Synthesis and characterization of ruthenium(II) complexes of 2′-hydroxychalcones

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Reaction of *cis*-$RuCl_2(DMSO)_4$ with the potassium salts of 2′-hydroxychalcones **L** leads to the stable complexes $RuL_2(DMSO)_2$. For each ligand **L** three isomers of each bis(dimethyl sulfoxide)bis(chalconato)ruthenium(II) complex were found; in two of them the two chalconates and the two DMSO ligands are equivalent, while in the third one the chalconates and DMSO ligands are inequivalent. Only two isomers of the $RuL_2(DMSO)_2$ complex were obtained by the reaction of *cis*-$RuCl_2(DMSO)_4$ with the potassium salt of the 2′-hydroxy-3,4,4′,5,6′-pentamethoxydihydrochalcone. One of these isomers was also obtained by the reduction of the appropriate bis(dimethyl sulfoxide)bis(chalconato)ruthenium(II) complex. All these complexes were fully characterized by extensive NMR studies, mass spectrometry and elemental analysis. The unequivocal stereochemistry of each $RuL_2(DMSO)_2$ complex was established by NOESY experiments.

Chalconoids constitute an important class of naturally occurring flavonoid compounds exhibiting a wide spectrum of biological activities, which include potential applications as artificial sweeteners, new drugs or agrochemicals.[1-8] The term chalconoid has been used to designate the whole family of compounds possessing a 1,3-diarylpropane skeleton, which can be modified in the propane chain by the presence of an olefinic bond, keto and/or hydroxyl groups. The most common and widespread compounds of the chalconoid group are the chalcones, which possess a 1,3-diaryl-2-propen-1-one carbon framework.[1,3,5] However, there are also other important derivatives of this family, such as the dihydrochalcones.[2,8]

The antioxidant activity of flavonoids is basically associated with the reduction or inhibition of lipid peroxidation, which is strongly related with aging and carcinogenesis, by their ability to act as free radical scavengers and also to chelate transition metals ions, in order to avoid the involvement of iron and copper ions in the initiation of free radical reactions.[9,10] Substances that can limit lipoperoxidation processes can be of considerable interest for therapeutic research on diseases in which free radicals are implicated. Having in mind these facts and that the 2′-hydroxychalcone and 2′-hydroxydihydrochalcone flavonoids present antioxidant activity,[7,11] it is of interest to study the complexation of these compounds with transition metal ions.

Studies on 2′-hydroxychalcone complexation with some transition metal ions (Co^{II}, Ni^{II}, Cu^{II}, Pt^{II} and Pd^{II}) led to stable complexes, with a square planar configuration, in a 1:2 metal:ligand stoichiometry.[12,13] Rao *et al.* have also reported the synthesis and characterization of complexes of the diamagnetic transition metal ion Ru^{II} with 2′-hydroxychalcones.[13] These complexes were obtained by treating *cis*-$RuCl_2(DMSO)_4$ with appropriate chalcones under reflux in a 3:1 mixture of toluene : methanol. In spite of the diamagnetic properties of such ruthenium(II) species, the complexes obtained were not characterized by NMR.

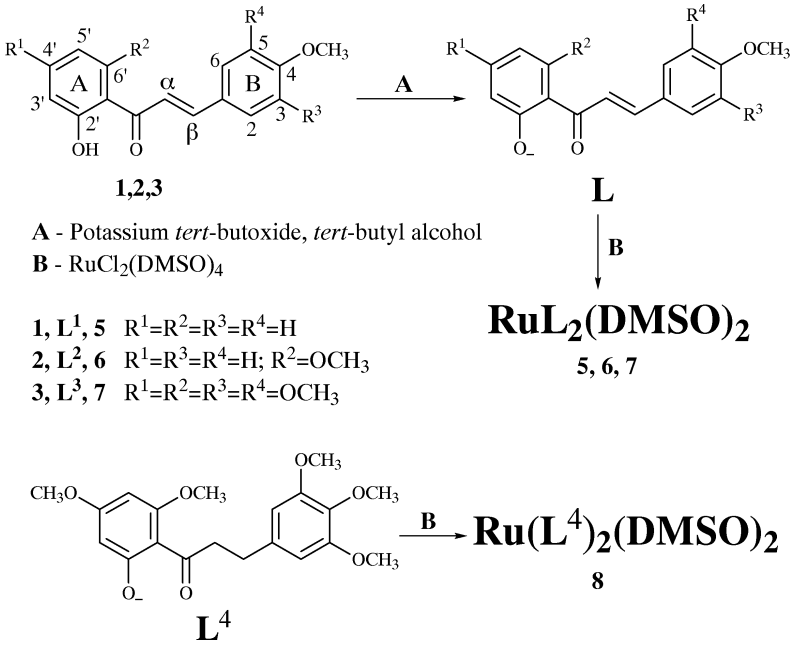
In this paper we will report the synthesis and characterization, by ^1H and ^{13}C NMR, mass spectrometry and elemental analysis, of the new bis(dimethyl sulfoxide)-bis(chalconato)ruthenium(II) **5**–**7** and bis(dimethyl sulfoxide)bis(dihydrochalconato)ruthenium(II) **8** complexes, which are respectively formed by treating *cis*-$RuCl_2(DMSO)_4$ with chalconates $\mathbf{L^1}$–$\mathbf{L^3}$ and dihydrochalconate $\mathbf{L^4}$ (Scheme 1). The complex bis(dimethyl sulfoxide)bis(dihydrochalconato)ruthenium(II) **8h** was also obtained by reduction of the corresponding bis(dimethyl sulfoxide)bis-(chalconato)ruthenium(II) complex **7i** with ammonium formate and Pd/C (10%).

Results and discussion

Synthesis and characterization of bis(dimethyl sulfoxide)bis(chalconato or dihydrochalconato)ruthenium(II) complexes

We have followed the complexation of chalconates with ruthenium(II) by ^1H NMR as in our previous work.[14] A solution of 2′-hydroxy-3,4,4′,5,6′-pentamethoxychalcone **3** in methanol-d_4 was treated with a molar equivalent of an aqueous solution of sodium hydroxide (some drops of dimethyl sulfoxide-d_6 were added to homogenize the reaction mixture) and was refluxed for 15 min. By ^1H NMR analysis, it was possible to observe the presence of a small amount of starting material and signals corresponding to the expected 3,4,4′,5,6′-pentamethoxychalconate $\mathbf{L^3}$. However, it may be noticed that the intensity of the integral of the vinylic proton resonance of this chalconate $\mathbf{L^3}$ is almost half of that corresponding to H-2,6 and decreases after more reflux time, suggesting that α-deuteriation has taken place.[15] To improve the synthesis of the chalconates $\mathbf{L^1}$–$\mathbf{L^3}$, the corresponding 2′-hydroxychalcones **1**–**3** were treated with a molar equivalent of potassium *tert*-butoxide in different solvents. After several assays, dimethyl sulfoxide-d_6, a solvent without exchangeable deuterium atoms, was chosen for NMR studies and anhydrous *tert*-butyl alcohol for the synthesis of ruthenium(II) complexes of chalconates $\mathbf{L^1}$–$\mathbf{L^3}$.

Treatment of *cis*-$RuCl_2(DMSO)_4$ with two molar equivalents of chalconates $\mathbf{L^1}$–$\mathbf{L^3}$ gave the corresponding



Scheme 1.

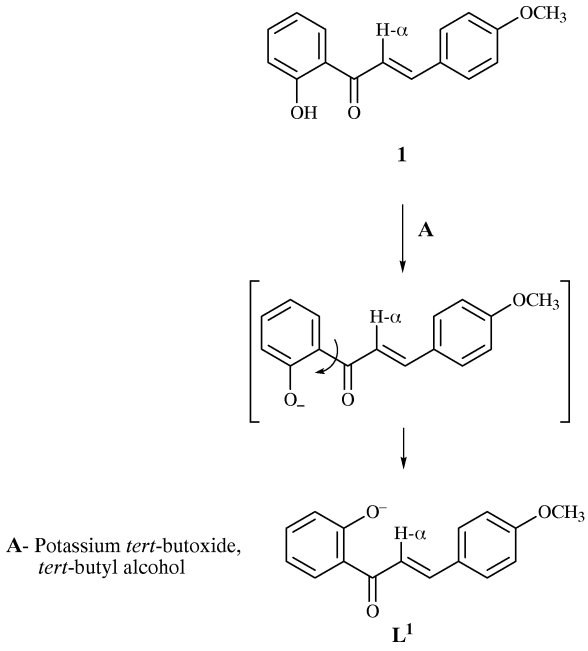
bis(dimethyl sulfoxide)bis(chalconato)ruthenium complexes **5**–**7**. For each chalconate L^1–L^3 three isomers have been obtained for each bis(dimethyl sulfoxide)bis(chalconato)ruthenium(II) complex, which have been separated by thin layer chromatography and identified in each case as **h** (higher), **i** (intermediate) and **l** (lower), following their R_f values in thin layer chromatographic analysis. In the case of 3,4,4′,5,6′-pentamethoxydihydrochalconate L^4 only two isomers, **8h** and **8l**, of the corresponding bis(dimethyl sulfoxide)bis(dihydrochalconato)ruthenium(II) complex have been obtained and separated by thin layer chromatography. The bis(dimethyl sulfoxide)bis(3,4,4′,5,6′-pentamethoxydihydrochalconato)ruthenium(II) complex **8h** was also obtained by treatment of bis(dimethyl sulfoxide)bis(3,4,4′,5,6′-pentamethoxychalconato)ruthenium(II) **7i** with ammonium formate and Pd/C (10%). In this transformation hydrogenation of the chalconate ligand double bonds took place.

The ^{1}H and ^{13}C NMR spectral data of the 2′-hydroxychalcones **1**–**3**, corresponding chalconates L^1–L^3 and their ruthenium(II) complexes **5**–**7** are given in Tables 1 and 2. The assignments of all proton and protonated carbon resonances were determined by 2D NMR experiments (COSY, NOESY, HETCOR and HMBC, Heteronuclear Multiple-Bond Correlation).

As shown in Table 1, the resonances corresponding to the A ring protons of chalconates L^1–L^3 are shielded relative to those of the corresponding 2′-hydroxychalcones **1**–**3**, because of the increased electronic density effects on all the protons of the chalconate A ring due to the anion charge, which most strongly affects the *para* position. The H-α and H-β resonances in **1**–**3** appeared as two doublets. The coupling constant ($^3J_{H\alpha\text{-}H\beta}$ 15.5–15.7 Hz) indicates the *trans* configuration of the vinylic system. The unequivocal assignment of these resonances were made by using HMBC experiments, in which the resonance of H-α presents connectivities with C=O, C-1 and C-1′ and that of H-β with C=O, C-1 and C-2,6. In the NOESY spectra of compounds **1**–**3**, NOE cross peaks were observed between the resonances of H-β and H-2,6 and also between H-α and H-2,6 and H-6′, for **5**, or 6′-OCH_3, for **6** and **7**.

2′-Hydroxychalcones have a strong hydrogen bond involving the carbonyl and the proton of the 2′-hydroxyl groups, inducing a delocalization along the α,β-unsaturated keto moiety of the molecule. In the chalconates L^1–L^3 this hydrogen bond does not exist and, as a consequence, this delocalization effect is decreased and H-β is shielded (∼ −0.6 ppm).

In the NOESY spectra of chalconates L^1–L^3, NOE cross peaks were observed between the resonances of H-2,6 and those of H-α and H-β. No cross peaks were observed between the signal of H-α and that of H-6′ in L^1 or of 6′-OCH_3 in L^2 and L^3, which indicates that these protons are not spatially close. In 4-methoxychalconate L^1, due to the repulsive effect between the anion and the carbonyl group, there is rotation around the C1′—C=O bond, which places the anion and H-α in close proximity (Scheme 2). Due to this spatial proximity H-α is strongly deshielded (+1.05 ppm) compared to H-α in the corresponding 2′-hydroxychalcone **1**. In the case of chalconates L^2 and L^3, there is also a repulsive effect between the anions and the carbonyl groups with a consequent rotation around the C1′—C=O bond. However, in this case the steric hindrance due to the presence of the 6′-methoxyl group implies that the A ring of these compounds will be perpendicular to the other part of the molecule (Scheme 3). As a consequence, H-α does not feel the through-space deshielding effect of the 6′-methoxyl oxygen, which is significant in the corresponding 2′-hydroxychalcones **2**,**3**. These effects are



Scheme 2.

Table 1 ^{1}H chemical shifts[a,b] of the 2′-hydroxychalcones **1**–**3** and 2′-hydroxydihydrochalcone **4**, their chalconates $\mathbf{L}^1$–$\mathbf{L}^3$ and dihydrochalconate $\mathbf{L}^4$ and of the corresponding bis(dimethyl sulfoxide)bis(chalconato or dihydrochalconato)ruthenium(II) complexes **5**–**8**

	OH-2′	H-3′	H-4′	H-5′	H-6′	H-α	H-β	H-2,6	H-3,5	*S*-DMSO
1	12.95	7.02	7.48	6.93	7.92	7.54	7.90	7.62	6.95	—
	(s)	(dd; 8.4, 1.2)	(dt; 7.8, 1.7)	(ddd; 7.8, 7.6, 1.2)	(dd; 7.6, 1.7)	(d; 15.5)	(d; 15.5)	(d; 8.6)	(d; 8.6)	—
$\mathbf{L}^1$	—	6.23	6.86	5.88	7.49	8.60	7.36	7.56	6.96	—
		(d; 8.6)	(dt; 7.4; 1.9)	(dd; 7.6, 7.4)	(dd; 7.6, 1.9)	(d; 15.9)	(d; 15.9)	(d; 8.7)	(d; 8.7)	
5h	—	6.55	7.13	6.46	7.73	7.42	7.56	7.57	6.93	2.97; 3.35
		(d; 8.4)	(t; 7.9)	(t; 7.9)	(d; 7.9)	(d; 16.0)	(d; 16.0)	(d; 8.6)	(d; 8.6)	(2 s)
5i	—	6.73	7.12	6.44	7.72	7.35	6.96	7.34	6.84	2.90; 3.22
		(dd; 8.4, 1.0)	(dt; 7.7, 1.6)	(dt; 7.7, 1.0)	(dd; 8.6, 1.6)	(d; 15.0)	(d; 15.0)	(d; 8.8)	(d; 8.8)	(2 s)
		6.94	7.18	6.48	7.81	7.46	7.66	7.62	6.94	3.19; 3.37
		(dd; 8.6, 1.0)	(dt; 7.7, 1.6)	(dt; 7.7, 1.0))	(dd; 8.6, 1.6)	(d; 16.0)	(d; 16.0)	(d; 8.8)	(d; 8.8)	(2 s)
5l	—	6.98	7.24	6.45	7.65	7.34	7.13	7.36	6.85	3.05; 3.32
		(d; 8.0)	(dt; 7.6, 1.6)	(dd; 7.6, 7.5)	(dd; 7.5, 1.6)	(d; 15.3)	(d; 15.3)	(d; 8.8)	(d; 8.8)	(2 s)
2	13.32	6.61	7.35	6.42	—	7.77	7.81	7.57	6.93	—
	(s)	(d; 7.6)	(t; 7.6)	(d; 7.6)		(d; 15.7)	(d; 15.7)	(d; 8.1)	(d; 8.1)	
$\mathbf{L}^2$	—	6.01	6.75	5.74	—	6.99	7.18	7.51	6.93	—
		(d; 8.2)	(t; 8.2)	(t; 8.2)		(d; 16.0)	(d; 16.0)	(d; 8.7)	(d; 8.7)	
6h	—	5.99	6.90	5.97	—	7.38	7.49	7.51	6.90	2.99; 3.29
		(d; 7.9)	(dd; 8.4, 7.9)	(d; 8.4)		(d; 15.6)	(d; 15.6)	(d; 8.7)	(d; 8.7)	(2 s)
6i	—	6.32	6.96	5.96	—	7.37	7.07	7.33	6.84	2.87; 3.19
		(dd; 8.6, 0.7)	(dd; 8.6, 8.0)	(d; 8.0)		(d; 15.4)	(d; 15.4)	(d; 8.7)	(d; 8.7)	(2 s)
	—	6.53	7.05	5.99	—	7.40	7.58	7.55	6.91	3.12; 3.34
		(dd; 8.6, 0.8)	(dd; 8.6, 7.7)	(d; 7.7)		(d; 15.6)	(d; 15.6)	(d; 8.7)	(d; 8.7)	(2 s)
6l	—	6.59	7.12	5.98	—	7.34	7.19	7.38	6.85	3.02; 3.29
		(dd; 8.6, 0.8)	(dd; 8.6, 7.8)	(d; 7.8)		(d; 15.5)	(d; 15.5)	(d; 8.8)	(d; 8.8)	(2 s)
3	14.36	6.11	—	5.96	—	7.82	7.68	6.84	—	—
	(s)	(d; 2.4)		(d; 2.4)		(d; 15.5)	(d; 15.5)	(s)		
$\mathbf{L}^3$	—	5.36	—	5.16	—	7.32	7.11	6.82	—	—
		(s; broad)		(s; broad)		(d; 15.8)	(d; 15.8)	(s)		
7h	—	5.66	—	5.56	—	7.37	7.39	6.78	—	3.01; 3.28
		(d; 2.1)		(d; 2.1)		(d; 16.0)	(d; 16.0)	(s)		(2 s)
7i	—	5.88	—	5.59	—	7.29	7.02	6.63	—	2.93; 3.15
		(d; 2.3)		(d; 2.3)		(d; 15.3)	(d; 15.3)	(s)		(2 s)
	—	6.05	—	5.64	—	7.35	7.48	6.81	—	3.15; 3.34
		(d; 2.3)		(d; 2.3)		(d; 15.5)	(d; 15.5)	(s)		(2s)
7l	—	6.11	—	5.62	—	7.36	7.08	6.66	—	3.06; 3.28
		(d; 2.3)		(d; 2.3)		(d; 15.4)	(d; 15.4)	(s)		(2 s)
4	14.00	6.08	—	5.93	—	3.31	2.94	6.46	—	—
	(s)	(d; 2.2)		(d; 2.2)		(t; 7.4)	(t; 7.4)	(s)		
$\mathbf{L}^4$	—	6.21	—	5.80	—	3.35	3.10	6.54	—	—
		(s; broad)		(s; broad)		(t; 7.4)	(t; 7.4)	(s)		
8h	—	5.98	—	5.61	—	3.11	2.48	6.31	—	2.77; 3.11
		(d; 2.3)		(d; 2.3)		(m)	(m)	(s)		(2 s)
	—	6.04	—	5.65	—	3.27	2.88	6.37	—	3.11; 3.31
		(d; 2.3)		(d; 2.3)		(m)	(m)	(s)		(2 s)
8l	—	5.59	—	5.59	—	3.20	2.77	6.32	—	2.82; 3.18
		(s)		(s)		(m)	(m)	(s)		(2 s)

[a] The resonances of the methoxyl groups are given in the Experimental. [b] In parentheses is shown the multiplicity of each signal and the corresponding coupling constants in hertz.

responsible for the shift to lower frequency values (−0.50 to −0.78 ppm) of the H-α resonance in $\mathbf{L}^2$,$\mathbf{L}^3$ relative to that in 2′-hydroxychalcones **2**,**3**.

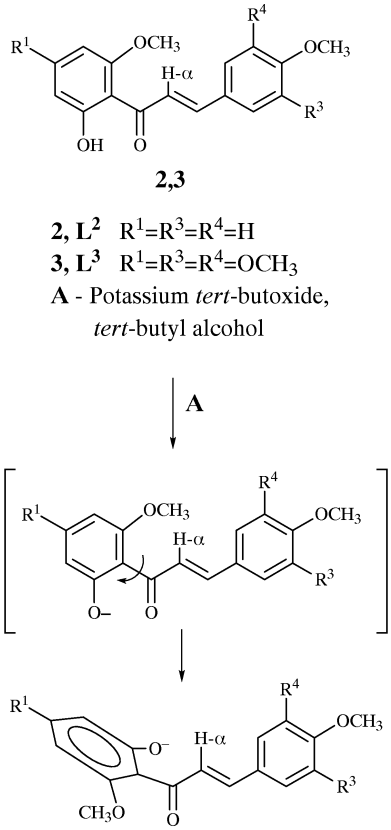
In the case of 3,4,4′,5,6′-pentamethoxydihydrochalconate $\mathbf{L}^4$, benzene-d_6 was chosen as solvent for the NMR characterization, because in this solvent no α-deuteriation could occur. Comparison between the resonances of dihydrochalcone **4** and the corresponding dihydrochalconate $\mathbf{L}^4$ is not possible because the ^{1}H NMR spectra of these two compounds were recorded in very different solvents.

Upon complexation of chalconates $\mathbf{L}^1$–$\mathbf{L}^3$ the A ring protons are deshielded (Table 1), as reported in the case of flavonate complexation with ruthenium(II).[14] Due to the complexation of chalconates $\mathbf{L}^1$–$\mathbf{L}^3$ as bidentate ligands it is important to notice that the conformational effects referred to above and shown in Schemes 2 and 3 have now disappeared; H-α is now shielded (−1.13 to −1.25 ppm) in complex **5** and deshielded in complexes **6** and **7**, but this effect is stronger in **6** (+0.35 to +0.41 ppm).

As shown in Table 2, the effects observed in the ^{13}C NMR spectra of 2′-hydroxychalcones **1**–**3**, their chalconates $\mathbf{L}^1$–$\mathbf{L}^3$ and the corresponding ruthenium(II) complexes **5**–**7** are similar to those already reported for 5-hydroxyflavones, the corresponding flavonates and their ruthenium(II) complexes.[14] These effects are a consequence of the electronic processes referred to above, and the most affected resonances are those of the A ring, C-α, C-β and of the carbonyl group. The comparison of the ^{13}C NMR spectra of 2′-hydroxy-3,4,4′,5,6′-pentamethoxydihydrochalcone **4**, the corresponding 3,4,4′,5,6′-pentamethoxydihydrochalconate $\mathbf{L}^4$ and their bis(dimethyl sulfoxide)bis(3,4,4′,5,6′-pentamethoxydihydrochalconato)-ruthenium(II) complexes **8h** and **8l** allowed us to conclude that the electronic processes affect essentially the resonances of the A ring and of the carbonyl group.

Structures of the new complexes

Mass spectra and elemental analysis of the synthesized complexes **5**–**8** suggest their composition as $RuL_2(DMSO)_2$ (L = chalconates $\mathbf{L}^1$–$\mathbf{L}^3$ or dihydrochalconate $\mathbf{L}^4$). The stereochemistry of these complexes will be discussed from the results of ^{1}H and ^{13}C NMR spectroscopy, because our attempts to



Scheme 3.

grow single crystals for X-ray analysis were unsuccessful.

The methyl carbon resonances of the DMSO ligands is a general and reliable criterion to establish their coordination mode, as *S*- or *O*-bonded.[16] In our case, these carbon resonances appear at higher frequency values (42.3–44.7 ppm) than that of free DMSO (40.1 ppm in $CDCl_3$), which indicates that in all the synthesized complexes the DMSO ligands are *S*-bonded.[17]

The presence of two unsymmetrical bidentate chalconate or dihydrochalconate ligands and of two *S*-bonded DMSO ligands may give rise to five diastereoisomers of the ruthenium(II) complexes **5**–**8**, three of which have enantiomers (forms C, D and E) (Scheme 4). However, in the case of chalconates L^1–L^3 and dihydrochalconate L^4 only three and two diastereoisomes have been respectively obtained; their structures are discussed below.

The ^{1}H NMR spectra of complexes **5h**, **6h** and **7h** (Table 1) present signals corresponding to two equivalent chalconate ligands and two other broad signals of equal intensity (6H each) in the *S*-bonded DMSO region (2.97–3.35 ppm). The broadness of these signals and the strong NOE cross peaks between them, observed in the NOESY spectra, led us to conclude that they are due to the resonance of two diastereotopic methyl groups[18] of two equivalent DMSO ligands. This broadness is due to the ^{1}H–^{1}H coupling between the diastereotopic methyl groups on the same DMSO.

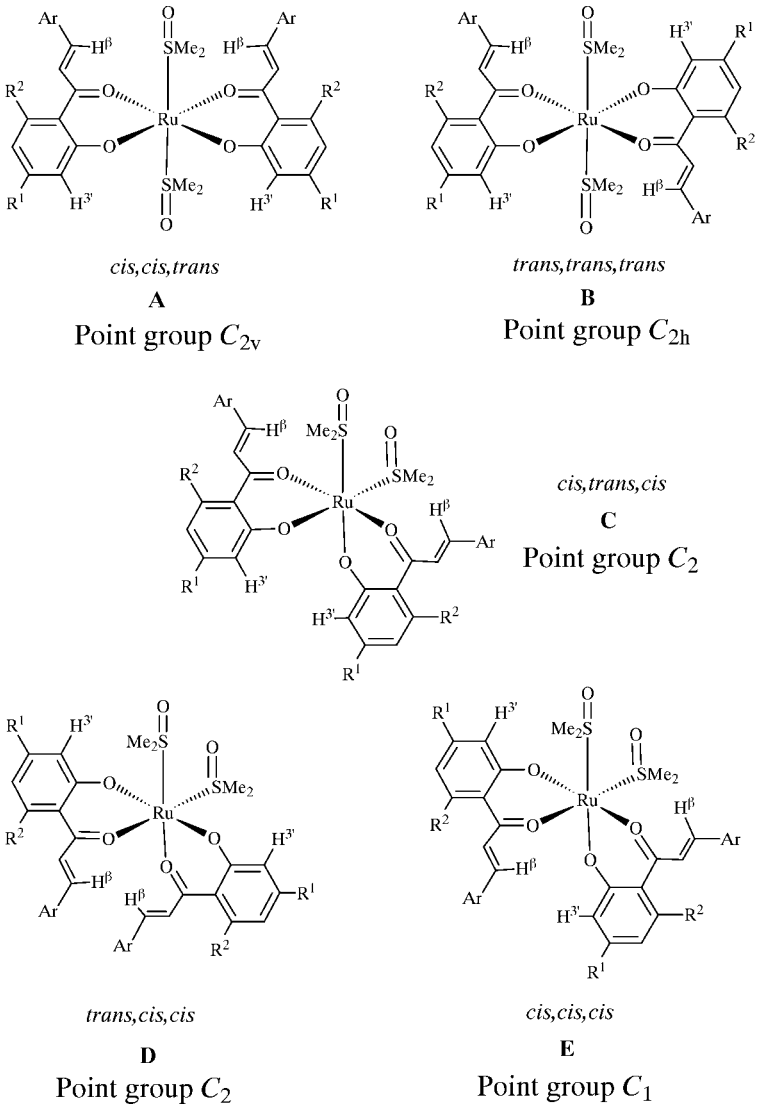
Of the five possible isomers of complexes **5h**, **6h** and **7h** (Scheme 4), the structures corresponding to forms A and E (or their enantiomer) are ruled out. In form A the two DMSO ligands are equivalent because of the horizontal plane of symmetry, while the vertical plane through the two sulfur atoms makes the methyl groups on each DMSO equivalent. On the other hand, in form E the two chalconate and the two DMSO ligands are inequivalent, because this form has only a C_1 axis of symmetry. Considering these facts and the NOE cross peaks, observed in the NOESY spectra, between the methyl proton resonances of the DMSO ligands and that of the H-β of chalconates, one can establish that the structures of complexes **5h**, **6h** and **7h** are represented by form C (or its enantiomer).

In the NOESY spectra of all the synthesized complexes **5**, **6** and **7**, NOE cross peaks were observed between the resonances of H-β and those of H-2,6 and also between H-α and H-2,6 and H-6′, for **5**, or 6′-OCH_3, for **6** and **7**. These data allowed us to conclude that in these complexes the stereochemistry of the ligands is similar to that of the 2′-hydroxychalcones **1**–**3** mentioned above.

Table 2 ^{13}C chemical shifts[a] of the 2′-hydroxychalcones **1**–**3** and 2′-hydroxydihydrochalcone **4**, their chalconates L^1–L^3 and dihydrochalconate L^4 and of the corresponding bis(dimethyl sulfoxide)bis(chalconato or dihydrochalconato) ruthenium(II) complexes **5**–**8**

	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	C=O	C-α	C-β	C-1	C-2,6	C-3,5	C-4	*S*-DMSO
1	120.1	163.6	118.6	136.2	118.8	127.4	193.7	117.6	145.4	127.4	129.5	114.5	162.0	—
L^1	125.7	176.1	126.2	133.2	107.1	131.1	189.5	128.6	135.9	129.3	129.2	114.2	159.8	—
5h	122.9	171.6	125.3	135.1	114.0	131.4	190.2	120.6	143.1	128.1	130.0	114.5	161.4	43.5; 44.3
5i	122.1	172.3	125.8	134.4	114.0	131.2	187.3	120.9	143.3	128.0	129.9	114.2	161.1	44.0; 44.2
	123.6	173.6	126.5	135.2	114.3	131.8	191.6	121.2	143.4	128.3	130.1	114.5	161.5	42.4; 44.3
5l	122.8	175.4	127.1	134.6	113.8	131.9	187.4	120.6	144.0	128.1	130.0	114.3	161.4	43.5; 44.2
2	112.0	164.8	110.9	135.7	101.5	160.9	194.3	125.1	143.1	128.0	130.3	114.4	161.5	—
L^2	118.5	173.9	114.3	130.0	92.5	158.7	195.1	128.1	137.7	128.7	129.4	114.3	160.2	—
6h	118.6	173.2	117.1	133.9	96.2	161.3	191.5	126.1	140.4	128.5	129.8	114.3	161.1	43.4; 44.0
6i	117.9	173.8	118.1	133.5	96.6	161.2	188.6	126.0	140.5	128.4	129.7	114.1	160.9	43.9; 44.6
	118.8	175.8	118.6	134.1	96.8	161.9	192.9	126.1	140.9	128.8	129.9	114.4	161.2	42.3; 44.7
6l	118.7	176.9	119.0	133.7	96.5	161.9	189.9	126.3	140.9	128.6	129.8	114.2	161.0	43.9; 44.3
3	106.3	168.8	93.8	166.6	91.3	162.8	192.3	126.9	142.4	131.1	105.5	153.4	140.0	—
L^3	113.1	175.6	97.8	162.7	81.3	161.2	190.9	134.1	132.3	131.9	104.6	153.0	137.9	—
7h	113.5	175.9	98.2	165.5	88.7	162.5	188.8	127.9	139.6	131.6	105.1	153.4	139.6	43.7; 44.3
7i	112.3	175.9	99.0	165.1	89.0	162.3	185.4	127.7	139.6	131.5	104.9	153.3	139.4	43.9; 44.6
	113.5	177.6	99.4	165.5	89.3	162.9	189.9	128.3	139.6	132.1	105.1	153.4	139.7	42.6; 44.7
7l	113.0	178.7	99.5	165.2	89.3	163.1	185.8	128.1	140.1	131.7	105.0	153.3	139.4	43.9; 44.3
4	105.8	167.6	93.7	166.0	90.9	162.7	204.4	45.8	31.1	137.5	105.4	153.1	136.2	—
L^4	110.0	171.8	96.7	163.5	89.9	166.3	205.3	47.2	32.6	138.5	107.4	154.6	138.5	—
8h	111.4	175.2	98.7	165.0	88.6	163.2	197.8	44.9	32.3	135.9	105.1	153.0	137.1	43.3; 44.2
	112.1	176.5	99.1	165.5	88.7	163.5	202.1	45.7	33.1	136.1	105.2	153.1	138.1	42.5; 44.4
8l	112.1	175.1	98.0	165.5	88.2	163.0	201.6	45.6	33.0	136.0	105.2	153.0	137.2	43.6; 43.6

[a] The resonances of the methoxyl groups are given in the Experimental.



Scheme 4.

The ^{1}H NMR spectra of complexes **5l**, **6l** and **7l** (Table 1) also present signals of equivalent chalconate ligands and of two diastereotopic methyl groups[18] of two equivalent DMSO ligands. In the NOESY spectra of these complexes, NOE cross peaks between the methyl proton resonances of the two DMSO ligands and that of the H-3′ of the chalconate were observed, establishing form D (or its enantiomer) as representing the structures of complexes **5l**, **6l** and **7l**.

The ^{1}H NMR spectra of complexes **5i**, **6i** and **7i** (Table 1) present the signals of two inequivalent chalconate ligands and of four inequivalent methyl groups of two DMSO ligands, as expected for a molecule belonging to the C_1 symmetry point group. In the NOESY spectra of these complexes, NOE cross peaks were observed between the two methyl proton resonances of the DMSO ligand *trans* to the carbonyl oxygen (2.90, 3.22 for **5i**; 2.99, 3.29 for **6i** and 2.93, 3.15 ppm for **7i**) and that of H-3′ of one chalconate ligand and also between the two methyl proton resonances of the DMSO ligand *trans* to the phenoxide (3.19, 3.37 for **5i**; 3.12, 3.34 for **6i** and 3.15, 3.34 ppm for **7i**) and that of H-β of the other chalconate ligand (Scheme 4). These results led us to conclude that the structure of complexes **5i**, **6i** and **7i** is represented by form E (or its enantiomer).

In the ^{1}H NMR spectrum of complex **8h** were observed the signals corresponding to two inequivalent dihydrochalconate ligands and of four inequivalent methyl groups of two DMSO ligands (Table 1). These results and their similarity to those of complexes **5i**, **6i** and **7i** allowed us to establish the structure of complex **8h** as being represented by an analogous form of E (or its enantiomer) (Scheme 4). The ^{1}H NMR spectrum of complex **8l** presents the signals of two equivalent dihydrochalconate ligands and of two diastereotopic methyl groups[18] of two equivalent DMSO ligands. These results and the NOE cross peaks, observed in the NOESY spectrum, between the methyl proton resonances of the DMSO ligands and that of H-β of the dihydrochalconate ligands, led us to establish an analogous form of C (or its enantiomer) as representing the structure of complex **8l**.

Experimental

Measurements

Melting points were determined on a Reichert Thermovar apparatus fitted with a microscope and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in diluted deuteriochloroform solutions (*ca.* 0.3%), except those of chalconates (DMSO-d_6) and dihydrochalconate (C_6D_6), on a Bruker AMX 300 spectrometer, at 300.13 and 75.47 MHz, respectively; the chemical shifts are expressed in ppm relative to tetramethylsilane (TMS) as internal reference. ^{1}H assignments were made by using 2D COSY and NOESY (mixing time of 800 ms) experiments, while ^{13}C assignments were made using HETCOR and HMBC (delay for long-range J C–H couplings were optimized for 7 Hz) experiments. Electron impact mass spectra were obtained at 70 eV electron impact ionization using a VG Autospec Q mass spectrometer. Fast atom bom-

bardment mass spectra were run on a Jeol JMX DX-33 mass spectrometer, using 3-nitrobenzyl alcohol as a matrix. Elemental analyses were carried out in the "Service Central de Microanalyse du Centre National de la Recherche Scientifique de Montpellier". Preparative thin layer chromatography was carried out on silica gel plates (Riedel silica gel 60 DGF_{254}). Column chromatography was also performed on silica gel (Merck silica gel 60, 70–230 mesh).

Reagents and syntheses

cis-$RuCl_2(DMSO)_4$ was obtained from Johnson Matthey Alfa Products. All other chemicals and solvents used herein were obtained from commercial sources and used as received or dried using standard procedures.

2′-Hydroxychalcones. These were synthesized by known procedures.[19]

2′-Hydroxy-4-methoxychalcone **1**. (85%), mp 89–91 °C (lit.[20] 95 °C). ^{1}H NMR: δ = 3.86 (s, 3H, 4-OCH_3). ^{13}C NMR: δ = 55.5 (4-OCH_3).

2′-Hydroxy-4,6′-dimethoxychalcone **2**. (89%), mp 112–114 °C. ^{1}H NMR: δ = 3.85 (s, 3H, 4-OCH_3), 3.94 (s, 3H, 6′-OCH_3). ^{13}C NMR: δ = 55.4 (6′-OCH_3), 55.9 (4-OCH_3). FAB$^+$-MS: *m*/*z* (rel. int.) 285 [(M + H)$^+$, 100], 284 (11), 269 (5), 153 (3), 241 (3), 177 (15), 161 (15), 151 (95), 135 (12), 134 (11), 121 (70), 103 (15), 91 (10). Anal. calcd. $C_{17}H_{16}O_4$: C 71.82, H 5.67; found: C 71.50, H 5.47%.

2′-Hydroxy-3,4,4′,5,6′-pentamethoxychalcone **3**. (86%), mp 183–185 °C (lit.[21] 176–178 °C). ^{1}H NMR: δ = 3.84 (s, 3H, 4-OCH_3), 3.90 (s, 3H, 6′-OCH_3), 3.91 (s, 3H, 4′-OCH_3), 3.91 [s, 6H, 3,5-(OCH_3)$_2$]. ^{13}C NMR: δ = 55.4 (6′-OCH_3), 55.8 (4′-OCH_3), 56.1 [3,5-(OCH_3)$_2$], 61.0 (4-OCH_3).

2′-Hydroxy-4,4′,5,6,6′-pentamethoxydihydrochalcone 4. Ammonium formate (3.0 g, 48 mmol) and Pd/C (10%) (0.8 g) were added to a solution of **3** (1.5 g, 4 mmol) in acetone (60 ml). The reaction mixture, with magnetic stirring and under nitrogen, was refluxed for 1 h, filtered through a column of celite and the solvent evaporated to dryness. The obtained residue was taken up in chloroform and purified by silica gel column chromatography, using a 9 : 1 mixture of CH_2Cl_2–acetone as eluent. After solvent evaporation the residue was crystallized from EtOH, giving **4** in 89% yield (1.34 g), mp 118–120 °C. ^{1}H NMR: δ = 3.84 (s, 3H, 4-OCH_3), 3.90 (s, 3H, 6′-OCH_3), 3.91 (s, 3H, 4′-OCH_3), 3.92 [s, 6H, 3,5-(OCH_3)$_2$]. ^{13}C NMR: δ = 55.6 (6′-OCH_3), 55.6 (4′-OCH_3), 56.1 [3,5-(OCH_3)$_2$], 61.0 (4-OCH_3). EI-MS: *m*/*z* (rel. int.) 376 (M$^{+\bullet}$, 36), 375 (100), 327 (6), 195 (66), 194 (57), 181 (98), 179 (20), 167 (10), 151 (9), 138 (9), 121 (5), 95 (7). Anal. calcd. $C_{20}H_{24}O_7$: C 63.82, H 6.43; found: C 63.61, H 6.17%.

Chalconates L^1-L^3. (NMR characterisation only) A solution of the appropriate 2′-hydroxychalcone **1**–**3** (0.1 mmol) in DMSO-d_6 (0.6 ml), was treated with a molar equivalent of potassium *tert*-butoxide. The reaction mixture was heated at 40 °C, with magnetic stirring and under nitrogen, for 30 min and then ^{1}H and ^{13}C NMR spectra were recorded. These values are shown in Tables 1 and 2; however, the proton and carbon assignments of the methoxyl groups are as follows.

4-Methoxychalconate **L^1**. ^{1}H NMR: δ = 3.77 (s, 3H, 4-OCH_3). ^{13}C NMR: δ = 55.2 (4-OCH_3).

4,6′-Dimethoxychalconate **L^2**. ^{1}H NMR: δ = 3.56 (s, 3H, 6′-OCH_3), 3.77 (s, 3H, 4-OCH_3,). ^{13}C NMR: δ = 54.9 (6′-OCH_3), 55.2 (4-OCH_3).

3,4,4′,5,6′-Pentamethoxychalconate **L^3**. ^{1}H NMR: δ = 3.53 (s, 3H, 6′-OCH_3), 3.59 (s, 3H, 4-OCH_3, s), 3.66 (s, 3H, 4′-OCH_3, s), 3.79 [s, 6H, 3,5-(OCH_3)$_2$]. ^{13}C NMR: δ = 54.0 (4′-OCH_3), 54.6 (6′-OCH_3), 55.8 [3,5-(OCH_3)$_2$], 60.1 (4-OCH_3).

3,4,4′,5,6′-Pentamethoxydihydrochalconate **L^4**. (NMR characterization only) A suspension of **4** (0.1 mmol) in C_6H_6-d_6 (0.6 ml) was treated with a one molar equivalent of potassium *tert*-butoxide. The reaction mixture was heated at 40 °C, with magnetic stirring and under nitrogen, for 30 min and then ^{1}H and ^{13}C NMR spectra were recorded. These values are shown in Tables 1 and 2; however, the proton and carbon assignments of the methoxyl groups are as follows. ^{1}H NMR: δ = 3.28 (s, 3H, 4′-OCH_3), 3.47 (s, 3H, 6′-OCH_3), 3.62 [s, 6H, 3,5-(OCH_3)$_2$], 3.90 (s, 3H, 4-OCH_3). ^{13}C NMR: δ = 55.3 (4′-OCH_3), 55.4 (6′-OCH_3), 56.6 [3,5-(OCH_3)$_2$], 61.0 (4-OCH_3).

Bis(dimethyl sulfoxide)bis (chalconato)ruthenium (II) complexes 5–7. To a solution of the appropriate 2′-hydroxychalcone **1**–**3** (1.0 mmol) in *tert*-butyl alcohol (10 ml), potassium *tert*-butoxide (112 mg, 1.0 mmol) was added. The mixture was heated at reflux, with magnetic stirring and under nitrogen, for 30 min, giving a red clear solution of the chalconate anion. *cis*-$RuCl_2(DMSO)_4$ (243 mg, 0.5 mmol) was then added and the reflux was continued for the appropriate time (2 days for **2** and **3**, and 6 days for **1**).

Upon cooling, CH_2Cl_2 (100 ml) was added to the reaction mixture and the organic layer was washed with water (2 × 100 ml), dried over anhydrous sodium sulfate and the solvent evaporated to dryness. The obtained residue was chromatographed on several preparative thin layer chromatography plates, eluting with an 8 : 2 $CHCl_3$–acetone mixture. In decreasing R_f order, in each case, three fractions were collected and identified as **h** (higher), **i** (intermediate) and **l** (lower). After crystallization from a CH_2Cl_2–C_6H_{12} mixture, the yields obtained were as follows. (*a*) Starting from **1** the following isomers have been obtained: **5h**, 36 mg, 19%; **5i**, 97 mg, 51%; and **5l**, 7 mg, 4%. (*b*) When using **2** as reagent: **6h**, 32 mg, 15%; **6i**, 92 mg, 45%; and **6l**, 8 mg, 4% have been obtained. (*c*) When using **3** as reagent: **7h**, 45 mg, 18%; **7i**, 88 mg, 35%; and **7l**, 5 mg, 2% have been obtained.

Bis(dimethyl sulfoxide)bis(4-methoxychalconato)ruthenium(II) **5h**. Mp 105–108 °C. ^{1}H NMR: δ = 3.86 (s, 6H, 2 × 4-OCH_3). ^{13}C NMR: δ = 55.4 (2 × 4-OCH_3). FAB$^+$-MS: *m*/*z* (rel. int.) 764 (M$^{+\bullet}$, 8), 608 (25), 355 (10), 255 (64). Anal. calcd. for $RuC_{36}H_{38}O_8S_2$: C 56.60, H 5.01, S 8.40; found: C 56.49, H 5.03, S 8.01%.

Bis(dimethyl sulfoxide)bis(4-methoxychalconato)ruthenium(II) **5i**. Mp 127–130 °C. ^{1}H NMR: δ = 3.82 and 3.87 (2s, 2 × 3H, 2 × 4-OCH_3). ^{13}C NMR: δ = 55.35 and 55.44 (2 × 4-OCH_3). FAB$^+$-MS: *m*/*z* (rel. int.) 764 (M$^{+\bullet}$, 15), 608 (74), 355 (27), 255 (43). Anal. calcd. for $RuC_{36}H_{38}O_8S_2 \cdot 0.5C_6H_{12}$: C 58.12, H 5.50, S 7.96; found: C 58.54, H 5.57, S 8.01%.

Bis(dimethyl sulfoxide)bis(4-methoxychalconato)ruthenium(II) **5l**. Mp 125–128 °C. ^{1}H NMR: δ = 3.82 (s, 6H, 2 × 4-OCH_3). ^{13}C NMR: δ = 55.4 (2 × 4-OCH_3). FAB$^+$-MS: *m*/*z* (rel. int.) 764 (M$^{+\bullet}$, 4), 608 (12), 355 (9), 255 (75). Anal. calcd. for $RuC_{36}H_{38}O_8S_2 \cdot 0.5C_6H_{12}$: C 58.12, H 5.50, S 7.96; found: C 58.34, H 5.77, S 8.26%.

Bis(dimethyl sulfoxide)bis(4,6′-dimethoxychalconato)ruthenium(II) **6h**. Mp 125–128 °C. ^{1}H NMR: δ = 3.846 (s, 6H, 2 × 6′-OCH_3), 3.851 (s, 6H, 2 × 4-OCH_3). ^{13}C NMR: δ = 55.4 (2 × 4-OCH_3), 55.6 (2 × 6′-OCH_3). FAB$^+$-MS: *m*/*z* (rel. int.) 827 [(M + 3)$^+$, 4], 825 [(M + H)$^+$, 6], 668 (25), 285 (10), 269 (2). Anal. calcd. for $RuC_{38}H_{42}O_{10}S_2 \cdot 0.5C_6H_{12}$: C 56.87, H 5.59, S 7.41; found: C 56.87, H 5.55, S 7.50%.

Bis(dimethyl sulfoxide)bis(4,6′-dimethoxychalconato)ruthenium(II) **6i**. Mp 127–130 °C. ^{1}H NMR: δ = 3.79 and 3.87 (2s, 2 × 3H, 2 × 6′-OCH_3), 3.82 and 3.85 (2s, 2 × 3H, 2 × 4-OCH_3). ^{13}C NMR: δ = 55.35 and 55.41 (2 × 4-OCH_3), 55.6 and 55.9 (2 × 6′-OCH_3). FAB$^+$-MS: *m*/*z* (rel. int.) 827 [(M + 3)$^+$, 16], 825 [(M + H)$^+$, 23], 668 (59), 387 (12), 285 (10), 269 (3). Anal. calcd. for $RuC_{38}H_{42}O_{10}S_2 \cdot 0.5C_6H_{12}$: C 56.87, H 5.59, S 7.41; found: C 56.88, H 5.60, S 7.69.%

Bis(dimethyl sulfoxide)bis(4,6′-dimethoxychalconato)ruthenium(II) **6l**. Mp 96–99 °C. ^{1}H NMR: δ = 3.64 (s, 6H, 2 × 6′-OCH_3), 3.82 (s, 6H, 2 × 4-OCH_3). ^{13}C NMR: δ = 55.4 (2 × 6′-OCH_3), 55.7 (2 × 4-OCH_3). FAB$^+$-MS: *m*/*z* (rel. int.)

825 [(M + H)$^+$, 4], 668 (8), 387 (4), 285 (59), 269 (1). Anal. calcd. for $RuC_{38}H_{42}O_{10}S_2 \cdot 0.5C_6H_{12}$: C 56.87, H 5.59, S 7.41; found: C 57.08, H 5.87, S 7.83%.

Bis(dimethyl sulfoxide)bis(3,4,4′,5,6′-pentamethoxychalconato)ruthenium(II) **7h**. Mp 119–122 °C. ^{1}H NMR: δ = 3.60 (s, 6H, 2 × 6′-OCH_3), 3.79 (s, 6H, 2 × 4′-OCH_3), 3.88 (s, 6H, 2 × 4-OCH_3), 3.90 [s, 12H, 2 × 3,5-(OCH_3)$_2$]. ^{13}C NMR: δ = 55.2 (2 × 6′-OCH_3), 55.5 (2 × 4-OCH_3), 56.2 [2 × 3,5-(OCH_3)$_2$], 61.0 (2 × 4-OCH_3). FAB$^+$-MS: *m/z* (rel. int.) 1004 (M$^{+\cdot}$, 3), 848 (15), 375 (20). Anal. calcd. for $RuC_{44}H_{54}O_{16}S_2$: C 52.63, H 5.42, S 6.39; found: C 52.75, H 5.48, S 6.09%.

Bis(dimethyl sulfoxide)bis(3,4,4′,5,6′- pentamethoxychalconato)ruthenium(II) **7i**. Mp 120–123 °C. ^{1}H NMR: δ = 3.62 and 3.77 (2s, 2 × 3H, 2 × 6′-OCH_3), 3.78 and 3.79 (2s, 2 × 3H, 2 × 4′-OCH_3), 3.87 and 3.89 (2s, 2 × 3H, 2 × 4-OCH_3), 3.87 and 3.90 [2s, 2 × 6H, 2 × 3,5-(OCH_3)$_2$]. ^{13}C NMR: δ = 55.2 and 55.3 (2 × 6′-OCH_3), 55.5 (2 × 4-OCH_3), 56.1 and 56.2 [2 × 3,5-(OCH_3)$_2$], 61.0 (2 × 4-OCH_3). FAB$^+$-MS: *m/z* (rel. int.) 1006 [(M + 2)$^{+\cdot}$, 2], 1005 [(M + H)$^+$, 2], 1004 (M$^{+\cdot}$, 1), 850 (5), 849 (5), 848 (55), 477 (5), 375 (20). Anal. calcd. for $RuC_{44}H_{54}O_{16}S_2 \cdot 0.5C_6H_{12}$: C 53.96, H 5.78, S 6.13; found: C 53.54, H 5.67, S 6.30.%

Bis(dimethyl sulfoxide)bis(3,4,4′,5,6′-pentamethoxychalconato)-ruthenium(II) **7l**. Mp 138–141 °C. ^{1}H NMR: δ = 3.61 (s, 6H, 2 × 6′-OCH_3), 3.80 (s, 6H, 2 × 4′-OCH_3), 3.86 (s, 6H, 2 × 4-OCH_3), 3.88 [s, 12H, 2 × 3,5-(OCH_3)$_2$]. ^{13}C NMR: δ = 55.4 (2 × 6′-OCH_3), 55.6 (2 × 4′-OCH_3), 56.1 [2 × 3,5-(OCH_3)$_2$], 61.0 (2 × 4-OCH_3). FAB$^+$-MS: *m/z* (rel. int.) 1006 [(M + 2)$^{+\cdot}$, 2], 848 (0.1), 375 (74). Anal. calcd. for $RuC_{44}H_{54}O_{16}S_2 \cdot 0.5C_6H_{12}$: C 53.96, H 5.78, S 6.13; found: C 53.66, H 5.47, S 5.98.%

Bis(dimethyl sulfoxide)bis (3,4,4′,5,6′-pentamethoxydihydrochalconato) ruthenium(II) complexes 8.

Using **4** and the same experimental procedure described for the preparation of complexes **7**, two fractions have been collected from preparative layer plates. The fraction having the higher R_f value is the bis(dimethyl sulfoxide)bis(3,4,4′,5,6′-pentamethoxydihydrochalconato) ruthenium(II) complex **8h**, whereas the other fraction is the isomer **8l**. After evaporating the solvents to dryness the residues were crystallized from a CH_2Cl_2–C_6H_{12} mixture.

Bis(dimethyl sulfoxide)bis (3,4,4′,5,6′-pentamethoxydihydrochalconato)ruthenium(II) **8h**. (53%), mp 83–85 °C. ^{1}H NMR: δ = 3.72 and 3.75 (2 × 3H, 2 × 6′-OCH_3), 3.77 and 3.78 (2s, 2 × 3H, 2 × 4′-OCH_3), 3.851 and 3.854 [2s, 2 × 6H, 2 × 3,5-(OCH_3)$_2$], 3.87 (s, 6H, 2 × 4-OCH_3). ^{13}C NMR: δ = 55.2 and 55.3 (2 × 4′-OCH_3), 55.3 and 55.4 (2 × 6′- OCH_3),56.0 [2 × 3, 5-(OCH_3)$_2$], 60.8 (2 × 4-OCH_3). FAB$^+$-MS: *m/z* (rel. int.) 1008 (M$^{+\cdot}$, 11), 478 (4), 376 (76). Anal. calcd. for $RuC_{44}H_{58}O_{16}S_2$: C 52.42, H 5.80, S 6.36; found: C 52.87, H 5.69, S 5.96.%

Bis(dimethyl sulfoxide)bis(3,4,4′,5,6′-pentamethoxydihydrochalconato)ruthenium(II) **8l**. (7%), mp 93–96 °C. ^{1}H NMR: δ = 3.61 (s, 6H, 2 × 6′-OCH_3), 3.76 (s, 6H, 2 × 4′-OCH_3), 3.80 [s, 12H, 2 × 3,5-(OCH_3)$_2$], 3.81 (s, 6H, 2 × 4-OCH_3). ^{13}C NMR: δ = 55.2 (2 × 4′-OCH_3), 55.3 (2 × 6′-OCH_3), 56.0 [2 × 3,5-(OCH_3)$_2$], 60.8 (2 × 4-OCH_3). FAB$^+$-MS: *m/z* (rel. int.) 1009 [(M + H)$^+$, 1], 1008 (M$^{+\cdot}$, 1), 477 (2). Anal. calcd. for $RuC_{44}H_{58}O_{16}S_2$: C 52.42, H 5.80, S 6.36; found: C 52.67, H 5.99, S 6.16%.

Bis(dimethyl sulfoxide)bis(3,4,4′,5,6′-pentamethoxydihydrochalconato)ruthenium(II) 8h. Ammonium formate (38 mg, 0.6 mmol) and Pd/C (10%) (20 mg) were added to a solution of **7i** (100 mg, 0.1 mmol) in acetone (10 ml). The reaction mixture, with magnetic stirring and under nitrogen, was refluxed for 1 h, filtered through a column of celite and the solvent evaporated to dryness. The residue was crystallized from a CH_2Cl_2–C_6H_{12} mixture, giving **8h** in 58% yield (58 mg).

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