

0040-4039(95)00954-X

## Evidence for the Existence of a Cyclic Ruthenium (VI) Diester as an Intermediate in the Oxidative Scission of $(-)-\alpha$ -Pinene with RuO4<sup>1</sup>.

## Laura Albarella,<sup>a</sup> Federico Giordano,<sup>b</sup> Maria Lasalvia,<sup>a</sup> Vincenzo Piccialli<sup>\*a</sup> and Donato Sica<sup>a</sup>

a. Dipartimento di Chimica Organica e Biologica, Università degli Studi di Napoli "Federico II", Via Mezzocannone 16, 80134 Napoli, Italy.

b. Dipartimento di Chimica, Università degli Studi di Napoli "Federico II", Via Mezzocannone 4, 80134 Napoli, Italy.

Abstract. The reaction of (-)- $\alpha$ -pinene (1) with RuO<sub>4</sub> in CCl<sub>4</sub> at room temperature affords the ketoaldehyde 3 as the sole product. Evidence is reported that the oxidative scission of the olefinic substrate to 3 proceeds through a ruthenium (VI) diester intermediate for which we propose structure 2 on the basis of spectral evidence and comparison with the osmium-containing analogue of 2, synthesised by reaction of (-)- $\alpha$ -pinene with OsO<sub>4</sub> in dioxane and whose structure has been determinated by single crystal X-ray diffraction analysis. Compound 2 was also shown to be an intermediate compound in the RuO<sub>4</sub> oxidation of (-)- $\alpha$ -pinene performed in acetone-water (2:1) which gives  $\alpha$ -ketol 4 as the sole oxidation product.

As a part of our continuing studies on the oxidation of alkenes using stoichiometric amounts of  $RuO_4$ ,  $2^{-5}$  we report here on the RuO<sub>4</sub> oxidation of (-)- $\alpha$ -pinene performed both in CCl<sub>4</sub> and acetone-water (2:1) solution. RuO<sub>4</sub> oxidation of (-)- $\alpha$ -pinene in CCl<sub>4</sub> at room temperature gave the scission product  $3^6$  in 20% yield<sup>7</sup> as the sole oxidation product but, very interestingly, its formation was seen to proceed through the preliminary formation of a highly unstable, brownish, species for which we propose the ruthenium (VI) diester structure 2, that successively evolves to the ketoaldehyde 3 (Scheme).

Although the existence of a cyclic ruthenium (VI) diester as an intermediate in the RuO<sub>4</sub> oxidative scission of alkenes had previously been suggested,<sup>8</sup> no evidence that could support this hypothesis has been provided to date. On the other hand, we have recently shown that the RuO<sub>4</sub> oxidation of 7-dehydrocholesteryl acetate to a mixture of  $5\alpha$ -cholest-7-en-3 $\beta$ ,5,6 $\alpha$ -triol 3-acetate and 3 $\beta$ -acetoxy-5-hydroxy-5 $\alpha$ -cholest-7-en-6-one, performed in acetone-water (1:1) at -60 °C, in turn proceeds through the



Scheme

formation of a cyclic ruthenium (VI) diester intermediate (a coloured, unstable, product in this case too) which has been isolated and characterised as  $5^4$ . However, no trace of a scission product was detected in this case among the oxidation products and thus no evidence could be gained on the eventual involvement of the isolated ruthenate ester in the scission reaction of the  $\Delta^7$  carbon-carbon double bond (the one interesting for the oxidation process) as well.



The presence of a reactive, coloured product both in the  $RuO_4$  oxidation of (-)- $\alpha$ -pinene and 7dehydrocholesteryl acetate suggested to us that in the former case also the transient species could be a ruthenate ester. This observation prompted us to further investigate the oxidation of the monoterpene substrate.

When the reaction was performed on a 300 mg amount of  $(-)-\alpha$ -pinene, just as observed for the analogous reaction performed on 7-dehydrocholesteryl acetate, the ruthenate diester (2) readily precipitated after the addition of the oxidant and, by silica gel TLC analysis, the coloured material could be seen to migrate without appreciable decomposition. However, in contrast to what happens for the steroidal derivative, all the attempts to isolate the above product resulted in its decomposition. Thus, in order to have structural information on this compound, we planned to follow the RuO<sub>4</sub> oxidation of  $(-)-\alpha$ -pinene by NMR spectroscopy performing the reaction in CDCl<sub>3</sub> solution. The change in the solvent system (CDCl<sub>3</sub> in place of CCl<sub>4</sub>), in fact, did not affect the course of the reaction and the reaction performed in CDCl<sub>3</sub> solution produced a coloured substance having the same chromatographic behaviour as that obtained from the reaction conducted in CCl<sub>4</sub> and, finally, gave the same ketoaldehyde 3 as the sole oxidation product.

One of the NMR experiments was performed as follows. RuO4 was generated by vigorously stirring the required (stoichiometric) amount (1.2 mg) of RuO<sub>2</sub>·2H<sub>2</sub>O and a 6 molar excess of NaIO<sub>4</sub> (9.0 mg) in the biphasic system CDCl<sub>3</sub>-D<sub>2</sub>O (0.5:1 mL) and the organic layer was added portion wise to  $(-)-\alpha$ pinene (1 mg) dissolved in CDCl<sub>3</sub> (0.4 mL) and placed into a 5 mm diameter NMR tube. After each addition of the reactant (overall three sequential additions) the reaction was followed by registering a series of proton spectra at successive times. Good quality <sup>1</sup>H-NMR spectra, as well as the shortening of the time required for the optimisation of the homogeneity condition of the magnetic field of the instrument after each addition of the oxidant into the NMR tube, could be obtained using only small amounts of the substrate (1-2 mg) for the reaction due to the precipitation of RuO<sub>2</sub> concomitant to the oxidation process. This necessarily required the use of a high field (400 MHz) spectrometer to collect the NMR data in the minimum time. All the above operations, including registration of the first proton spectrum, required no more than 1.5 min., a time in which the ruthenate ester concentration in solution was high enough to allow accurate <sup>1</sup>H-NMR measurements. After the first addition of oxidant all the signals pertinent to compound 2 persisted in solution up to 5 min. Their disappearence was only accompanied by the increasing of the signals pertinent to the ketoaldehyde 3 while no trace of other possible oxidation products, such as (1S, 2S, 3R, 5S)-2,3-pinanediol (the hydrolysis product of diester 2) or the corresponding  $\alpha$ -ketol (4), could be detected in the reaction mixture. The successive two additions of oxidant regenerated signals relevant to 2 while causing the lowering of the intensities of those pertinent to the olefin and, ultimately, leading to their disappearence.

The most significant feature of the proton spectrum of the reaction mixture, that indicated the existence in solution of compound 2, was the presence of a double doublet signal at  $\delta$  5.56 (J=8.5 and 3.0 Hz)

that was easily attributed to the proton vicinal to ruthenium (H-3) in compound 2, on comparison of its chemical shift value with that exhibited by the proton vicinal to the metal in the ruthenate diester 5 obtained from 7-dehydrocholesteryl acetate, which resonated at  $\delta$  4.99 in its proton spectrum<sup>4</sup>. Furthermore, the multiplicity and coupling constants of the above signal at  $\delta$  5.56 well agree with those expected for H-3, which is only vicinally coupled with the H<sub>2</sub>-4 methylene protons, as indicated by the examination of a molecular model of 2. The proton spectrum of the reaction mixture also included methyl singlet signals at  $\delta$  1.52, 1.39 and 1.02 attributable to the methyls Me-8, Me-9 and Me-10 of 2 (possibly, the signal at  $\delta$  1.52 should be attributed to Me-10; its deshielded position could be due to the vicinity of the Ru=O grouping).

Further corroboration for the presence of a ruthenate ester intermediate in the RuO<sub>4</sub> oxidation of (-)- $\alpha$ -pinene came from a <sup>13</sup>C-NMR experiment performed on a 50 mg amount of the substrate using the same experimental procedure as that detailed above for the <sup>1</sup>H-NMR experiment. In the course of this experiment it was possible to notice the presence in the <sup>13</sup>C-NMR spectrum of the reaction mixture of a low-intensity, quickly disappearing, carbon signal at  $\delta$  95.5 which was attributed to one of the two carbon atoms geminal to ruthenium (carbons C-2 and C-3 in 2) of each of the two coordinated pinene units. This attribution once again was suggested by the comparison of the structure of 2 with that of the ruthenium (VI) diester 5 (both 2 and 5 have a (C-O)<sub>4</sub>-Ru=O, pyramidally arranged substructure) whose <sup>13</sup>C-NMR spectrum contained resonances for carbon atoms geminal to ruthenium at  $\delta$  101.03 and 88.95, very close to the above value of 95.5 ppm.

At this stage we synthesised the osmium-containing analogue of 2 (differing from 2 only by the presence of osmium in place of ruthenium in the structure) by reaction of OsO<sub>4</sub> with (-)- $\alpha$ -pinene in dioxane at room temperature. We reasoned that this compound could indirectely provide further information on the structure of the compound under investigation. Our expectations were based on the fact that compound 5 (the ruthenate diester of 7-dehydrocholesteryl acetate) and its osmium-containing analogue, recently synthesised by reaction of 7-dehydrocholesteryl acetate with OsO<sub>4</sub>, in dioxane,<sup>9</sup> possess astonishingly similar <sup>1</sup>H- and <sup>13</sup>C-NMR spectra (in particular, carbon atoms geminal to osmium in the above osmate ester resonate at  $\delta$  98.71and 88.07 while these carbons resonated in 5 at  $\delta$  101.03 and 88.95). This similarity strongly suggested to us that also the osmium-containing analogue of 2 could have spectral properties very similar to those exhibited by 2 itself, thus furnishing a further evidence for the identity of this compound.

Indeed, osmilation of (-)- $\alpha$ -pinene in dioxane afforded a brownish osmate ester (6) which showed chromatographic mobility and NMR characteristics very similar to those exhibited by its analogue 2 (both 2 and its osmium-containing analogue have the very same R<sub>f</sub> value on silica gel TLC; hexane-EtOAc, 8:2, Rf=0.60). In particular, the proton spectrum of 6 contained singlet methyl resonances at  $\delta$  1.48, 1.32 and 0.96 and the H-3 double doublet signal at  $\delta$  5.26 (J= 8.8 and 2.4 Hz) while the <sup>13</sup>C-NMR spectrum included resonances at  $\delta$  98.12 and 93.22 for carbons geminal to osmium. X-ray analysis of compound 6 performed on a single crystal obtained by slow evaporation from petroleum ether (80-100°)-CH<sub>3</sub>OH (1:1) revealed, as expected, <sup>10</sup> that this compound had a structure identical to that attributed to 2 (except for the nature of the metal), in which osmium adopts a square-based pyramidal five-coodination by connecting two  $\alpha$ -pinene units<sup>11</sup>. The figure shows a view of the X-ray model of osmate ester 6<sup>11</sup>.

Finally, compound 2 was also seen to be an intermediate compound in the RuO<sub>4</sub> oxidation of (-)- $\alpha$ -pinene performed in deuteriumacetone-D<sub>2</sub>O (2:1). This reaction was monitored by <sup>1</sup>H-NMR as described for the oxidation of the same substrate performed in CDCl<sub>3</sub> and gave  $\alpha$ -ketol 4 in 50% yield as the sole oxidation product (Scheme) which had spectral properties identical to those reported <sup>12</sup>. RuO<sub>4</sub> was generated in D<sub>2</sub>O (1 mL) from a stoichiometric amount of RuO<sub>2</sub>·2H<sub>2</sub>O and a 6 molar excess of NaIO<sub>4</sub>. Excess NaIO<sub>4</sub> was precipitated by adding 0.5 mL of deuteriumacetone and removed by centrifugation. In this case the oxidant was added in one time to the alkene (the amount of (-)- $\alpha$ -pinene oxidised was 1 mg in this case as well.). The presence of diester 2 as an intermediate in this reaction as well, was indicated by the presence of the H-3 resonance at  $\delta$  5.65 (J=8.5 and 3.0 Hz) and the methyl

resonances at  $\delta$  1.47, 1.35 and 0.99 (Me-8, Me-9 and Me-10), in the proton spectrum of the reaction mixture. The chemical shift values of the above signals well matched those of the corresponding proton signals in the ruthenium diester intermediate (2) for the oxidation performed in CDCl<sub>3</sub>.



In conclusion, the RuO<sub>4</sub> oxidation of  $(-)-\alpha$ -pinene performed either in CCl<sub>4</sub> or acetone-water seems to proceed through the same ruthenium (VI) diester 2 which is or oxidatively cleaved, in the first solvent, to give an aldehydic product, or undergoes oxidative decomposition to an  $\alpha$ -ketol, in the second solvent system. How the solvent could control the reaction towards either of the two oxidation products is still an open question.

Acknowledgments. This research was supported by a grant of MURST. Throughout the NMR work the facilities of the "Centro di Metodologie Chimico-Fisiche dell'Università degli Studi di Napoli" were used.

## **References and Notes**

- 1. Part 5 in the series "Reaction of RuO<sub>4</sub> with carbon-carbon double bonds". For part 4 see ref. 5.
- 2. Piccialli, V.; Smaldone, D.; Sica, D. Tetrahedron 1993, 49, 4211-4228.
- 3. Notaro, G.; Piccialli, V.; Sica, D.; Smaldone, D. Tetrahedron 1994, 50, 4835-4852.
- 4. Piccialli, V.; Sica, D.; Smaldone, D. Tetrahedron Lett. 1994, 35, 7093-7096.
- 5. Giordano, F.; Piccialli, V.; Sica, D.; Smaldone, D. J. Chem. Res. (S) 1995, 52-53.
- 6. Compound 3 was identified on comparison with an authentic sample prepared by Pb(OAc)<sub>4</sub> oxidation of commercially available (1S,2S,3R,5S)-pinanediol.
- The yields of this process are low possibly due to the strong absorption of the aldehyde product on the ruthenium dioxide surface.
- 8. Lee, D. G.; Spitzer, U. A. J. Org. Chem. 1976, 41, 3644.
- 9. Work in preparation.
- 10. Philips, F. L.; Skapsky, A. C. Acta Cryst. 1975, B31, 1814-1818.
- 11. X-ray crystallographyc analysis will be published elsewhere.
- 12. Thomas, A. F; Rey, F. Tetrahedron 1992, 48, 1927-1942.

(Received in UK 18 April 1995; revised 23 May 1995; accepted 26 May 1995)