Oxidative Transformations of 4-Methylcoumarins Using Dimethyldioxirane

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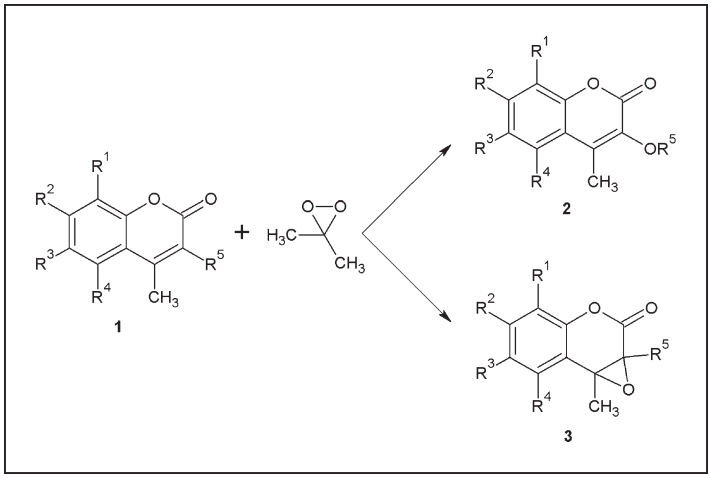

Efficient regioselective oxidation of the double C—C bond of 4-methylcoumarins with isolated dimethyldioxirane was performed, and related hydroxy and epoxy derivatives were obtained in good yields. All of obtained epoxides and most of hydroxy derivatives are novel compounds. The position of different electron-donating groups attached at the aromatic part of molecule shows significant influence on kinetics and course of the reaction.

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INTRODUCTION

Coumarins occupy an important place in the realm of natural products and synthetic organic chemistry. Many compounds containing the *2H*-1-benzopyran-2-one subunit exhibit useful and diverse biological activity and find their application in pharmaceuticals, fragrances, agrochemicals, and insecticides [1,2].

Studying the metabolic pathways of coumarin, it was found that it is also toxic, due to the formation of coumarin-3,4-epoxide, which decomposes to toxic *o*-hydroxyphenylacetaldehyde [3–5]. The 4-methylcoumarins are known to be less toxic compared with coumarin [6–8], but there is lack of data about products of their reactions with reactive oxygen species. The 4-methylcoumarins are also implicated to have several beneficial pharmacological effects [3,6–9]. It has been noted that the selective hydroxylation of coumarins by cytochrome P-450 enzymes and dimethyldioxirane have several features in common [10,11]. The reaction of oxidation involves insertion of oxygen into C—H bonds very efficiently and can discriminate between different sites in the same molecule. The selectivity is often as high as those that enzymes are able to achieve.

The fact that excess of dimethyldioxirane oxidize the double C—C bond of few 4-methlycoumarins in regioselective manner has already been reported [12]. Kinetic analyses demonstrate two independent reaction pathways, epoxidation and hydroxylation, respectively, which was also confirmed using kinetic isotope effect methods.

As a part of a continuing effort in our laboratory toward the examinations of oxidation of biologically relevant heterocyclic compounds [9,12], here we report the synthesis of novel 4-methlycoumarin derivatives, obtained from their reaction with dimethyldioxirane. Special attention was paid to reaction kinetics, which was examined by UV/vis and EPR spectroscopy.

RESULTS AND DISCUSSION

The synthesis of 4-methylcoumarins (**1a–j**) was carried out according to the slightly modified Pechmann method [13,14], which involves the condensation of

different phenols with β-keto esters in the presence of acidic condensing agents, such as concentrated sulfuric acid and/or anhydrous aluminum chloride. The yields of obtained 4-methylcoumarins were, in general, very high regardless to the structural variations of phenol substrates. The purity of synthesized 4-methylcoumarins was determined by GC/MS technique and by elemental analysis. Structural confirmation was done using ^{1}H-NMR, ^{13}C-NMR, and EI mass spectrometric methods. The characterizations of these compounds are identical with the literature reports [15].

A solution of dimethyldioxirane was prepared in pure acetone, according to the methods described in the literature [16], and its content was determined using GC/MS analysis of its reaction with thioanisole [17]. The analysis is done quantitatively by determining the response factors of the sulfides.

The reactions of 0.12 mol/L isolated dimethyldioxirane (12 equiv) and selected 4-methylcoumarins (**1a–j**) were carried out at room temperature, in dry acetone solution, in the absence of sunlight and air. The progress of oxidation was monitored by GC/MS sampling the reaction mixture every 30 min. The yields of reaction products are calculated using semiquantitative analysis carried out directly from peak areas in the GC profile. Detailed chromatographic and spectral study of reaction between selected 4-methylcoumarins and dimethyldioxirane showed that main oxidation products are corresponding hydroxy derivatives (**2a–j**) and epoxides (**3a–j**). All of obtained epoxides [3,4-dihydro-4-methyl-2*H*-oxireno[c]chromen-2-one (**3a**), 3,4-dihydro-4,6-dimethyl-2*H*-oxireno[c]chromen-2-one (**3b**), 3,4-dihydro-4,7-dimethyl-2*H*-oxireno[c]chromen-2-one (**3d**), 3,4-dihydro-4-methyl-6-methoxy-2*H*-oxireno[c]chromen-2-one (**3e**), 6-hydroxy-4-methyl-2*H*-oxireno[c]chromen-2-one (**3g**), and 6-hydroxy-4,7-dimethyl-2*H*-oxireno[c] chromen-2-one (**3j**)], and some of hydroxy derivatives [3-hydroxy-4-methyl-7-methoxy-2*H*-chromen-2-one (**2f**), 3,7-dihydroxy-4-methyl-2*H*-chromen-2-one (**2h**), 3,7-dihydroxy-4,8-dimethyl-2*H*-chromen-2-one (**2i**), and 3,6-dihydroxy-4,7-dimethyl-2*H*-chromen-2-one (**2j**)] are novel compounds. The proposed reaction route is given in Figure 1. In addition, an experiment under inert atmosphere (argon) was carried out to double-check if hydroxylation product is a direct reaction product.

At the end of the reaction, solvent was evaporated under argon, reaction mixture was dissolved in acetone-d_6 and/or DMSO-d_6, and products were determined with GC/MS and NMR techniques. The Mass and ^{1}H-NMR spectral data of the main products of oxidation are presented in the ''Experimental Section.''

The mass spectra of coumarin hydroxy and epoxy derivatives showed a prominent molecular ion, and fragments corresponding to the loss of HCO $[M - 29]^+$ and HCO_2 $[M - 44]^+$, i.e., benzofuranylium and benzofuran

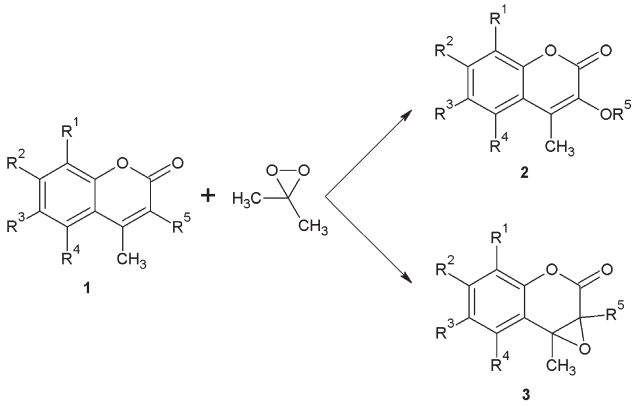

Figure 1. Proposed reaction route of oxidation of 4-methylcoumarins using dimethyldioxirane.

methylium ion, respectively. Both oxidative products have the same fragments, but in different abundances (''Experimental Section''). All other examined compounds showed the same fragmentation under EI conditions. In general, base peak of hydroxy derivatives is molecular peak $[M]^+$, whereas base peak of epoxides is fragment corresponding to loss of HCO_2 following the loss of methylene group on a pyrone ring (Fig. 2).

The proton NMR of DMSO solution containing the corresponding epoxide and hydroxide showed resonance peaks characteristic for hydrogen atoms located at the aromatic part of coumarin molecule, ranging δ 6.83–7.55 (d). Methyl group at the position C-4 showed singlets ranging δ 2.29–2.44, whereas those attached at the benzene ring were shifted upfield, ranging δ 2.03–3.31 (s). Methoxy group located in the aromatic moiety of the molecule showed singlet chemical shifts at δ 3.82–3.84. Proton from aromatic hydroxy group showed singlet at δ 9.22–9.81. All of these chemical shifts can be compared with those displayed from corresponding coumarin substrate and demonstrate that the aromatic part of the coumarin structures remain unchanged in their reaction with dimethyldioxirane.

Loss of peak characteristic for hydrogen atoms located at the 3-positon on pyrone ring proves that oxidation occurs at this position. 4-Methylcoumarin epoxides (**3a–j**) showed chemical shifts ranging δ 3.73–3.83 (s), whereas corresponding 3-hydroxy derivatives (**2a–j**) displayed singlets ranging δ 4.47–5.37. In general, compounds containing aromatic hydroxy group showed singlets for these hydrogen atoms shifted upfield in

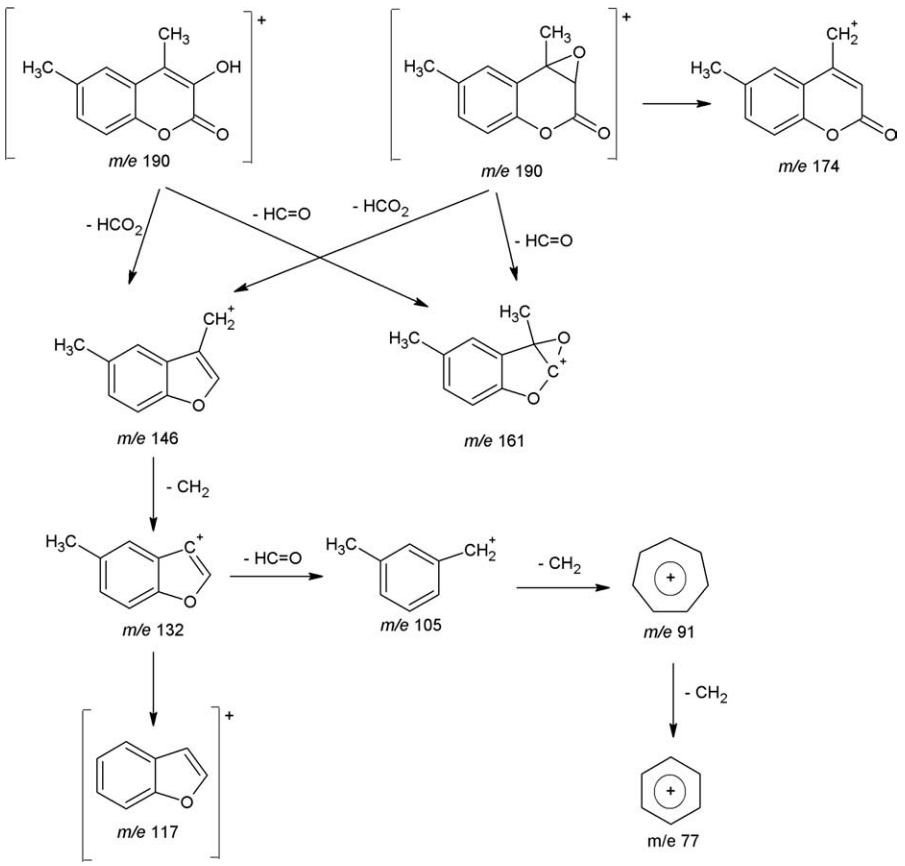

Figure 2. Proposed rationalization of fragmentation of 3-hydroxy-4,6-dimethyl-2H-chromen-2-one (**2b**), and 3,4-dihydro-4,6-dimethyl-2H-oxireno[c]chromen-2-one (**3b**) under EI conditions.

comparison with those without hydroxy group. Presented results are in agreement with those found in literature [3,12].

The epoxide and hydroxy hydrogen atoms were shifted downfield compared with the H-3 atoms in the corresponding coumarin molecules (δ 5.99–6.92). The chemical shifts of protons positioned at C-3 atom, for epoxide and hydroxy derivative, were not detected in the reaction between dimethyldioxirane and 4,6-dimethyl-2*H*-chromen-2-one deuterated at 3-positon (**1c**). Moreover, the mass spectra of these two products showed similarity with mass spectra of oxidation products of 4,6-dimethyl-2*H*-chromen-2-one (**1b**), with mass fragments increased by 1 due to the presence of deuterium atom. These outcomes prove the fact that described epoxides and hydroxy derivatives are the main products of oxidation of 4-methylcoumarins by dimethyldioxirane. No effort was made to purify the products because unreacted coumarins served as a convenient internal standard during sample analysis. It should be noted that isolation of the main products of oxidation could not be possible due to its high instability under atmospheric conditions, especially for epoxides.

As it has been reported [12], kinetic study of the reaction indicates that hydroxy and epoxy derivatives of 4-methylcoumarins are independently produced. The reactions were proven to be of the second order, overall. Results show a significant influence of the substituent position on kinetic rate constants and activation parameters. Some previous studies [18–22] of oxidations of similar natural products showed that hydroxylation occurs on the aromatic part of the molecule. Generally, hydroxylation is much faster than epoxidation, but epoxidation is energetically favored reaction. Activation energies span from (16.21 ± 0.07) to (38.45 ± 0.15) kJ/kmol for hydroxy derivatives and from (15.06 ± 0.10) to (33.64 ± 0.12) kJ/kmol for epoxy derivatives, respectively. Values of logarithm of frequency factor and negative values of entropy of activation in all examined cases indicate bimolecular behavior of reaction. Introducing the methyl group, as a δ-donor, on a benzene ring of a molecule, the reaction rate slightly increases. Moreover, in the case of 4-methylcoumarins with the π-donor groups, methoxy and hydroxy group at the aromatic part of coumarin structure, reaction rate increases, especially in the case of hydroxylation.

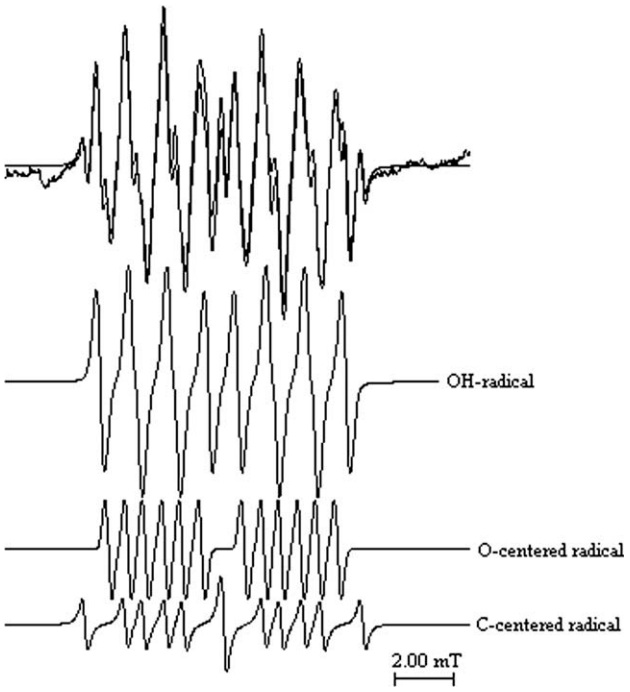

Figure 3. Simulated EPR spectra of the reaction mixture (4-methylcoumarin derivative and dimethyldioxirane).

In addition, reaction between selected 4-methylcoumrins and dimethyldioxirane has been examined by EPR spectroscopy. Immediately after mixing the degassed solutions of dimethyldioxirane (0.12 mol/L) and 4-methylcoumarin (0.01 mol/L) in acetone, the solution of spin-trap compound was added, and EPR spectra were recorded. The same experiments were repeated after a particular time period (30, 60, and 120 min). During the course of the study, DEPMPO has been chosen as a spin-trap compound. The hyperfine splitting constants of radical adducts were calculated from simulations of experimental. Presented spectra (Fig. 3) show that reaction mixture contained three radical adducts, hydroxy radical, O-centered radical, and C-centered radical, in different portions which rate was changing during the reaction. The hyperfine splitting constants for OH radical (after 30 min) were $a_P = 4.73$ mT, $a_H = 1.10$ mT, and $a_N = 1.32$ mT, for O-centered radical adduct were $a_P = 4.66$ mT, $a_H = 0.79$ mT, and $a_N = 1.27$ mT, and for C-centered radical adduct were $a_P = 4.80$ mT, $a_H = 1.95$ mT, and $a_N = 1.39$ mT. These results are comparable with those found in literature [23–25]. However, a portion of hydroxyl and C-centered radical adduct increased during the reaction, whereas a portion of O-radical adduct decreased. The presence of hydroxyl radical can be explained by reaction of the proton of the hydroxy group attached at aromatic part of coumarin molecule. Resulting phenoxyl radical of coumarin substrate can be stabilized by resonance [6]. In addition, the presence of C-centered radical adduct can be explained by elimination of proton from 4-CH_3 group from coumarin. As a consequence, the obtained methylene radical can be stabilized by resonance [26]. The EPR study confirmed the fact that dimethyldioxirane probably acts as radical oxygen species, which produce hydroxy derivatives of corresponding 4-methylcoumarin.

CONCLUSIONS

Study of the oxyfunctionalization of 4-methylcoumarins by dimethyldioxirane presents a new insight into introducing an epoxide and hydroxy group to a substrate molecule under mild conditions. All of obtained epoxides and most of hydroxy derivatives are novel compounds.

The presented findings open a new perspective of the site-selective oxyfunctionalization of molecules with a heteroconjugated system. This study could aid the development of methods for quantifying epoxidation and hydroxylation of coumarin derivatives, and contribute to understanding antioxidant activity of coumarins, a biological property currently considered as a promising approach for the treatment of different diseases.

EXPERIMENTAL SECTION

General. All reagents were purchased from Sigma-Aldrich, Fluka, and Kemika Chemical Company. Synthesized 4-methylcoumarins were identified by determination of melting points on Kofler microscope hot stage apparatus, using elemental analysis on CHN Analyzer, GC/MS and NMR techniques.

The GC conditions were as follows: the fused-silica HP-5 column (5% phenyl methyl siloxane; 30 m × 250 μm × 0.25 μm), carriers gas He (1.1 mL/min), temperature program: 20°C/min from 100 to 270°C; the injection port temperature was 250°C; detector temperature 280°C. Ionization of the sample components was performed in the EI mode, (70 eV). The NMR spectra were recorded in $CDCl_3$, acetone-d_6 and DMSO-d_6 at 300 MHz using Bruker DPX 300 NMR spectrometer. The EPR spectra of the reaction were measured with a Bruker ELEXSYS E500 spectrometer (X band, 9.33 GHz) at room temperature (~20°C). The operating conditions were as follows: microwave power 20.06 mW, center field 332.67 mT, sweep width 16.0 mT, modulation frequency 100 kHz, modulation amplitude 0.1 mT, gain 60 dB, time constant 1.28 ms. A computer simulation of the hyperfine coupling constants was carried out using the WIN-EPR software package (Bruker, USA) and EPRISM-C Wizard 6.2 software.

General procedure for the preparation of 4-methlycoumarin hydroxy and epoxy derivatives. A flask containing 2.5-mL dimethyldioxirane solution (0.12 mol/L) and 0.5 mL solution of 4-methylcoumarin (0.01 mol/L) was carried at room temperature, in dry acetone solution, in the absence of sunlight and air. The progress of reaction was monitored by GC/MS. The yields of reaction products are calculated using semi-quantitative analysis carried out directly from peak areas

in the GC profile. At the end of the reaction, products were determined with different 1D and 2D NMR techniques. In addition, an experiment under inert atmosphere (argon) was carried out to confirm that obtained products are direct oxidation products.

Reaction kinetics. Kinetic studies of reaction between dimethyldioxirane (12 equiv) and 4-methylcoumarins were carried at various temperatures in a thermostated cell (20, 25, 30, and 40°C), using UV–vis spectrophotometric method, for 2–5 h. Data for kinetic analyses were collected using Varian Cary 50 Bio UV–vis spectrophotometer. UV–vis spectra were recorded at wavelength range from 300 to 800 nm, using Xenon lamp. All kinetics experiments were carried out in triplicate.

3-Hydroxy-4-methyl-2H-chromen-2-one (2a). Yield 59.4%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.57–7.18 (m, 4H, Ar—H), 5.37 (s, 1H, 3-OH), 2.34 (s, 3H, 4-CH_3). MS (EI, 70 eV): *m/z* (%) = 65 (11), 77 (9), 91 (35), 120 (23), 147 (37), 176 $[M]^+$ (100).

3,4-Dihydro-4-methyl-2H-oxireno[c]chromen-2-one (3a). Yield 39.5%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.55–7.21 (m, 4H, Ar—H), 3.83 (s, 1H, 3-H), 2.38 (s, 3H, 4-CH_3). MS (EI, 70 eV): *m/z* (%) = 43 (11), 51 (18), 65 (24), 77 (22), 91 (99), 105 (43), 120 (18), 132 (100), 147 (14), 176 $[M]^+$ (41).

3-Hydroxy-4,6-dimethyl-2H-chromen-2-one (2b). Yield 83.2%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.40 (d, J_1 = 7.2, 1H, 5-H), 7.21 (d, J_2 = 2.7 Hz, 1H, 8-H), 7.12 (dd, J_1 =7.2 Hz, J_2 =2.7 Hz, 1H, 7-H), 5.29 (s, 1H, 3-OH), 2.41 (s, 3H, 4-CH_3), 2.12 (s, 3H, 6-CH_3). MS (EI, 70 eV): *m/z* (%) = 51 (10), 77 (14), 91 (20), 105 (10), 115 (12), 132 (21), 161 (32), 190 $[M]^+$ (100).

3,4-Dihydro-4,6-dimethyl-2H-oxireno[c]chromen-2-one (3b). Yield 13.8%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.62 (d, J_2 = 2.3 Hz, 1H, 5-H),7.30 (dd, J_1 = 7.6 Hz, J_2 = 2.3 Hz, 1H, 7-H), 7.13 (d, J_1 = 7.6 Hz, 1H, 8-H), 5.41 (s, 1H, 3-H), 2.46 (s, 3H, 4-CH_3), 2.03 (s, 3H, 6-CH_3). MS (EI, 70 eV): *m/z* (%) = 51 (37), 65 (23), 77 (38), 91 (67), 103 (39), 117 (44), 132 (26), 139 (2), 146 (100), 161 (22), 174 (24), 190 $[M]^+$ (39).

3-(D)Hydroxy-4,6-dimethyl-2H-chromen-2-one (2c). Yield 43.1%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.41 (d, J_1= 7.6 Hz, 1H, 5-H), 7.13 (d, J_2 = 2.9 Hz, 1H, 8-H), 6.98 (dd, J_1 = 7.6 Hz, J_2 = 2.9 Hz, 1H, 7-H), 2.31 (s, 3H, 4-CH_3), 2.19 (s, 3H, 6-CH_3). MS (EI, 70 eV): *m/z* (%) = 51 (13), 53 (15), 77 (19), 133 (48), 162 (34), 191 $[M]^+$ (100).

3,4-(3D)Dihydro-4,6-dimethyl-2H-oxireno[c]chromen-2-one (3c). Yield 11.5%. ^{1}H-NMR (300.13 MHz, DMSO-d_6 δ 7.17 (d, J_1 = 7.9 Hz, 1H, 5-H), 7.10 (d, J_2 = 3.1 Hz, 1H, 8-H), 7.03 (dd, J_1 = 7.9 Hz, J_2 = 3.1 Hz, 1H, 7-H), 2.30 (s, 3H, 4-CH_3), 2.16 (s, 3H, 6-CH_3). MS (EI, 70 eV): *m/z* (%) = 51 (41), 78 (56), 92 (46), 133 (100), 147 (100), 162 (43), 191 $[M]^+$ (27).

3-Hydroxy-4,7-dimethyl-2H-chromen-2-one (2d). Yield 47.5%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.62 (d, J_2 = 2.3 Hz, 1H, 5-H), 7.30 (dd, J_1 = 7.6 Hz, J_2 = 2.3 Hz, 1H, 6-H), 7.13 (d, J_1 = 7.6 Hz, 1H, 8-H), 5.41 (s, 1H, 3-OH), 2.28 (s, 3H, 4-CH_3), 2.03 (s, 3H, 7-CH_3). MS (EI, 70 eV): *m/z* (%) = (13), 91 (15), 105 (10), 134 (21), 161 (26), 190 $[M]^+$ (100).

3,4-Dihydro-4,7-dimethyl-2H-oxireno[c]chromen-2-one (3d). Yield 42.2%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.19 (d, J_2 = 2.8 Hz, 1H, 5-H), 7.12 (d, J_1 = 7.7 Hz, J_2 = 2.8 Hz, 1H, 6-H), 6.88 (d, J_1 = 7.7 Hz, 1H, 8-H), 3.82 (s, 1H, 3-H), 2.38 (s, 3H, 4-CH_3), 2.11 (s, 3H, 7-CH_3). MS (EI, 70 eV): *m/z* (%) = 51 (33), 65 (15), 77 (34), 91 (56), 105 (32), 117 (34), 133 (33), 146 (100), 162 (21), 174 (42), 190 $[M]^+$ (79).

3-Hydroxy-6-methoxy-4-methyl-2H-chromen-2-one (2e). Yield 54.8%. ^{1}H-NMR (300.13 MHz, DMSO-d_6 δ 7.32 (d, J_1 = 8.3 Hz, 1H, 5-H), 7.21 (d, J_2 = 3.2 Hz, 1H, 8-H), 7.06 (dd, J_1 = 8.3 Hz, J_2 = 3.2 Hz, 1H, 7-H), 5.32 (s, 1H, 3-OH), 3.84 (s, 3H, 6-OCH_3), 2.43 (s, 3H, 4-CH_3). MS (EI, 70 eV): *m/z* (%) = 77 (16), 91 (7), 135 (34), 150 (20), 178 (10), 191 (10), 206 $[M]^+$ (100).

3,4-Dihydro-6-methoxy-4-methyl-2H-oxireno[c]chromen-2-one (3e). Yield 29.3%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.11 (d, J_1 = 8.5 Hz, 1H, 5-H), 7.04 (d, J_2 = 3.0 Hz, 1H, 8-H), 6.96 (dd, J_1 = 8.5 Hz, J_2 = 3.0 Hz, 1H, 7-H), 3.88 (s, 1H, 3-H), 3.84 (s, 3H, 6-OCH_3), 2.32 (s, 3H, 4-CH_3). MS (EI, 70 eV): *m/z* (%) = 51 (21), 57 (39), 65 (27), 69 (30), 77 (38), 85 (18), 91 (51), 97 (22), 107 (25), 111 (15), 119 (26), 135 (67), 147 (66), 162 (100), 178 (10), 190 (77), 206 $[M]^+$ (79).

3-Hydroxy-7-methoxy-4-methyl-2H-chromen-2-one (2f). Yield 23.1%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 7.94 (d, J_2 = 2.1 Hz, 1H, 5-H), 7.12 (dd, J_1 = 8.2 Hz, J_2 = 2.1 Hz, 1H, 6-H), 7.03 (d, J_1 = 8.2 Hz, 1H, 8-H), 4.96 (s, 1H, 3-OH), 3.82 (s, 3H, 7-OCH_3), 2.26 (s, 3H, 4-CH_3). MS (EI, 70 eV): *m/z* (%) = 44 (18), 69 (13), 77 (13), 89 (12), 135 (10), 163 (55), 191 (19), 206 $[M]^+$ (100).

3,6-Dihydroxy-4-methyl-2H-chromen-2-one (2g). Yield 28.4%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 9.76 (s, 1H, 6-OH), 7.19 (d, J_1 = 7.8 Hz, 1H, 5-H), 7.11 (d, J_2 = 2.9 Hz, 1H, 8-H), 6.83 (d, J_1 = 7.8 Hz, J_2 = 2.9 Hz, 1H, 7-H), 4.47 (s, 1H, 3-OH), 2.29 (s, 3H, 4-CH_3). MS (EI, 70 eV): *m/z* (%) = 43 (10), 53 (13), 107 (10), 121 (36), 137 (34), 163 (32), 192 $[M]^+$ (100).

3,4-Dihydro-6-hydroxy-4-methyl-2H-oxireno[c]chromen-2-one (3g). Yield 62.8%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 9.81 (s, 1H, 6-OH), 7.20 (d, J_1 = 8.0 Hz, 1H, 5-H), 7.15 (d, J_2 = 2.8 Hz, 1H, 8-H), 6.88 (dd, J_1 =8.0 Hz, J_2 = 2.8 Hz, 1H, 7-H), 3.73 (s, 1H, 3-H), 2.32 (s, 3H, 4-CH_3). MS (EI, 70 eV): *m/z* (%) = 55 (12), 80 (10), 107 (13), 121 (22), 136 (50), 148 (17), 163 (18), 176 (100), 192 $[M]^+$ (62).

3,7-Dihydroxy-4-methyl-2H-chromen-2-one (2h). Yield 49.3%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 9.22 (s, 1H, 7-OH), 7.64 (d, J_2 = 2.8 Hz, 1H, 5-H), 7.11 (dd, J_1 = 8.0 Hz, J_2 = 2.8 Hz, 1H, 6-H), 7.01 (d, J_1 = 8.0 Hz, 1H, 8-H), 4.74 (s, 1H, 3-OH), 2.09 (s, 3H, 4-CH_3). MS (EI, 70 eV): *m/z* (%) = 53 (10), 69 (10), 77 (10), 107 (10), 121 (13), 136 (23), 147 (10), 164 (32), 192 $[M]^+$ (100).

3,7-Dihydroxy-4,8-dimethyl-2H-chromen-2-one (2i). Yield 34.9%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 9.48 (s, 1H, 7-OH), 7.24 (d, J_1 = 2.2 Hz, 1H, 5-H), 6.91 (d, J_1 = 2.2 Hz, 1H, 6-H), 4.92 (s, 1H, 3-OH), 2.43 (s, 3H, 4-CH_3), 2.31 (s, 3H, 8-CH_3). MS (EI, 70 eV): *m/z* (%) = 77 (17), 83 (3), 107 (10), 135 (19), 150 (19), 178 (28), 206 $[M]^+$ (100).

3,6-Dihydroxy-4,7-dimethyl-2H-chromen-2-one (2j). Yield 45.7%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 9.64 (s, 1H, 6-OH), 7.26 (s, 1H, 5-H), 7.04 (s, 1H, 8-H), 4.86 (s, 1H, 3-OH, 2.39 (s, 3H, 4-CH_3), 2.23 (s, 3H, 7-CH_3). MS (EI, 70 eV): *m/z* (%) = 51 (10), 77 (19), 107 (12), 135 (27), 150 (21), 163 (11), 178 (32), 206 $[M]^+$ (100).

3,4-Dihydro-6-hydroxy-4,7-dimethyl-2H-oxireno[c]chromen-2-one (3j). Yield 62.8%. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ 9.56 (s, 1H, 6-OH), 7.21 (s, 1H, 5-H), 7.07 (s, 1H, 8-H), 3.79 (s, 1H, 3-H), 2.31 (s, 3H, 4-CH_3), 2.19 (s, 3H,

7-CH_3). MS (EI, 70 eV): *m/z* (%) = 51 (15), 65 (12), 69 (10), 77 (23), 91 (15), 103 (12), 107 (12), 115 (11), 133 (13), 150 (15), 162 (100), 178 (22), 190 (79), 206 $[M]^+$ (73).

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