One-pot Synthesis of Novel *N*-Cyclopropyldecahydroacridine-1,8-dione Derivatives under Microwave Irradiation

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A series of new *N*-cyclopropyldecahydroacridine-1,8-dione derivatives were synthesized by one-pot reaction of aromatic aldehyde, dimedone (or 1,3-cyclohexanedione) and cyclopropanamine in solution of glycol and water under microwave irradiation with excellent yields (78-94%) and short reaction time (5-10 min).

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Many natural and synthetic compounds containing the acridine skeleton display interesting biological and physical activities [1]. Acridinedione, for example, has been identified as antimalarial and antitumor agents [2]. Decahydroacridine-1,8-dione derivatives are also reported to possess important properties such as high fluorescence efficiency [3]. As a consequence, the interest of organic chemists in the synthesis or structure modifications of acridine derivatives remains high.

Apart from the synthesis of decahydroacridine-1,8-diones reported by Martin, Suarez and us [4-6], it has also been discovered that the introduction of aryl or methyl group to the nitrogen atom of these compounds leads to enhanced fluorescence activity [7-8].

Recently, Hubschwerlen *et al* found that the introduction of a cyclopropyl group to the nitrogen atom of the pyridine ring results in a wide spectrum of antibacterial activities [9]. Since the pyridine scaffold is included in decahydroacridine-1,8-diones, a question was aroused whether the same modification on the nitrogen of the decahydroacridine-1,8-dione may bring about some significant activity. However, the introduction of a cyclopropyl group to the nitrogen atom of the decahydroacridine-1,8-dione has not been reported yet. It would seem, therefore, that further investigations are needed in order to screen novel compounds with peculiar properties.

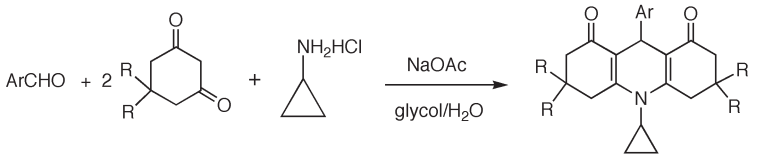
Since 1986 when microwave heating was first used in organic synthesis by Gedye [10], microwave irradiation has been widely utilized in the synthesis of heterocyclic compounds such as hexahydroquinolines [11], unsymmetrical 1,4-dihydropyridines [11], octahydroquinolines [12], dihydropyridones [13], pyridopyrimidones [14] as well as decahydroacridines [15] with good yields and short reaction time. The efficiency of microwave irradiation (MWI) in promoting organic synthesis and the success of its application in these heterocyclic syntheses triggered us to extend those procedures to the nitrogen modification of decahydroacridine-1,8-diones.

In our previous study [10], we have introduced hydroxyl group to the nitrogen atom of decahydroacridine-1,8-dione under microwave irradiation. Through intensive research, we have successfully achieved the introduction of cyclopropyl group to the nitrogen atom of these compounds under microwave irradiation with excellent yields and short reaction time.

Herein, we would like to describe the one-pot synthesis of this novel type of heterocyclic compounds, the *N*-cyclopropyldecahydroacridine-1,8-dione derivatives.

For the aim of contrast, we carried out the reaction not only under microwave irradiation but under traditional heating conditions (Scheme 1). As a result, we found that microwave can efficiently promote this reaction. By employing microwave irradiation, the reaction time was shortened to 5-10 min from 10 hours required in the conventional heating mode and the yields were sharply increased to 78%-94% from the 15% afforded in the conventional heating mode.

Scheme 1



1 **2** **3** **4**

In addition, we discovered that the reaction condition was crucial to the procedure. Firstly, cyclopropanamine is easy to volatilize because of its lower boiling point (30 °C), so we convert it into the hydrochloride salt and then add NaOAc to liberate the free amine. Secondly, the com-

position of the solvent plays a key role in the process. For example, when anhydrous ethanol or glycol is used as a solvent, the main product is **10** (yield: 92% or so) or **11** (yield: 90% or so), while **4** is the by-product (Scheme 2). When water acts as solvent, **11** and **4** can be obtained simultaneously. Therefore, we investigated the relationship between the contents of **4** and the ratio of water to glycol by HPLC. The optimal ratio of water to glycol is found to be 2:1 (Table 1).

Scheme 2

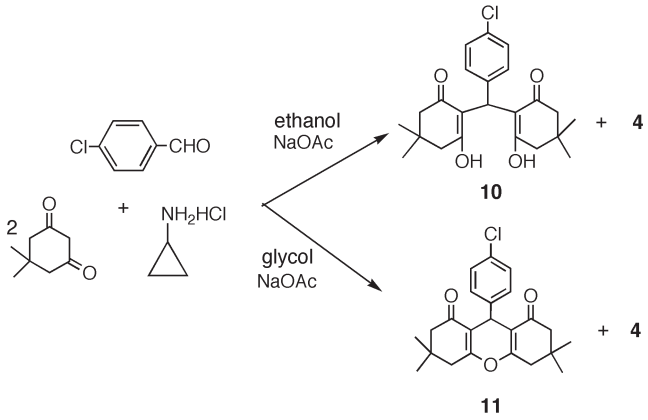


Table 1

The Relationship Between the Contents of **4c** and the Ratio of Water to Glycol by HPLC (water is 0.50 mL)

Volume of glycol (mL)	Content of **4c** (%)	Content of **11** (%)
0.00	48.1	52.9
0.13	43.7	56.3
0.19	50.6	49.4
0.25	98.2	1.8
0.31	24.8	75.2
0.38	25.6	74.4
0.50	9.8	90.2

The results (Table 2) show that a series of aromatic aldehydes can undergo the cyclocondensation reaction to give products in excellent yields (78-94%).

This reaction may occur *via* a mechanism of condensation, addition, cyclization and elimination (Scheme 3). At first, the condensation between aldehyde and dimedone gave 2-aryllidene-5,5-dimethyl-1,3-cyclohexanedione (**5**). Then, Michael addition between **5** and **6** obtained from dimedone and cyclopropanamine furnished the intermediate **7**, which tautamerized to **8**. After that, intermolecular cyclization of **8** gave **9**, which finally afforded **4** by dehydration.

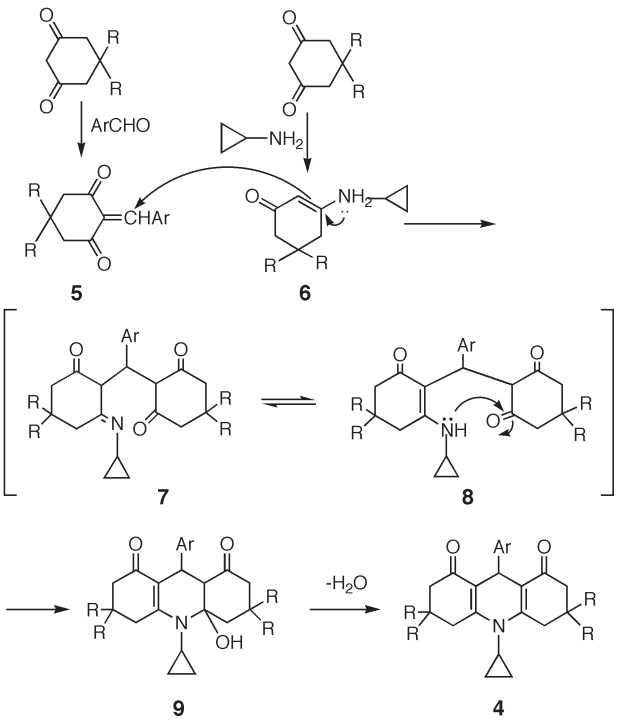
All the products were characterized by IR, ^{1}H NMR and elemental analysis. Moreover, the structure of **4a** and **4l** were further conformed by X-ray crystallographic analysis

Table 2

Synthesis of **4** Under Microwave Irradiation

Entry	Ar	R	Time (min)	Yield (%)	Mp (°C)
4a	3-OCH_3-4-OHC_6H_3	CH_3	6	85	274-275
4b	3-$NO_2C_6H_4$	CH_3	7	80	235-236
4c	4-ClC_6H_4	CH_3	6	79	202-203
4d	4-BrC_6H_4	CH_3	6	85	204-205
4e	4-$CH_3OC_6H_4$	CH_3	6	88	248-250
4f	3,4-$Cl_2C_6H_3$	CH_3	7	82	230-231
4g	2-ClC_6H_4	CH_3	9	85	226-227
4h	4-FC_6H_4	CH_3	7	80	227-228
4i	4-BrC_6H_4	H	5	92	222-223
4j	4-$NO_2C_6H_4$	H	6	85	222-223
4k	3-$NO_2C_6H_4$	H	10	78	193-194
4l	4-$CH_3OC_6H_4$	H	5	94	233-234
4m	3,4-$Cl_2C_6H_3$	H	6	90	230-231
4n	2-ClC_6H_4	H	6	86	234-235
4o	3-OCH_3-4-OHC_6H_3	H	8	88	242-243
4p	4-ClC_6H_4	H	6	90	204-205

Scheme 3



(Figure 1-2). In the structure of **4a** and **4l**, the aromatic rings are vertical to the pyridine rings which adopt the boat conformation, whereas both of the cyclohexanone rings adopt envelope conformations. The dihedral angles of **4a** and **4l** between the pyridine rings and the cyclopropyl rings are 72.19° and 66.01°, respectively. The ^{1}H NMR

data of all the compounds are consistent with their assigned structures.

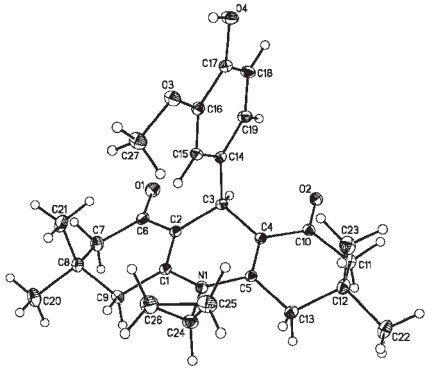


Figure 1 The structure of **4a**.

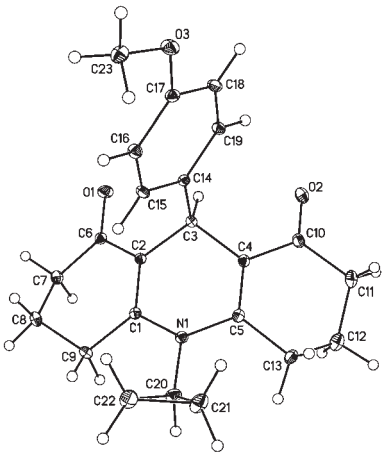


Figure 2 The structure of **4l**.

In conclusion, we have disclosed a novel microwave-assisted reaction by aromatic aldehyde, 1,3-cyclohexanedione or dimedone and cyclopropanamine, thus realizing the introduction of cyclopropyl group on the nitrogen atom of decahydroacridine-1,8-dione derivatives. Therefore, this one-pot synthesis of *N*-cyclopropyldecahydroacridine-1,8-dione derivatives therefore is a simple, timesaving, high-yielding and environmentally friendly process. Great efforts are underway to clarify the bioactivity of these new compounds and the results will be reported in due course.

EXPERIMENTAL

Microwave irradiation was carried out with a modified commercial microwave oven (2450 MHz, 650W) under atmospheric pressure. Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Shimadzu spectrometer. ^{1}H NMR spectra were measured on a DPX 400 MHz spectrometer using TMS as an internal standard, DMSO-d_6 as solvent. Elemental analysis was determined by using a Perkin-Elmer 240c elemental analysis instrument. X-ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

General Procedure for the Synthesis of 9-Aryl-3,3,6,6-tetramethyldecahydroacridine-1,8-diones **4a-4h**.

A solution of the appropriate aromatic aldehyde (2 mmol), dimedone (4 mmol), cyclopropanammonium chloride (4 mmol) and NaOAc (4 mmol) in glycol (0.25 mL) and water (0.50 mL) was irradiated for 6-9 min. The reaction mixture was cooled to room temperature, then poured into water (50 mL), filtered to give the crude product, which was further purified by recrystallization from 95% EtOH.

3,3,6,6-Tetramethyl-*N*-cyclpropyl-9-(3-methoxyl-4-hydroxylphenyl)-decahydroacridine-1,8-dione (**4a**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3185, 2954, 1646, 1635, 1569, 1510, 1465,1428, 1370, 1370, 1269, 1226, 1141, 1040, 845, 743, 666, 568, 466. ^{1}H NMR (δ, ppm): 8.58(s, 1H, OH), 6.54-6.40(m, 3H, ArH), 4.93(s, 1H, CH), 3.63(s, 3H, OCH_3), 3.09-3.06(m, 1H, CH), 3.00-2.96(m, 2H, CH_2), 2.57-2.52(m, 2H, CH_2), 2.22-2.12(m, 4H, CH_2), 1.18-1.16(m, 2H, CH_2), 1.04(s, 6H, CH_3), 1.01(s, 6H, CH_3), 0.59-0.57(m, 2H, CH_2).

Anal. Calcd. for $C_{27}H_{33}NO_4$: C, 74.45; H, 7.64; N, 3.22. found: C, 74.57; H, 7.83; N, 3.12.

3,3,6,6-Tetramethyl-*N*-cyclpropyl-9-(3-nitrophenyl)-decahydroacridine-1,8-dione (**4b**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3083, 2953, 2866, 1670, 1626, 1570, 1525, 1467, 1452, 1369, 1344, 1318, 1273, 1221, 1120, 977, 909, 810, 846, 733, 710, 589. ^{1}H NMR (δ, ppm): 7.97-7.94 (m, 1H, ArH), 7.51-7.49 (m, 2H, ArH), 7.23-7.16 (m, 1H, ArH), 5.12 (s, 1H, CH), 3.12-3.09 (m, 1H, CH), 3.04-3.00 (m, 2H, CH_2), 2.62-2.59 (m, 2H, CH_2), 2.24-2.17(m, 4H, CH_2), 1.24-1.19 (m, 2H, CH_2), 1.03 (s, 6H, CH_3), 0.99 (s, 6H, CH_3), 0.71-0.68 (m, 2H, CH_2).

Anal. Calcd. for $C_{26}H_{30}N_2O_4$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.98; H, 6.84; N, 6.32.

3,3,6,6-Tetramethyl-*N*-cyclpropyl-9-(4-cholorophenyl)-decahydroacridine-1,8-dione (**4c**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3001, 2954, 2868, 1636, 1565, 1485, 1364, 1316, 1224, 1116, 1009, 855, 830, 773, 528, 456. ^{1}H NMR (δ, ppm): 7.21 (d, 2H, *J*=8.0 Hz, ArH), 6.98 (d, 2H, *J*= 8.0 Hz, ArH), 5.01 (s, 1H, CH), 3.08-3.05 (m, 1H, CH), 3.00-2.96 (m, 2H, CH_2), 2.58-2.54 (m, 2H, CH_2), 2.23-2.17 (m, 4H, CH_2), 1.18-1.13 (m, 2H, CH_2), 1.01 (s, 6H, CH_3), 0.99 (s, 6H, CH_3), 0.63-0.58 (m, 2H, CH_2).

Anal. Calcd. for $C_{26}H_{30}ClNO_2$: C, 73.65; H, 7.13; N, 3.30. Found: C, 73.78; H, 7.01; N, 3.33.

3,3,6,6-Tetramethyl-*N*-cyclpropyl-9-(4-bromophenyl)-decahydroacridine-1,8-dione (**4d**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 2954, 2868, 2089, 1633, 1570, 1480, 1363, 1316, 1224, 1144, 1122, 1029, 999, 860, 707, 522. ^{1}H NMR (δ, ppm): 7.34 (d, 2H, *J*=8.8 Hz, ArH), 6.92 (d, 2H, *J*= 8.8 Hz, ArH), 4.99 (s, 1H, CH), 3.09-3.03 (m, 1H, CH), 3.00-2.96 (m, 2H, CH_2), 2.58-2.54

(m, 2H, CH_2), 2.23-2.13 (m, 4H, CH_2), 1.18-1.13 (m, 2H, CH_2), 1.01 (s, 6H, CH_3), 0.99 (s, 6H, CH_3), 0.63-0.58 (m, 2H, CH_2).

Anal. Calcd. for $C_{26}H_{30}BrNO_2$: C, 66.67; H, 6.46; N, 2.99; found: C, 6652; H, 6.32; N, 3.12.

3,3,6,6-Tetramethyl-*N*-cyclpropyl-9-(4-methoxylphenyl)-decahydroacridine-1,8-dione (**4e**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3062, 3001, 2950, 2832, 1637, 1625, 1565, 1508, 1366, 1292, 1246, 1127, 1106, 1031, 942, 830, 707, 548 cm^{-1}. ^1H NMR (δ, ppm): 6.88(d, 2H, *J*=8.8 Hz, ArH), 6.70 (d, 2H, *J*= 8.8 Hz, ArH), 4.95 (s, 1H, CH), 3.65 (s, 3H, OCH_3), 3.08-3.03 (m, 1H, CH), 2.99-2.95 (m, 2H, CH_2), 2.57-2.53 (m, 2H, CH_2), 2.17-2.13 (m, 4H, CH_2), 1.17-1.14 (m, 2H, CH_2), 1.01 (s, 6H, CH_3), 0.99 (s, 6H, CH_3), 0.62-0.58 (m, 2H, CH_2).

Anal. Calcd. for $C_{27}H_{33}NO_3$: C, 77.29; H, 7.93; N, 3.34. Found: C, 77.41; H, 7.77; N, 3.39.

3,3,6,6-Tetramethyl-*N*-cyclpropyl-9-(3,4-dicholorophenyl)-decahydroacridine-1,8-dione (**4f**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3093, 3006, 2960, 2863, 1630, 1572, 1462, 1387, 1361, 1302, 1265, 1222, 1146, 1119, 1019, 983, 886, 830, 778, 676, 599, 548, 440. ^1H NMR (δ, ppm): 7.43 (d, 1H, *J*= 8.4 Hz, ArH), 7.13-6.93 (m, 2H, ArH), 5.00 (s, 1H, CH), 3.11-3.05 (m, 1H, CH), 3.03-2.98 (m, 2H, CH_2), 2.59-2.55 (m, 2H, CH_2), 2.25-2.14 (m, 4H, CH_2), 1.21-1.16 (m, 2H, CH_2), 1.01 (s, 6H, CH_3), 1.00 (s, 6H, CH_3), 0.63-0.59 (m, 2H, CH_2).

Anal. Calcd. for $C_{26}H_{29}Cl_2NO_2$: C, 68.12; H, 6.38; N, 3.06; found: C, 68.29; H, 6.29; N, 6.28.

3,3,6,6-Tetramethyl-*N*-cyclpropyl-9-(2-cholorophenyl)-decahydroacridine-1,8-dione (**4g**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3088, 3016, 2956, 2929, 2868, 1637, 1576, 1465, 1368, 1385, 1338, 1304, 1216, 1180, 1144, 1120, 1037, 944, 906, 840, 748, 702, 650, 579, 471. ^1H NMR (δ, ppm): 7.19-7.01 (m, 4H, ArH), 5.25 (s, 2H, CH), 3.09-3.05 (m, 1H, CH), 3.02-2.98 (m, 2H, CH_2), 2.60-2.55 (m, 2H, CH_2), 2.15-2.08 (m, 4H, CH_2), 1.26-1.22 (m, 2H, CH_2), 1.00 (s, 6H, CH_3), 0.97 (s, 6H, CH_3), 0.83-0.79 (m, 2H, CH_2).

Anal. Calcd. for $C_{26}H_{30}ClNO_2$: C, 73.65; H, 7.13; N, 3.30. Found: C, 73.52; H, 7.32; N, 3.38.

3,3,6,6-Tetramethyl-*N*-cyclpropyl-9-(4-fluorophenyl)-decahydroacridine-1,8-dione (**4h**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3093, 3006, 2960, 2863, 1630, 1572, 1462, 1387, 1361, 1302, 1265, 1222, 1146, 1119, 1019, 983, 886, 830, 778, 676, 599, 548, 440. ^1H NMR (δ, ppm): 7.01-6.94 (m, 4H, ArH), 5.01 (s, 1H, CH), 3.09-3.04 (m, 1H, CH), 3.01-2.96 (m, 2H, CH_2), 2.58-2.51 (m, 2H, CH_2), 2.23-2.13 (m, 4H, CH_2), 1.18-1.13 (m, 2H, CH_2), 1.01 (s, 6H, CH_3), 0.99 (s, 6H, CH_3), 0.62-0.58 (m, 2H, CH_2).

Anal. Calcd. for $C_{26}H_{30}FNO_2$: C, 76.63; H, 7.42; N, 3.44. Found: C, 76.52; H, 7.25; N, 3.61.

General Procedure for the Synthesis of 9-Aryl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-diones **4i-4p**.

A solution of the appropriate aromatic aldehyde (2 mmol), 1,3-cyclohexanedione (4 mmol), cyclopropanammonium chloride (4 mmol) and NaOAc (4 mmol) in glycol (0.25 mL) and water (0.50 mL) was irradiated for 5-10 min. The reaction mixture was cooled to r.t., then poured into water (50 mL), the solid produce was collected by filtration to give the crude product, which was further purified by recrystallization from 95% EtOH.

N-Cyclpropyl-9-(4-bromophenyl)-decahydroacridine-1,8-dione (**4i**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3088, 2939, 2858, 1632, 1569, 1366, 1293, 1231, 1181, 1134, 1071, 1036, 1008, 937, 896, 835, 543, 466. ^1H NMR (δ, ppm): 7.33 (d, 2H, *J*=8.4 Hz, ArH), 6.93 (d, 2H, *J*= 8.4 Hz, ArH), 5.01 (s, 1H, CH), 3.08-3.05 (m, 1H, CH), 3.04-3.01 (m, 2H, CH_2), 2.72-2.66 (m, 2H, CH_2), 2.33-2.24 (m, 4H, CH_2), 1.98-1.93 (m, 4H, CH_2), 1.11-1.06 (m, 2H, CH_2), 0.67-0.63 (m, 2H, CH_2).

Anal. Calcd. for $C_{22}H_{22}BrNO_2$: C, 64.09; H, 5.38; N, 3.40. Found: C, 64.18; H, 5.16; N, 3.33.

N-Cyclpropyl-9-(4-nitrophenyl)-decahydroacridine-1,8-dione (**4j**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 2945, 2919, 1632, 1563, 1519, 1360, 1286, 1231, 1180, 1106, 1052, 942, 901, 814, 702, 604, 471. ^1H NMR (δ, ppm): 8.03 (d, 2H, *J*=8.4 Hz, ArH), 7.24 (d, 2H, *J*= 8.4 Hz, ArH), 5.15 (s, 1H, CH), 3.46-3.43 (m, 1H, CH), 3.09-3.06 (m, 2H, CH_2), 2.75-2.72 (m, 2H, CH_2), 2.33-2.27 (m, 4H, CH_2), 2.21-1.95 (m, 4H, CH_2), 1.12-1.05 (m, 2H, CH_2), 0.72-0.68 (m, 2H, CH_2).

Anal. Calcd. for $C_{22}H_{22}N_2O_4$: C, 69.83; H, 5.86; N, 7.40. Found: C, 70.00; H, 5.99; N, 7.22.

N-Cyclpropyl-9-(3-nitrophenyl)-decahydroacridine-1,8-dione (**4k**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3078, 2939, 2919, 2868, 1632, 1568, 1532, 1429, 1363, 1345, 1289, 1230, 1182, 1134, 906, 825, 671, 548. ^1H NMR (δ, ppm): 7.95-7.93 (m, 1H, ArH), 7.88-7.86 (m, 1H, ArH), 7.74-7.46 (m, 2H, ArH), 5.12 (s, 1H, CH), 3.12-3.08 (m, 1H, CH), 3.05-3.02 (m, 2H, CH_2), 2.76-2.68 (m, 2H, CH_2), 2.33-2.22 (m, 4H, CH_2), 1.98-1.92 (m, 4H, CH_2), 1.16-1.11 (m, 2H, CH_2), 0.75-0.71 (m, 2H, CH_2).

Anal. Calcd. for $C_{22}H_{22}N_2O_4$: C, 69.83; H, 5.86; N, 7.40. Found: C, 70.01; H, 5.77; N, 7.23.

N-Cyclpropyl-9-(4-methoxylphenyl)-decahydroacridine-1,8-dione (**4l**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3001, 2950, 1637, 1625, 1565, 1508, 1366, 1292, 1246, 1292, 1284, 1031, 942, 830, 707, 548. ^1H NMR (δ, ppm): 6.88 (d, 2H, *J*=8.8 Hz, ArH), 6.79(d, 2H, *J*=8.8 Hz, ArH), 4.97(s, 1H, CH), 3.65(s, 3H, OCH_3), 3.07-3.04(m, 1H, CH), 3.03-3.00(m, 2H, CH_2), 2.70-2.63(m, 2H, CH_2), 2.33-2.18(m, 4H, CH_2), 1.96-1.90(m, 4H, CH_2), 1.12-1.07(m, 2H, CH_2), 0.65-0.61(m, 2H, CH_2).

Anal. Calcd for $C_{23}H_{25}NO_3$: C, 76.01; H, 6.93; N, 3.85. Found: C, 76.22; H, 6.84; N, 3.61.

N-Cyclpropyl-9-(3,4-dicholorophenyl)-decahydroacridine-1,8-dione (**4m**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3083, 3062, 2939, 2863, 1631, 1568, 1469, 1403, 1385, 1359, 1296, 1229, 1181, 1131, 1028, 943, 910, 825, 753, 661, 533, 420. ^1H NMR (δ, ppm): 7.40 (d, 1H, *J*=8.0 Hz, ArH), 7.14 (s, 1H, ArH), 6.93-6.91 (m, 1H, ArH), 5.01 (s, 1H, CH), 3.09-

3.06 (m, 1H, CH), 3.05-3.01 (m, 2H, CH_2), 2.73-2.66 (m, 2H, CH_2), 2.36-2.20 (m, 4H, CH_2), 1.98-1.93 (m, 4H, CH_2), 1.13-1.09 (m, 2H, CH_2), 0.68-0.64 (m, 2H, CH_2).

Anal. Calcd. for $C_{22}H_{21}Cl_2NO_2$: C, 65.68; H, 5.26; N, 3.48. Found: C, 65.54; H, 5.10; N, 3.31.

N-Cyclpropyl-9-(2-cholorophenyl)-decahydroacridine-1,8-dione (**4n**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3073, 2949, 1634, 1570, 1473, 1452, 1436, 1357, 1297, 1230, 1181, 1134, 1040, 965, 907, 838, 744, 537, 468. ^{1}H NMR (δ, ppm): 7.18-6.98 (m, 4H, ArH), 5.26 (s, 1H, CH), 3.09-3.06 (m, 1H, CH), 3.04-2.99 (m, 2H, CH_2), 2.74-2.67 (m, 2H, CH_2), 2.26-2.13 (m, 4H, CH_2), 1.94-1.89 (m, 4H, CH_2), 1.19-1.14 (m, 2H, CH_2), 0.84-0.80 (m, 2H, CH_2).

Anal. Calcd. for $C_{22}H_{22}ClNO_2$: C, 71.83; H, 6.03; N, 3.81. Found: C, 71.98; H, 5.88; N, 3.62.

N-Cyclpropyl-9-(3-methoxyl-4-hydroxylphenyl)-decahydroacridine-1,8-dione (**4o**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3401, 2949, 1626, 1564, 1511, 1453, 1432, 1364, 1288, 1231, 1182, 1116, 1034, 946, 906, 625, 476. ^{1}H NMR (δ, ppm): 8.52 (s, 1H, OH), 6.52-6.37 (m, 3H, ArH), 4.94 (s, 1H, CH), 3.64 (s, 3H, OCH_3), 3.08-3.05 (m, 1H, CH), 3.04-3.01 (m, 2H, CH_2), 2.70-2.50 (m, 2H, CH_2), 2.32-2.20 (m, 4H, CH_2), 1.97-1.92 (m, 4H, CH_2), 1.13-1.08 (m, 2H, CH_2), 0.65-0.61 (m, 2H, CH_2).

Anal. Calcd. for $C_{23}H_{25}NO_4$: C, 72.80; H, 6.64; N, 3.69; found: C, 72.98; H, 6.83; N, 3.60.

N-Cyclpropyl-9-(4cholophenyl)-decahydroacridine-1,8-dione (**4p**).

This compound has the following properties: IR (KBr, ν, cm^{-1}): 3416, 3257, 2937, 1644, 1596, 1488, 1366 1293, 1232, 1183, 1136, 1087, 1037, 1011, 944, 908, 836, 758, 650, 534. ^{1}H NMR (δ, ppm): 7.20 (d, 2H, *J*=8.4 Hz, ArH), 6.99(d, 2H, *J*=8.4 Hz, ArH), 5.03(s, 1H, CH), 3.08-3.05(m, 1H, CH), 3.03-3.00(m, 2H, CH_2), 2.73-2.64(m, 2H, CH_2), 2.35-2.22(m, 4H, CH_2), 1.98-1.91(m, 4H, CH_2), 1.11-1.08(m, 2H, CH_2), 0.66-0.63(m, 2H, CH_2).

Anal. Calcd. for $C_{22}H_{22}ClNO_2$: C, 71.83; H, 6.03; N, 3.81. Found: C, 72.01; H, 5.98; N, 3.53.

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REFERENCE AND NOTES

[1a] B. Wysocka-Skrzela and A. Ledochowski, *Roccz. Chem.*, **50**, 127 (1976); [b] A. Nasim and T. Brychey, *Muta. Res.*, **65**, 261, (1979); [c] U. Thull and B. Testa, *Biochem. Pharmacol.*, **47**, 2307 (1994); [d] E. Reil, M. Scoll, K. Masson and W. Oettmeier, *Biochem. Soc. Trans.*, **22**, 62 (1994); [e] Y. Mandi, K. Regely, I. Ocsovszky, J. Barbe, J. P. Galy and J. Molnar, *Anticaner Res.*, **14**, 2633 (1994).

[2a] J. M. Khurana, G.. C. Maikap and S. Mehta, *Synthesis* 731, (1990); [b] H. Matsumoto, T. Arai, M. Takahashi, T. Ashizawa, T. Nakano and Y. Nagai, *Bull. Chem. Soc. Jpn.* **56**, 3009 (1983); [c] T. Nakano, M. Takahashi, T. Arai, S. Seki, H. Matsumoto and Y. Nagai, *Chem. Lett.* 613, (1982).

[3] P. Shanmugasundaram, P. Amurugan, V. T. Ramakrishnam, N. Srividya and P. Ramamurthy, *Heteroatom. Chem.*, **7,** 17 (1996).

[4] N. Martin, M. Quinteio and C. Seoane, *J. Heterocyclic Chem.*, **32**, 235 (1995).

[5] M. Suarez, A. Loupy, E. Salfran, L. Moran and E. Rolando, *Heterocycles* **51**, 21 (1999).

[6] S. J. Tu, Z. S. Lu, D. Q. Shi, C. S. Y. Yao, Gao and C. Guo, *Synth. Commun.*, **32**, 2181 (2002).

[7] V. Ondru?, M. Orság, L. Fi?era and N. Prónayová, *Tetrahedron* **55,** 10425 (1999).

[8] P. Roman, H. Shengkui and D. C. Neckers, *Photochem. and Photobio. A: Chem.*, **110**, 79 (1997).

[9] C. Hubschwerlen, J. L. Specklin, C. H. Sigwalt and S. H. Locher, *Bioorg. Med. Chem.*, **11**, 2313 (2003).

[10] R. Gedye, F. Smith, K. Westawaym, A. Humera, L. Baldisern, L. Laberge and J. Rousell, *Tetrahedron Lett.*, **27** 279 (1986),

[11] S. J. Tu, Q. H. Wei, H. J. Ma, D. Q. Shi, Y. Gao and G. Y. Cui, *Synth. Commun.*, **17**, 2675 (2001).

[12] S. J. Tu, D. Q. Shi and J. C. Feng, *Chin. J. of Chem.*, **19**, 714 (2001).

[13] T. Quiroga, C. Cisneros, B. Insuasty, R. Abonia, M. Nogueras and A. Sanchez, *Tetrahedron Lett.*, **42,** 5625 (2001).

[14] S. J. Tu, J. F. Zhou, P. J. Cai and J. Z. Feng, *Synth. Commun.*, **24**, 3729 (2001).

[15] S. J. Tu, Z. S. Lu, D. Q. Shi, C. S. Yao, Y. Gao and C. Guo, *Synth. Commun.*, **14**, 2181 (2002).

[16] S. J. Tu, C. B. Miao, Y. Gao, F. Fang, Q. Y. Zhuang, Y. J. Feng and D. Q. Shi, *Synlett.*, **2**, 255 (2004).

[17] The sing-crystal growth was carried out in ethanol at room temperature. X-ray crystallographicanalysis was performed with a Siemens SMART CCD and a Semens P4 diffractometer. Crystal data for **4a**: $C_{27}H_{33}NO_4$, yellow, crystal dimension 0.30x0.22x0.19 mm, monoclinic, space group P21/n, *a*=9.6559(11), *b*=14.9830(16), *c*=16.5393(19) ≈, α=γ=90°, β=102.754(1)°, *V*=2333.8(5) ≈^{3}, *Mr*=386.28, *Z*=4, *Dc*=1.525 g/cm^3, λ=0.71070 Å, μ(*Mok*α)=0.082 mm^{-1}, *F(000)*=9366, R_1=0.0607, wR_2=0.1290. Crystal data for **4l**: $C_{23}H_{25}NO_3$, yellow, crystal dimension 0.50x0.30x0.20 mm, monoclinic, space group P21/c, *a*=11.2668(10), *b*=16.4542(12), *c*=10.8049(9) ≈, α=γ=90°, β=111.798(1)°, *V*=2333.8(5) ≈^{3}, *Mr*=363.44, *Z*=4, *Dc*=1.298 g/cm^3, λ=0.71070 Å, μ(*Mok*α)=0.085 mm^{-1}, *F(000)*=776, R_1=0.0678, wR_2=0.1415.