Oxidative Cyclization of 5-Hydroxyalkenes With Rhenium Oxide, Utilizing a Co-Oxidant. IV

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Abstract: 5-Hydroxylalkenes react with rhenium(VII) oxide in the presence of another oxidant, H5IO₆, to provide substituted tetrahydrofurans. The yield and stereoselectivity are comparable to stoichiometric results.

A number of natural products, such as polyether antibiotics, are comprised of tetrahydrofuran rings rich in stereochemical complexity.¹ Notable methods have been developed in recent years to access these heterocycles.² We have recently reported a new method for assembling substituted tetrahydrofurans via oxidative cyclization of 5-hydroxyalkenes with rhenium(VII) oxide.³ Despite high stereoselectivity, a disadvantage of these reactions is the necessity of a stoichiometric excess of rhenium(VII) oxide needed to force these reactions to completion. Herein we report a new method requiring significantly smaller amounts of rhenium oxide.

The general procedure is as follows: To a mixture of 1.0 mmol 5-hydroxyalkene and 1.3 mmol periodic acid (H₅IO₆) in CH₂Cl₂ at room temperature, was added 0.5 mmol rhenium(VII) oxide (Re₂O₇). The reaction was monitored by TLC until all starting material was consumed (about 15 hr). Then, 10 equivalents of NaHSO₃ as 1.0 M aqueous solution was added. After stirring for 30 min, the reaction mixture was diluted with CH₂Cl₂ and the product was purified in normal fashion.

Schemes 1, 2, and 3 outline oxidation of several 5-hydroxylalkenes by 50 mol% rhenium(VII) oxide (Re₂O₇) in the presence of another oxidant, H₅IO₆.^{4,5,6} The yields and stereoselectivity are comparable to previous results where a 2-3 times mol excess of rhenium(VII) oxide was utilized.^{3,7} For substrates with trisubstituted double bonds such as 3 and 6, non-oxidative cyclization products 5 and 8 were also isolated. This occurs because the reaction conditions are quite acidic.⁸ A variety of bases were examined to suppress formation of these by-products. However, in all attempts only starting material was recovered. Addition of base appears to precipitate H₅IO₆ and perrhenic acid as their conjugate bases.

Interestingly, when t-BuOOH was used as co-oxidant, product 9, resulting from rhenium catalyzed epoxidation of the double bond followed by intramolecular cyclization, was isolated in high yield (eq. 1).⁹

$$C_{5}H_{11} \xrightarrow{\mathsf{R}} \begin{array}{c} 10 \mod \% \operatorname{Re}_{2}O_{7}, 1.1 \text{ eq. t-BuOOH} \\ \hline \mathsf{n}, 15 \text{ hr, CH}_{2}Cl_{2} \\ \mathsf{N} = H \\ \mathbf{1} \\ \mathsf{R} = M \\ \mathsf{R} = M \\ \mathsf{e} \\ \end{array} \begin{array}{c} 67.0\% (1:1 \text{ mixture}) \\ \mathsf{9} \end{array} \begin{array}{c} \mathsf{H} \\ \mathsf{OH} \\ \mathsf{H} \\ \mathsf{OH} \\ \mathsf{OH} \\ \mathsf{H} \\ \mathsf{OH} \\ \mathsf{OH} \\ \mathsf{H} \\ \mathsf{OH} \\ \mathsf{H} \\ \mathsf{OH} \\ \mathsf{OH} \\ \mathsf{OH} \\ \mathsf{OH} \\ \mathsf{H} \\ \mathsf{OH} \\ \mathsf$$



Scheme 2



	3	4 Yield% (<i>Trans/Cis</i>) (previous results) ^{ref. 3}	by-product 5Yield%
8	$R=R_2=R_3=H$, $R_1=Me$, $R_4=n-C_6H_{13}$	36.2 (>99:1) (61.6%, >99:1)	59.9
b	R=n-C ₅ H ₁₁ , R ₁ =Me, R ₂ =R ₃ =R ₄ =H	77.0 (85.5%)	19.8
c	$R=n-C_5H_{11}, R_1=R_4=Me, R_2=R_3=H$	44.8 (>99:1) (75.0%, 13.5:1)	48.5
d	$R=n-C_{5}H_{11}, R_{1}=R_{3}=Me, R_{2}=R_{4}=H$	52.4 (1:29) (86.7%, 1:29)	43.5
e	$R=n-C_{5}H_{11}$, $R_{1}=R_{2}=Me$, $R_{3}=R_{4}=H$	62.7 (<8:1) (92.0%, 8:1)	35.6





It is critical that at least 50 mol% rhenium(VII) oxide (Re₂O₇) be used in this reaction. When 10 mol% rhenium(VII) oxide (Re₂O₇) was used on substrate 1a in the presence of 1.3 equivalents of periodic acid (H₅IO₆), only a 41% yield of product 2a was obtained. ¹H NMR (400 MHz) studies show the rhenium(VII) species to be strongly bound to the tetrahydrofuran products. This may explain the need for at least 100 mol% of rhenium atom.

Finally, when Z-5-undecen-2-ol (1c) and 1-undecen-5-ol (1e) were treated with 1.0 equivalent of ReO_3^{10} and 1.3 equivalents of H_5IO_6 in CH_2Cl_2 at room temperature for 21 hr, *trans* product 2c and 2e were isolated in 61.0 and 51.0% yield as a single isomer (eq. 2,3).



We have developed a practical method for the oxidative cyclization of 5-hydroxyalkenols to tetrahydrofuran derivatives with far less Re₂O₇ by using a co-oxidant, H₅IO₆. This procedure gives comparable results, considering yield and stereoselectivity, to previous reactions where 2-3 mol excess Re₂O₇ was required.

Reference and notes

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- 7. For substrate 1c, quantitative yield with the same ratio was obtained when 1.0 equivalent of rhenium(VII) oxide and 1.3 equivalent of H₅IO₆ were used.
- 8. (a) It has been shown that Re₂O₇ is an effective olefin hydration catalyst. see: Chem. Abstr. 1973, 79, 31479y. (b) We have previously observed that the substrate 1, when exposed to Re₂O₇ alone, provides non-oxidative cyclization product 2 as the major product.



- 9. It has been reported that Re₂O₇ catalyzes epoxidation of cyclohexene by PhCHMeOOH. see: Chem. Abstr. 1977, 86, 189687u.
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