Synthesis of Acrimarins from 1,3,5-Trioxygenated-9-acridone Derivatives

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1,3,5-Trihydroxy-9(10*H*)-acridinone (**1**) was prepared from 3-hydroxyanthranillic acid with phloroglucinol. 1,3-Dihydroxy-5-methoxy-9(10*H*)-acridinone (**2**) was prepared from 3-methoxyanthranillic acid and phloroglucinol. Methylation of **1** under different conditions gave 1-hydroxy-3,5-dimethoxy (**3**), 1-hydroxy-3,5-dimethoxy-10-methyl (**4**), 1-hydroxy-3,5-dimethoxy-4-methyl (**5**), 1,3,5-trimethoxy-10-methyl (**6**) and 1,3,5-trimethoxy-4,10-dimethyl (**7**) analogues. Demethylation of **4** afforded the 1,3,5-trihydroxy-10-methyl analogue **8**. Condensation of acridones **1**, **2**, **3** and **4** individually with *E*-suberenol (**9**) gave four novel acrimarins (acridone-coumarin dimers) **10**, **11**, **12** and **13** respectively, while the acridone **8** gave previously reported acrimarin-G (**14**).

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Acridone alkaloids constitute a small group of natural products found mainly in the Rutaceae family of higher plants. This class of compounds has generated considerable interest due to high anti-tumour activity of acronycine [1,2] and the versatile biological activity shown by most other acridones [2]. Though acronycine and the majority of other acridone alkaloids exhibit a wide range of *in-vitro* biological activity, *in-vivo* experiments have shown limited success due to their extremely low solubility in common solvents [2]. Therefore, the preparation of biologically active acridones and their derivatization to more soluble prodrugs are of great interest. Most of the biologically active acridone alkaloids such as acronycine possess a 1,3-dioxygenated system. Therefore, we focused our attention on the synthesis of different types of new and naturally occurring acridone alkaloids with oxygenated functions at 1 and 3 positions.

In previous studies we reported the synthesis of 1,3-dioxygenated acridone alkaloids with a 3-hydroxy-3-methyl-1-butenyl moiety [3], 1,3,7,8-tetraoxygenated acridone alkaloids [4] and some acridone-coumarin dimers (acrimarins) [5]. Acrimarins are a class of compounds isolated from various *Citrus* plants and their hybrids. So far fourteen acrimarins (acrimarin A - N) have been reported from *Citrus* hybrids [6-10]. Both acridones and coumarins have shown wide range of biological activities. Therefore, acrimarins are also expected to show some interesting bioactivity. However, none of them has been tested for bioactivities due to the lack of materials. As a result, the synthesis of acrimarins is becoming very important. In this paper we describe the total synthesis of a number of 1,3-dioxygenated acridone analogoues, which have an additional oxygen function at the C-5 position, *i.e.* 1,3,5-trioxygenated-9-acridinones. Furthermore, the syntheses of the corresponding acrimarins of most of the above acridones have also been presented (Figure-1).

1,3,5-Trihydroxy-9(10*H*)-acridinone (**1**) and 1,3-dihydroxy-5-methoxy-9(10*H*)-acridinone (**2**) have not yet been reported as natural products. However, N-methyl derivatives of both **1**, [1,3,5-trihydroxy-10-methyl-9-acridinone

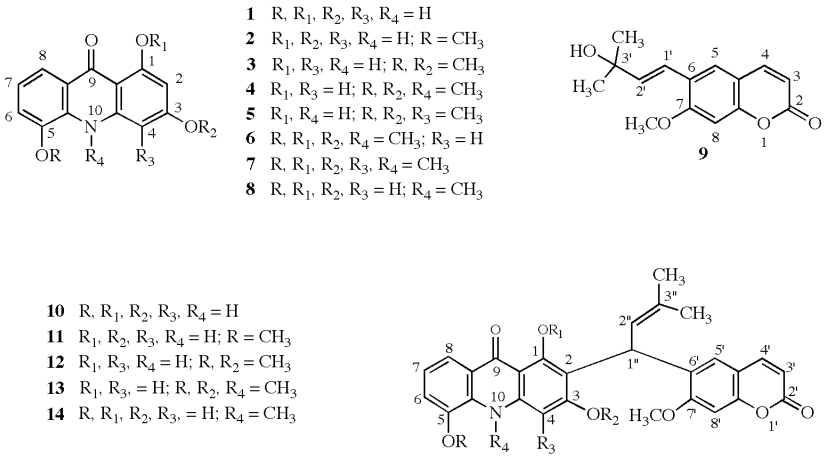
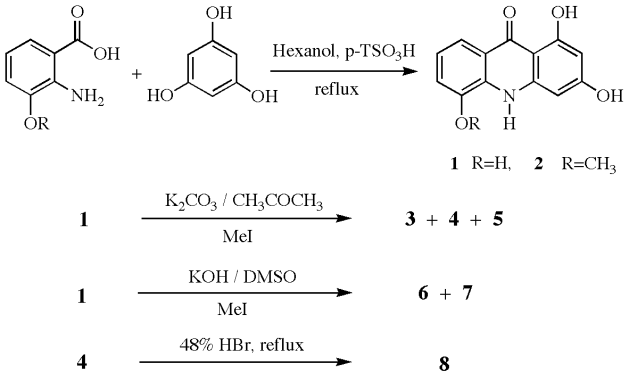


Figure -1

(**8**)] and **2**, [1,3-dihydroxy-5-methoxy-10-methyl-9-acridinone (yokodiene)] have been isolated from the root of Yahala [10] and *Citrus yoko* [11] respectively. 1-Hydroxy-3,5-dimethoxy-9(10*H*)-acridinone (**3**) is another compound, which has not been found in nature to date, but the synthesis of **3** has been described [12]. 1-Hydroxy-3,5-dimethoxy-10-methyl-9-acridinone (**4**) has been reported as yokodinine from *Citrus yoko* [11]. This is the first report of compounds, 1-hydroxy-3,5-dimethoxy-4-methyl-9(10*H*)-acridinone (**5**) and 1,3,5-trimethoxy-4,10-dimethyl-9-acridinone (**7**). 1,3,5-Trimethoxy-10-methyl-9-acridinone (**6**) has previously been reported from *Teclea boiviniana* [13]. Further, in this study we discuss the total synthesis of five acrimarins (**10** – **14**). Among these acrimarins only compound **14** has previously been reported as a natural product from *Citrus funadoko* (acrimarin–G) [6]. Though the other acrimarins have not yet been reported as naturally occurring compounds, the possibility of their natural occurrence cannot be ruled out. It is interesting to note that the acrimarin-M was isolated from *Citrus funadoko* [9] after we reported the total synthesis of this compound [5].

Treatment of 2-amino-3-hydroxybenzoic acid with phloroglucinol in 1-hexanol using *p*-toluenesulphonic acid as a catalyst gave acridone **1**. Methylation of **1** with MeI/anhydrous K_2CO_3 in acetone gave compound **3** as the major product and compounds **4** and **5** as by-products (Scheme 1). Two sharp methoxy singlets appeared at δ 3.80 and 4.00 in the ^{1}H nmr of **3**, indicating methylation of the two hydroxyl groups attached to C-3 and C-5 carbons of compound **1**. The ^{1}H and ^{13}C nmr spectra of compound **5** were almost identical to that of compound **3**. However, the sharp singlet at δ 2.18 in the ^{1}H nmr and the methyl carbon signal at δ 29.7 in the ^{13}C nmr of **5** showed the presence of an additional CH_3 group. Further, the sharp singlet at δ 6.29 revealed the replacement of the proton either at C-2 or C-4 by that CH_3 group. The strong correlation indicated by the methyl proton singlet at δ 2.18 with C-3 and C-4a, and the singlet at 6.29 with C-4 and C-9a in the HMBC spectrum of compound **5** confirmed that the proton is at C-2 and the methyl group is attached to C-4. The sharp singlet at δ 14.13 and the broad singlet at 8.33 in the ^{1}H nmr spectrum of **5** indicated the presence of a chelated OH group at C-1 and the NH group, respectively.

Scheme 1



The methylation of **1** with MeI/KOH in DMSO gave compounds **6** and **7** as major products (Scheme 1). The structure of compound **6** was suggested as 1,3,5-trimethoxy-10-methyl-9(10*H*)-acridinone since the spectral data agreed with that of the previously reported naturally occurring compound [13]. According to the spectral data, the structure of compound **7** was very similar to **6**, but it showed an additional methyl group at C-4, as in compound **5**. The presence of the additional methyl group was indicated by the sharp singlet at δ 2.31, and the methyl carbon signal at 13.4 in the ^{1}H and ^{13}C nmr, respectively. A sharp singlet at δ 6.38 due to the proton at C-2 confirmed the replacement of the C-4 proton by a methyl group. Further, HMBC spectrum of **7** confirmed that the substitution of the methyl group was at C-4. Hence, the structure 1,3,5-trimethoxy-4,10-dimethyl-9(10*H*)-acridinone was proposed for compound **7**. Demethylation of compound **4** with 48% HBr gave 1,3,5-trihydroxy-10-methyl-9(10*H*)-acridinone (**8**). The structure was confirmed by comparing the spectral data with those of the previously reported natural product [10].

Each of acridones **1**, **2**, **3**, **4** and **8** was treated with *E*-suberenol (**9**) (Scheme 2) in the presence of Nafion NR-50 resulting in the acridone coumarin dimers (acrimarins) **10**, **11**, **12**, **13** and **14** respectively. The acridones **5**, **6** and **7** did not react under the same conditions. The total synthesis of *E*-suberenol (**9**) had been previously described [14].

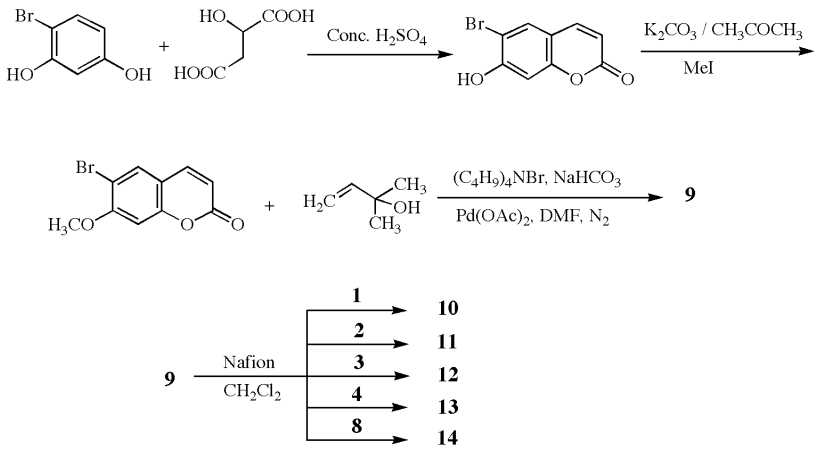
The high-resolution mass spectrum of compound **10** showed that its molecular formula is $C_{28}H_{23}NO_7$. The AB

Table 1

^{13}C NMR Spectral Data of Compounds **1** – **8**

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1	163.4	164.2	163.2	165.3	162.6	162.6	160.1	164.3
2	91.9	91.2	90.1	90.7	92.1	91.1	90.4	91.0
3	163.8	164.7	165.0	166.0	162.8	164.0	162.4	163.9
4	95.6	95.7	94.7	94.3	98.5	92.6	108.0	95.6
4a	143.6	147.1	142.9	147.6	139.2	149.4	152.6	124.7
5	145.4	147.3	147.3	149.5	146.6	149.9	150.7	146.8
6	114.8	119.9	112.5	116.0	111.7	114.8	114.3	116.2
7	120.8	122.2	120.7	122.1	120.6	122.0	122.7	119.3
8	115.9	115.8	116.2	118.4	117.2	119.2	118.5	121.9
8a	119.8	123.0	119.6	120.7	119.9	128.0	129.3	120.9
9	180.0	179.5	180.1	180.8	181.6	177.1	179.5	180.2
9a	103.4	103.7	104.3	105.7	104.5	109.1	111.9	106.6
10a	131.4	133.3	131.7	128.8	131.5	134.6	138.5	123.3
OCH_3		56.0	55.2	55.5	55.8	56.4	56.2	
			56.1	56.5	56.0	56.1	56.0	
						55.4	55.7	
NCH_3				41.8		42.3	46.9	40.5

Scheme 2



doublet at δ 7.50 and 6.21 (J= 10 Hz) and two singlets at δ 6.72 and 7.67 showed the presence of a 6,7-disubstituted coumarin moiety. The signal of the 7-methoxy group of the coumarin moiety appeared at δ 3.80. Three double doublets at δ 7.75 (8-H), 7.20 (7-H), 7.19 (6-H) and the singlet at 6.31 (4-H) indicated the presence of a 1,2,3,5-tetrasubstituted 9-acridone moiety. The singlet at δ 14.45 and broad singlet at 9.40 (D_2O exchangeable) were assigned to three hydroxy groups at C-1, C-3 and C-5 of the acridone residue. Two singlets at δ 1.80(3H) and 1.73(3H) accounted for the two vinylic methyl groups of the prenyl unit. Two doublets at δ 5.73 (1H) and 6.04 (1H) with J= 9.8Hz were assigned to 1"–H and 2"–H, respectively. Further, the prominent peak at m/z 242 (78%) in the MS spectrum of **10** also revealed the presence of a coumarin moiety with the prenyl unit in the molecule. According to the ^1H and ^{13}C nmr spectral data of compound **10**, the prenylated coumarin moiety could be bridged either through C-2 or C-4 positions of the acridone molecule. However, the HMQC and HMBC studies revealed that the bridging occurs at C-2. Further, the corresponding signals for both acridone and prenylated coumarin residues, indicated in the ^{13}C nmr spectrum of **10** (Table 2) provided additional evidence for the proposed structure of 1,3,5-trihydroxy-2-[1"-(7'-methoxy-2'-oxo-2*H*-chromen-6'-yl)-3"-methyl-2"-butenyl]-9(10*H*)-acridinone (**10**).

Table 2

^{13}C nmr Data of Compounds **10** – **14**

	10	**11**	**12**	**13**	**14**
1	163.3	162.2	161.4	161.5	162.3
2	110.8	110.3	111.0	111.5	109.8
3	163.8	152.3	164.0	163.8	164.1
4	91.3	91.0	86.9	87.3	91.4
4a	142.0	140.7	142.2	142.3	137.9
5	142.6	146.8	148.2	147.4	148.2
6	112.3	111.5	112.8	118.4	112.2
7	120.1	120.2	120.3	120.0	120.2
8	116.9	116.8	117.0	117.4	117.5
8a	121.7	120.4	121.8	122.0	124.2
9	182.0	180.4	180.9	180.7	181.8
9a	105.0	105.7	105.0	105.9	109.3
10a	134.0	132.8	132.3	133.7	132.6
2'	160.1	161.0	160.5	160.9	161.8
3'	112.1	114.4	112.0	112.2	113.6
4'	146.1	145.0	145.8	145.3	145.6
4'a	112.3	110.3	113.4	113.7	112.9
5'	129.4	128.5	129.1	128.3	129.5
6'	133.5	130.6	130.2	130.3	131.6
7'	162.0	162.7	161.3	161.8	162.3
8'	99.0	98.2	99.4	98.3	99.2
8'a	154.9	154.0	154.6	154.2	154.8
1"	33.5	32.9	32.9	32.6	33.2
2"	125.2	124.3	125.7	124.3	125.8
3"	131.5	130.6	131.9	132.8	132.5
OCH_3	56.3	61.1, 55.7	64.5, 56.1, 50.6	62.3, 55.4, 51.2	55.8, 55.8
NCH_3	-	-	-	41.7	40.8
CH_3	26.0,18.2	25.9, 17.6	26.5, 18.7	26.2, 18.2	25.7, 18.0

As in acrimarin **10**, the ^1H and ^{13}C nmr and mass spectral data of acrimarins **11, 12, 13** and **14** also indicated the presence of identical coumarin and prenyl units and their respective acridone moieties. Further, their molecular formulae suggested by MS and confirmed by HRMS were also in agreement with the proposed structures. The allylic moiety of *E*-suberenol (**9**) could be linked to the acridone moiety, either through C-2 or C-4. However, the HMBC studies suggested that the coumarin unit with the prenyl group is attached to the C-2 position of each acridone moiety. Hence, the pertinent structures were assigned for the other four acrimarins.

EXPERIMENTAL

1,3,5-Trihydroxy-9(10*H*)-acridinone (**1**).

A mixture of 2-amino-3-hydroxybenzoic acid (1 g), phloroglucinol (1.2 g) and *p*-toluenesulphonic acid (50 mg) in 1-hexanol (30 ml) was refluxed for 6 h. The mixture was allowed to cool, stirred well with 100 ml of hexane and filtered. The residue was thoroughly

washed with hexane (3 x 100 ml) and dichloromethane (2 x 100 ml) to remove hexanol and traces of 2-amino-3-hydroxybenzoic acid and *p*-toluenesulphonic acid. The dried crude yellow residue was recrystallized from acetone/water to give bright yellow prisms of **1**. Yield: 1.4 g (88%); mp >320 °C (lit. [15] 319–320 °C); ^{1}H nmr (400 MHz, DMSO): δ 14.37 (s, 1H, chelated OH), 11.2 (br.s., 1H, NH), 10.5 (br.s., OH), 7.59 (dd, 1H, 8-H, J=7.9, 1.5 Hz), 7.13 (dd,1H, 6-H, J=7.6, 1.5 Hz), 7.04 (dd, 1H, 7-H, J=7.9, 7.6 Hz,), 6.67 (d, 1H, 4-H, J=2.0 Hz), 5.98 (d, 1H, 2-H, J=2.0 Hz); ^{13}C nmr (100 MHz, DMSO): (Table 1); ms: *m/z* (%) = 243 (M^+, 100), 215 (10), 187 (8); hrms: *m/z* calcd. for $C_{13}H_9NO_4$: 243.0531; found 243.0525.

1,3–Dihydroxy-5-methoxy-9(10*H*)-acridinone (**2**).

A mixture of 2-amino-3-methoxybenzoic acid (1 g), phloroglucinol (762 mg), and *p*-toluenesulphonic acid (60 mg) in 1-hexanol (40 ml) was heated to reflux for 12 h. The mixture was allowed to cool, stirred well with hexane (3 x 100 ml) and dichloromethane (2 x 100 ml). The dried crude yellow residue was recrystallized from ethanol/water to give bright yellow needles of **2**. Yield: 1.20 g (80.0%); mp 278–280 °C (lit. [16] 275–280 °C). ^{1}H nmr: (400 MHz, $CDCl_3/CD_3OD$): δ 14.07 (s, H, chelated OH), 11.80 (br.s., 1H, NH), 10.20 (br.s., OH), 7.75 (dd, 1H, 8-H, J = 7.6, 2.2 Hz), 7.05 (m, 2H, 6-H and 7-H), 6.30(d, 1H, 2-H J = 1.8 Hz), 6.10 (d, 1H, 4-H, J = 1.8 Hz); ^{13}C nmr: (100 MHz, $CDCl_3/CD_3OD$): (Table 1); ms: *m/z* (%) = 257 (M^+, 100), 242 (37), 228 (17), 200 (22), 185 (13); hrms *m/z* calcd. for $C_{14}H_{11}NO_4$: 257.0688; found 257. 0672.

Methylation of 1,3,5-Trihydroxy-9(10*H*)-acridinone (**1**).

Method A.

A mixture of compound **1** (120 mg), anhydrous K_2CO_3 (103 mg) in acetone (10 ml) was heated to reflux temperature for 1 h and allowed to cool. Then MeI (2 ml) was added, and the mixture was stirred for another 30 min at room temperature. The usual work up procedure followed by preparative thin layer chromatography gave compounds **3**, **4** and **5**.

Method B.

Compound **1** (150 mg) in DMSO was stirred with KOH (200 mg) in an ice-water bath for 30 min., MeI (2 ml) was added, and the mixture was stirred for another 30 min. The mixture was then diluted with distilled water (25 ml), neutralized with 2 *N* HCl and partitioned with CH_2Cl_2 (3 x 25 ml). The organic layer was evaporated to dryness and separated by preparative TLC to give compounds **6** and **7**.

1-Hydroxy-3,5-dimethoxy-9(10*H*)-acridinone (**3**).

This compound was obtained in 50% yield (68 mg) as yellow prisms from DMSO/water mp 220–222 °C (lit. [12] 215–218 °C) ^{1}H nmr (400 MHz, DMSO): δ 14.19 (s, 1H, chelated OH), 11.25 (s, 1H, NH), 7.72 (dd, 1H, 8-H, J=8.0, 1.4 Hz), 7.24 (dd, 1H, 6-H, J=7.8, 1.4 Hz), 7.13 (dd, 1H, 7-H, J=8.0, 7.8 Hz), 6.83 (d, 1H, 4-H, J=2.3 Hz), 6.08 (d, 1H, 2-H, J=2.3 Hz), 4.00 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3); ^{13}C nmr (100 MHz, DMSO): (Table 1); ms: *m/z* (%) = 271 (M^+, 100), 256 (65), 242 (28), 228 (12), 213 (9), 200 (12), 185 (11), 135 (8); hrms: Calcd. for $C_{15}H_{13}NO_4$: 271.0844; found 271.0837.

1-Hydroxy-3,5-dimethoxy-10-methyl-9-acridinone (**4**).

This compound was obtained in 17% yield (24 mg) as yellow needles from $CHCl_3$/hexane, mp 148–150 °C (lit. [11] yellow oil) ^{1}H nmr (400 MHz, $CDCl_3$): δ 14.54 (s, 1H, chelated OH), 8.03 (dd, 1H, 8-H, J=7.4, 2.0 Hz), 7.22 (dd, 1H, 7-H, J=7.7, 7.4 Hz), 7.17 (dd, 1H, 6-H, J=7.7, 2.0 Hz), 6.28 (s, 2H, 2-H & 4-H), 3.95 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.90 (s, 3H, NCH_3); ^{13}C nmr (100 MHz, $CDCl_3$): (Table 1); ms: *m/z* (%) = 285 (M^+, 100), 270 (49), 256 (17), 240 (13), 227 (22), 213 (11), 199 (17), 170 (10), 77 (12); hrms: *m/z* calcd. for $C_{16}H_{15}NO_4$: 285.1001; found 285.0994.

1-Hydroxy-3,5-dimethoxy-4-methyl-9(10*H*)-acridinone (**5**).

This compound was obtained in 19% yield (28 mg) as yellow prisms from $CHCl_3$/hexane, mp 185–186 °C; ^{1}H mnr(400 MHz, $CDCl_3$): δ 2.18 (s, 3 H, $ArCH_3$), 3.89 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 6.29 (s, 1 H, 4-H), 7.02 (dd, 1 H, 6-H, J=7.8, 1.5 Hz), 7.11 (dd, 1 H, 7-H, J=7.8, 7.8 Hz), 7.84 (dd, 1 H, 8-H, J=7.9, 1.5 Hz), 8.33 (br.s., 1 H, NH), 14.13 (s, 1 H, chelated OH); ^{13}C nmr (100 MHz, $CDCl_3$): (Table 1); ms: *m/z* (%) = 285 (M^+, 100), 270 (55), 256 (12), 240 (14), 227 (30), 212 (10), 77 (12); hrms: *m/z* calcd for $C_{16}H_{15}NO_4$: 285.1001; found 285.0988.

Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36, H, 5.30, N, 4.91. Found C, 67.41, H, 5.37, N, 4.87.

1,3,5-Trimethoxy-10-methyl-9-acridinone (**6**).

This compound was obtained in 40% yield (51 mg) as colourless plates from CH_2Cl_2/hexane, mp 142–143 °C (lit. [13] 140–141 °C); ^{1}H mnr (400 MHz, $CDCl_3$): δ 8.02 (dd, 1H, 8-H, J=7.8, 1.8Hz), 7.17(t, 1H, 7-H, J=7.8 Hz), 7.11 (dd, lH, 6-H, J=7.8, 1.7 Hz), 6.38(d, 1H, 4-H, J=2.1 Hz), 6.26 (d, 1H, 2-H, J=2.1 Hz), 3.96 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.92 (s, 3H, NCH_3), 3.86 (s, 3H, OCH_3). ^{13}C mnr(100 MHz, $CDCl_3$): (Table 1); ms: *m/z* (%) = 299 (M^+, 37), 285 (100), 270 (54), 256 (23), 240 (13), 227 (22), 199 (17); hrms: Calcd. For $C_{17}H_{17}NO_4$: 299.1157; found 299.1161.

1,3,5-Trimethoxy-4,10-dimethyl-9-acridinone (**7**).

This compound was obtained in 25% yield (33 mg) as pale yellow needles from $CHCl_3$/hexane, mp 183–184 °C; ^{1}H nmr (400 MHz, $CDCl_3$): δ 2.31 (s, 3 H, 4 CH_3), 3.47 (s, 3 H, NCH_3), 3.95 (s, 3 H, OCH_3), 3.98 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 6.38 (s, 1 H, 2-H), 7.09 (dd, 1 H, 6-H, J=8.0, 1.5 Hz), 7.18 (dd, 1 H, 7-H, J=8.1, 7.8 Hz), 7.86 (dd, 1 H, 8-H, J=7.8, 1.5 Hz); ^{13}C nmr (100 MHz, $CDCl_3$): (Table 1); ms: *m/z* (%)= 313 (M^+, 11), 299 (100), 285(67), 270 (35), 240 (17), 227 (34), 170 (10); hrms: *m/z* calcd for $C_{18}H_{19}NO_4$: 313.1314; found 313.1320.

Anal. Calcd for $C_{18}H_{19}NO_4$: C, 68.99, H, 6.11, N, 4.47. Found C, 68.91, H, 5.97, N, 4.62.

1,3,5-Trihydroxy-10-methyl-9-acridinone (**8**)**.**

A mixture of compound **6** (50 mg) and 48% HBr (20 ml) was refluxed for 1 h. Preparative TLC separation of the mixture yielded compound **8** as pale yellow oil. Yield: 32 mg (78%); (lit. [10], yellow oil); ^{1}H nmr (400 MHz, $CDCl_3/CD_3OD$): δ 14.30 (s, 1H, chelated OH), 10.5 (br.s., OH), 7.87 (dd, 1H, 8-H, J = 7.1 & 2.0 Hz), 7.75 (dd, 1H, 6-H, J =7.3, 2.0 Hz,), 7.15 (t, 1H, 7-H, J = 7.2 Hz), 6.15 (d, 1H, 4-H, J = 2.0 Hz), 6.02 (d, 1H, 2-H, J=2.0 Hz,) and 4.05 (s, 3H, NCH_3); ^{13}C nmr (100 MHz, $CDCl_3/CD_3OD$): (Table 1); ms: *m/z* (%) = 257 (M^+, 100), 243 (72), 187 (28); hrms: Calcd. for $C_{14}H_{11}NO_4$: 257.0688; found 257.0697.

E-Suberenol [6-(3'-hydroxy-3'-methyl-1'-butenyl)-7-methoxycoumarin)] (**9**).

E-Suberenol was synthesized from 4-bromoresurcinol (1 g) according to a previously recorded procedure [14] and recrystal-

lized from hexane/CH_2Cl_2 to give pale yellow crystals. Yield: 0.87 g (63%); mp 172–174 °C (lit. [14], 174-175 °C); ^{1}H nmr (200 MHz, $CDCl_3$): δ 7.75 (d, 1H, 4-H, J = 9.4 Hz), 7.65 (s, 1H, 5-H), 6.85 (d, 1H, 1'-H, J = 16.0 Hz), 6.81 (s, 1H, 8-H), 6.38 (d, 1H, 2'-H, J = 16.0 Hz), 6.27 (d, 1H, 3-H, J = 9.4 Hz), 3.96 (s, 3H, OCH_3), 1.44 (s, 6H, 2x CH_3); ^{13}C nmr (50 MHz, $CDCl_3$): δ 162.3(C-2), 160.3 (C-7), 155.0 (C-8a), 144.3 (C-4), 139.6 (C-2'), 125.5 (C-5), 124.6 (C-6), 119 .5 (C-1'), 112.8 (C-3, 112.3 (C-4a), 98.8 (C-8), 70.6 (C-3'), 55.7 (OCH_3), 29.1 (2x CH_3); ms: *m/z* (%) = 260 (M^+, 26), 245 (48), 203 (64), 189 (100), 159 (17), 131 (10), 119 (11), 58(12).

General Procedure for the Synthesis of Acrimarins.

The appropriate acridone (100 mg) and *E*-suberenol (**9**), (50 mg) were dissolved in absolute ethanol (5–10 ml) and Nafion NR-50 (mesh 35–60) [17] was added to the mixture while stirring at room temperature. After 6 h the TLC monitoring of the reaction was started and further amounts of *E*-suberenol (10 mg aliquots at a time) were added at given intervals (1–2 h) while stirring until TLC indicated the disappearance of the acridone or no further changes in the reaction mixture. The products of the reaction mixture were purified by preparative TLC followed by recrystallization to give the respective pure acrimarins. The acridones **1**, **2**, **3**, **4** and **8** subjected to the above procedure gave acrimarins **10**, **11**, **12**, **13** and **14,** respectively, but there was no reaction observed for the acridones **5**, **6** and **7** even after continuous stirring for 96 h.

1,3,5-Trihydroxy-2-[1"-(7'-methoxy-2'-oxo-2*H*chromen-6'-yl)-3"-methyl-2"-butenyl]-9(10*H*)-acridinone (**10**).

This compound was obtained in 61% yield (118.5 mg) as bright yellow needles from CH_2Cl_2/CH_3OH, mp 202 –204 °C, ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.73 (s, 3 H, CH_3), 1.80 (s, 3 H, CH_3), 3.80 (s, 3 H, OCH_3), 5.73 (d, 1 H, 1"-H, J =9.8 Hz), 6.04 (br.d, 1 H, 2"-H, J=9.8 Hz), 6.21 (d, 1H, 3'-H, J=10 Hz), 6.31 (s, 1 H, 4-H), 6.72 (s, 1 H, 8'-H), 7.19(dd, 1 H, 6-H, J= 8.0 & 2.0 Hz), 7.20 (dd, 1 H, 7-H, J= 8.5 & 7.9 Hz), 7.50 (d, 1 H, 4'-H, J=10.0 Hz), 7.67 (s, 1 H, 5'-H), 7.75 (dd, 1 H, 8-H, *J*= 8.5 & 2.0 Hz), 9.40 (br.s, 2 H, 3-OH and 5-OH), 14.45 (s, 1 H, 1-OH); ^{13}C nmr (100 MHz, $CDCl_3$): (Table 2); ms: m/z (%) = 485 (M^+, 3), 429 (10), 386 (20), 359 (35), 242 (78), 229 (59), 147 (57), 129 (100), 111 (44), 73 (37), 55 (39); hrms: m/z calcd for $C_{28}H_{23}NO_7$: 485.1474; found 485.1468,

Anal. Calcd for $C_{28}H_{23}NO_7$: C, 69.27, H, 4.78, N, 2.89. Found C, 69.41, H, 4.77, N, 2.87.

1,3-Dihydroxy-5-methoxy-2-[1"-(7'-methoxy-2'-oxo-2*H*-chromen-6'-yl)-3"-methyl-2"-butenyl]-9(10*H*)-acridinone (**11**).

This compound was obtained in 57% yield (111.8 mg); yellow needles from CH_2Cl_2/CH_3OH, mp 164–165 °C, ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.72 (s, 3 H, CH_3), 1.80 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 5.72 (d, 1 H, 1"-H, J=9.1 Hz), 6.03 (br.d, 1 H, 2"-H, J =9.0 Hz), 6.21 (d, 1 H, 3'-H, J=9.4 Hz), 6.37 (s, 1 H, 4-H), 6.76 (s, 1 H, 8'-H), 7.05 (dd, 1 H, 6-H, J=8.0 & 2.0 Hz), 7.10 (dd, 1 H, 7-H, J=7.8 & 8.0 Hz), 7.67 (s, 1 H, 5'-H), 7.78 (d, 1 H, 4'-H, J =9.5 Hz), 7.85 (dd, 1 H, 8-H, J =8.0 & 1.9 Hz), 10.52 (br.s, 1 H, 3-OH), 11.40(br.s, NH), 14.20 (s, 1 H, 1-OH); ^{13}C nmr ($CDCl_3$, 100 MHz): (Table 2); ms: m/z (%) = 500 (M^++1, 21) 456 (100), 441 (14), 257 (15), 242 (28), 227(20); hrms: m/z calcd for $C_{29}H_{25}N0_7$: 499.1631; found 499.1647.

Anal. Calcd for $C_{29}H_{25}NO_7$: C, 69.73, H, 5.04, N, 2.80. Found C, 69.64, H, 5.07, N, 2.83.

3,5-Dimethoxy-1-hydroxy-2-[1"-(7'-methoxy-2'-oxo-2*H*-chromen-6'-yl)-3"-methyl-2"-butenyl]-9(10*H*)-acridinone (**12**).

This compound was obtained in 35% yield (62.8 mg) as yellow prisms from CH_2Cl_2/hexane mp 147–149 °C, ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.62 (s, 3 H, CH_3), 1.69 (s, 3 H, CH_3), 3.74 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 4.01 (s, 3 H, OCH_3), 5.64 (d, 1 H, 1"-H, J = 9.5 Hz), 5.92 (d, 1 H, 2"-H, J = 9.5 Hz), 6.19 (d, 1 H, 1H, 3'- H, J = 9.5 Hz), 6.94 (s, 1 H, 4-H), 6.89 (s, 1 H, 8'-H), 7.17 (dd, 1 H, 7-H, J= 8.1, 8.0Hz), 7.29 (dd, 1 H, 6-H, J= 7.9, 1.0 Hz), 7.60 (s, 1 H, 5'-H), 7.71 (dd, 1 H, 8-H, J=8.2, 1.0 Hz), 8.02 (d, 1 H, 4'-H, J=9.5 Hz), 14.31 (s, 1 H, 1-OH); ^{13}C nmr (100 MHz, $CDCl_3$): (Table 2); ms: m/z (%) = 513 (M^+, 11), 457 (72), 442 (24), 256 (15), 242 (58), 228 (22), 146 (37), 129 (100) and 112 (34); hrms: m/z calcd for $C_{30}H_{27}NO_7$: 513.1787; found 513.1781.

Anal. Calcd for $C_{30}H_{27}NO_7$: C, 70.16, H, 5.30, N, 2.73. Found C, 70.21, H, 5.47, N, 2.87.

3,5-Dimethoxy-1-hydroxy-10-methyl-2-[1"-(7'-methoxy-2'-oxo-2*H*-chromen-6-yl)-3-methyl-2"-butenyl-9-acridinone (**13**).

This compound was obtained in 48% yield (88.6 mg) as yellow needles from CH_2Cl_2/hexane, mp 142–143 °C, ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.64 (s, 3 H, CH_3), 1.72 (s, 3 H, CH_3), 3.76 (s, 3 H, OCH_3), (s, 3 H, OCH_3), 3.87 (s, 3 H, NH_3), 3.97 (s, 3H, OCH_3), 5.66 (d, 1 H, 1"-H, J =9.5Hz), 5.90 (br.d, 1 H, 2"-H, J = 9.5 Hz), 6.14 (d, 1 H, 3'-H, J = 9.2 Hz), 6.24 (s, 1 H, 4H), 6.63 (s, 1 H, 8'-H), 6.98 (dd, 1 H, 6-H J=7.5, 1.9 Hz), 7.14 (dd, 1 H, 7-H, J= 8.1, 7.6 Hz), 7.52 (s, 1 H, 5'-H), 7.64 (d, 1 H, 4'-H, J=9.3 Hz), 7.81 (dd, 1 H, 8-H, J=8.0, 2.0 Hz), 14.25 (s, 1 H, 1-OH); ^{13}C nmr (100 MHz, $CDCl_3$): (Table 2); ms: m/z (%) = 528 (M^++1, 9), 498 (18), 387 (23), 359 (35), 339 (48), 243 (80), 230 (39), 148 (47) and 129 (100); hrms: m/z calcd for $C_{31}H_{29}NO_7$: 527.1944; found 527.1957,

Anal. Calcd for $C_{31}H_{29}NO_7$: C, 70.58, H, 5.54, N, 2.65. Found C, 70.41, H, 5.37, N, 2.87.

1,3,5-Trihydroxy-10-methyl-2-[1"-(7'-methoxy-2'-oxo-2*H*-chromen-6'-yl)-3"-methyl-2"-butenyl]-9(10*H*)-acridinone (**14**).

This compound was obtained in 51% yield (99.2 mg) as pale yellow semi-solid; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.73 (s, 3 H, CH_3), 1.78 (s, 3 H, CH_3), 3.85 (s, 3 H, OCH_3), 3.92 (s, 3 H, NH_3), 5.78 (d, 1 H, 1"-H, J =9.0 Hz), 6.06 (br.d, 1 H, 2"-H, J=9.0 Hz), 6.18 (d, 1 H, 3'-H, J= 9.5 Hz), 6.38 (s, 1 H, 4-H), 6.82 (s, 1 H, 8'-H), 7.17 (dd, 1 H, 7-H, J=8.0 & 7.9 Hz), 7.27 (dd, 1 H, 6-H, J= 8.0 & 2.0 Hz), 7.70 (s, 1 H, 5'-H), 7.84 (d, 1 H, 4'-H, J= 9.5 Hz), 7.87 (dd, 1 H, 8-H, J= 8.0 & 1.9 Hz), 10.20 (br.s, 2 H, 3-OH and 5-OH), 14.75 (s, 1 H, 1-OH); ^{13}C nmr (100 MHz, $CDCl_3$): (Table 2); ms: m/z (%) =500 (M^++1, 23), 386 (20), 359 (35), 339(48), 256 (24), 242 (100), 229 (59), 147 (57) and 129 (60); hrms: m/z calcd for $C_{29}H_{25}NO_7$: 499.1631; found 499.1658.

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