Epoxidation Studies of 2-Styrylchromones using Jacobsen's Catalyst and Hydrogen Peroxide and Iodosylbenzene as Oxidants

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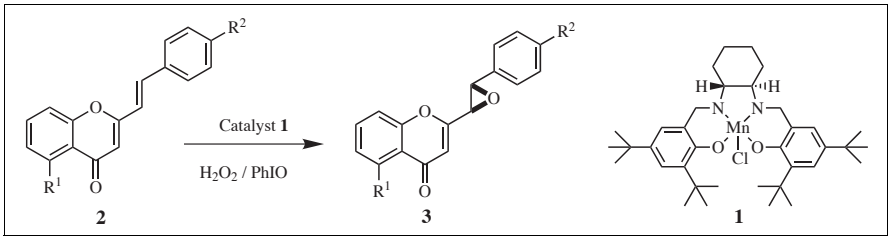

The epoxidation of 2-styrylchromones **2a-h** using Jacobsen's Mn(III)[salen] complex **1** as catalyst is reported for the first time. Several studies were performed using both hydrogen peroxide and iodosylbenzene as oxidants, in order to obtain the α,β-epoxy-2-styrylchromones **3a-h** regioselectively. Due to the low reactivity of the substrates and the highly unstable character of the formed epoxides, reactions should be interrupted at lower conversions to obtain acceptable yields, especially when hydrogen peroxide is used.

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Introduction.

2-Styrylchromones constitute a small group of natural oxygen heterocyclic compounds [1-3]. Both natural and synthetic derivatives possess significant biological properties such as anti-allergic [4], anti-tumour [5] and cytotoxic activity against human leukaemia cells [6,7]. Certain synthetic derivatives have also been reported to show important antiviral activity [8] and they can also interact with the oxidative phosphorylation system [9]. In our recent studies several polyhydroxylated 2-styrylchromones were found to act as potent inhibitors of xanthine oxidase [10] and as promising hepatoprotectors against *tert*-butyl-hydroperoxide [11].

In continuation of our studies on the synthesis of new 2-styrylchromone derivatives for further assessment of their biological activity, namely the antioxidant activity, we decided to study their epoxidation using various oxidants. The expected epoxides could be easily transformed into a large variety of compounds *via* regio- and stereoselective ring-opening.

Epoxidation of substituted alkenes can be performed by using several oxidising species such as peracids, perborate and percarbonate, hydrogen peroxide and *tert*-butyl hydroperoxide, sodium hypochlorite, Oxone®, O_2/aldehyde and various dioxiranes [12-16]. However, most of the oxidizing agents suffer from the disadvantage that not only epoxide but stoichiometric amount of a waste product are also formed. From this point of view, the use of hydrogen peroxide is a particularly attractive option both on environmental and economic grounds. It is cheap, readily available and reasonably stable giving only water as a by-product. The main problem associated with this oxidant, is the homolytic cleavage of the weak O-O bond, which leads to the formation of radicals and, therefore, indiscriminate oxidation. One possible solution is the use of various metal-containing catalysts to give reactive metal-oxo species in the presence of hydrogen peroxide as terminal oxidant. The use of nitrogen heterocyclic co-catalysts such as imidazoles, pyridines and tertiary amine-*N*-oxides acting as either bases or axial ligands for the transition metal catalyst can improve their efficiency.

Cationic Mn(III)-salen complexes have been successfully used as catalysts for the epoxidation of isolated olefins. The first report on the epoxidation of olefins with iodosylbenzene as terminal oxidant and Mn(III)-salen complexes as catalyst was published by Kochi *et al*. [17]. Only a few years after this key publication an asymmetric version of this epoxidation was reported by the groups of Jacobsen [18] and Katsuki [19] using chiral Mn(III)-salen complexes as catalyst. Iodosylbenzene [17-23] and sodium hypochlorite [24-26] are the most frequently used terminal oxidants but other oxygen sources such as hydrogen peroxide [27-30], dimethyldioxirane (DMD) [31-33], Oxone® [34], tetrabutylammonium monopersulfate [35], tetrabutylammonium periodate [36], *m*-chloroperoxybenzoic acid [37] and even molecular oxygen [38] have been reported. Iodosylbenzene is a

polymeric substance, prepared by base-induced hydrolysis of the commercially available iodobenzene diacetate, and the role of the catalyst in homogeneous catalysis is to solubilise it in its monomeric form. The essential mechanistic feature of this process is not yet clarified. When iodosylbenzene is used, no oxo intermediates take place as it can be observed when the oxygen comes from a peroxide or a peroxyacid; instead, the oxygen is bound through single bonds to both the metal center and the iodine atom [23].

In this report we describe the epoxidation studies of 2-styrylchromones **2a-h** with DMD, hydrogen peroxide and iodosylbenzene as oxidants and using *N,N'*-bis-(3,5-di-*t*-butylsalicilidene)-1,2-cyclohexanediamino-manganese(III) chloride **1** (Jacobsen's catalyst) as catalyst in combination with the latter two reagents.

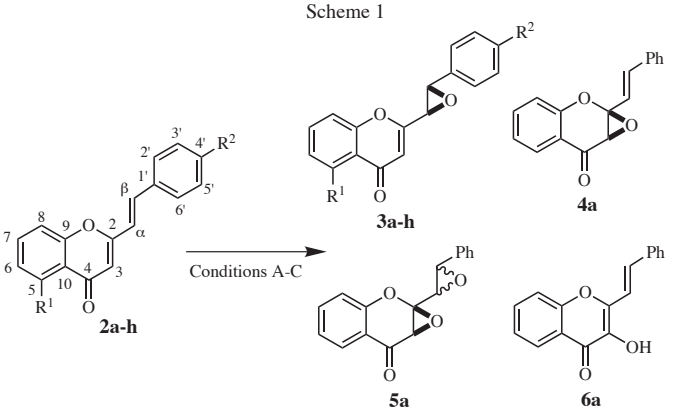
Results and Discussion.

Chemistry.

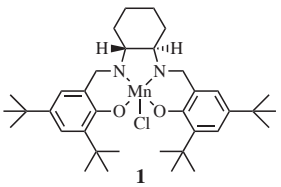
Since we have found that DMD is a reagent of choice to oxidize various heterocyclic substrates [14,39 and the references cited therein], first we investigated the epoxidation of 2-styrylchromone **2a** with isolated DMD in acetone or in acetone-free chloroform solution (Scheme 1, Method A). In a slow reaction the formation of a highly unstable product mixture was observed, a high excess (*ca.* 6 equiv.) of DMD was needed to complete the oxidation. Using various eluents, we were able to isolate some components of the reaction mixture such as α,β-epoxy-2-styrylchromone **3a** (6%), 2,3:α,β-diepoxy-2-styrylchromone **5a** (33%) as a 45:55 mixture of the two possible diastereomers and 3-hydroxy-2-styrylchromone **6a** (11%), while other components decomposed during silica chromatography. Considerable amount of cinnamic acid has also been identified in the reaction mixture. It seems very likely that both chromone **6a** and cinnamic acid originate from the labile intermediate epoxide **4a** by opening of the oxirane ring followed by elimination of water and further oxidation, respectively. Clearly, DMD discriminates poorly between the two double bonds, a similar situation has previously been observed in the DMD oxidation of *E,E*-cinnamylideneacetophenones [40]. Thus, we can conclude that, due to the low reactivity of the substrate, the poor regioselectivity of the reagent and the unstable character of the products, DMD has little synthetic value in the epoxidation of 2-styrylchromones.

Next, we tested the epoxidation of 2-styrylchromones **2a-h** with hydrogen peroxide in the presence of a catalytic amount of the Mn(III)-salen complex **1** (Scheme 1, Method B). Optimization experiments were done with the parent compound **2a** using dichloromethane/methanol (1:1, v/v) mixture as solvent, since it is known that the use of this mixture is important to solubilize the substrate and

Scheme 1



2,3 a: R^1 = H, R^2 = H; **b:** R^1 = H, R^2 = Cl; **c:** R^1 = H, R^2 = CH_3; **d:** R^1 = H, R^2 = NO_2; **e:** R^1 = OH, R^2 = H; **f:** R^1 = OH, R^2 = Cl; **g:** R^1 = OH, R^2 = CH_3; **h:** R^1 = OH, R^2 = NO_2



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Methods:
A: DMD/Me_2CO-CH_2Cl_2 or $CHCl_3$
B: Catalyst **1**, cocatalyst, H_2O_2, CH_2Cl_2:CH_3OH (1:1)
C: Catalyst **1**, cocatalyst, PhIO, solvent

to mix it with hydrogen peroxide [28,30]. Surprisingly, treatment of **2a** with an excess of hydrogen peroxide or alkaline hydrogen peroxide, with or without catalyst **1**, at room temperature failed to give any epoxide. Only the unreacted starting material **2a** was recovered, in some cases decomposition was also observed. However, when hydrogen peroxide and Mn(III)-salen complex **1** were used in the presence of 1-methylimidazole as co-catalyst, the corresponding epoxide **3a** was obtained in a small amount (Table 1, entry 1). An increase in the amount of oxidant and the reaction period usually resulted in an improvement in the yield (Table 1, entries 1-6). The best result (65% effective yield) was achieved using high excess of hydrogen peroxide at elevated temperature (Table 1, entry 6). By changing 1-methylimidazole for its 2-methyl isomer led to lower conversions (Table 1, entries 7-9). Other ligands, such as pyridine *N*-oxide or 4-phenylpyridine *N*-oxide, which have been successfully used previously to improve the efficiency the Mn(III)-salen-catalyzed epoxidations, gave no better results (Table 1, entries 10-12 and 13-15). The crucial role of an added co-ligand was further supported by the application of ammonium acetate (Table 1, entries 16,17). On the other hand, very long reaction periods led to diminished yields in some cases (compare Table 1, entries 2,3 and 10,11). The conversions were much poorer than in the case of DMD applied either in acetone-dichloromethane or chloroform solution. Either the change in the oxidizing species or in the solvent may result in this diminished reactivity. These results suggest this epoxidation is quite sensitive to the reaction conditions, in accordance with the

above-mentioned low reactivity of the substrate and the unstable character of the product. We have to emphasize that the epoxidation took place with complete regio-selectivity and no 2,3-epoxy-2-styrylchromones could be detected in the reaction mixture.

no epoxidation was observed in the polar-protic solvent methanol (Table 2, entry 5). Use of higher oxidant amount resulted in better yields (Table 2, entries 3,4). Once again, the reaction period played an important role in the yields of epoxide **3a**, the yields with various

Table 1

Epoxidation of 2-styrylchromone **2a** using catalyst (*S*,*S*)-**1** and hydrogen peroxide as oxidant.[a]

Entry	Co-catalyst (equivalent)	Oxidant (equivalent)	Temperature (ºC)	Time (h)	Conversion (%)	Yield[b] (**3a**, %)	Effective yield[c] (**3a**, %)
1	1-MeIm	3	r.t.	12	16.8	0.8	4.9
2	1-MeIm	3	r.t.	24	10.6	6.7	62.0
3	1-MeIm	3	r.t.	48	13.0	3.8	29.2
4	1-MeIm	3	40	24	8.0	1.9	23.8
5	1-MeIm	10	40	24	16.3	6.6	40.4
6	1-MeIm	10	40	48	12.5	8.1	64.8
7	2-MeIm	3	r.t.	24	4.6	2.5	54.3
8	2-MeIm	3	40	48	4.2	3.1	73.8
9	2-MeIm	10	40	48	9.1	4.4	48.4
10	PyNO	3	r.t.	24	13.3	5.2	39.1
11	PyNO	3	r.t.	48	9.3	1.8	19.4
12	PyNO	10	40	48	14.8	6.2	41.9
13	PPNO	3	r.t.	24	15.2	4.5	29.6
14	PPNO	3	r.t.	48	6.5	4.1	63.1
15	PPNO	10	40	48	13.1	5.2	39.7
16	NH_4OAc	3	r.t.	48	8.5	5.0	58.8
17	NH_4OAc	10	40	48	9.3	5.5	59.1

a) Ratio 2-styrylchromone: catalyst: co-catalyst = 1:0.05:0.7. b) Yield of the isolated epoxide **3a**. c) Yield calculated on the basis the reacted 2-styrylchromone **2a**. 1-MeIm: 1-methylimidazole, 2-MeIm: 2-methylimidazole, PyNO: pyridine *N*-oxide, PPNO: 4-phenylpyridine *N*-oxide.

When the best conditions (Table 1, entry 6) were applied in the epoxidation of substituted 2-styryl-chromones **2b-d**, the corresponding epoxides **3b-d** were obtained in 32-37% effective yields (*vide experimental*). It is noteworthy that all reaction mixtures were separated by silica gel thin layer chromatography, the first spot with lower R_f corresponded to the unreacted starting material **2a-d** and the second spot, which appeared just above it, belonged to the α,β-epoxy-2-styrylchromones **3a-d** in each case.

Then, we investigated the epoxidation of 2-styryl-chromones **2a-d** with iodosylbenzene, another widely used oxygen source in the Mn(III)-salen-catalyzed oxidations (Scheme 1, Method C) and some selected results are shown by Table 2. We started our study with the epoxidation of **2a** using a stoichiometric amount of iodosylbenzene in the presence of catalyst **1** and acetonitrile as solvent. The reaction took place with much better conversion than in the case of hydrogen peroxide and the desired epoxide **3a** was obtained in 7% isolated yield (Table 2, entry 1). As before, the addition of a co-catalyst, such as pyridine *N*-oxide, improved the efficiency although this effect was less pronounced (Table 2, entry 2). In dichloromethane similar results were achieved as in acetonitrile (Table 2, entries 2,3) but reaction periods fitted a maximum curve (Table 2, entries 6-10). Again, this fact clearly shows that the epoxide **3a** is formed and destroyed after a certain period of time in the reaction medium. These results support our idea on the instability of the epoxide **3a** under the reaction conditions. Unlike method B, the increase of temperature did not increase the yield of the epoxide **3a** (Table 2, entries 9,12). The use of iodosylbenzene as oxidant and acetonitrile as solvent resulted in much better conversions and effective yields than the conditions of Method B. It seems likely that both the higher reactivity of the oxidizing reagent and the lower nucleophilicity of the solvent are responsible for this effect. The epoxidation of 2-styrylchromones **2b-d** were also carried out applying iodosylbenzene as oxidant under the best conditions (Table 2, entry 7) and the corresponding epoxides **3b-d** were obtained in 13-36% effective yields (*vide experimental*). Comparison of the yields of methods B and C using the same substrate reveals the greater synthetic utility of the latter protocol which can be interpreted in terms of the higher lifetime of the unstable epoxides **3a-d** in the aprotic solvent acetonitrile. Again, a complete regioselectivity with exclusive attack of the oxidant at the styryl double bond was observed.

Table 2
Epoxidation of 2-styrylchromone **2a** using catalyst (*S*,*S*)-**1** and iodosylbenzene as oxidant.[a]

Entry	Co-catalyst (equivalent)	Oxidant (equivalent)	Solvent	Temperature (ºC)	Time (h)	Conversion (%)	Yield[b] (**3a** %)	Effective Yield[c] (**3a** %)
1	no ligand	1	CH_3CN	r.t.	24	58.1	6.5	11.2
2	PyNO	1	CH_3CN	r.t.	24	30.2	7.1	23.5
3	PyNO	1	CH_2Cl_2	r.t.	24	31.9	9.8	30.7
4	PyNO	2	CH_2Cl_2	r.t.	24	43.3	11.3	26.1
5	PyNO	2	CH_3OH	r.t.	24	0.0	0.0	0.0
6	PyNO	2	CH_3CN	r.t.	4	52.1	14.6	28.0
7	PyNO	2	CH_3CN	r.t.	12	66.9	29.0	43.3
8	PyNO	2	CH_3CN	r.t.	18	71.8	26.8	37.3
9	PyNO	2	CH_3CN	r.t.	24	60.2	16.9	28.1
10	PyNO	2	CH_3CN	r.t.	48	78.3	22.8	29.1
11	PyNO	2	CH_3CN	r.t.	96	40.2	16.3	40.5
12	PyNO	2	CH_3CN	reflux	24	49.0	16.5	33.7

a) Ratio 2-styrylchromone: catalyst: co-catalyst = 1 : 0.05 : 0.5. b) Yield of the isolated epoxide **3a.** c) Yield calculated from the reacted 2-styrylchromone **2a**.
PyNO: pyridine *N*-oxide.

Since we used catalyst (*S*,*S*)-**1** in each case and, therefore, the epoxidation was performed by a chiral, non-racemic Mn(V)oxo species in both methods, it was an important point to determine the enantiomeric ratio of the obtained epoxides. Unfortunately, HPLC measurements of epoxides **3a-c** on chiral column Chiralcel OD showed that no stereodifferentiation took place and the products were racemic mixtures of the two enantiomers.

The optimized conditions of Methods B and C (Table 1, entry 6 and Table 2, entry 7) were applied to 5-hydroxy-2-styrylchromones **2e-h**, as well. Although TLC analysis of the reaction mixture showed only one spot in various eluents, the ^{1}H NMR measurements revealed the presence of two compounds, two singlets were observed at ~ δ 6.3-6.5 ppm belonging to the resonance of 3-H of two different chromones. The presence of two doublets at δ ~ 3.7-3.8 ppm and δ ~ 4.2-4.3 ppm indicated that one of these structures were the desired epoxides **3e-h**. Since all of our attempts to find the appropriate eluent for the TLC or column chromatography separation failed, we decided to separate these mixtures by HPLC on a reverse phase RP-18 column. After some optimization experiments methanol/water (8:2, v/v) mixture was found to be an ideal eluent for a base-line separation. The first peak identified in each case as α,β-epoxy-5-hydroxy-2-styrylchromone **3e-h** appeared at about 8 minutes, while the second component which proved to be the starting material **2e-h** appeared at about 15 minutes. Thus, we were able to obtain a small amount of the new epoxides **3e-h** to perform their full spectral characterization. The yields of these reactions were calculated from the ^{1}H NMR spectra of the obtained reaction mixtures on the basis of the 3-H integrals of the epoxides **3e-h** and those of the starting materials **2e-h**.

Nuclear Magnetic Resonance Spectroscopy.

α,β-Epoxy-2-styrylchromones **3a-h** could be easily identified by their singlet at δ = 6.37-6.49 ppm corresponding to the resonances of the 3-H and, in the case of the compounds **3c**,**g**, by the singlets of the 4'-methyl groups at δ = 2.38 ppm. Another main feature in their ^{1}H and ^{13}C NMR spectra were the resonances assigned to β-H (δ = 4.16-4.38 ppm) and C-β (δ = 59.1-60.9 ppm) which appeared at higher frequency than that of α-H (δ = 3.74-3.80 ppm) and C-α (δ = 58.3-59.0 ppm). The coupling constant $^3J_{H\alpha\text{-}H\text{-}\beta}$ = 1.6-1.7 Hz of compounds **3a-h** were consistent with those of *trans*-1,2-disubstituted epoxides, this relative configuration was expected for an epoxide obtained from a *trans*-alkene [41-43].

The most important characteristics of the ^{13}C NMR spectra of epoxides **3a-h** were the signals of the carbonyl carbon. Incorporation of the 5-hydroxyl group resulted in a marked downfield shift (δ = 177.5-177.7 ppm for the epoxides **3a-d** and δ = 182.9-183.1 ppm for the 5-hydroxy-epoxides **3e-h**), this great difference offers a diagnostic tool for identifying this substitution pattern.

A detailed analysis of the ^{1}H, ^{13}C, HSQC and HMBC NMR spectra of all epoxides **3a-h** allowed the assignment of the 6-H, 8-H and 7-H proton resonances which appeared at δ = 6.82-7.45, 6.90-7.48 and 7.54-7.72 ppm, respectively. The 5-H resonances of α,β-epoxy-2-styrylchromones **3a-d** always appeared as a double doublet a δ = 8.20-8.22 ppm, this extremely high chemical shift is the consequence of the carbonyl group at *peri* position. When the 5-position is substituted by a hydroxyl group (epoxides **3e-h**), the proton resonance of the hydroxyl group is identified as a singlet appearing at δ = 12.33-12.41 ppm due to the intramolecular hydrogen bond between the 5-hydroxyl group and the carbonyl. The assignment of the other proton and carbon resonances of

epoxides **3a-h** was confirmed by the connectivities found in their HMBC spectra, the most important C-H connectivities are shown by Figure 1.

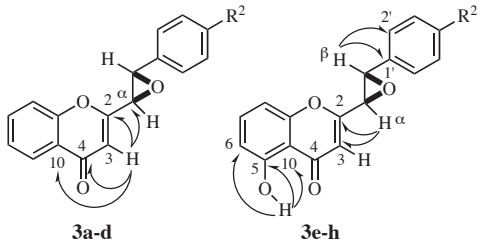

Figure 1. Main connectivities found in the HMBC spectra of compounds **3a-h**.

Conclusions.

We have verified the possibility of the epoxidation of 2-styrylchromones with hydrogen peroxide and iodosylbenzene in the presence of Mn(III)-salen complex but our results clearly show difficulties of this reaction. Due to the low reactivity of the substrates and the highly unstable character of the epoxides formed, the reactions should be finished at lower conversion to obtain the products in acceptable yields, especially in the case of using hydrogen peroxide as oxidant. Our results clearly show that both the reactivity of the substrates and the stability of the products depend on the structure of the oxidant and the reaction medium. Addition of ligands to increase the reactivity of the oxidizing species Mn(V)oxo complex is necessary for the successful reaction. 1-Methylimidazole was the most appropriate co-catalyst when hydrogen peroxide was used while pyridine *N*-oxide proved to be the most effective in the case of iodosylbenzene. In general, the best isolated yields were obtained using iodosylbenzene as oxidant.

EXPERIMENTAL

Melting points were measured in a Reichert Thermovar apparatus fitted with a microscope and are uncorrected. NMR spectra were recorded on a Bruker Avance 300 spectrometer (300.13 for ^{1}H and 75.47 MHz for ^{13}C), with $CDCl_3$ as a solvent. Chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. The internal standard was TMS. ^{13}C assignments were made with the aid of 2D *g*HSQC and *g*HMBC (delays for one bond and long-range *J* C/H couplings were optimised for 145 and 7 Hz, respectively) experiments. Electron impact (EI, 70 eV) MS were recorded with VG Autospec Q and M spectrometers. Elemental analyses were obtained with Carlo Erba 1108 and LECO 932 CHNS analysers. Preparative thin layer chromatography was performed with Riedel silica gel DGF_{254} while the column chromatography was done on Merck silica gel 60 (70-230 mesh). HPLC separations were performed on a Merck–Hitachi apparatus using a reversed phase LiChrospher 100 RP-18 (5 μm) column, at room temperature (eluent: methanol/water (8:2, v/v); flow rate: 0.7 ml/min). Detection was carried out at 254 nm with a Merck-Hitachi UV-Vis detector. Chiral HPLC measurement was performed with a Barspec system using a Chiralcel OD column, eluent: hexane/2-propanol (90:10, v/v), flow rate: 0.7 ml/min. Under these conditions enantiomers of epoxide **3a-3c** were detected at retention times 42-52 min and 56-66 min, respectively.

2-Styrylchromones **2a-h** [44,45], DMD solutions in acetone [46] and in acetone-free chloroform [47] were prepared according to literature procedures. Iodosylbenzene was obtained by hydrolysis of commercially available iodobenzene diacetate under basic conditions [17].

Dimethyldioxirane epoxidations of 2-styrylchromone (**2a**).

Oxidation by DMD/chloroform solution.

To a stirred solution of 2-styrylchromone **2a** (248 mg, 1.0 mmol) in chloroform (12 ml) 84 ml of isolated aceton-free DMD in chloroform (0.075 *M*) was added in four portions at room temperature. The column chromatography (eluent: toluene/ethyl acetate = 4:1, v/v) of the concentrated reaction mixture yielded 15 mg (5.7%) epoxide **3a** (*vide infra*).

Oxidation by DMD/acetone solution.

To a stirred solution of 2-styrylchromone **2a** (125 mg, 0.5 mmol) in dichloromethane (5 ml) 25 ml of isolated DMD in acetone (0.09 *M*) was added at room temperature. After 1 hour another batch of DMD (10 ml, 0.09 *M*) was added, the mixture was stirred for 6 hrs and evaporated. The oily residue was dissolved in dichloromethane, dried ($MgSO_4$) and purified by column chromatography (eluent: hexane/acetone = 1:1, v/v) to give 46 mg (32.9%) of diepoxide **5a** and 15 mg (11.4%) of 3-hydroxy-2-styrylchromone **6a**.

2,3:α,β-Diepoxy-2-styrylchromone (**5a**).

This compound was obtained as a yellow oil; ^{1}H nmr (hexadeuterioacetone): 3.80 (d, 1H, β-H (minor), J = 1.2 Hz), 3.94 (d, 1H, β-H (major), J = 1.3 Hz), 4.00 (s, 1H, 3-H (minor)), 4.02 (s, 1H, 3-H (major)), 4.28 (d, 1H, α-H (minor), J = 1.2 Hz), 4.34 (d, 1H, α-H (major), J = 1.3 Hz), 7.21 (d, 1H, 8-H (minor), J = 8.3 Hz), 7.23 (d, 1H, 8-H (major), J = 8.3 Hz), 7.28 (m, 1H, 6-H), 7.43 (m, 5H, 2'-, 3'-, 4'-, 5'-, 6'-H), 7.72 (m, 1H, 7-H), 7.89 (d, 1H, 5-H, J = 8.0 Hz); ^{13}C nmr (hexadeuterioacetone): 56.0 (C-β (minor)), 56.2 (C-β (major)), 58.1 (C-α (minor)), 58.5 (C-3 (major) + C-α (major)), 58.9 (C-3 (minor)), 84.3, 85.2 (C-2), 118.2 (C-8), 119.8, 120.0 (C-10), 124.1 (C-6), 126.6, 129.1, 129.3 (C-2',3',4',5',6'), 127.3 (C-5), 136.1 (C-1'), 137.0 (C-7), 156.2 (C-9), 187.6 (C-4).

Anal. Calcd. for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 73.06; H, 4.51.

3-Hydroxy-2-styrylchromone (**6a**).

This substance was obtained as a yellow crystalline powder, mp 198-199°; ir: OH 3210 br, CO 1616, 1562, 1478, 1468, 1426, 1250, 1214, 1200, 754 cm^{-1}; ^{1}H nmr: 7.33-7.75 (m, 10H, Ar-H), 8.24 (dd, 1H, 5-H, J = 1.6 and 8.0 Hz).

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found: C, 77.01; H, 4.49.

Synthesis of α,β-Epoxy-2-styrylchromones (**3a-h**).

Method B**.**

To a solution of the appropriate 2-styrylchromone **2a-h** (0.4 mmol), 1-methylimidazole (23.0 mg, 0.28 mmol) and catalyst **1**

(12.7 mg, 0.02 mmol) in a 1:1 mixture of dichloromethane/ methanol (4 ml) 30% aqueous H_2O_2 (0.4 ml, 12 mmol) was added. The mixture was stirred at 40°C for 2 days. Then, the mixture was diluted with dichloromethane and the organic layer was separated and concentrated.

In the case of the epoxides **3a-d**, the residue was separated by preparative silica gel thin layer chromatography (eluent: light petroleum/dichloromethane (1:2, v/v)) to give the unreacted starting materials **2a-d** and the epoxides **3a-d**. In the case of the products **3e-h**, the residue was purified by silica gel column chromatography (eluent: light petroleum/dichloromethane, (1:2, v/v)) and the obtained mixture containing the starting material **2e-h** and the epoxide **3e-h** were submitted to separation by HPLC. The yields/effective yields of the epoxidations were as follows: **3a** (8.1%, 64.8%), **3b** (4.0%, 32.3%), **3c** (7.6%, 34.7%), **3d** (2.7%, 37.2%), **3e** (2.9%, 13.5%), **3f** (3.4%, 38.0%), **3g** (3.3%, 26.6%), **3h** (2.6%, 4.3%).

Method C.

Catalyst **1** (12.7 mg, 0.02 mmol) was added to a solution of the appropriate 2-styrylchromone **2a-h** (0.4 mmol) and pyridine *N*-oxide (19.0 mg, 0.2 mmol) in acetonitrile (4 ml). Then iodosylbenzene (0.18 g, 0.8 mmol) was added and the mixture was stirred at room temperature for 12 hours. The mixture was concentrated and separated in the same manner as described at method C. The yields/effective yields of the epoxidations were as follows: **3a** (29.0%, 43.3%), **3b** (9.7%, 36.2%), **3c** (15.3%, 27.0%), **3d** (4.4%, 13.1%), **3e** (22.2%, 39.3%), **3f** (11.8%, 21.8%), **3g** (3.8%, 16.2%), **3h** (7.3%, 20.1%).

α,β-Epoxy-2-styrylchromone (**3a**).

This compound was obtained as white needles (mixture of dichloromethane:cyclohexane), mp 97-99°; ^{1}H nmr: δ 3.80 (d, 1H, α-H, J = 1.7 Hz), 4.24 (d, 1H, β-H, J = 1.7 Hz), 6.47 (s, 1H, 3-H), 7.35-7.46 (m, 6H, 6-, 2'-, 3'-, 4'-, 5'- and 6'-H), 7.47 (d, 1H, 8-H, J = 8.2 Hz), 7.69 (dt, 1H, 7-H, J = 1.7 and 8.2 Hz), 8.21 (dd, 1H, 5-H, J = 1.7 and 8.0 Hz); ^{13}C nmr: δ 58.6 (C-α), 60.4 (C-β), 109.4 (C-3), 118.0 (C-8), 124.2 (C-10), 125.5 (C-6), 125.7 (C-2',6'), 125.8 (C-5), 128.8 (C-3',5'), 129.1 (C-4'), 133.9 (C-7), 135.0 (C-1'), 156.1 (C-9), 162.8 (C-2), 177.6 (C-4); ms (EI): m/z 264 ($M^{+\bullet}$, 5), 247 (11), 236 (74), 235 (100), 207 (17), 191 (12), 179 (16), 121 (47), 115 (22), 102 (20), 90 (46), 89 (48), 83 (25), 77 (33), 76 (25), 63 (29), 51 (25).

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found: C, 77.02; H, 4.60.

4'-Chloro-α,β-epoxy-2-styrylchromone (**3b**).

This compound was obtained as white needles (mixture of dichloromethane:cyclohexane), mp 161-163°; ^{1}H nmr: δ 3.76 (d, 1H, α-H, J = 1.7 Hz), 4.23 (d, 1H, β-H, J = 1.7 Hz), 6.46 (s, 1H, 3-H), 7.31 (d, 2H, 2'-, 6'-H, J = 8.5 Hz), 7.40 (d, 2H, 3'-, 5'-H, J = 8.5 Hz), 7.43 (dd, 1H, 6-H, J = 7.6 and 7.9 Hz), 7.47 (dd, 1H, 8-H, J = 0.9 and 7.9 Hz), 7.70 (ddd, 1H, 7-H, J = 1.6 and 7.6 Hz), 8.21 (dd, 1H, 5-H, J = 1.6 and 7.6 Hz); ^{13}C nmr: δ 58.6 (C-α), 59.7 (C-β), 109.6 (C-3), 118.0 (C-8), 124.2 (C-10), 125.5 (C-6), 125.9 (C-5), 127.0 (C-2',6'), 129.0 (C-3',5'), 133.5 (C-1'), 134.0 (C-7), 135.0 (C-4'), 156.1 (C-9), 162.4 (C-2), 177.6 (C-4); ms (EI): m/z 298 ($M^{+\bullet}$, 7), 281 (9), 272 (33), 271 (55), 270 (90), 269 (100), 243 (8), 235 (29), 234 (87), 205 (10), 178 (23), 139 (16), 121 (41), 111 (16), 102 (25), 92 (25), 89 (87), 77 (16), 76 (29), 75 (19), 64 (16), 63 (33), 57 (13), 51 (13).

EI-HMRS. Calcd. for $C_{17}H_{11}{}^{35}ClO_3$, $M^{+\bullet}$: 298.0391. Found: 298.0397. EI-HMRS. Calcd. for $C_{17}H_{11}{}^{37}ClO_3$, $M^{+\bullet}$: 300.0373. Found: 300.0367.

α,β-Epoxy-4'-methyl-2-styrylchromone (**3c**).

This compound was obtained as white needles (mixture of dichloromethane:cyclohexane), mp 141-142°; ^{1}H nmr: δ 2.38 (s, 3 H, 4'-CH_3), 3.78 (d, 1H, α-H, J = 1.7 Hz), 4.21 (d, 1H, β-H, J = 1.7 Hz), 6.45 (s, 1H, 3-H), 7.22 (d, 2H, 3'-, 5'-H, J = 8.4 Hz), 7.26 (d, 2H, 2'-, 6'-H, J = 8.4 Hz), 7.42 (ddd, 1H, 6-H, J = 0.8, 7.7 and 7.8 Hz), 7.47 (dd, 1H, 8-H, J = 0.8 and 8.0 Hz), 7.69 (ddd, 1H, 7-H, J = 1.6, 7.7 and 8.0 Hz), 8.20 (dd, 1H, 5-H, J = 1.6 and 7.8 Hz); ^{13}C nmr: δ 21.3 (4'-CH_3), 58.6 (C-α), 60.5 (C-β), 109.4 (C-3), 118.0 (C-8), 124.2 (C-10), 125.5 (C-6), 125.6 (C-2',6'), 125.8 (C-5), 129.5 (C-3',5'), 131.9 (C-1'), 133.9 (C-7), 139.1 (C-4'), 156.2 (C-9), 163.0 (C-2), 177.7 (C-4); ms (EI): m/z 278 ($M^{+\bullet}$, 8), 251 (13), 250 (70), 249 (100), 235 (11), 234 (37), 221 (11), 178 (12), 158 (8), 145 (8), 129 (11), 121 (37), 103 (33), 92 (16), 91 (23), 78 (28), 77 (22), 65 (15), 63 (16), 51 (11).

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found: C, 77.29; H, 5.34.

α,β-Epoxy-4'-nitro-2-styrylchromone (**3d**).

This compound was obtained as white needles (mixture of dichloromethane:cyclohexane), mp 181-183°; ^{1}H nmr: δ 3.80 (d, 1H, α-H, J = 1.7 Hz), 4.38 (d, 1H, β-H, J = 1.7 Hz), 6.49 (s, 1H, 3-H), 7.45 (dt, 1H, 6-H, J = 1.0 and 7.7 Hz), 7.48 (d, 1H, 8-H, J = 8.2 Hz), 7.57 (d, 2H, 2'-, 6'-H, J = 8.8 Hz), 7.72 (ddd, 1H, 7-H, J = 1.6, 7.7 and 8.2 Hz), 8.22 (dd, 1H, 5-H, J = 1.6, 7.7 and 7.7 Hz), 8.29 (d, 2H, 3'-, 5'-H, J = 8.8 Hz); ^{13}C nmr: δ 59.0 (C-α), 59.1 (C-β), 110.1 (C-3), 118.0 (C-8), 124.1 (C-3',5'), 124.2 (C-10), 125.7 (C-6), 126.0 (C-5), 126.6 (C-2',6'), 134.2 (C-7), 142.2 (C-1'), 148.4 (C-4'), 156.1 (C-9), 161.6 (C-2), 177.5 (C-4); ms (EI): m/z 309 ($M^{+\bullet}$, 30) 293 (10), 281 (93), 263 (5), 235 (32), 234 (100), 233 (33), 205 (29), 189 (10), 178 (17), 121 (30), 104 (24), 102 (34), 92 (30), 89 (60), 77 (24), 76 (41), 63 (45), 51 (25).

Anal. Calcd. for $C_{17}H_{11}NO_5$: C, 66.02; H, 3.58; N, 4.53. Found: C, 66.23; H, 3.92; N, 4.51.

α,β-Epoxy-5-hydroxy-2-styrylchromone (**3e**).

This compound was obtained as yellowish oil, ^{1}H nmr: δ 3.78 (d, 1H, α-H, J = 1.6 Hz), 4.20 (d, 1H, β-H, J = 1.6 Hz), 6.39 (s, 1H, 3-H), 6.83 (d, 1H, 6-H, J = 8.3 Hz), 6.91 (d, 1H, 8-H, J = 8.4 Hz), 7.34-7.37 (m, 2H, 2'-, 6'-H), 7.40-7.43 (m, 3H, 3'-, 4'- and 5'-H), 7.54 (dd, 1H, 7-H, J = 8.3 and 8.4 Hz), 12.41 (s, 1H, 5-O*H*); ^{13}C nmr: δ 58.4 (C-α), 60.8 (C-β), 107.0 (C-8), 107.8 (C-3), 111.2 (C-10), 111.8 (C-6), 125.7 (C-2',6'), 128.9 (C-3',5'), 129.3 (C-4'), 134.8 (C-1'), 135.6 (C-7), 156.4 (C-9), 160.9 (C-5), 164.4 (C-2), 183.1 (C-4); ms (EI): m/z 280 ($M^{+\bullet}$, 50), 263 (5), 252 (54), 251 (100), 234 (8), 223 (10), 207 (14), 178 (7), 167 (8), 149 (9), 137 (35), 121 (7), 115 (13), 105 (17), 90 (35), 89 (39), 77 (25), 64 (10), 63 (14), 57 (7), 51 (15).

EI-HMRS. Calcd. for $C_{17}H_{12}O_4$, $M^{+\bullet}$: 280.0736. Found: 280.0732.

4'-Chloro-α,β-epoxy-5-hydroxy-2-styrylchromone (**3f**).

This compound was obtained as yellowish oil, ^{1}H nmr: δ 3.74 (d, 1H, α-H, J = 1.6 Hz), 4.18 (d, 1H, β-H, J = 1.6 Hz), 6.38 (s, 1H, 3-H), 6.83 (d, 1H, 6-H, J = 8.4 Hz), 6.90 (d, 1H, 8-H, J = 8.4 Hz), 7.30 (d, 2H, 2'-, 6'-H, J = 8.5 Hz), 7.40 (d, 2H, 3'-, 5'-H, J =

8.5 Hz), 7.54 (t, 1H, 7-H, J = 8.4 Hz), 12.37 (s, 1H, OH-5); ^{13}C nmr: δ 58.3 (C-α), 60.1 (C-β), 107.0 (C-8), 107.9 (C-3), 111.1 (C-10), 111.9 (C-6), 127.0 (C-2',6'), 129.1 (C-3',5'), 133.3 (C-1'), 135.2 (C-4'), 135.7 (C-7), 156.3 (C-9), 160.9 (C-5), 163.9 (C-2), 183.0 (C-4); ms (EI): m/z 314 ($M^{+\bullet}$, 40), 285 (100), 250 (39), 137 (28), 124 (10), 108 (12), 92 (10), 89 (57), 63 (12), 51 (7).

EI-HMRS. Calcd. for $C_{17}H_{11}{}^{35}ClO_4$, $M^{+\bullet}$: 314.0346. Found: 314.0359. EI-HMRS. Calcd. for $C_{17}H_{11}{}^{37}ClO_4$, $M^{+\bullet}$: 316.0316. Found: 316.0318.

α,β-Epoxy-5-hydroxy-4'-methyl-2-styrylchromone (**3g**).

This compound was obtained as yellowish oil, ^{1}H nmr: δ 2.38 (s, 3H, 4'-CH_3), 3.77 (d, 1H, α-H, J = 1.7 Hz), 4.16 (d, 1H, β-H, J = 1.7 Hz), 6.37 (s, 1H, 3-H), 6.82 (dd, 1H, 6-H, J = 0.8 and 8.3 Hz), 6.90 (dd, 1H, 8-H, J = 0.8 and 8.4 Hz), 7.22 (d, 2H, 3'-, 5'-H, J = 8.3 Hz), 7.25 (d, 2H, 2'-, 6'-H, J = 8.3 Hz), 7.54 (dd, 1H, 7-H, J = 8.3 and 8.4 Hz); 12.41 (s, 1H, 5-O*H*); ^{13}C nmr: δ 21.3 (4'-CH_3), 58.3 (C-α), 60.9 (C-β), 107.0 (C-8), 107.6 (C-3), 111.2 (C-10), 111.8 (C-6), 125.7 (C-2',6'), 129.5 (C-3',5'), 131.7 (C-1'), 135.6 (C-7), 139.3 (C-4'), 156.4 (C-9), 160.9 (C-5), 164.5 (C-2), 183.1 (C-4); ms (EI): m/z 294 ($M^{+\bullet}$, 24), 266 (50), 265 (100), 250 (12), 237 (6), 22 (8), 137 (26), 135 (8), 119 (7), 103 (20), 91 (12), 78 (18), 77 (11), 65 (6), 63 (6), 51 (5).

EI-HMRS. Calcd. for $C_{18}H_{14}O_4$, $M^{+\bullet}$: 294.0892. Found: 294.0898.

α,β-Epoxy-5-hydroxy-4'-nitro-2-styrylchromone (**3h**).

This compound was obtained as yellowish oil, ^{1}H nmr: δ 3.78 (d, 1H, α-H, J = 1.6 Hz), 4.34 (d, 1H, β-H, J = 1.6 Hz), 6.41 (s, 1H, 3-H), 6.85 (dd, 1H, 6-H, J = 0.7 and 8.2 Hz), 6.91 (dd, 1H, 8-H, J = 0.7 and 8.4 Hz), 7.56 (d, 2H, 2'-, 6'-H, J = 8.8 Hz), 7.56 (dd, 1H, 7-H, J = 8.2 and 8.4 Hz), 8.30 (d, 2H, 3'-, 5'-H, J = 8.8 Hz), 12.33 (s, 1H, 5-O*H*); ^{13}C nmr: δ 58.6 (C-α), 59.3 (C-β), 107.0 (C-8), 108.4 (C-3), 111.2 (C-10), 112.1 (C-6), 124.1 (C-3',5'), 126.6 (C-2',6'), 135.8 (C-7), 141.9 (C-1'), 149.1 (C-4'), 156.3 (C-9), 160.9 (C-5), 163.0 (C-2), 182.9 (C-4); ms (EI): m/z 325 ($M^{+\bullet}$, 100), 309 (16), 296 (59), 279 (9), 250 (72), 221 (14), 205 (17), 190 (10), 165 (10), 137 (16), 120 (12), 108 (28), 91 (29), 89 (48), 77 (15), 63 (34), 51 (19).

EI-HMRS. Calcd. for $C_{17}H_{11}NO_6$, $M^{+\bullet}$: 325.0586. Found: 325.0590.

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