A Green Procedure for the Synthesis of 1,8-Dioxodecahydroacridine Derivatives under Microwave Irradiation in Aqueous Media without Catalyst

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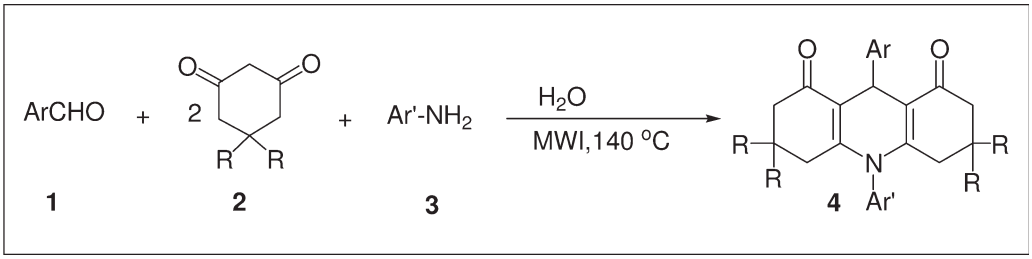

A green procedure for the synthesis of 1,8-dioxo-decahydroacridine derivatives is developed under microwave irradiation without catalyst in water. This method provides several advantages such as excellent yields (86–96%), simple workup procedure, and environment friendliness.

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INTRODUCTION

Water as a solvent has many advantages in organic synthesis, both from economic and from environmental points of view. Water has, therefore, become an attractive medium for many organic reactions. Many important types of heterocyclic compounds, such as triazines [1], acridines [2], quinolines [3], pyridines [4], indoles [5], pyrazines [6], furans [7], and pyrimidines [8] have been synthesized in aqueous media.

4-Aryl-1,4-dihydropyridines (1,4-DHPs) have proved to be valuable as drugs for the treatment of cardiovascular disorders [9] and constitute an important class of calcium channel blockers [10]. It is well established that slight structural modification on the DHP ring may result in remarkable change of pharmacological effect [11–14]. With a 1,4-DHP parent nucleus, acridine-1,8-diones have been shown to have very high lasing efficiencies [15] and used as photoinitiators [16]. Recently, many methods have become available for the synthesis of these important class of derivatives, We have synthesized these compounds from schiff's base and dimedone or 1,3-cyclohexanedione or three-component (aldehyde, dimedone, and arylamines) in glycol under microwave [17,18]. Jin et al. [19] reported that this reaction could be carried out catalyzed by *p*-dodecylben-zensulfonic acid (DBSA) in water. However, these reactions must be carried out by impetus of catalyst or in organic solvents. Wang et al. [20] reported the same reaction proceeded in an ionic medium, and Wang and Miao [21] achieved the reactions in aqueous solvent at traditional heating. The reaction time was 10 h, the yield was 72–75%. Arylamine used was only *p*-toluidine. Microwave-assisted organic reaction using water as solvent has peculiarity of ''safe solvents'' and ''energy efficiency.'' It was widely used in the organic synthesis [22]. In this article, we would like to report the green synthesis of 1,8-dioxo-9,10-diaryl-decahydracidines without catalyst *via* the combination of aqueous solvent and microwave heating, using a variety of arylamines including the anilines contained electron-withdrawing groups and electron-donating groups (Scheme 1).

RESULTS AND DISCUSSION

When treating aldehyde **1** with dimedone or 1,3-cyclohexanedione **2** and primary arylamines **3** under microwave irradiation, the target compound **4** were obtained.

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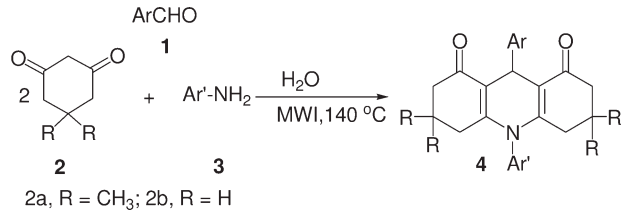
Scheme 1



To demonstrate the efficiency and the applicability of this method, we investigated the reaction of a variety of aromatic aldehydes **1**, dimedone, and a variety of primary arylamines **3** at 140°C in aqueous media. As shown in Table 1, a series of **1** and **3**, in which the aromatic ring contained electron-withdrawing groups (such as halo or nitro) or electron-donating groups (such as methyl or methyloxy), reacted with **2a** under the same reaction conditions to give the corresponding product **4** in good yields (entries 1–14), We thus concluded that there were no obvious electronic effect of the substituents on the aromatic rings. To further expand the scope of the present method, the replacement of dimedone **2a** with 1,3-cyclohexanedione **2b** was examined. To our delight, under the same conditions, the reactions proceeded steadily to afford a series of 1,8-dioxo-decahydroacridine derivatives in good yields (Table 1, entries 15–25).

The structures of all the synthesized compounds were established on the basis of their spectroscopic data (IR and ^{1}H NMR). In addition, the X-ray diffraction analysis of product **4e** [23], **4k** [24], **4l** [25], **4n** [26], was carry out to confirm its structure. The crystal structure of **4k** is shown in Figure 1.

In conclusion, we have developed a green chemistry method for the synthesis of 1,8-dioxo-decahydroacridine derivatives. Excellent yields were obtained not only for anilines substituted with electron-donating groups but also for ones containing electron-withdrawing groups, The method avoided using organic solvents and had the main advantages of convenient procedure and environmental friendliness.

EXPERIMENTAL

Microwave irradiation was carried out with microwave oven Emrys^{TM} Creator from Personal Chemistry, Uppsala, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were taken on a TENSOR 27 spectrometer in KBr and reported in cm^{-1}. ^{1}H NMR spectra were measured on a Bruke DPX 400 MHz spectrometer in DMSO-d_6 with chemical shift (δ) given in ppm relative to TMS as internal standard, Elemental analyses were determined by using a Perkin-Elmer 240c elemental analysis instrument. X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Semens P4 diffractometer.

General procedure for the synthesis of compound 4 with microwave irradiation. In a 10 mL Emrys^{TM} reaction vial, an aldehyde **1**(1 mmol), dimedone or 1,3-cyclohexanedione **2**(2 mmol), primary arylamines **3**(1 mmol) and water (1.0 mL)

Table 1

Physical data of compounds **4**.

Entry	Product	Ar	2	Ar′-NH$_2$	Time (min)	Mp (°C)	Yield (%)
1	**4a**	4-Chlorophenyl	**2a**	*p*-Toluidine	7	283–285	96
2	**4b**	4-Bromophenyl	**2a**	*p*-Toluidine	8	277–278	93
3	**4c**	4-Nitrophenyl	**2a**	*p*-Toluidine	8	>300	87
4	**4d**	4-Methoxyphenyl	**2a**	*p*-Toluidine	10	241–243	90
5	**4e**	Benzo[*d*][1,3]dioxol-5-yl	**2a**	*p*-Toluidine	10	263–264	92
6	**4f**	4-Chlorophenyl	**2a**	4-Aminophenol	8	>300	90
7	**4g**	4-Bromophenyl	**2a**	4-Aminophenol	8	>300	88
8	**4h**	4-Chlorophenyl	**2a**	4-Chlorobenzenamine	8	>300	89
9	**4i**	4-Bromophenyl	**2a**	4-Chlorobenzenamine	8	>300	87
10	**4j**	4-Nitrophenyl	**2a**	4-Chlorobenzenamine	8	>300	85
11	**4k**	Benzo[*d*][1,3]dioxol-5-yl	**2a**	4-Chlorobenzenamine	10	287–288	88
12	**4l**	4-Methoxyphenyl	**2a**	4-Chlorobenzenamine	8	269–270	87
13	**4m**	4-Bromophenyl	**2a**	Aniline	8	245–247	92
14	**4n**	4-Fluorophenyl	**2b**	*p*-Toluidine	8	267–269	95
15	**4o**	Benzo[*d*][1,3]dioxol-5-yl	**2b**	*p*-Toluidine	8	236–238	89
16	**4p**	4-Fluorophenyl	**2b**	*p*-Toluidine	8	263–264	93
17	**4q**	4-Bromophenyl	**2b**	*p*-Toluidine	9	>300	89
18	**4r**	4-Nitrophenyl	**2b**	*p*-Toluidine	8	>300	87
19	**4s**	4-Methoxyphenyl	**2b**	*p*-Toluidine	8	261–262	88
20	**4t**	4-Chlorophenyl	**2b**	4-Aminophenol	8	>300	92
21	**4u**	4-Methoxyphenyl	**2b**	4-Chlorobenzenamine	8	270–272	86
22	**4v**	4-Fluorophenyl	**2b**	4-Chlorobenzenamine	8	298–300	91
23	**4w**	4-Chlorophenyl	**2b**	4-Chlorobenzenamine	8	255–257	89
24	**4x**	4-Chlorophenyl	**2b**	Aniline	8	288–290	92
25	**4y**	4-Methoxyphenyl	**2b**	Aniline	8	290–291	87

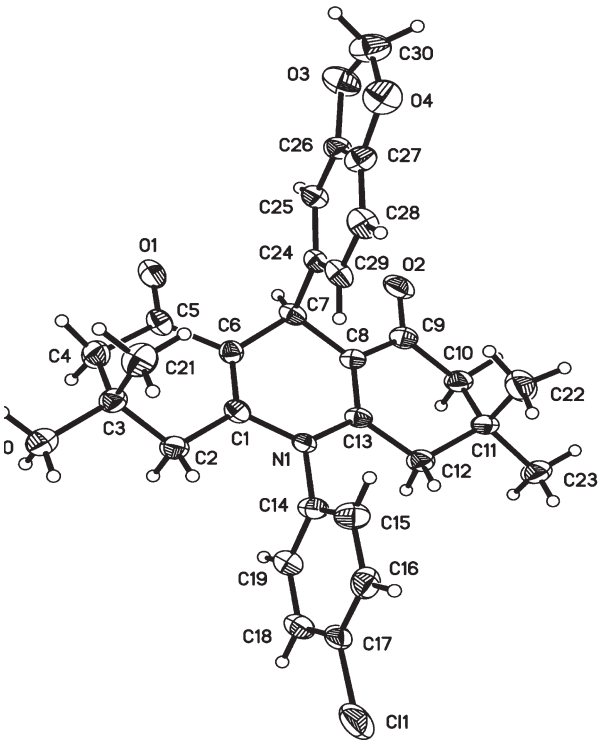


Figure 1. Molecular structure of **4k**.

was mixed and then capped. The mixture was irradiated for a given time at power of 200 W at 140°C. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature. The solid product was filtered to give the crude product, which was further purified by recrystallization from EtOH (95%).

9-(4-Chlorophenyl)-10-(p-tolyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4a). mp 283–285°C. (lit. mp: 265–267°C) [19]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3058, 2958, 2888, 1639, 1575, 1511, 1486, 1450, 1361, 1278, 1221, 1144, 1089, 841. ^{1}H NMR: 7.41 (d, 2H, ArH, J = 8.4 Hz), 7.29–7.31 (m, 6H, ArH), 5.02 (s, 1H, CH), 2.50 (s, 3H, CH_3), 2.17–2.22 (m, 4H, $2CH_2$), 2.00 (d, 2H, CH_2, J = 16.0 Hz), 1.77 (d, 2H, CH_2, J = 17.2 Hz), 0.88 (s, 6H, CH_3), 0.71 (s, 6H, CH_3). Anal calcd. for $C_{30}H_{32}ClNO_2$: C, 76.01; H, 6.80; N, 2.95. Found: C, 76.25; H, 6.71; N, 3.02.

9-(4-Bromophenyl)-10-(p-tolyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4b). mp 277–278°C. (lit. mp: 265–267°C) [20]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3035, 2957, 2870, 1640, 1576, 1511, 1471, 1362, 1278, 1222, 1145, 1069, 842. ^{1}H NMR: 7.40–7.45 (m, 4H, ArH), 7.25–7.32 (m, 4H, ArH), 5.00 (s, 1H, CH), 2.42 (s, 3H, CH_3), 2.17–2.22 (m, 4H, $2CH_2$), 1.99 (d, 2H, CH_2, J = 16.0 Hz), 1.77 (d, 2H, CH_2, J = 16.0 Hz), 0.88 (s, 6H, CH_3), 0.71(s, 6H, CH_3). Anal calcd. for $C_{30}H_{32}BrNO_2$: C, 69.50; H, 6.22; N, 2.70. Found: C, 69.39; H, 6.13; N, 2.82.

9-(4-Nitrophenyl)-10-(4-tolyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]dione (4c). mp >300°C. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2959, 2930, 1639, 1573, 1512, 1343, 1222, 1146, 834. ^{1}H NMR: 8.14–8.16 (m, 2H, ArH), 7.57–7.59 (m, 2H, ArH), 7.42 (d, 2H, ArH, J = 6.8), 7.35 (d, 2H, ArH, J = 7.6), 5.14 (s, 1H, CH), 2.43 (s, 3H, CH_3), 2.19–2.24 (m, 4H, $2CH_2$), 2.00 (d, 2H, CH_2, J = 16.0 Hz), 1.80 (d, 2H, CH_2, J = 17.2 Hz), 0.88 (s, 6H, CH_3), 0.70 (s, 6H, CH_3). Anal calcd. for $C_{30}H_{32}N_2O_4$, C, 74.36; H, 6.66; N, 5.78. Found: C, 74.16; H, 6.79; N, 5.73.

9-(4-Methoxyphenyl)-10-(4-tolyl)-3,3,6,6-tetrameth-yl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4d). mp: 281–283°C. (lit. mp: 285–287°C) [20]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3039, 2947, 2865, 1672, 1572, 1484, 1359, 1175, 1010, 837. ^{1}H NMR: 7.41 (d, 3H, ArH, J = 8.0 Hz), 7.20 (d, 3H, ArH, J = 8.8 Hz), 7.80 (d, 2H, ArH, J = 8.4 Hz), 4.98 (s, 1H, CH), 3.69 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3), 2.16–2.22 (m, 4H, $2CH_2$), 1.99 (d, 2H, CH_2, J = 16.0 Hz), 1.76 (d, 2H, CH_2, J = 17.2 Hz), 0.88 (s, 6H, CH_3), 0.72 (s, 6H, CH_3). Anal calcd. for $C_{31}H_{35}NO_3$. C, 79.28; H, 7.51; N, 2.98. Found: C, 79.47; H, 7.62; N, 2.79.

9-(Benzo[d][1,3]dioxo-5-yl)-10-(p-tolyl)-3,3,6,6-tetra methyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4e). mp 263–264°C. (lit. mp: 272–274°C) [20]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2954, 2871, 1640, 1576, 1486, 1420, 1361, 1278, 1254, 1142, 1042, 813. ^{1}H NMR: 7.16–7.21(m, 4H, ArH), 6.72–6.83 (m, 3H, ArH), 5.94 (s, 2H, CH_2) 4.96 (s, 1H, CH), 2.50 (s, 3H, CH_3), 2.16–2.20 (m, 4H, $2CH_2$), 2.02 (d, 2H, CH_2, J = 16.0 Hz), 1.78 (d, 2H, CH_2, J = 17.2 Hz), 0.88 (s, 6H, CH_3), 0.74 (s, 6H, CH_3). Anal calcd. for $C_{31}H_{33}NO_4$: C, 76.99; H, 6.88; N, 2.90. Found: C, 76.78; H, 6.98; N, 2.69.

9-(4-Chlorophenyl)-10-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4f). mp >300°C. (lit. mp: >300°C) [17]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3262, 2960, 2875, 1642, 1640, 1566, 1515, 1451, 1364, 1316, 1264, 1225, 1177, 1145, 1090, 1013, 886, 852, 782. ^{1}H NMR: 10.0 (s, 1H, OH), 6.92–7.30 (m, 8H, ArH), 5.01 (s, 1H, CH), 2.17–2.22 (m, 4H, $2CH_2$), 1.83–2.00 (m, 4H, $2CH_2$), 0.90 (s, 6H, CH_3), 0.72 (s, 6H, CH_3). Anal calcd. for $C_{29}H_{30}ClNO_3$: C, 73.17; H, 6.35; N, 2.94. Found: C, 73.32; H, 6.21; N, 3.02.

9-(4-Bromophenyl)-10-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4g). mp >300°C. (lit. mp: >300°C) [17]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3162, 2958, 2875, 1638, 1564, 1513, 1463, 1365, 1316, 1264, 1178, 1146, 1070, 1009, 887, 850, 734, 779. ^{1}H NMR: 10.0 (s, 1H, OH), 7.42 (d, 2H, ArH, J = 8.0 Hz), 7.24 (d, 2H, ArH, J = 8.0 Hz), 6.90–7.22 (m, 4H, ArH), 5.1 (s, 1H, CH), 2.16–2.23 (m, 4H, $2CH_2$), 1.83–2.00 (m, 4H, $2CH_2$), 0.90 (s, 6H, CH_3), 0.72 (s, 6H, CH_3). Anal calcd. for $C_{29}H_{30}BrNO_3$. C, 66.92; H, 5.81; N, 2.69. Found: C, 67.08; H, 5.65; N, 2.54.

9-(4-Chlorophenyl)-10-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4h). mp >300°C. (lit. mp: 284–286°C) [20]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2958, 2870, 1639, 1578, 1490, 1361, 1361, 1263, 1221, 1145, 1090, 1014, 840, 739. ^{1}H NMR: 7.68 (d, 2H, ArH, J = 12.0 Hz), 7.47–7.49 (m, 2H, ArH), 7.28–7.33 (m, 4H, ArH), 5.01 (s, 1H, CH), 2.17–2.22 (m, 4H, $2CH_2$), 2.01

(d, 2H, CH_2, J = 16.0 Hz), 1.77 (d, 2H, CH_2, J = 16.0 Hz), 0.89 (s, 6H, CH_3), 0.72 (s, 6H, CH_3). Anal calcd. for $C_{29}H_{29}Cl_2NO_2$: C, 70.44; H, 5.91; N, 2.83. Found: C, 70.21; H, 6.02; N, 2.71.

9-(4-Bromophenyl)-10-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4i). mp: 254–256°C. (lit. mp: 249–251°C) [20]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2958, 2869, 1639, 1578, 1577, 1491, 1361, 1221, 1145, 1089, 1009, 839. ^{1}H NMR: 7.68 (d, 2H, ArH, J = 8.0 Hz), 7.42–7.48 (m, 4H, ArH), 7.26 (d, 2H, ArH, J = 8.0 Hz), 4.99 (s, 1H, CH), 2.17–2.23 (m, 4H, $2CH_2$), 2.01 (d, 2H, CH_2, J = 16.0 Hz), 1.76 (d, 2H, CH_2, J = 16.0 Hz), 0.89 (s, 6H, CH_3), 0.72 (s, 6H, CH_3). *Anal* calcd. for $C_{29}H_{29}BrClNO_2$: C, 64.63; H, 5.42; N, 2.60. Found: C, 64.81; H, 5.28; N, 2.68.

9-(4-Nitrophenyl)-10-(4-chlorophenyl)-3,3,6,6-tetra methyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4j). mp >300°C. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2959, 2870, 1638, 1577, 1491, 1361, 1342, 1222, 1145, 1089, 1009, 831. ^{1}H NMR: 7.67–7.70 (m, 2H, ArH), 7.48–7.50 (m, 2H, ArH), 7.28–7.33 (m, 4H, ArH), 5.01 (s, 1H, CH), 2.17–2.22 (m, 4H, $2CH_2$), 2.02 (d, 2H, CH_2, J = 16.0 Hz), 1.77 (d, 2H, CH_2, J = 16.0 Hz), 0.89 (s, 6H, CH_3), 0.72 (s, 6H, CH_3). Anal calcd. for $C_{29}H_{29}ClN_2O_4$: C, 68.97; H, 5.79; N, 5.55. Found: C, 69.14; H, 5.61; N, 5.42.

9-(Benzo[d][1,3]dioxo-5-yl)-10-(4-chlorophenyl)-3,3, 6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4k). mp 287–288°C. (lit. mp: 287–288°C) [24]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2955, 2871, 1641, 1578, 1490, 1360, 1254, 1221, 1141, 1042, 921, 813. ^{1}H NMR: 7.68 (d, 2H, ArH, J = 8.8 Hz), 7.42–7.45 (m, 2H, ArH), 6.77–6.79 (m, 3H, ArH), 5.94 (s, 2H, CH_2), 4.96 (s, 1H, CH), 2.16–2.20 (m, 4H, $2CH_2$), 2.03 (d, 2H, CH_2, J = 17.6 Hz), 1.78 (d, 2H, CH_2, J = 17.2 Hz), 0.89 (s, 6H, CH_3), 0.75 (s, 6H, CH_3). Anal calcd. for $C_{30}H_{30}ClNO_4$: C, 71.49; H, 6.00; N, 2.78. Found: C, 71.23; H, 6.18; N, 2.69.

9-(4-Methoxyphenyl)-10-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine1,8-[2H,5H]-dione (4l). mp 269–270°C. (lit. mp: 269–271°C) [27]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2952, 1641, 1578, 1491, 1361, 1259, 1173, 1140, 998, 834, 740. ^{1}H NMR: 7.68 (d, 2H, ArH, J = 8.0), 7.44–7.47 (m, 2H, ArH), 7.21 (d, 2H, ArH, J = 8.0 Hz), 6.80 (d, 2H, ArH, J = 8.0 Hz), 4.97 (s, 1H, CH), 3.69 (s, 3H, OCH_3), 2.16–2.22 (m, 4H, $2CH_2$), 2.00 (d, 2H, CH_2, J = 16.0 Hz), 1.77 (d, 2H, CH_2, J = 17.6 Hz), 0.89 (s, 6H, CH_3), 0.73 (s, 6H, CH_3). Anal calcd. for $C_{30}H_{32}ClNO_3$: C, 73.53; H, 6.58; N, 2.86. Found: C, 73.73; H, 6.62; N, 2.71.

9-(4-Bromophenyl)-10-phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4m). mp 285–287°C. (lit. mp: > 300°C) [20]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3060, 2956, 2869, 1639, 1577, 1491, 1452, 1361, 1261, 1176, 1008, 838. ^{1}H NMR: 7.55–7.64 (m, 3H, ArH), 7.45 (d, 4H, ArH, J = 8.0 Hz), 7.27 (d, 2H, ArH, J = 8.0 Hz), 5.01 (s, 1H, CH), 2.18–2.23 (m, 4H, $2CH_2$), 2.01 (d, 2H, CH_2, J = 16.0 Hz), 1.75 (d, 2H, CH_2, J = 16.0 Hz), 0.87 (s, 6H, CH_3), 0.71 (s, 6H, CH_3). Anal calcd. for $C_{29}H_{30}BrNO_2$: C, 69.05; H, 5.99; N, 2.78. Found: 69.18; H, 5.76; N, 2.54.

9-(4-Fluorophenyl)-10-(4-tolyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine1,8-[2H,5H]-dione (4n). mp 267–269°C. (lit. mp: 262–294°C) [17]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3063, 2931, 2870, 1651, 1575, 1508, 1451, 1142, 1000, 843. ^{1}H NMR: 7.41 (d, 2H, ArH, J = 7.6 Hz), 7.30–7.34 (m, 4H, ArH), 7.04–7.08 (m, 2H, ArH), 5.03 (s, 1H, CH), 2.42 (s, 3H, CH_3), 2.20–2.22 (m, 4H, $2CH_2$), 2.00 (d, 2H, CH_2, J = 16.0 Hz), 1.77 (d, 2H, CH_2, J = 17.6 Hz), 0.88 (s, 6H, CH_3), 0.71 (s, 6H, CH_3). Anal calcd. for $C_{30}H_{32}FNO_2$: C, 78.75; H, 7.05; N, 3.06. Found: C, 78.94; H, 7.18; N, 3.02.

9-(Benzo[d][1,3]dioxo-5-yl)-10-(4-tolyl)-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4o). mp 236–238°C. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3031, 2945, 2888, 1642, 1570, 1486, 1362, 1285, 1231, 1135, 1040, 857, 799. ^{1}H NMR: 7.37 (d, 3H, ArH, J = 8.0 Hz), 7.16–7.18 (m, 1H, ArH), 6.72–6.79 (m, 3H, ArH), 5.94 (s, 2H, CH_2), 5.06 (s, 1H, CH), 2.97 (s, 3H, CH_3), 2.18–2.24 (m, 6H, $3CH_2$), 1.91–1.96 (m, 2H, CH_2), 1.76–1.84 (m, 2H, CH_2), 1.59–1.65 (m, 2H, CH_2). Anal calcd. for $C_{27}H_{25}NO_4$: C, 75.86; H, 5.89; N, 3.28. Found: 75.81; H, 6.01; N, 3.41.

9-(4-Fluorophenyl)-10-(p-tolyl)-3,4,6,7,9,10-hexahy-droacridine-1,8-[2H,5H]-dione (4p). mp 263–264°C. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3059, 2929, 2870, 1633, 1571, 1507, 1360, 1284, 1231, 1134, 839. ^{1}H NMR: 7.37–7.39 (m, 3H, ArH), 7.19–7.31 (m, 3H, ArH), 7.02–7.07 (m, 2H, ArH), 5.13 (s, 1H, CH), 2.40 (s, 3H, CH_3), 2.18–2.22 (m, 6H, $3CH_2$), 1.92–1.97 (m, 2H, CH_2), 1.79–1.84 (m, 2H, CH_2), 1.63–1.65 (m, 2H, CH_2). Anal calcd. for $C_{26}H_{24}FNO_2$: C, 77.78; H, 6.03; N, 3.49. Found: C, 77.94; H, 5.85; N, 3.31.

9-(4-Bromophenyl)-10-(p-tolyl)-3,4,6,7,9,10-hexahy-droacridine-1,8-[2H,5H]-dione (4q). mp >300°C. (lit. mp: > 300°C) [17]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3040, 2923, 2867, 1644, 1572, 1510, 1485, 1361, 1283, 1230, 1134, 1069, 831. ^{1}H NMR: 7.37–7.43 (m, 5H, ArH), 7.24 (d, 2H, ArH, J = 8.4 Hz), 7.14 (d, 1H, ArH, J = 8.4 Hz), 5.10 (s, 1H, CH), 2.40 (s, 3H, CH_3), 2.18–2.21 (m, 8H, $4CH_2$), 1.92–1.97 (m, 2H, CH_2), 1.77–1.85 (m, 2H, CH_2). Anal calcd. for $C_{26}H_{24}BrNO_2$: C, 67.54; H, 5.23; N, 3.03. Found: C, 67.72; H, 5.06; N, 3.19.

9-(4-Nitrophenyl)-10-(p-tolyl)-3,4,6,7,9,10-hexahy-droacridine-1,8-[2H,5H]-dione (4r). mp >300°C. (lit. mp: > 300°C) [17]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2953, 2915, 1631, 1600, 1574, 1511, 1342, 1284, 1230, 1179, 1132. ^{1}H NMR: 7.31–8.13 (m, 8H, ArH), 5.23 (s, 1H, CH), 2.40 (s, 3H, CH_3), 1.94–2.89 (m, 8H, $4CH_2$), 1.79–1.85 (m, 2H, CH_2), 1.62–1.65 (m, 2H, CH_2). Anal calcd. for $C_{26}H_{24}N_2O_4$: C, 72.88; H, 5.65; N, 6.54. Found: C, 72.72; H, 5.84; N, 6.70.

9-(4-Methoxyphenyl)-10-(p-tolyl)-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4s). mp 241.2–243.0°C. (lit. mp: 256–257°C) [17]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2938, 1637, 1569, 1509, 1360, 1287, 1232, 1181, 1130, 954, 913, 825, 758. ^{1}H NMR: 7.37–7.86 (m, 4H, ArH), 7.18 (d, 2H, ArH, J = 8.8 Hz), 6.80 (d, 2H, ArH, J = 8.4 Hz), 5.07 (s, 1H, CH), 3.70 (s, 3H, OCH_3), 2.40 (s, 3H, CH_3), 2.18–2.25 (m, 6H, $3CH_2$), 1.80–1.83 (m, 4H, $2CH_2$), 1.59–1.61 (m, 2H, CH_2). Anal calcd. for $C_{27}H_{27}NO_3$: C, 78.42; H, 6.58; N, 3.39. Found: C, 78.69; H, 6.72; N, 3.12.

9-(4-Chlorophenyl)-10-(4-hydroxyphenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4t). mp >300°C. (lit. mp: >300°C) [17]. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3161, 1636, 1561, 1489, 1453, 1385, 1362, 1269, 1234, 1140, 1088, 959. ^{1}H NMR: 9.94 (s, 1H, OH), 6.89–7.28 (m, 8H, ArH), 5.11 (s, 1H, CH), 2.17–2.25 (m, 6H, $3CH_2$), 1.96–2.04(m, 2H, CH_2), 1.80–1.86 (m, 2H, CH_2), 1.59–1.67 (m, 2H, CH_2). Anal calcd. for $C_{25}H_{22}ClNO_3$: C, 71.51; H, 5.28; N, 3.34. Found: C, 71.38; H, 5.32; N, 3.40.

9-(4-Methoxyphenyl)-10-(4-chlorophenyl)-3,4,6,7,9, 10-hexahydro acridine-1,8-[2H,5H]-dione (4u). mp 270–272°C. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2938, 1634, 1569, 1509, 1363, 1284, 1230, 1181, 1132, 955, 846, 756. ^{1}H NMR: 7.68 (d, 2H, ArH, J = 12.0), 7.45–7.47 (m, 2H, ArH), 7.21 (d, 2H, ArH, J = 8.0 Hz), 6.80 (d, 2H, ArH, J = 8.0 Hz), 4.97 (s, 1H, CH), 3.69 (s, 3H, OCH_3), 2.19–2.23 (m, 6H, $3CH_2$), 1.82–1.84 (m, 4H, $2CH_2$), 1.59–1.62 (m, 2H, CH_2). Anal calcd. for $C_{26}H_{24}ClNO_3$: C, 71.97; H, 5.57; N, 3.23. Found: C, 72.12; H, 5.38; N, 3.32.

9-(4-fluorophenyl)-10-(4-chlorophenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4v). mp 298–299°C. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2962, 1634, 1572, 1505, 1360, 1283, 1232, 1182, 1132, 956, 839, 759. ^{1}H NMR: 7.65 (d, 2H, ArH, J = 8.0), 7.29–7.33 (m, 3H, ArH), 7.02–7.06 (m, 3H, ArH), 5.12 (s, 1H, CH), 2.19–2.24 (m, 6H, $3CH_2$), 1.92–1.97 (m, 2H, CH_2), 1.80–1.84 (m, 2H, CH_2), 1.62–1.65 (m, 2H, CH_2). Anal calcd. for $C_{25}H_{21}ClFNO_2$: C, 71.17; H, 5.02; N, 3.32. Found: C, 71.02; H, 5.18; N, 3.21.

9-(4-Chlorophenyl)-10-(4-chlorophenyl)-3,4,6,7,9,10-hexahydroacridine-1,8[2H,5H]-dione (4w). mp 255–257°C. This compound was obtained according to earlier general procedure. IR (potassium bromide): 2946, 1633, 1571, 1489, 1362, 1284, 1183, 1134, 1089, 858, 821, 757. ^{1}H NMR: 7.63–7.66 (m, 2H, ArH), 7.53–7.57 (m, 2H, ArH), 7.17–7.20 (m, 2H, ArH), 6.79 (d, 2H, ArH, J = 8.0), 5.06 (s, 1H, CH), 2.18–2.26 (m, 6H, $3CH_2$), 1.91–1.97 (m, 2H, CH_2), 1.80–1.85 (m, 2H, CH_2), 1.59–1.65 (m, 2H, CH_2). Anal calcd. For $C_{25}H_{21}Cl_2NO_2$: C, 68.50; H, 4.83; N, 3.20. Found: C, 68.38; H, 4.99; N, 3.07.

9-(4-Chlorophenyl)-10-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8-[2H,5H]-dione (4x). mp 288–290°C. This compound was obtained according to earlier general procedure. IR (potassium bromide): 3044, 2953, 1637, 1570, 1489, 1425, 1360, 1269, 1281, 1137, 1088, 956, 835. ^{1}H NMR: δ7.53–7.60 (m, 3H, ArH), 7.19–7.33 (m, 6H, ArH), 5.13 (s, 1H, CH), 2.19–2.25 (m, 6H, $3CH_2$), 1.90–1.95 (m, 2H, CH_2), 1.79–1.81 (m, 2H, CH_2), 1.60–1.63 (m, 2H, CH_2). Anal calcd. for $C_{25}H_{22}ClNO_2$: C, 74.34; H, 5.49; N, 3.47. Found: C, 74.18; H, 5.62; N, 3.31.

9-(4-Methoxyphenyl)-10-phenyl-3,4,6,7,9,10-hexa-hydroacridine-1,8-[2H,5H]-dione (4y). mp 290–291°C. (lit. mp: 270–272°C) [28]. IR (potassium bromide): 2943, 2887, 1635, 1569, 1509, 1359, 1284, 1229, 1181, 1132, 953, 857. ^{1}H NMR: 7.55–7.57 (m, 4H, ArH), 7.30–7.35 (m, 1H, ArH), 7.18–7.21 (m, 2H, ArH), 6.79–7.82 (m, 2H, ArH), 5.09 (s, 1H, CH), 3.70 (s, 3H, OCH_3), 2.19–2.24 (m, 6H, $3CH_2$), 1.84–1.90 (m, 2H, CH_2), 1.79–1.81 (m, 2H, CH_2),1.60–1.64 (m, 2H, CH_2). Anal calcd. for $C_{26}H_{25}NO_3$: C, 78.17; H, 6.31; N, 3.51. Found: C, 78.01; H, 6.52; N, 3.58.

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[22] The 12 principles are as follows: prevention, atom economy, less hazardous chemical synthesis, designing safer chemicals, safer solvents, design for energy efficiency, use of renewable feedstocks, reduce derivatives, catalysis, design for degradation, real-time analysis for pollution prevention, inherently safer chemistry for accident prevention.

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