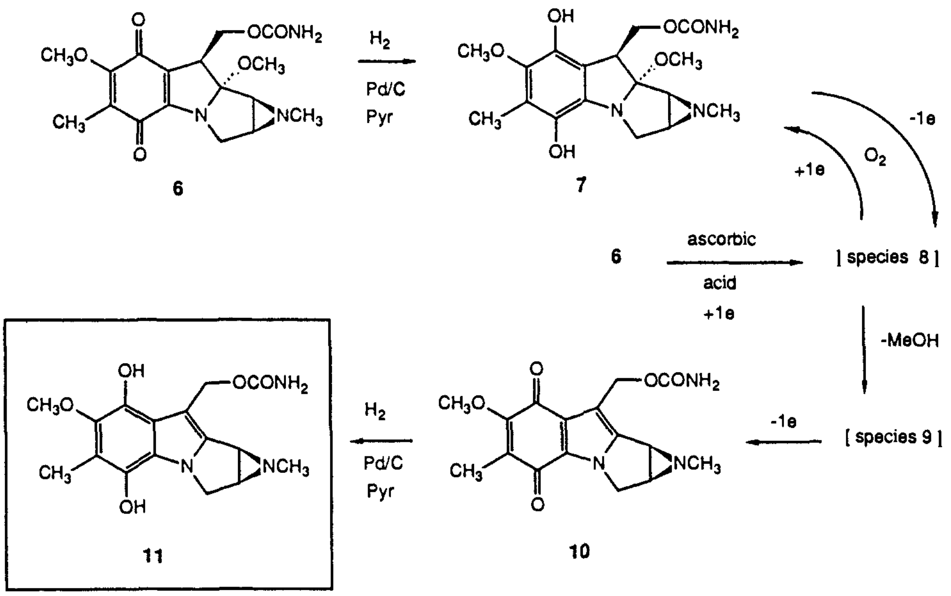
Scheme II



(i.e., species **8** of undefined protonation state). Elimination of methanol from **8** would afford the semiquinonoidal form of the mitosene (species **9**, of undefined protonation state). In the presence of oxygen, semiquinone **9** would be oxidized to the observed **10**. In the absence of external oxygen, **9** reacts with **8** in a disproportionation reaction to provide the observed **7** + **10**. The intervention of semiquinones in the mitomycin activation cycle is also suggested by the interesting findings of Bachur.[14b]

Support for this permissable though not obligatory formulation was obtained from the reaction of **6** in pyridine with ascorbic acid (catalytic) in pyridine. *A 90% yield of **10** was obtained.* A control experiment revealed that ascorbic acid in pyridine failed to effect elimination of methanol from leucomitomycin **7**. Since compound **7** is much more labile toward direct elimination than is **6**, it seems particularly unlikely that the conversion of **6** to **10** by ascorbic acid is a simple acid-catalyzed elimination process. More likely is the possibility that **6** undergoes one-electron reduction by the ascorbate,[15] producing the indolinosemiquinone equivalent **8**. This suffers elimination of methanol to afford the indolosemiquinone **9**.[16] The latter is oxidized to give **10**.

With preparatively sound routes to aziridinomitosene **10** in hand, attention was directed toward its reduction under substantially the same conditions used for the reduction of **6**. *There was thus obtained for the first time a solution of the unstable leucoaziridinomitosene* **11**. The structure of this substance follows unambiguously from its 250-MHz NMR spectrum[12c] and from its reoxidation (via oxygen) to **10** in 66% yield (Scheme II).

We are currently sorting out the chemistry of compound **11**. It is already clear that this leuco system is highly reactive. Compound **11** may be the operative bioelectrophilic form of a mitomycin. However, there is, in principle, a relationship between the methanol expulsion and the aziridine displacement processes in their dependency on electronic accession from the indolic nitrogen. Since the elimination process occurs most readily, at least in our experiment, on an oxidized (one electron) version of **7** (cf. semiquinone **8**), the aziridine opening reaction might well operate on an oxidized (one electron) version of **11** (cf. species **9**).[16]

Future research in the mitomycin area will strive for greater definition of species **8** and **9** and for elucidation of the chemistry of compound **11**, including its behavior in simulated biological systems. With the series **6** → **7** → **10** → **11** now characterized for the first time, the prospectus for progress toward these goals would seem to be realistic. Conceivably, new chemical insights could find application to the preparation of more active mitomycin congeners.

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Supplementary Material Available: Copies of the NMR spectra of compounds **6**, **7**, **10**, and **11** (4 pages). Ordering information is given on any current masthead page.

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(14) (a) For the involvement of semiquinones in biological electron transport processes, see: Crofts, A. R. In *The Enzymes of Biological Membranes*; Plenum Press: New York, 1985; Vol. 4, pp 347-382. (b) For a previous suggestion as to the involvement of semiquinones in the activation cascade, see: Pan, S. S.; Andrews, P. A.; Glover, C. J.; Bachur, N. R. *J. Biol. Chem.* **1984**, *259*, 959.

(15) Sieb, P. A.; Tolbert, B. M.; Bielski, B. H. J. *Ascorbic Acid: Chemistry, Metabolism and Uses*; Advances in Chemistry 200; American Chemistry Society: Washington, DC, 1982; pp 81-100.

(16) Without any justification or comment, a species analogous to **9** appears in ref 3c as a possible biological alkylating agent.

On the Interaction of Poly(pyridine)ruthenium(II) Optical Antipodes Intercalated in Montmorillonite Clay

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We report here the UV-vis absorption spectra of (−)-RuL$_3^{2+}$ (L = 2,2′-bipyridine; 1,10-phenanthroline), (+)-RuL$_3^{2+}$, and (±)-RuL$_3^{2+}$ adsorbed on montmorillonite clay. Our results provide compelling evidence of selective interactions between the optical antipodes of RuL$_3^{2+}$, when as few as 2–4% of the available cation exchange sites in clay are loaded with the Ru(II) complex.

Several unusual features of smectite clay–ML$_3^{2+}$ adducts have been reported in recent years.[1-5] Most notable among these is

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(1) Yamagishi, A.; Soma, M. *J. Am. Chem. Soc.* **1981**, *103*, 4640.

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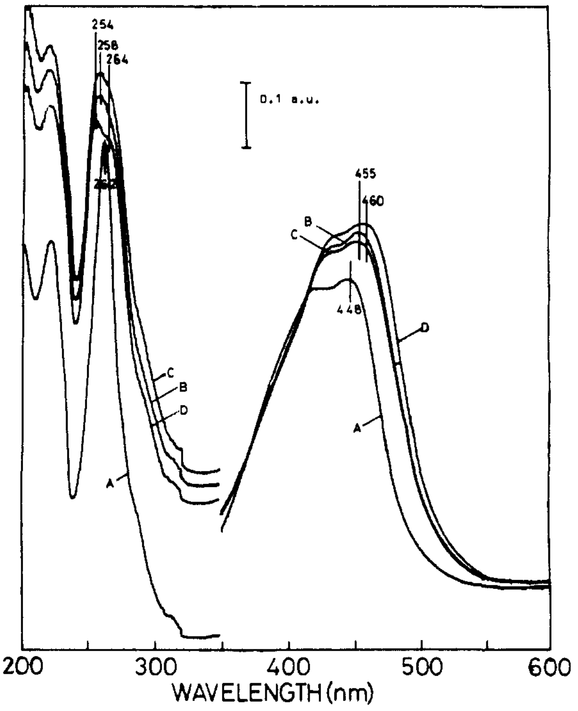

Figure 1. Visible absorption spectra of 2×10^{-5} M (−)-Ru(phen)$_3^{2+}$ (B), (+)-Ru(phen)$_3^{2+}$ (C), and (±)-Ru(phen)$_3^{2+}$ (D) adsorbed in montmorillonite clay (1 g/L aqueous dispersion). The corresponding UV spectra were recorded following 3-fold dilution of the above samples with water. The spectrum of Ru(phen)$_3^{2+}$ in water, which was the same for the enantiomers and the racemic mixture, is shown in trace A. There were marginal differences in the optical purity and concentration of samples B and C. The UV spectra have been offset for the sake of clarity, and all spectra were recorded against suitable references. All experiments were carried out under ambient conditions, and the solution temperature typically ranged from 28 to 30 °C.

Yamagishi & Soma's observation that such complexes are intercalated in clay as a racemic pair.[1] This remarkable property of the smectites has led to the development of versatile clay columns suitable for optical resolution of racemic mixtures.[6-10] Our own research in this area has also yielded encouraging results. For example, Ru(bpy)$_2$L$_2^{2+}$ (L = 4,4′-dicarboxy-2,2′-bipyridine) could be completely resolved on a (−)-Ru(phen)$_3^{2+}$–montmorillonite column by using a pH-based elution scheme.[11] These results have motivated us to better understand the principles underlining such separations; specifically, we have been interested in probing possible interactions between optical antipodes adsorbed in the clay interlayer.

Previous work by Yamagishi and co-workers employed clay samples saturated with ML$_3^{2+}$ (M = Ni, Fe, Ru). It was shown that adsorption of racemic ML$_3^{2+}$ in clay results in a 2-fold denser degree of stacking than that found for a single enantiomer. For example, clay samples saturated with (−)-Fe(phen)$_3^{2+}$ adsorb an additional equivalent of (+)-Fe(phen)$_3^{2+}$.[1] These results were attributed to the formation of racemic pairs resulting from the improved packing of optical antipodes in the clay interlayer.[1,6-10] Subsequent experiments revealed that formation of pseudoracemic pairs between optical antipodes of different molecules is also possible.[9] In the experiment described below, possible interactions between optical antipodes have been probed under conditions in which the adsorbed ions are lightly packed in clay. Such an experiment may be used to test Yamagishi's hypothesis concerning the role of packing in the formation of racemic pairs.

Figure 1 shows the UV-vis absorption spectra of (−)-Ru(phen)$_3^{2+}$ (B), (+)-Ru(phen)$_3^{2+}$ (C), and (±)-Ru(phen)$_3^{2+}$ (D) in an aqueous montmorillonite dispersion.[12,13] High-speed (20000 rpm) centrifugation of the above samples indicated that all of the Ru(II) complex was adsorbed in clay. The estimated loading level of the complex ion is 4% of the cation exchange capacity (cec) of this montmorillonite clay,[13] so that the packing parameter is unimportant under these conditions. It can be seen from the figure that while the spectral profiles for the (+) and (−) enantiomers are similar ($\lambda_{\max,\pi-\pi^*} = 258$ nm; $\lambda_{\max,\mathrm{MLCT}} = 455$ nm), there are obvious differences in the spectrum of the racemic complex.[14] Most significantly, the MLCT (metal-to-ligand charge transfer) maximum is red-shifted to 460 nm, while the ligand based $\pi-\pi^*$ band is partially split into two peaks with $\lambda_{\max}$ values of 254 and 264 nm, respectively. Slight changes in molar absorptivity have also been observed. We note that there are no discernible differences between the spectrum of the racemic complex and those for the pure enantiomers in aqueous solution not containing clay (trace A). The results were similar for the Ru(bpy)$_3^{2+}$ complex: For example, the visible charge transfer maximum for the adsorbed enantiomers was located at 462 nm as compared to a value of 470 nm for the racemic mixture. The latter value is in good accord with published literature data on racemic Ru(bpy)$_3^{2+}$ intercalated in montmorillonite clay.[2-4]

The above results strongly suggest molecule–molecule interactions between the optical antipodes of RuL$_3^{2+}$, even when <5% of the exchangeable sites in clay are loaded with the metal complex. The interaction energy estimated from the observed spectral shifts amounts to 1–2 kcal/mol and is presumably what drives the pairing of optical antipodes under conditions in which such ions would have normally remained separated in the interlayer.

In conclusion, we have successfully monitored selective interactions between the optical antipodes of RuL$_3^{2+}$ intercalated in montmorillonite clay. These results lend strong support to Yamagishi's model of racemic pairs in the clay interlayer and help account for the efficacy with which racemic complexes are resolved on chirally modified clay columns. Such interactions may also be responsible for the clustering of (±)-Ru(bpy)$_3^{2+}$ noted earlier by Ghosh and Bard.[2] While the origin of such selective interactions between optical antipodes remains to be understood, our results indicate that Yamagishi's hypothesis of improved packing efficiency of optical antipodes as the reason behind racemic pairing is not entirely satisfactory.[1,6-10] Finally, previous explanations concerning spectral shifts observed for intercalated (±)-Ru(bpy)$_3^{2+}$ need to be revised. Such shifts are in part due to clay–molecule interactions, as earlier proposed,[3,4] and in part due to interaction between optical antipodes.

Registry No. (+)-Ru(bpy)$_3^{2+}$, 24162-12-7; (−)-Ru(bpy)$_3^{2+}$, 52389-25-0; (±)-Ru(bpy)$_3^{2+}$, 15158-62-0; (+)-Ru(phen)$_3^{2+}$, 19368-51-5; (−)-Ru(phen)$_3^{2+}$, 24162-09-2; (±)-Ru(phen)$_3^{2+}$, 22873-66-1; montmorillonite, 1318-93-0.

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(10) Yamagishi, A.; Ohnishi, R. *Inorg. Chem.* **1982**, *21*, 4233.

(11) Kotkar, D.; Ghosh, P. K., unpublished results.

(12) (−)-Ru(phen)$_3^{2+}$ and (+)-Ru(phen)$_3^{2+}$ were obtained in 92% and 97% enantiomeric excess, respectively, from the resolution of (±)-Ru(phen)$_3$Cl$_2$·2H$_2$O with potassium antimonyl tartrate (Dwyer, F. P.; Gyarfas, E. C. *J. Proc. R. Soc. N. S. W.* **1949**, *83*, 170) and isolated as their perchlorate salts. Elemental analysis data for both enantiomeric salts [(−) isomer: C 48.78%, N 9.64%, H 2.85%; (+) isomer: C = 48.57%, N = 9.52%, H = 2.87%] are in reasonable agreement with their formulation as Ru(phen)$_3$(ClO$_4$)$_2$·2H$_2$O (calcd: C = 49.31%, N = 9.58%, H = 3.19%). (±)-Ru(phen)$_3^{2+}$ used in the present experiments was prepared by premixing aqueous solutions of the above enantiomeric salts. The results were similar to that found for authentic (±)-Ru(phen)$_3$(ClO$_4$)$_2$.

(13) Grade GK-129 montmorillonite clay from Georgia Kaolin Co. was employed in the present experiments. Aqueous dispersions of Na–montmorillonite were prepared by the procedure described in ref 2, and the cation exchange capacity of the dispersed clay was ~1 mequiv/g. Typically, absorption spectra were recorded for samples containing $1-2 \times 10^{-5}$ M Ru(II) and 1 g/L clay, which corresponded to a loading level of 2–4%.

(14) All spectra were recorded for freshly prepared samples. The experiments were repeated several times in this laboratory and the results were entirely reproducible. The results were the same for different batches of Ru(phen)$_3^{2+}$.