.53 g, 5.0 mmol) was heated at 100° until consumption of **3a** had been confirmed by TLC (SiO_2; AcOEt/hexane 1:3; *ca.* 5 h). The mixture was cooled to r.t. and dissolved in DMF (6 ml). Then, NaH (60% in mineral oil; 80 mg, 2.0 mmol) was added, and the mixture was stirred overnight at the same temp. To the cooled (0°) mixture were added H_2O (30 ml) and sat. aq. NH_4Cl soln. (5 ml). The precipitate was collected by filtration and recrystallized from hexane/CH_2Cl_2 to give **7a** (0.23 g, 80%). Yellow solid. M.p. 178–180° ([8a]: 180–181°). The ^{1}H-NMR data for this product were identical to those reported in [8b].

*2-Chloro-10-(phenylmethyl)acridin-9(10*H*)-one* (**7b**). Yellow solid. M.p. 194–196° (hexane/CH_2Cl_2). IR (KBr): 1630. ^{1}H-NMR (500 MHz): 5.59 (*s*, 2 H); 7.19 (*d*, $J = 6.9$, 2 H); 7.29–7.38 (*m*, 6 H); 7.55 (*dd*, $J = 9.2$, 2.9, 1 H); 7.65 (*ddd*, $J = 9.2$, 7.4, 1.7, 1 H); 8.54 (*d*, $J = 2.9$, 1 H); 8.57 (*dd*, $J = 8.0$, 1.7, 1 H). ^{13}C-NMR: 50.91; 115.23; 117.03; 121.99; 122.42; 123.38; 125.54; 126.89; 127.60; 127.82; 127.98; 129.33; 134.07; 134.38; 135.01; 140.91; 142.39; 177.13. MS: 319 (100, M^+). Anal. calc. for $C_{20}H_{14}ClNO$ (319.78): C 75.12, H 4.41, N 4.38; found: C 74.91, H 4.26, N 4.28.

*2-Chloro-10-[(4-chlorophenyl)methyl]acridin-9(10*H*)-one* (**7c**). Yellow solid. M.p. 221–223° (hexane/CH_2Cl_2). IR (KBr): 1631. ^{1}H-NMR (500 MHz): 5.55 (*s*, 2 H); 7.13 (*d*, $J = 8.0$, 2 H); 7.25 (*d*, $J = 9.2$, 1 H); 7.30–7.35 (*m*, 4 H); 7.56 (*dd*, $J = 9.2$, 2.9, 1 H); 7.66 (*dd*, $J = 8.0$, 7.4, 1 H); 8.54 (*d*, $J = 2.9$, 1 H); 8.58 (*d*, $J = 8.0$, 1 H). ^{13}C-NMR: 50.34; 114.98; 116.78; 122.14; 122.41; 123.39; 126.99 (two overlapped C-atoms); 127.74; 127.90; 129.53; 133.52; 133.89; 134.14; 134.46; 140.70; 142.18; 177.03. MS: 353 (100, M^+). Anal. calc. for $C_{20}H_{13}Cl_2NO$ (354.23): C 67.81, H 3.70, N 3.95; found: C 68.01, H 3.62, N 4.03.

*2-Chloro-10-[(4-methoxyphenyl)methyl]acridin-9(10*H*)-one* (**7d**). Yellow solid. M.p. 205–207° (hexane/CH_2Cl_2). IR (KBr): 1634. ^{1}H-NMR (500 MHz): 3.79 (*s*, 3 H); 5.53 (*s*, 2 H); 6.89 (*d*, $J = 9.2$, 2 H); 7.10 (*d*, $J = 9.2$, 2 H); 7.30–7.33 (*m*, 2 H); 7.38 (*d*, $J = 8.6$, 1 H); 7.56 (*dd*, $J = 9.2$, 2.3, 1 H); 7.66 (*dd*, $J = 8.6$, 6.9, 1 H); 8.54 (*d*, $J = 2.3$, 1 H); 8.57 (*d*, $J = 8.0$, 1 H). ^{13}C-NMR: 50.36; 55.27; 114.68; 115.28; 117.11; 121.92; 122.33; 123.28; 126.72; 126.77; 127.49; 127.72 (two overlapped C-atoms); 134.02; 134.34; 140.84; 142.33; 159.27; 177.11. MS: 349 (100, M^+). Anal. calc. for $C_{21}H_{16}ClNO_2$ (349.81): C 72.10, H 4.61, N 4.00; found: C 72.26, H 4.65, N 3.73.

*3-Chloro-10-[(4-methylphenyl)methyl]acridin-9(10*H*)-one* (**7e**). Yellow solid. M.p. 197–199° (hexane/CH_2Cl_2). IR (KBr): 1637, 1607. ^{1}H-NMR (500 MHz): 2.36 (*s*, 3 H); 5.52 (*s*, 2 H); 7.09 (*d*, $J = 8.0$, 2 H); 7.18 (*d*, $J = 8.0$, 2 H); 7.25 (*d*, $J = 1.7$, 1 H); 7.31–7.36 (*m*, 3 H); 7.64 (*ddd*, $J = 8.6$, 6.9, 1.7, 1 H); 8.52 (*d*, $J =$ 8.6, 1 H); 8.57 (*dd*, $J = 8.0$, 1.7, 1 H). ^{13}C-NMR: 21.08; 50.73; 114.92; 115.41; 120.95; 122.09; 122.31; 122.68; 125.49; 127.71; 129.42; 130.01; 131.69; 134.27; 137.78; 140.47; 142.52; 143.24; 177.51. MS: 333 (100, M^+). Anal. calc. for $C_{21}H_{16}ClNO$ (333.81): C 75.56, H 4.83, N 4.20; found: C 75.43, H 4.87, N 4.08.

*3-Chloro-10-[(4-methoxyphenyl)methyl]acridin-9(10*H*)-one* (**7f**). Yellow solid. M.p. 199–201° (hexane/CH_2Cl_2). IR (KBr): 1637. ^{1}H-NMR (500 MHz): 3.80 (*s*, 3 H); 5.50 (*s*, 2 H); 6.91 (*d*, *J* = 8.6, 2 H); 7.12 (*d*, *J* = 8.6, 2 H); 7.25 (*dd*, *J* = 8.0, 1.7, 1 H); 7.32 (*dd*, *J* = 8.0, 6.9, 1 H); 7.36 (*d*, *J* = 1.7, 1 H); 7.37 (*d*, *J* = 7.4, 1 H); 7.65 (*ddd*, *J* = 8.6, 6.9, 1.7, 1 H); 8.52 (*d*, *J* = 8.6, 1 H); 8.57 (*dd*, *J* = 8.0, 1.7, 1 H). ^{13}C-NMR: 50.42; 55.32; 114.75; 114.92; 115.40; 120.93; 122.10; 122.28; 122.67; 126.53; 126.77; 127.72; 129.43; 134.29; 140.48; 142.50; 143.24; 159.31; 177.50. MS: 349 (100, M^+). Anal. calc. for $C_{21}H_{16}ClNO_2$ (349.81): C 72.10, H 4.61, N 4.00; found: C 72.07, H 4.62, N 3.73.

*6-Chloro-2-methoxy-10-[(4-methoxyphenyl)methyl]acridin-9(10*H*)-one* (**7g**). Yellow solid. M.p. 205–207° (hexane/CH_2Cl_2). IR (KBr): 1637, 1619. ^{1}H-NMR (500 MHz): 3.79 (*s*, 3 H); 3.94 (*s*, 3 H); 5.50 (*s*, 2 H); 6.89 (*d*, *J* = 8.6, 2 H); 7.10 (*d*, *J* = 8.6, 2 H); 7.24 (*d*, *J* = 8.6, 1 H); 7.28 (*dd*, *J* = 9.2, 2.9, 1 H); 7.33 (*d*, *J* = 9.2, 1 H); 7.36 (*s*, 1 H); 7.96 (*d*, *J* = 2.9, 1 H); 8.53 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR: 50.40; 55.32; 55.82; 106.69; 114.67; 114.74; 117.20; 120.16; 121.98; 124.82; 126.65; 126.74 (two overlapped C-atoms); 129.44; 137.19; 140.25; 142.73; 155.00; 159.33; 176.98. MS: 379 (100, M^+). Anal. calc. for $C_{22}H_{18}ClNO_3$ (379.84): C 69.57, H 4.78, N 3.69; found: C 69.67, H 4.70, N 3.68.

*2,7-Dichloro-10-(phenylmethyl)acridin-9(10*H*)-one* (**7h**). Yellow solid. M.p. 280–282° (hexane/$CHCl_3$). IR (KBr): 1630. ^{1}H-NMR (500 MHz): 5.58 (*s*, 2 H); 7.16 (*d*, *J* = 7.4, 2 H); 7.30 (*d*, *J* = 9.2, 2 H); 7.34–7.39 (*m*, 3 H); 7.57 (*dd*, *J* = 9.2, 2.3, 2 H); 8.51 (*d*, *J* = 2.3, 2 H). ^{13}C-NMR: 51.13; 117.14; 123.24; 124.87; 125.46; 127.14; 128.18; 129.55; 134.47; 134.55; 140.92; 176.07. MS: 353 (100, M^+). Anal. calc. for $C_{20}H_{13}Cl_2NO$ (354.23): C 67.81, H 3.70, N 3.95; found: C 67.73, H 3.75, N 3.86.

*2,7-Dichloro-10-[(4-methoxyphenyl)methyl]acridin-9(10*H*)-one* (**7i**). Yellow solid. M.p. 283–285° (hexane/$CHCl_3$). IR (KBr): 1632. ^{1}H-NMR (500 MHz): 3.79 (*s*, 3 H); 5.51 (*s*, 2 H); 6.89 (*d*, *J* = 8.6, 2 H); 7.07 (*d*, *J* = 8.6, 2 H); 7.32 (*d*, *J* = 9.2, 2 H); 7.57 (*dd*, *J* = 9.2, 2.9, 2 H); 8.50 (*d*, *J* = 2.9, 2 H). ^{13}C-NMR: 50.56; 55.31; 114.79; 117.18; 123.14; 126.27; 126.67; 126.85; 127.94; 134.37; 140.71; 159.41; 175.99. MS: 383 (100, M^+). Anal. calc. for $C_{21}H_{15}Cl_2NO_2$ (384.26): C 65.64, H 3.93, N 3.65; found: C 65.53, H 3.88, N 3.54.

We are indebted to Mrs. *Miyuki Tanmatsu* of our University for recording mass spectra and performing combustion analyses.

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Received July 3, 2012