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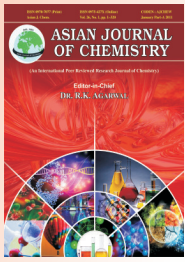

Synthesis and NMR of 4-Aryl-3,4-dihydrocoumarins and 4-Arylcoumarins

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This paper described the synthesis and ^{1}H and ^{13}C NMR chemical shifts of a series of 4-aryl-3,4-dihydrocoumarin and 4-arylcoumarin derivatives based on a combination of ^{1}H and ^{13}C NMR, HSQC and HMBC experiments.

Keywords: ^{1}H NMR, ^{13}C NMR, 2D NMR, 4-Aryl-3,4-dihydrocoumarins, 4-Arylcoumarins, Synthesis.

INTRODUCTION

The compounds 4-arylcoumarin and 4-aryl-3,4-dihydrocoumarin constitute a specific branch of coumarin derivatives regarded as a rare subgroup of flavonoids. In recent years, several 4-arylcoumarins and 4-aryl-3,4-dihydrocoumarins have been shown to possess antidiabetic[1], antiinflammatory[2,3], cytotoxic[4-6] and antifungal[7] effects.

We have investigated the design, synthesis and potential therapeutic properties of a series of arylcoumarins. In this paper, to address the paucity of fully assigned NMR spectral data for these types of compounds, a series of 4-arylcoumarin and 4-aryl-3,4-dihydrocoumarin of varying complexity were synthesized and their ^{1}H and ^{13}C NMR spectral data fully assigned based on a combination of 1D and 2D NMR experiments including HSQC and HMBC.

EXPERIMENTAL

Melting points were determined using a Thiele tube and were uncorrected. The FT-IR spectra were recorded using an Analect RFX-65A spectrometer with KBr pellets. Spin multiplets are given as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Mass spectra were obtained with a Shimadzu QP-5050A spectrometer.

NMR spectra: Chemical shifts were reported on a δ scale (ppm) with $CDCl_3$ or CD_3COCD_3 as the solvents. The ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker DRX-400 spectrometer with TMS as the external standard. Chemical shifts are reported in ppm (δ) and referenced to TMS (δH = 0 ppm) in ^{1}H NMR spectra or to residual $CDCl_3$ (δH = 7.25 ppm, δC = 77 ppm) in heteronuclear 2D spectra. Scalar couplings are reported in hertz. Typically, 20-30 mg of sample was dissolved in 1 mL of $CDCl_3$ and 0.7 mL of the solution transferred into a 5 mm Norell ST500 NMR tube. The ^{1}H and ^{13}C NMR spectra of compounds were recorded on a Bruker DRX-400 spectrometer operating at 400.13 and 100.6 MHz, respectively, equipped with a 5 mm QNP $^{13}C/^{1}H/^{31}P/^{15}N$ probe head. The ^{1}H spectra were recorded with 32 scans, 3s relaxation delay, 1.36 s acquisition time, 0.367 Hz digital FID resolution, 16384 FID size, with 6009 Hz spectral width. The ^{13}C spectra were recorded with Waltz 16 ^{1}H broadband decoupling, 300 scans, 5s relaxation delay, 0.3 s acquisition time, 1.5 Hz digital FID resolution, 16384 FID size, 25063 Hz spectral width. 2D spectra were recorded on a Bruker DRX 400 spectrometer (400.13 MHz for ^{1}H, 100.6 MHz for ^{13}C) equipped with QNP probe head. Standard pulse sequences were used for 2D spectra. Data processing was performed on a 1K × 512 data matrix. Inverse-detected 2D heteronuclear correlated spectra were measured over 2048 complex points in F2 and 256 increments in F1, collecting 64 (HSQC) or 128 (HMBC) scans per increment with a relaxation delay of 2 s. The spectral widths were 4 and 22 kHz in F2 and F1 dimensions, respectively. The HSQC experiments were optimized for C-H couplings of 145 Hz; the HMBC experiments were optimized for long-range C-H couplings of 3 Hz. Fourier transforms were performed on a 2048 × 512 data matrix. π/2 shifted sine-squared window functions were used along F1 and F2 axes for all 2D spectra.

Synthesis of 5,7,4'-trimethoxy-4-phenylcoumarin (1a) and 5,7-dimethoxy-4-phenylcoumarin (1b): Ponndorf reaction of phenylpropiolic acid (10 mmol) with phloroglucinol (10 mmol) in the presence of CF_3COOH (7 mL) at room temperature. The reaction mixture was poured into ice water, washed with water (150 mL) and dried to obtain hydroxylated 4-arylcoumarins. To a mixture of hydroxylated 4-arylcoumarins,

potassium carbonate (45m mol) and acetone (150 mL) was added and then refluxed for 4 h. Filtrate the reaction mixture and dried. Crude product can be purified either by column chromatography on silica gel or by washing with water, dried and then crystallized from ethyl acetate and petroleum ether for two or three times[8].

5,7-Dimethoxy-4-phenylcoumarin (1a): White crystals; m.p. 151-152 °C; Yield: 62.8 %; IR (KBr, ν_{max}, cm^{-1}): 1712, 1624, 1591, 1510, 1460, 1356, 1244, 1228, 1203, 1157, 1107; EI-MS: *m/z*: 312 $[M]^+$, 284 $[M\text{-}CO]^+$, 269 $[M\text{-}CO\text{-}Me]^+$, 226, 211, 167, 149.

5,7,4'-Trimethoxy-4-phenylcoumarin (1b): Yellow crystals; m.p. 213-215 °C; Yield: 66.2 %; IR (KBr, ν_{max}, cm^{-1}): 1716, 1612, 1460, 1352, 1227, 1205, 1159, 1111; EI-MS: *m/z*: 282 $[M]^+$, 254 $[M\text{-}CO]^+$, 239 $[M\text{-}CO\text{-}Me]^+$, 211, 196, 168, 152, 139.

Synthesis of 4-arylcoumarins (1c-1g): A solution of the appropriate phenol (11 mmol) and the appropriate aryl-propargyl acid (10 mmol) in 10 mL of CF_3COOH was stirred at room temperature for 4-8 h. The reaction mixture was poured onto ice water. It was extracted with ethyl acetate (2 × 150 mL), washed with water (150 mL) and dried. The solvent was removed under reduced pressure to obtain the crude product, which was then purified by chromatography on silica gel.

4-(3,4-Dimethoxyphenyl)-7-hydroxycoumarin (1c): White crystals, m.p. 233-234 °C, Yield: 56.4 %; IR (KBr, ν_{max}, cm^{-1}): 3194 (OH), 1695 (CO), 1624, 1599, 1518, 1263 and 1140; MS *m/z* (%) 298 $[M]^+$, 283 $[M\text{-}CH_3]^+$, 270, 255, 227, 199, 184, 113.

4-(3,4-Dimethoxyphenyl)-7,8-dihydroxycoumarin (1d): White crystals, m.p. 271-272 °C, Yield: 58 %; IR (KBr, ν_{max}, cm^{-1}): 2987, 1726 (CO), 1618, 1518, 1379, 1255, 1147 and 814; MS *m/z* (%) 314 $[M]^+$, 286 $[M\text{-}CO]^+$, 271 $[M\text{-}CO\text{-}CH_3]^+$, 161, 133, 115, 103.

4-(3,4-Dimethoxyphenyl)-7-methoxycoumarin(1e): White crystals, m.p. 148-149 °C, Yield: 53.8 %; IR (KBr, ν_{max}, cm^{-1}): 3411 (CO), 1695 (CO), 1606, 1518, 1448, 1173 and 1140; MS *m/z* (%) 312 $[M]^+$, 297 $[M\text{-}CH_3]^+$, 284 $[M\text{-}CO\text{-}CH_3]^+$, 269, 213, 183, 139.

7,8-Dihydroxy-4-(3-hydroxy-4-methoxyphenyl) coumarin (1f): Yellow crystals, m.p. 176-177 °C, Yield: 53.7 %; IR (KBr, ν_{max}, cm^{-1}): 3371 (OH), 1695 (CO), 1653, 1599, 1448, 1240, 1178 and 1130; MS *m/z* (%) 300 $[M]^+$, 272 $[M\text{-}CO]^+$, 257 $[M\text{-}CO\text{-}CH_3]^+$, 229, 115.

7-Methoxy-4-(4-methoxyphenyl)coumarin (1g): White crystals, m.p. 155-157 °C, Yield: 69 %; IR (KBr, ν_{max}, cm^{-1}): 3440, 3064, 2993, 1738 (CO), 1612, 1510, 1375, 1250, 825; MS *m/z* (%) 282 $[M]^+$, 254 $[M\text{-}CO]^+$, 239 $[M\text{-}CO\text{-}CH_3]^+$, 211, 196, 168, 152, 140, 127.

General procedure for the synthesis of 4-aryl-3,4-dihydrocoumarins (2a-2l): To a mixture of $POCl_3$ (10 mmol) and BF_3-Et_2O (20 mmol) at 0 °C, substituted cinnamic acid (5 mmol) was added and the reaction mixture was stirred for 15 min at 0 ºC. Substituted phenol (5 mmol) was added and the mixture stirred at room temperature for 4-18 h. The reaction mixture was poured onto ice water, extracted with ethyl acetate (2 × 150 mL), washed with water (150 mL) and dried. The solvent was evaporated under reduced pressure to obtain the crude product, which was purified by chromatography on silica gel or by crystallization from acetone and water. Physical properties of the synthesized compounds are listed below.

(±)-7,8-Dihydroxy-4-(3-hydroxy-4-methoxyphenyl)-3,4-dihydrocoumarin (2a): White crystals, m.p. 188-190 °C, Yield: 69.5 %; IR (KBr, ν_{max}, cm^{-1}): 3498 (OH), 3417, 1753 (CO), 1516, 1468, 1271, 1198, 1174 and 1126; MS *m/z* (%) 302 $[M]^+$, 284 $[M\text{-}H_2O]^+$, 269 $[M\text{-}CH_3\text{-}H_2O]^+$, 259, 243, 229, 194, 179.

(±)-7-Hydroxy-4-(3,4,5-trimethoxyphenyl)-3,4-dihydrocoumarin (2b): White crystals, m.p. 176-178 °C, Yield: 70 %; IR (KBr, ν_{max}, cm^{-1}): 3381 (OH), 1747 (CO), 1626, 1597, 1510, 1456, 1358, 1230, 1271, 1240, 1122, 987 and 968; MS *m/z* (%) 330 $[M]^+$, 315 $[M\text{-}CH_3]^+$, 297 $[M\text{-}CH_3\text{-}H_2O]^+$, 287, 273, 257, 213, 128, 107.

(±)-4-(3,4-Dimethoxyphenyl)-7-hydroxy-3,4-dihydrocoumarin (3c): Yellow crystals, m.p. 144-146 °C, Yield: 60.7 %; IR (KBr, ν_{max}, cm^{-1}): 3429 (OH), 1761 (CO), 1626, 1597, 1516, 1462, 1419, 1335, 1271, 1244, 1159, 1103, 1024, 991, 847 and 812; MS *m/z* (%) 300 $[M]^+$, 282 $[M\text{-}H_2O]^+$, 267 $[M\text{-}CH_3\text{-}H_2O]^+$, 257, 243, 227, 190 ,163, 129.

(±)-6-Hydroxy-4-(3,4,5-trimethoxyphenyl)-3,4-dihydrocoumarin (3d): White crystals, m.p. 174-176 °C, Yield: 71.4%; IR (KBr, ν_{max}, cm^{-1}): 3421 (OH), 1757 (CO), 1504, 1454, 1232, 1195 and 1122; MS *m/z* (%) 330 $[M]^+$, 312 $[M\text{-}H_2O]^+$, 297 $[M\text{-}H_2O\text{-}CH_3]^+$, 257, 213, 181, 128.

(±)-7-Hydroxy-4-(3-hydroxy-4-methoxyphenyl)-3,4-dihydrocoumarin (2e): White crystals, m.p. 165-168 °C, Yield: 55.2 %; IR (KBr, ν_{max}, cm^{-1}): 3513 (OH), 3334, 1733 (CO), 1627, 1597, 1513, 1450, 1300, 1273, 1223, 1151 and 815; MS *m/z* (%) 286 $[M]^+$, 268 $[M\text{-}H_2O]^+$, 253 $[M\text{-}CH_3\text{-}H_2O]^+$, 243, 227, 213, 176, 115.

(±)-4-(3,4-Dimethoxyphenyl)-7,8-dihydroxy-3,4-dihydrocoumarin(2f): White crystals, m.p. 174-176 °C, Yield: 72.8 %; IR (KBr, ν_{max}, cm^{-1}): 3423 (OH), 1755 (CO), 1516, 1468, 1275, 1238, 1192, 1169 and 1020; MS *m/z* (%) 316 $[M]^+$, 298 $[M\text{-}H_2O]^+$, 283 $[M\text{-}CH_3\text{-}H_2O]^+$, 273, 259, 243, 190.

(±)-7,8-Dihydroxy-4-(3,4,5-trimethoxyphenyl)-3,4-dihydrocoumarin(2g): White crystals, m.p. 221-223 °C, Yield: 52.6 %; IR (KBr, ν_{max}, cm^{-1}): 3471 (OH), 1751 (CO), 1597, 1512, 1466, 1311, 1246, 1122 and 1007; MS *m/z* (%) 346 $[M]^+$, 328 $[M\text{-}H_2O]^+$, 313 $[M\text{-}CH_3\text{-}H_2O]^+$, 273, 257, 243, 229, 181, 115.

(±)-7,8-Dihydroxy-4-(4-methoxyphenyl)-3,4-dihydrocoumarin (2h): White crystals, m.p. 166-168 °C, Yield: 62.2 %; IR (KBr, ν_{max}, cm^{-1}): 3413 (OH), 1751 (CO), 1612, 1514, 1311, 1284, 1247, 1180, 1144 and 1007; MS *m/z* (%) 286 $[M]^+$, 268 $[M\text{-}H_2O]^+$, 243, 229, 200, 115.

(±)-6-Hydroxy-4-(4-methoxyphenyl)-3,4-dihydrocoumarin (2i): White crystals, m.p. 170-172 °C, Yield: 52.2 %; IR (KBr, ν_{max}, cm^{-1}): 3320 (OH), 1732 (CO), 1510, 1456, 1309, 1252, 1194, 1155 and 831; MS *m/z* (%) 270 $[M]^+$, 252 $[M\text{-}H_2O]^+$, 227 $[M\text{-}H_2O\text{-}CH_3]^+$, 213, 197, 128.

(±)-7-Methoxy-4-(4-methoxyphenyl)-3,4-dihydrocoumarin(2j): White crystals, m.p. 136-137 °C, Yield: 52.1 %; IR (KBr, ν_{max}, cm^{-1}): 2937, 1761 (CO), 1510, 1252, 1124, 1030 and 831; MS *m/z* (%) 284 $[M]^+$, 256 $[M\text{-}CO]^+$, 241 $[M\text{-}CO\text{-}CH_3]^+$, 227, 211, 128.

(±)-7-Methoxy-4-(3,4,5-trimethoxyphenyl)-3,4-dihydrocoumarin (2k): White crystals, m.p. 131-133 °C, Yield:

57.2 %; IR (KBr, ν_{max}, cm^{-1}): 3456, 1761 (CO), 1593, 1506, 1460, 1130; MS *m/z* (%) 344 $[M]^+$, 329 $[M-CH_3]^+$, 311 $[M-CO-CH_3]^+$, 271, 220, 177, 121, 77.

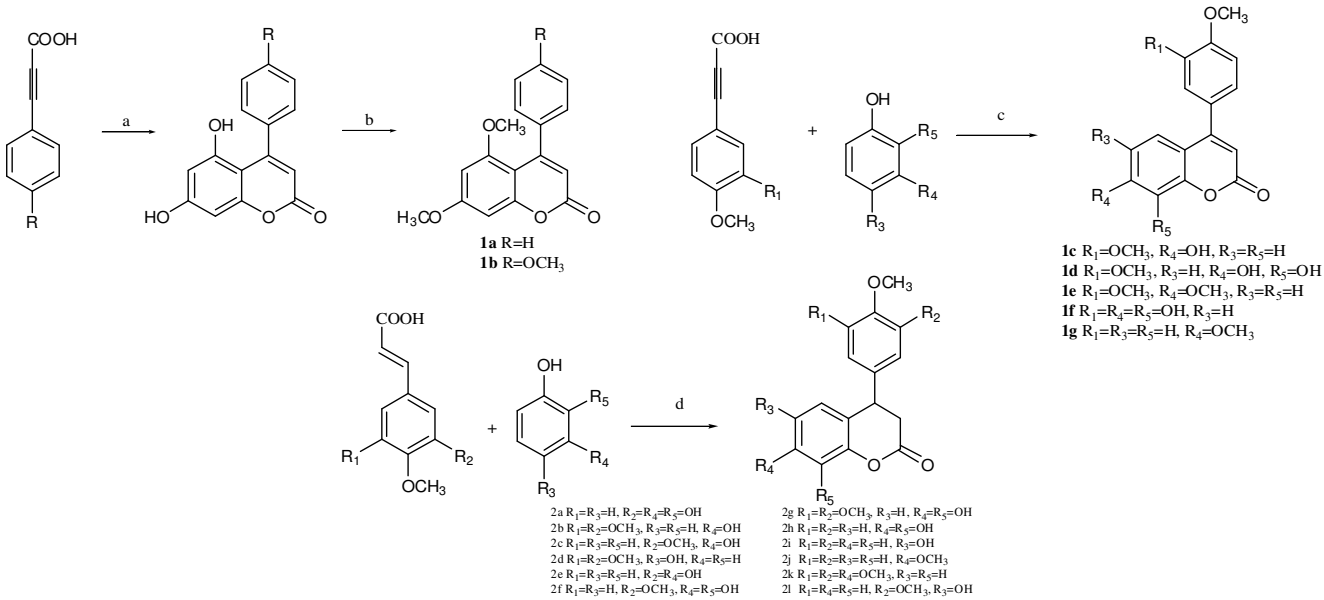
(±)-4-(3,4-Dimethoxyphenyl)-6-hydroxy-3,4-dihydrocoumarin(2l): White crystals, m.p. 168-170 °C, Yield: 62.3 %; IR (KBr, ν_{max}, cm^{-1}): 3273 (OH), 1714 (CO), 1521, 1487, 1247, 1244 and 1186; MS *m/z* (%) 300 $[M]^+$, 282 $[M-H_2O]^+$, 267 $[M-CH_3-H_2O]^+$, 257, 243, 227, 151, 115.

RESULTS AND DISCUSSION

As part of our ongoing program for the studies of bioactive arylcoumarins, we herein report a phenylpropiolic acid *via* Ponndorf reaction with corresponding polyphenols to afford 5,7-dimethoxy-4-phenylcoumarin (**1a**), 5,7,4'-trimethoxy-4-phenylcoumarin (**1b**) as well as their analogues compound **1c-1g** in mild conditions with satisfactory yields. Twelve 4-aryl-3,4-dihydrocoumarins were synthesized by the condensation of substituted cinnamic acids with the corresponding phenols in the presence of Friedel-Crafts catalyst BF_3-Et_2O and $POCl_3$. Twelve of the 4-aryl-3,4-dihydrocoumarins prepared were novel compound **2a-2l**, while 4-arylcoumarins (**1a-1g**) were reported previously[8]. However, only limited NMR data are available for the two known compounds **1a** and **1b** and thus their 2D-NMR spectral data, as well as the ^1H NMR spectral data, are reported here for the first time.

The structural and spectroscopic assignments were made through the combined use of 1D and 2D NMR experiments such as HMQC and HMBC. All the ^1H and ^{13}C chemical shifts and coupling constants for compounds **1a**, **1b** and **2a**, **2b** are given in Tables 1-4, along with the HMQC and HMBC on which the unambiguous assignments of all carbons and protons were made. The ^1H and ^{13}C chemical shifts and coupling constants for compounds **1c-1g** and **2c-2l** are given in Tables 5-8.

5,7-Dimethoxy-4-phenylcoumarin (**1a**) was obtained as white crystals. The IR spectrum shows characteristic vibrations



Scheme-I: Route to preparation of 4-arylcoumarin and 4-aryl-3,4-dihydrocoumarin; (a) phloroglucinol, CF_3COOH, r.t. or 60 °C, 4-12 h, (b) $(CH_3)_2SO_4$, K_2CO_3, $(Me)_2CO$, reflux, 4 h, (c) CF_3COOH, r.t., 4-8 h, (d) $POCl_3$ and BF_3–Et_2O, 0 °C → r.t., 4-18 h

TABLE-1
HMBC AND HSQC FOR 5,7-DIMETHOXY-4 PHENYLCOUMARIN (**1a**)

C	δ_C(ppm)	H	δ_H(ppm)	Multiplicity	Coupling constant (Hz)	HMBC	HSQC
2	160.9	—	—	—	—	—	—
3	112.6	3	5.99	s	—	2-C,1'-C,9-C	3-H
4	157.1	—	—	—	—	—	—
5	158.2	—	—	—	—	—	—
6	95.7	6	6.21	d	2.0	4-C,7-C, 8-C,9-C	6-H
7	163.3	—	—	—	—		
8	93.5	8	6.51	d	2.0	6-C,9-C, 10-C	8-H
9	103.5	—	—	—	—	—	—
10	155.7	—	—	—	—	—	—
1'	139.7	—	—	—	—	—	—
2'	127.3	2'	7.35	m	—	6'-C	2'-H
3'	127.1	3'	7.24	m	—	5'-C	3'-H
4'	127.9	4'	7.35	m	—	2'-C,6'-C, 1'-C	4'-H
5'	127.1	5'	7.24	m	—	3'-C	5'-H
6'	127.3	6'	7.35	m	—	2'-C	6'-H
5-OCH_3	55.7	5'-OCH_3	3.85	s	—	5'-C	5-OCH_3
7-OCH_3	55.4	7'-OCH_3	3.40	s	—	7'-C	7-OCH_3

TABLE-2
HMBC AND HSQC FOR 5,7-DIMETHOXY-4-(4 METHOXYPHENYL)COUMARIN (**1b**)

C	δ_C(ppm)	H	δ_H(ppm)	Multiplicity	Coupling constant (Hz)	HMBC	HSQC
2	160.9	—	—	—	—	—	—
3	112.5	3	5.97	s	—	9-C,1'-C,2-C	3-H
4	159.5	—	—	—	—	—	—
5	158.2	—	—	—	—	—	—
6	95.7	6	6.22	d	2.4	8-C,9-C	6-H
7	163.2	—	—	—	—	—	—
8	93.5	8	6.49	d	2.4	6-C,9-C	8-H
9	103.6	—	—	—	—	—	—
10	155.4	—	—	—	—	—	—
1'	132.0	—	—	—	—	—	—
2'	128.7	2'	7.20	dd	6.8,2	6'-C,4-C,4'-C	2'-H
3'	112.7	3'	6.87	dd	6.8,2	3-C,1'-C,4-C	3'-H
4'	157.2	—	—	—	—	—	—
5'	112.7	5'	6.87	dd	6.8,2	3-C,1'-C,4-C	5'-H
6'	128.7	6'	7.20	dd	6.8,2	6'-C,4-C,4'-C	6'-H
5-OCH_3	55.3	5-OCH_3	3.46	s	—	5-C	5-OCH_3
7-OCH_3	55.4	7-OCH_3	3.83	s	—	7-C	7-OCH_3
4'-OCH_3	55.7	4'-OCH_3	3.83	s	—	4'-C	4'-OCH_3

TABLE-3
HMBC AND HSQC FOR 7,8-DIHYDROXY-4-(3-HYDROXY-4-METHOXYPHENYL)-3,4-DIHYDROCOUMARIN (**2a**)

C	δ_C(ppm)	H	δ_H(ppm)	Multiplicity	Coupling constant (Hz)	HMBC	HSQC
2	168.0	—	—	—	—	—	—
3	37.9	3a,3b	2.99	m	—	2-C,4-C, 5-C,1'-C	3a-H,3b-H
4	40.4	4	4.19	t	6.4	3-C, 6-C,7-C, 6'-C1'-C	4-H
5	119.1	5	6.65	d	8	6-C,8-C, 10-C	5-H
6	118.6	6	6.43	d	8	7-C, 8-C	6-H
7	141.3	—	—	—	—	—	—
8	146.3	—	—	—	—	—	—
9	119.1	—	—	—	—	—	—
10	133.8	—	—	—	—	—	—
1'	135.5	—	—	—	—	—	—
2'	115.0	2'	6.69	d	2.4	5-C,4'-C	2'-H
3'	147.5	—	—	—	—	—	—
4'	147.6	—	—	—	—	—	—
5'	111.7	5'	6.77	d	8	1'-C,3'-C,4'-C	5'-H
6'	112.7	6'	6.59	dd	8, 2.4	3'-C,4'-C,2'-C	6'-H
4'-OCH_3	56.2	4'-OCH_3	3.86	s	—	4'-C	4'-OCH_3

TABLE-4
HMBC AND HSQC FOR 7-HYDROXY-4-(3,4,5-TRIMETHOXYPHENYL)-3,4-DIHYDROCOUMARIN (**2b**)

C	δ_C(ppm)	H	δ_H(ppm)	Multiplicity	Coupling constant (Hz)	HMBC	HSQC
2	167.9	—	—	—	—	—	—
3	37.4	3	3.01	m	—	4,2,9,1'	3a-H,3b-H
4	40.4	4	4.18	t	6	3,9,2',6',1'2	4-H
5	117.4	5	6.84	d	8.4	4,7,10	5-H
6	112.0	6	6.56	dd	2.4,8.4	8,9	6-H
7	156.3	—	—	—	—	—	—
8	104.3	8	6.64	d	2.4	—	8-H
9	129.1	—	—	—	—	—	—
10	152.3	—	—	—	—	—	—
1'	137.2	—	—	—	—	—	—
2'	104.5	2'	6.33	s	—	4,6',9,4'5'	2'-H
3'	153.6	—	—	—	—	—	—
4'	136.4	—	—	—	—	—	—
5'	153.6	—	—	—	—	—	—
6'	104.5	6'	6.33	s	—	4',2',4',3'	6'-H
3'-OCH_3	56.1	3'-OCH_3	3.78	s	—	3'-C	3'-OCH_3
4'-OCH_3	60.9	4'-OCH_3	3.82	s	—	4'-C	4'-OCH_3
5'-OCH_3	56.1	5'-OCH_3	3.78	s	—	5'-C	5'-OCH_3

TABLE-5
^{13}C NMR CHEMICAL SHIFTS (δ, ppm) of 4-ARYLCOUMARIN DERIVATIVES **1c–1g** (100.6 MHz, $CDCl_3$ or CD_3COCD_3)

C	1c	1d	1e	1f	1g
2	161.3	161.2	161.1	161.3	161.4
3	112.5	112.5	112.9	112.7	112.7
4	157.0	157.2	157.0	157.2	156.0
5	128.9	118.7	128.7	118.7	127.8
6	112.3	112.7	112.6	112.7	112.2
7	162.2	144.7	163.8	144.6	162.7
8	103.5	133.3	101.8	133.2	101.1
9	112.9	113.0	112.9	113.0	114.3
10	156.5	149.9	156.3	149.9	155.5
1’	129.3	129.1	129.0	129.3	129.9
2’	111.0	110.8	111.8	110.6	127.8
3’	151.4	151.4	151.5	147.4	111.4
4’	150.3	150.2	150.4	149.6	160.7
5’	113.6	113.0	113.2	112.4	111.4
6’	122.0	122.1	122.1	120.9	127.8
3’-OCH_3	56.2	56.2	56.2	–	–
4’-OCH_3	56.1	56.1	56.1	56.2	55.4
7-OCH_3	–	–	56.3	–	55.8

at 1712 cm^{-1} (CO). The H-3 proton appears as a singlet at δ5.99 ppm. The protons on carbons 3, 6, 8, 2', 3', 4', 5' and 6', which were easily assigned on the basis of chemical shift and multiplicity, enabled the assignment by direct correlation (HSQC) of carbons to which they are directly attached. Proton H-3 showed a long distance correlation with C9 and with two carbons at 160.9 and 139.7 ppm. The latter two signals were assigned to 2 and 1', respectively, owing to their markedly different chemical shifts. H-8 showed correlations with carbons 6, 9 and 10 and with two quaternary carbons at 95.7 and 155.7 ppm, which were assigned as 6 and 10, respectively. H-2'/H-6' are chemically equivalent and have a long-distance correlation (HMBC) with each other. Similarly, chemically equivalent protons H-3'/H-5' show a long-distance correlation with each other.

5,7,4'-Trimethoxy-4-phenylcoumarin (**1b**) was obtained as yellow crystals. In the case of the compound, protons 3, 6, 8, 2', 3', 5' and 6' and the corresponding carbon atoms were assigned as described above. The remaining correlations are similar to those observed for compound **1a**.

7,8-Dihydroxy-4-(3-hydroxy-4-methoxyphenyl)-3,4-dihydrocoumarin (**2a**) was obtained as white crystals. The IR

TABLE-6
^{1}H NMR CHEMICAL SHIFTS (δ, ppm) of 4-ARYLCOUMARIN DERIVATIVES **1c-1g** (400.13 MHz, $CDCl_3$ or CD_3COCD_3)

H	1c	1d	1e	1f	1g
3	6.20(s)	6.07(s),	6.14(s)	6.03(s)	6.18(s)
5	7.45(d,8.8)	7.00(d, 8.8)	7.55(d,8.8)	6.98(d,8.8)	7.43(d, 8.8)
6	—	6.83(d, 8.8)	6.90(dd,8.8,2.4)	6.83(d,8.8)	6.78(dd,8.8, 2.4)
8	6.98 (d, 2)	—	6.94(d,2.4)	—	6.87 (1H,d, J=2.4Hz,
2’	6.91(d, 2.4)	7.10 (d, 2)	7.12(d,2.4)	6.98(d,2)	7.37(d,8)
3’	—	—	—	—	7.01(d,8)
4’	—	—	—	—	—
5’	6.97(1d,8)	7.06(dd,2,8.4)	7.12(d,8.4)	6.96(dd,8,2)	7.01(d,8)
6’	6.74(dd,2.4,8)	7.11(d, 8.4)	7.08(dd,8.4,2)	7.10(d,8)	7.37(d,8)
3’-OCH_3	3.94(s)	3.88(s)	3.89(s)	—	—
4’-OCH_3	3.90(s)	3.87(s)	3.88(s)	3.91(s)	3.68
7-OCH_3	—	—	3.93(s)	—	3.68

TABLE-7
^{13}C NMR CHEMICAL SHIFTS (δ, ppm) OF 4-ARYL-3,4-DIHYDROCOUMARIN DERIVATIVES **2c–2l** (100.6 MHz, $CDCl_3$)

C	2c	2d	2e	2f	2g	2h	2i	2j	2k	2l
2	168.5	168.1	168.2	166.9	166.7	167.9	168.2	167.7	167.6	168.2
3	37.5	36.8	37.9	37.4	37.3	37.9	37.0	37.4	37.4	36.9
4	39.6	41.0	39.9	40.0	40.7	40.2	39.9	39.2	40.5	40.4
5	119.7	115.5	119.1	118.9	117.6	118.5	114.6	117.9	117.4	114.5
6	110.5	153.6	112.3	111.3	111.3	111.7	152.3	110.6	110.8	152.5
7	156.3	114.5	158.5	144.2	144.3	146.3	114.5	159.8	160.0	111.6
8	104.2	118.0	104.2	139.3	139.3	141.2	118.0	102.4	104.4	119.9
9	129.1	137.2	129.9	119.7	119.0	129.3	131.9	128.7	128.9	132.3
10	152.2	145.3	153.4	132.7	136.0	134.5	145.5	152.3	152.4	145.4
1’	133.1	126.9	135.6	131.1	131.1	133.8	128.7	132.6	136.4	127.4
2’	111.6	104.6	112.7	110.6	104.5	119.1	127.5	128.4	102.5	110.6
3’	149.3	152.6	147.4	149.4	153.6	114.9	114.7	114.3	153.6	149.4
4’	148.3	135.7	147.6	148.5	136.0	159.6	159.0	158.8	137.3	148.5
5’	112.0	152.6	114.9	111.5	153.6	114.9	114.7	114.3	153.6	115.3
6’	117.7	104.6	117.9	118.1	104.5	119.1	127.5	128.4	102.5	118.0
3’-OCH_3	55.9	56.1	56.2	55.9	56.2	—	—	—	56.1	55.9
4’-OCH_3	55.9	60.8	—	55.9	60.9	55.4	55.3	55.2	60.8	55.9
5’-OCH_3	—	56.1	—	—	56.2	—	—	—	56.1	—
7-OCH_3	—	—	—	—	—	—	—	55.4	55.5	—

TABLE-8
^{1}H NMR CHEMICAL SHIFTS (δ, ppm) of 4-ARYL-3,4-DIHYDROCOUMARIN DERIVATIVES **2c–2l** (400.13 MHz, $CDCl_3$)

H	2c	2d	2e	2f	2g
3a,3b	2.98 (m)	2.98 (m)	2.98 (m)	3.03(m)	3.03(m)
4	4.20 (t, 6.0)	4.17 (t, 6.4)	4.16 (t, 6.4)	4.24 (t, 6.4)	4.22(dd,6,7.6)
5	6.67(d,8.4)	6.85 (d,8.6)	6.82(d,8.4)	6.66(d,8.4)	6.67(d,8.8)
6	6.56(dd, 2.4 8.4)	6.55(dd, 2.4,8.6)	6.54(dd, 2.4 8.4)	6.41(d,8.4)	6.45(d,8.8)
8	6.80 (d, 2.4)	6.64(d,2.4)	6.69 (d, 2.4)	—	—
2’	6.82 (d, 2.4)	6.33(s)	6.61 (d, 2.4)	6.66(d,2.4)	6.33(s)
5’	6.66(d,8.4)	—	6.78(d,8.4)	6.8(d,8.4)	—
6’	6.64(dd, 2.4 8.4)	6.33(s)	6.59(dd, 2.4 8.4)	6.64(dd, 2.4,8.4)	6.33(s)
3’-OCH_3	3.79(s)	3.77(s)	—	3.81(s)	3.78(s)
4’-OCH_3	3.84(s)	3.80(s)	3.68(s)	3.85(s)	3.82(s)
5’-OCH_3	—	3.77(s)	—	—	3.78(s)
H	2h	2i	2j	2k	2l
3a,3b	3.01(m)	2.96(m)	3.03(m)	3.00(m)	3.00(m)
4	4.24(t,6.8)	4.19(dd,6,8.4)	4.37(t,6.4)	4.19(t,7.6)	4.17(dd,6,8.4)
5	6.65(d,8.4)	6.38(d,2.4)	6.95(d,8.4)	6.89(d,8.4)	6.63(d,2.4)
6	6.39(d,8.4)	—	6.69(dd,2.4,8.4)	6.64(dd,2.4,8.4)	—
7	—	6.71(dd,3.2,8.8)	—	—	6.68(dd,2.4,8)
8	—	6.96(d,8.8)	6.66(d,2.4)	6.66(d,2.4)	6.79(d,8)
2’	7.04(d,8.8)	7.05(d,8.8)	7.11(d,8.8)	6.33(s)	6.41(d,2.8)
3’	6.85(d,8.8)	6.85(d,8.8)	6.89(d,8.8)	—	—
5’	7.04(d,8.8)	7.05(d,8.8)	6.89(d,8.8)	—	6.96(d,8.8)
6’	6.85(d,8.8)	6.85(d,8.8)	7.11(d,8.8)	6.33(s)	6.72(dd,2.8,8.8)
3’-OCH_3	—	—	—	3.78(s)	3.79(s)
4’-OCH_3	3.78(s)	3.75(s)	3.76(s)	3.79(s)	3.82(s)
5’-OCH_3	—	—	—	3.78(s)	—
7-OCH_3	—	—	3.81(s)	3.81(s)	—

spectrum shows characteristic vibrations at 1753 cm^{-1} (CO). The H-3a and H-3b proton appear as a multiplet at δ2.99 ppm. The H-4 proton appear as triplet at δ4.19 ppm. The protons on carbons 3, 4, 5, 6, 2', 5' and 6', which were easily assigned on the basis of chemical shift and multiplicity, enabled the assignment by direct correlation (HSQC) of carbons to which they are directly attached.

In the case of 7-hydroxy-4-(3,4,5-trimethoxyphenyl)-3,4-dihydrocoumarin (**2b**) was obtained as white crystals. The protons on carbons 3, 4, 5, 6, 8, 2' and 6' and the corresponding carbon atoms were assigned as described above. H-2'/H-6' are chemically equivalent. The remaining correlations are similar to those observed for compound **2a**.

The ^{1}H and ^{13}C NMR spectral data for the five other aryl-coumarins derivatives (**1c-1g**) and ten 4-aryl-3,4-dihydro-coumarins (**2c-2l**) were fully assigned using similar reasoning to that described above, with the results presented in Tables 5-8.

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