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Photochemistry of *trans*- and *cis*-[$RuCl_2(dmso)_4$] in Aqueous and Nonaqueous Solutions

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The photochemical behavior of the *trans*- and *cis*-[$RuCl_2(dmso)_4$] complexes has been investigated in organic coordinating solvents (dmso, CH_3CN) and aqueous solutions by means of electronic and ^1H NMR spectroscopy as well as chloride-selective electrode measurements. Excitation in the UVA and visible region of the *cis*-[$RuCl_2(dmso)_4$] complex in dmso leads to geometric isomerization with quantum yields $\Phi_{313} = 0.41$ and $\Phi_{365} = 0.49$ to give the photostable *trans* complex, whereas in acetonitrile and aqueous solutions, both isomerization and substitution processes occur. Moreover, in the latter two solvents, the *trans* isomer is photoactive and undergoes substitution reactions. In acetonitrile, for both *trans*- and *cis*-[$RuCl_2(dmso)_4$] isomers, selective photolabilization of the dimethylsulfoxide ligands results in the formation of the *trans*-[$RuCl_2(CH_3CN)_4$] complex. In aqueous solutions, the dmso and Cl^- ligands are gradually substituted by water molecules to give as a final product a mixture of (aqua)ruthenium(II) and (aqua)(chlorido)ruthenium(II) complexes. These species may prove to be useful in the binding of cellular components.

Introduction

The *trans* and *cis* isomers of the [$RuCl_2(dmso)_4$] complex exhibit antimetastasizing activity against several experimental tumors such as P388 leukemia, Lewis lung carcinoma, B16 melanoma, and MCa mammary carcinoma.[1–4] However, the side effects associated with the administration of the therapeutically required high doses of the compounds have promoted the search for alternative methods leading to enhanced anticancer activity of these complexes. A new approach involving site-specific photochemical activation of the metal complex in the tumor cells, which minimizes undesired toxic effects on normal cells, has been suggested recently.[5–8] Moreover, our previous results have shown that the cytotoxicity of the *trans* and *cis* isomers of [$RuCl_2(dmso)_4$] complexes against human (SK-Mel 188) and mouse (S91) melanoma cells is significantly increased by irradiation with UVA light.[9] It has been suggested that one of the factors that contribute to the enhanced antiproliferative activity of the two complexes after illumination is phototransformation of the complexes into more active species, which undergo reactions with cellular components.[9] In this respect it is interesting to understand the photochemical behavior of *trans* and *cis* isomers of ruthenium(II) complexes in greater detail. To the best of our knowledge, the photochemistry of the *cis*- and *trans*-[$RuCl_2(dmso)_4$] complexes in aqueous solution has never been investigated, and the only aspect mentioned in the literature concerns the application of light for the synthesis of the *trans* isomer from the *cis* analogue in dmso solution.[10] In this work we have investigated the photochemical behavior of the *trans*- and *cis*-[$RuCl_2(dmso)_4$] complexes upon irradiation with UVA and/or visible light in organic coordinating solvents like dimethylsulfoxide (dmso) and acetonitrile (CH_3CN) as well as in aqueous solutions. The results of Alessio et al.[10] are further corroborated by our present studies: the photochemistry is extended into a more synthetically useful area, and the photochemical properties of the [$RuCl_2(dmso)_4$] complexes are discussed in detail.

Results and Discussion

Photochemistry of *trans*- and *cis*-[$RuCl_2(dmso)_4$] in dmso

The electronic absorption spectra for the *trans*-[$RuCl_2(dmso)_4$] (**Ia**) and *cis*-[$RuCl_2(dmso)_4$] (**IIa**) complexes dissolved in dmso are presented in Figure 1 (see also Table 1S, Supporting Information).

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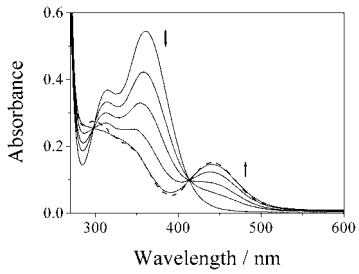


Figure 1. UV/Vis absorption spectra for a 1-mM dmso solution of *cis*-[$RuCl_2(dmso)_4$] irradiated at 365 nm at room temperature for 0, 0.5, 1, 2, and 5 min; the dashed line denotes the spectrum of *trans*-[$RuCl_2(dmso)_4$] in dmso solution.

The *cis* isomer is thermally very stable, whereas the *trans* complex can undergo isomerization to the *cis* analogue [Equation (1)]; however, this process is relatively slow at room temperature ($t_{1/2} \approx 75$ h).[10] Our results have shown that irradiation of a dmso solution of *cis*-[$RuCl_2(dmso)_4$] (**IIa**) with UVA (313 and 365 nm) or visible (400–600 nm) light results in the formation of *trans*-[$RuCl_2(dmso)_4$] (**Ia**). This is in agreement with a previous report by Alessio et al. showing that *trans*-[$RuCl_2(dmso)_4$] can be generated in situ by irradiation of *cis*-[$RuCl_2(dmso)_4$] dissolved in dmso solution with white light.[10]

$$cis\text{-}[RuCl_2(dmso)_3(dmso)] \underset{\Delta}{\overset{h\nu}{\rightleftharpoons}} trans\text{-}[RuCl_2(dmso)_4] \quad (1)$$

The photoisomerization process has been followed by UV/Vis spectroscopic measurements. The absorption band characteristic for the *cis* isomer (λ_{max} = 360 nm) decreases in intensity, and a new band characteristic for the *trans* isomer at 441 nm appears upon irradiation (Figure 1). Isosbestic points occurring at 415 and 298 nm confirm simple *cis* to *trans* isomerization. The quantum yields for the photoisomerization reaction have been found to be 0.41 ± 0.05 and 0.49 ± 0.03 for irradiation at 313 and 365 nm, respectively. The photoisomerization is an efficient process, and the quantum yields are nearly independent of the wavelength of irradiation. This indicates that a good internal conversion of the charge-transfer (CT) manifold to the lowest ligand-field (LF) excited state occurs as observed in early studies of Ru^{II} complexes.[11] No spectral changes have been observed during the irradiation of *trans*-[$RuCl_2(dmso)_4$].

Photochemistry of *trans*- and *cis*-[$RuCl_2(dmso)_4$] in CH_3CN

Given the potential synthetic utility of the photoreaction reported in the Equation (1), we decided to find out whether derivatives of [$RuCl_2(dmso)_4$] could be prepared by photolysis in the presence of almost any coordinating agent L. Our objective here was to see whether sequential substitution of dmso by L is possible until every dmso has been replaced, i.e. whether [$RuCl_2(dmso)_4$] can be converted to [$RuCl_2(CH_3CN)_4$] if L (CH_3CN in this case) resembles dmso in its bonding properties.

The analysis of ^1H NMR spectra for the *trans*- and *cis*-[$RuCl_2(dmso)_4$] complexes recorded after their dissolution in CD_3CN indicates that two dmso ligands from the *trans* isomer and one from the *cis* isomer are immediately released and substituted by solvent molecules (Figure 2). These results indicate the formation of [$RuCl_2(dmso)_2(CH_3CN)_2$] from the *trans* isomer and [$RuCl_2(dmso)_3(CH_3CN)$] from the *cis* analogue. The ^1H NMR observations are interpreted in terms of the pathways outlined in Scheme 1.

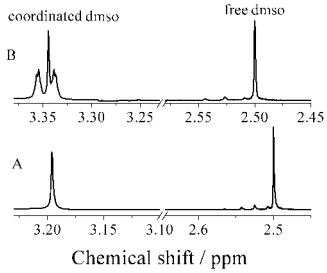
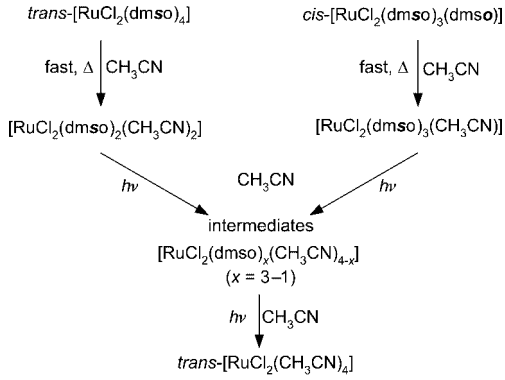


Figure 2. ^1H NMR spectra for *trans*-[$RuCl_2(dmso)_4$] (A) and *cis*-[$RuCl_2(dmso)_4$] (B) immediately after dissolution in CD_3CN solution (for the *trans* isomer, the ratio of the integration area of the peak at 3.20 ppm to that at 2.50 ppm is 1:1; for the *cis* isomer, the ratio of the integration area of the peaks at 3.35–3.34 ppm to that at 2.50 ppm is 3:1); T = 20 °C.



Scheme 1.

The electronic spectra for both complexes in acetonitrile indicated that the complexes are thermally relatively stable and that their further solvolysis process is slow enough not to interfere with our photochemical studies (see Figure 3 for the *trans* isomer).

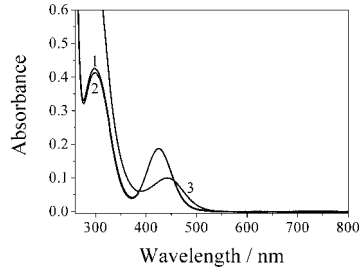


Figure 3. UV/Vis absorption spectra for a 1-mM acetonitrile solution of *trans*-[$RuCl_2(dmso)_4$] recorded immediately after dissolution (1), after 15 min at 20 °C (2), and upon irradiation at $\lambda_{irr} > 400$ nm for 15 min (3); T = 20 °C.

Irradiation of the *trans* complex with visible light ($\lambda_{irr} > 400$ nm) results in the gradual dissociation of the remaining coordinated dmso ligands, as revealed in the ^1H NMR spectra by the decrease in the intensity of the CH_3 resonance at $\delta = 3.20$ ppm originating from the coordinated dmso ligands and the concomitant increase in the intensity of the CH_3 resonance at $\delta = 2.50$ ppm ascribed to free dmso in CD_3CN solvent (Figure 4).

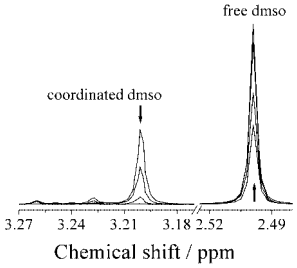


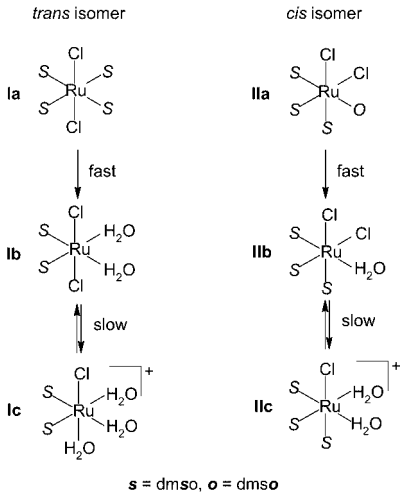
Figure 4. ^1H NMR spectra for *trans*-[$RuCl_2(dmso)_4$] (CD_3CN solution) before irradiation (the ratio of the integration area of the peak at 3.20 ppm to that at 2.50 ppm is 1:1) and after being irradiated for 1, 5, and 15 min at $\lambda_{irr} > 400$ nm; $T = 20$ °C.

The photolysis of the *cis* complex proceeds according to the same sequence as that of the *trans* isomer. The possible photolabilization of the Cl^- ligands can be excluded, because Cl^- ions were not detected after photolysis of the complex. Prolonged photolysis of concentrated solutions of the *trans*- or *cis*-[$RuCl_2(dmso)_4$] complexes in CH_3CN led to the formation of the complex *trans*-[$RuCl_2(CH_3CN)_4$]. This was established by elemental analysis, crystallographic data, and by ^1H NMR spectra. The resulting *trans* geometry of the complex (see crystallographic data in ref.[17]) was identical to that previously reported for *trans*-[$RuCl_2(CH_3CN)_4$] prepared by classical thermal routes[12–16] or by the photolysis of the [$RuCl_2(\eta^6$-*o*-*n*$Bu_2C_6H_4)]_2$ complex.[17] The new route for the synthesis of *trans*-[$RuCl_2(CH_3CN)_4$] by photosubstitution of dmso ligand with CH_3CN from either the *trans* or *cis* isomer of the [$RuCl_2(dmso)_4$] complex is reported in detail in the Experimental Section.

Photochemistry of *trans*- and *cis*-[$RuCl_2(dmso)_4$] in H_2O

To provide another possible pathway for the photochemical formation of the substitution products, we studied the photochemistry of *trans*- and *cis*-[$RuCl_2(dmso)_4$] in H_2O. In water solution, the complexes have been demonstrated[10,18,19] to undergo thermal hydrolysis as shown in Scheme 2.

According to Scheme 2, the two isomers, **Ia** and **IIa**, release two and one dmso ligands, directly after dissolution to afford *trans*,*cis*,*cis*-[$RuCl_2(dmso)_2(H_2O)_2$] (**Ib**) and *cis*,*fac*-[$RuCl_2(dmso)_3(H_2O)$] (**IIb**), respectively. For both complexes, a subsequent slow dissociation of chloride ions occurs. However, this is a very slow process: the half life of the reaction at 37 °C is ca. 1.5 and 1 h for the *trans* and *cis* isomer, respectively.[19] Binding of H_2O to the ruthenium center gives rise to new electronic spectral features for **Ib** and **IIb**. The electronic spectrum of *trans*,*cis*,*cis*-[$RuCl_2(dmso)_2(H_2O)_2$] (**Ib**) (Figure 5A, curve 1), consists of two bands at 432 and 322 nm assigned to LF transitions and one band at 227 nm of CT character.[20,21] Similarly, the electronic spectrum of *cis*,*fac*-[$RuCl_2(dmso)_3(H_2O)$] (**IIb**) is characterized by three bands at 355 nm (LF transition), 310 nm (LF transition), and 255 nm (CT transition)[22] (Figure 5B, curve 1). For both isomers, the molar absorption coefficients for the two lower-energy bands were found to be higher than those for the usual LF transition (Table 1S). This may be due to the mixing of the LF energy levels with those corresponding to the neighboring intense CT band.[22]



Scheme 2.

The irradiation of a deaerated aqueous solution of the *trans* complex, **Ib**, with visible light induces significant UV/Vis spectral changes as shown in Figure 5A. The absorption maxima at 322 and 432 nm decrease gradually, and a new very weak band at ca. 540 nm and a shoulder at ca. 400 nm appear. Three isosbestic points at 285, 349, and 417 nm are observed upon very short irradiation of **Ib** (up to ca. 1 min, Figure 1S, Supporting Information). Further irradiation leads to the disappearance of these isosbestic points. These results could be interpreted in terms of a subsequent photochemical reaction with conversion of the initial product into new species. Irradiation of a deaerated aqueous solution of the *cis* complex, **IIb**, leads to a regular decrease in the intensity of the band at 355 nm and the concomitant appearance of a shoulder at ca. 420 nm (after 3 min of irradiation, Figure 5B). Further irradiation gives rise to spectral changes similar to those observed for the primary photochemical process of the *trans* analogue. The UV/Vis spectral changes observed for aerated solutions of both isomers, **Ib** and **IIb**, during their irradiation with visible light indicate the initial formation of products similar to those found in the absence of oxygen (Figure 5C and Figure 5D, for **Ib** and **IIb**, respectively).

The prolonged photolysis of both solutions (up to 15 min) results in the appearance of a new relatively intense band at ca. 300 nm, which is not observed for the oxygen-

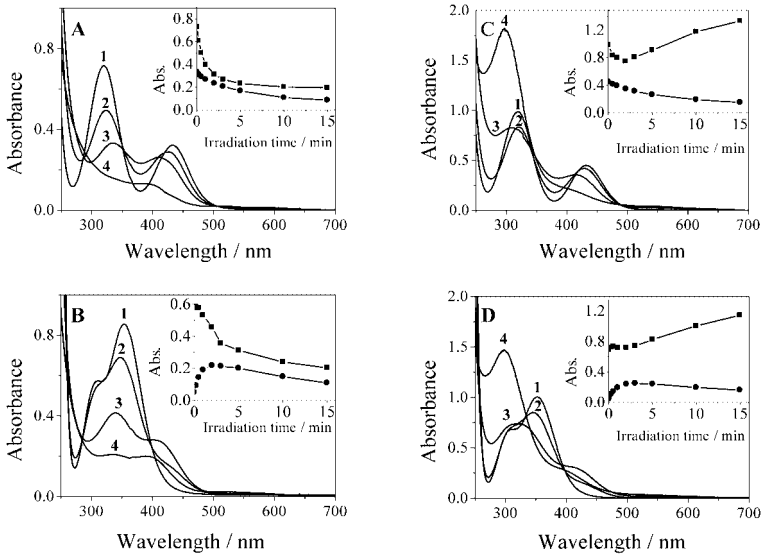


Figure 5. UV/Vis spectral changes during the photolysis (λ_{irr} in the range 400–600 nm) of 2-mM aqueous solutions of **Ib** (A) and **IIb** (B) in an argon-saturated solution, and **Ib** (C) and **IIb** (D) in an air-saturated solution at room temperature. Spectra recorded after irradiation times of: 0 (1), 0.5 (2), 3 (3), and 15 min (4); T = 20 °C. Insets: absorbance against irradiation time at 320 (■) and 432 nm (●).

free solution. The same product is also formed, as confirmed by UV/Vis spectra, when previously irradiated deaerated aqueous solutions of complexes **Ib** or **IIb** are purged with oxygen. These findings suggest that, after a long irradiation period in aerated solution, secondary thermal oxidation reactions of the primary photoproducts occur. Photolysis of **Ib** and **IIb** in the presence of Cl^- ions was expected to yield additional information on the reactivity. Irradiation of **Ib** and **IIb** in aqueous solution in the presence of excess of NaCl (0.2 M solution, 100-fold excess over Ru^{II} complexes) yielded the same spectral changes as those described above. The processes occurred with a lower efficiency, however, indicating that the overall mechanism includes a photodissociation of the Cl^- ligands. It is likely that the UV/Vis spectral changes observed for complexes **Ib** and **IIb** occur as a consequence of photosubstitution reactions of the dmso and Cl^- ligands with water molecules. To make sure that substitution of dmso by H_2O occurs, we decided to take advantage of the different chemical shifts in the ^1H NMR spectra of the free ligands and of those coordinated to the Ru^{II} center. The ^1H NMR spectrum of **Ib** recorded immediately after dissolution of the *trans* complex in D_2O consist of two resonances of equal intensity at 2.73 and 3.36 ppm assigned to the CH_3 groups of the free and coordinated dmso ligands, respectively.(Figure 6A and Table 1).

The observation of two resonances is consistent with the mechanism in Scheme 2 showing that dissolution of the *trans*-$[RuCl_2(dmso)_4]$ complex leads to the formation of *trans,cis,cis*-$[RuCl_2(dmso)_2(H_2O)_2]$ (**Ib**) and two free molecules of dmso. Observation of the increase in the intensity of the CH_3 resonance at δ = 2.73 ppm in the ^1H NMR spectra (Figure 6A) during photolysis of complex **Ib** is indicative of a gradual dissociation of the dmso ligand. The resulting mixture of products was analyzed by ^1H NMR, and it was determined that (99 ± 4)% of the final products is a complex without dmso and the remaining is a complex

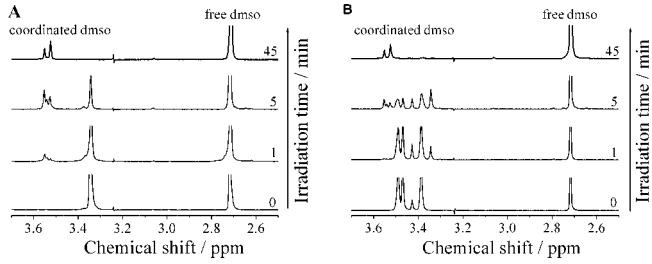


Figure 6. ^1H NMR spectra of the complex **Ib** (A) and **IIb** (B) (D_2O solution) at various irradiation times; λ_{irr} > 400 nm, T = 20 °C.

Table 1. ^1H NMR chemical shifts (δ/ppm) recorded for *trans,cis,cis*-$[RuCl_2(dmso)_2(H_2O)_2]$ (**Ib**) in D_2O solution after irradiation in the range 400–600 nm at T = 20 °C.

Irradiation time/min	δ/ppm				
0	2.73[a]	3.36			
1–15	2.73[a]	3.36	3.54	3.56	3.57
30–45	2.73[a]	–	**3.54**	–	**3.57**

[a] Resonance assigned to CH_3 protons of free dmso.

still containing the dmso ligand (Figure 6A, Figure 7, and Table 1). Upon further investigation, we determined that, during the course of the irradiation, the dmso ligand rather than the Cl^- ligand is labilized first. The analysis of the ^1H NMR spectrum indicates the absence of the resonance at δ = 3.39 ppm attributable to the CH_3 group of dmso in *cis,fac*-$[RuCl(dmso)_2(H_2O)_3]^+$ (**Ic**), a possible intermediate complex if Cl^- dissociation is operative in the primary photochemical event.[23] In addition, a comparison of the quantitative data for the release of dmso and Cl^- ligands (Figure 7 and Figure 8, respectively) supports the conclusion that the dmso ligand is more photolabile than the chlorido ligand.

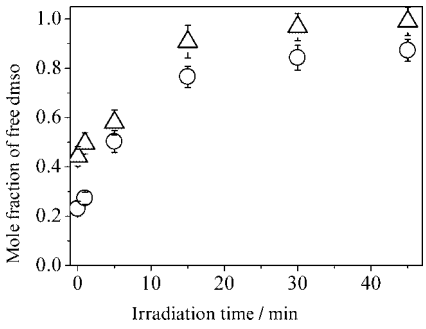


Figure 7. Mole fraction of free dmso molecules [defined as $(n_f)/(n_c + n_f)$, where n_f denotes the number of moles of free dmso and n_c denotes the number of moles of dmso coordinated to ruthenium ion] for **Ib** (Δ) and **IIb** (○) released during irradiation (λ_{irr} in the range 400–600 nm; T = 20 °C).

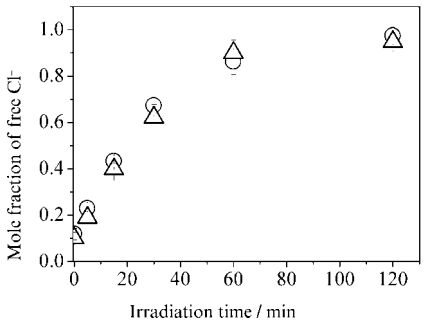


Figure 8. Mole fraction of free chloride ions [defined as $(n_f)/(n_c + n_f)$, where n_f denotes the number of moles of free chloride ions and n_c denotes the number of moles of chloride ions coordinated to ruthenium ion] for **Ib** (Δ) and **IIb** (○) released during irradiation (λ_{irr} in the range 400–600 nm; T = 20 °C).

Given the difficulties which can arise in elucidating the mechanism of the photoreactions described above, in order to conclude that Scheme 1 and Scheme 2 are the most likely pathways for the reactions, we felt that some care should be taken in ruling out other possibilities, especially those involving possible intermediates. The ^{1}H NMR spectrum of *cis,fac*-[$RuCl_2(dmso)_3(H_2O)$] (**IIb**) presents thee resonances at δ = 3.40, 3.48, and 3.50 ppm assigned to the CH_3 groups of the three coordinated dmso ligands (Table 2).

Table 2. ^{1}H NMR chemical shifts (δ/ppm) recorded for *cis,fac*-[$RuCl_2(dmso)_3(H_2O)$] (**IIb**) in D_2O solution after irradiation in the range 400–600 nm at T = 20 °C.

Irradiation time/min	δ/ppm								
0	2.73[a]		3.40	3.44	3.48	3.50			
1	2.73[a]	3.36	3.40	3.44	3.48	3.50			
5	2.73[a]	3.36	3.40	3.44	3.48	3.50	3.54	3.55	3.57
15	2.73[a]	3.36	–	–	–	–	3.54	3.55	3.57
30–45	2.73[a]	–	–	–	–	–	**3.54**	–	**3.57**

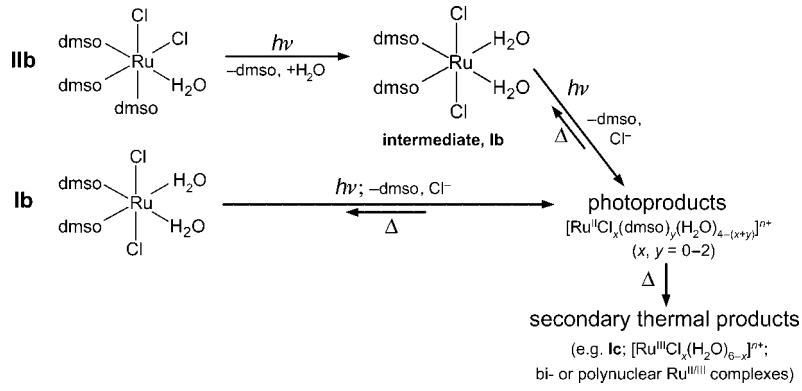
[a] Resonance assigned to CH_3 protons of free dmso.

The resonance at δ = 2.73 ppm is attributed to the CH_3 group of the free dmso present in the solution after dissolution of the *cis* isomer (Figure 6B, see also Scheme 2). A very small peak at δ = 3.44 ppm (the intensity is lower than 10% of the other resonances) is also observed and is attributed to one of the CH_3 groups of the dmso ligand in the hydrolyzed form of complex **IIb** (Scheme 2, complex **IIc**). The short irradiation of complex **IIb** leads to the formation of **Ib** as an intermediate. This is confirmed by the appearance in the ^{1}H NMR spectrum of the peak at 3.36 ppm, assignable to the CH_3 group of the dmso ligand in complex **Ib**. Longer irradiation results in further formation of the intermediate **Ib**, which is photochemically unstable and undergoes secondary photolysis. These processes give rise to changes in the ^{1}H NMR spectra leading to (i) gradual disappearance of peaks for the CH_3 protons of the dmso ligand of **IIb**; (ii) appearance of a new resonance, the same as that found for the irradiated complex **Ib**. The ^{1}H NMR spectrum for the final photoproducts of **IIb** is the same as that observed for complex **Ib** (Figure 6). For both ruthenium(II) complexes, **Ib** and **IIb**, the increase of the peak intensity at δ = 2.73 ppm assigned to free dmso is a consequence of photolysis, since the increase of the resonance is not observed in thermal hydrolysis. The concentration of dissociated dmso ligands has been estimated by calculation of the area under the CH_3 resonance peak at δ = 2.73 ppm. The relevant measurements indicate an almost complete photodissociation of dmso ligands (Figure 7).

The *trans,cis,cis*-[$RuCl_2(dmso)_2(H_2O)_2$] (**Ib**) and *cis,fac*-[$RuCl_2(dmso)_3(H_2O)$] (**IIb**) complexes have two chlorido ligands in the *trans* and *cis* configuration, respectively. To provide trustworthy estimates of the amount of Cl^- ions which might be present in the photoreaction mixture, we have carried out electrochemical experiments by using the ion-selective chloride electrode. Upon photolysis of complexes **Ib** and **IIb**, one begins to see the formation of Cl^- ions as quantitatively reported in Figure 8. It is important to note that the thermal hydrolysis of the chlorido ligand in both complexes is relatively slow (vide supra). Thus, at the selected temperature (20 °C), the major contribution to the amount of free chloride ions in solution originates from the photodissociation of Cl^- ligands. It appears that the release of chlorido ligands from both isomers takes place with similar yields. Longer irradiation (ca. 2 h) leads to nearly complete chloride dissociation.

The obtained results have shown that LF irradiation of *trans,cis,cis*-[$RuCl_2(dmso)_2(H_2O)_2$] (**Ib**) and *cis,fac*-[$RuCl_2(dmso)_3(H_2O)$] (**IIb**) leads to the photodissociation of dmso and Cl^- ligands, which are substituted by water molecules. The photolysis of the *cis* isomer, **IIb**, generates the *trans* analogue, **Ib**, as an intermediate, which itself is also photoactive, giving the same products as those obtained in the direct photolysis of the *trans* isomer, **Ib** (Scheme 3).

The photolysis of the *trans* and *cis* isomers, **Ib** and **IIb**, results in the formation of the same final products, as confirmed by UV/Vis and ^{1}H NMR spectra. On the basis of our findings and literature data,[24–27] these products could be a mixture of (aqua)ruthenium(II) and (aqua)(chlorido) ruthenium(II) complexes (Scheme 3). The photoproducts are very unstable in the presence of oxygen, as demonstrated by UV/Vis spectral changes. The gradual increase in



Scheme 3.

the intensity of the maximum at ca. 300 nm observed for aerated solutions, but not observed for deaerated solutions, could be ascribed to a slow thermal oxidation of the (aqua)-ruthenium(II) and (aqua)(chlorido)ruthenium(II) complexes to ruthenium(III) species.[25,27–30] Moreover, the prolonged thermal reaction (over a period of 24 h) at 20 °C results in a darkening of the irradiated solution. This result indicates that polymerization occurs along with hydrolysis, forming bi- or polynuclear species containing chlorido, oxido, or hydroxido bridges.[25,31] In addition to the above products, the ^{1}H NMR spectra of photolyzed solutions of complexes **Ib** and **IIb** kept in the dark for 24 h have shown that still minor amounts of **Ib** and **Ic** are present for both isomers. Only in the presence of an excess of chloride ions (ca. 17-fold excess over Ru^{II}) are the photoproducts converted back to complex **Ib** (up to 60%) in the prolonged thermal reaction (Scheme 3).

Conclusions

The various studies that have been conducted point to two main photoreactions of *trans*- and *cis*-$[RuCl_2(dmso)_4]$ complexes. The first is the photoinduced isomerization of the *cis* isomer to the *trans*-$[RuCl_2(dmso)_4]$ complex through the LF excited state. The second reaction appears to involve breakage of the metal–dmso bond, which results in the substitution of dmso with CH_3CN and H_2O, when the photoreaction is conducted in acetonitrile and in water, respectively. In aqueous solution, photolysis of *trans*- and *cis*-$[RuCl_2(dmso)_4]$ leads first to the dissociation of the dmso ligand and then, in a secondary photochemical event, dissociation of the Cl^- ligands. The ligand-loss photochemistry of *trans*- and *cis*-$[RuCl_2(dmso)_4]$ results in the formation of products of the type $[RuCl_x(dmso)_y(H_2O)_{4-(x+y)}]^{n+}$ (x, y = 0–2). These new species, formed upon irradiation in H_2O solution, have a considerable substitution lability relative to the *cis* and *trans*-$[RuCl_2(dmso)_4]$ complexes. These photoproducts may react quickly and with high efficiency with cellular components through sequential ligand exchange. This judgment is confirmed by our previous results,[9] which demonstrated an enhancement of the antiproliferative activity of the *trans*- and *cis*-$[RuCl_2(dmso)_4]$ complexes upon irradiation. Furthermore, the reaction of both isomers with a short oligonucleotide (T_2GGT_2) in aqueous solution is significantly facilitated by irradiation of the reaction mixture with UVA light.[9] These are interesting results, because they suggest that the photolysis of Ru^{II} complexes with photolabile ligands will allow the covalent binding of cellular components.

Experimental Section

Materials and Syntheses

The ruthenium complexes, *trans*-$[RuCl_2(dmso)_4]$ (**Ia**) and *cis*-$[RuCl_2(dmso)_4]$ (**IIa**) were synthesized and purified according to published procedures.[10,32] Both elemental analysis {For *trans*-$[RuCl_2(dmso)_4]$ (484.54): calcd. C 19.81, H 4.95, S 26.41; found C 19.72, H 5.01, S 26.83 and for *cis*-$[RuCl_2(dmso)_4]$ (484.54): calcd. C 19.81, H 4.95, S 26.41; found C 19.92, H 5.03, S 27.21.} and electronic spectroscopy have been used for checking their purity (Table 1S, Supporting Information).[10,20–22] All other chemicals used were of analytical grade.

Synthesis of *trans*-$[RuCl_2(CH_3CN)_4]$: The complex was synthesized by irradiation of *trans*- or *cis*-$[RuCl_2(dmso)_4]$ (200 mg, 0.41 mmol) dissolved in acetonitrile (20 cm^3) with visible light (500-W high-pressure mercury lamp, cut-off: 400 nm) for 1.5 h. The irradiation resulted in the precipitation of a yellow solid, which was collected by filtration, washed with a little acetonitrile, and vacuum-dried at room temperature (98 mg, 71%). $[RuCl_2(CH_3CN)_4]$ (336.19): calcd. C 28.58, H 3.59, N 16.66; found C 28.62, H 3.40, N 16.64. ^{1}H NMR (200 MHz, D_2O): δ = 2.60 (s) ppm. X-ray crystallographic analysis was used for the confirmation of the *trans* position of the chlorido ligands in this complex.

X-ray Structure Determination: An orange prismatic crystal of compound $[RuCl_2(CH_3CN)_4]$ was mounted on a Nonius Kappa CCD diffractometer with Mo-K_α radiation (λ = 0.71073 Å) at room temperature. The cell constants [a = 11.8001(3), b = 8.5722(3), c = 13.1258(4) Å, $\alpha = \beta = \gamma$ = 90°] and the space group *Pbca* were obtained by least-squares refinement of the diffraction data from 7566 reflections with $1° < \theta < 30°$. The obtained crystallographic data perfectly agree with a previous report,[17] showing that the crystals of compound $[RuCl_2(CH_3CN)_4]$ consist of molecules of the complex *trans*-tetrakis(acetonitrile)(dichlorido)ruthenium(II).

UV/Vis Spectroscopy: Electronic absorption spectra were recorded in 1-cm quartz cells with a Shimadzu UVPC 2100 or a Hewlett–Packard HP 8463 spectrophotometer.

^{1}H NMR Spectroscopy: ^{1}H NMR spectra were recorded with a BRUKER AC 200 spectrometer operating at 200.13 MHz. The chemical shift values were internally referenced to the dmso resonances (δ = 2.50 ppm in CD_3CN or 2.73 ppm in D_2O).

Chloride-Selective Electrode Measurements: A chloride-ion-selective electrode (Carison) was used for the determination of the free chloride ion concentration. Each point in the plot is an average value of at least three independent experiments, and the error corresponds to the standard deviation.

Photochemical Studies

Continuous photolysis was carried out in the λ_{irr} range from 400 to 600 nm by using a 500-W high-pressure mercury lamp equipped with a 400-nm cut-off filter (Oriel, Stradford – USA). The photolysis of *trans*- and *cis*-[$RuCl_2(dmso)_4$] complexes was carried out in solutions of dmso, CH_3CN, and H_2O in 1-cm quartz spectrophotometer cells or in deuterated solvents (CD_3CN and D_2O) in NMR tubes at 20 °C. All solutions of ruthenium(II) complexes were freshly prepared before use and deaerated when needed by bubbling argon through them. During irradiation, the solutions were stirred, and the temperature was kept at 20 °C by a refrigerated circulator (JULAB F12-EC). The progress of the photolysis was monitored by UV/Vis and ^{1}H NMR spectroscopy, and chloride-selective electrode measurements. For spectroscopic measurements, samples were used as prepared for irradiation (2-mM solutions for UV/Vis and 3.5 mg complex/0.6 mL solvent for ^{1}H NMR spectroscopy), whereas for the determination of free chloride ion concentration, the irradiated samples were diluted in 0.1-M KNO_3 solution.

For quantum yield determination, a 200-W high-pressure mercury lamp was used as a source of light, and interference filters (VEB Carl Zeiss JENA) were employed for wavelength selection (365 and 313 nm). Ferrioxalate actinometry was used at both wavelengths for light intensity determination.[33] Quantum yields of the photoisomerization of the *cis*-[$RuCl_2(dmso)_4$] into the *trans* analogue was determined from UV/Vis spectral changes upon irradiation of a 5.5-mM dmso solution of the *cis* isomer (the chosen concentration provides a complete absorption of light at both wavelengths).

Supporting Information (see footnote on the first page of this article): Electronic spectral data for complexes **Ia**, **IIa**, **Ib**, and **IIb**, and UV/Vis absorption spectra for a 2-mM, argon-saturated aqueous solution of **Ib** upon irradiation at T = 20 °C for various time intervals up to 1 min; ORTEP view of *trans*-[$RuCl_2(dmso)_4$].

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