Synthesis of γ-Butyrolactones by a Baeyer–Villiger Oxidation with Hydrogen Peroxide, Catalysed by Methyltrioxorhenium

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Keywords: Baeyer–Villiger reaction / Lactones / Methyltrioxorhenium / Catalysis / Oxidations / Cyclobutanones / Ketones

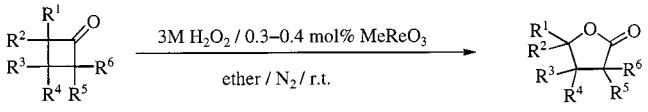
γ-Butyrolactones were obtained in good yields and high regioselectivity by a Baeyer–Villiger oxidation with H_2O_2 catalysed by methyltrioxorhenium. The lactonization was chemoselective in the presence of double bonds, aromatic rings, and chlorine substituents. A trimethylsiloxy-substituted ketone was converted directly into a hydroxylated lactone in good yield and regioselectively.

Introduction

The Baeyer−Villiger reaction,[1] the oxidation of ketones to esters, lactones, or derived alcohols and acids, which was first reported 100 years ago, is of considerable synthetic importance. It is used in areas as diverse as the synthesis of antibiotics, steroids, pheromones, monomers for polymerization, etc. The reaction also includes the parallel oxidation of aldehydes. The oxidation is accomplished with organic peroxoacids, H_2O_2, or alkyl hydroperoxides. Many of the widely used oxidants, such as CF_3CO_3H and MCPBA, are explosive and/or shock-sensitive and hence unsuitable for many industrial applications. They are used in stoichiometric quantities and sometimes at high temperatures, which increases the risks. Long reaction times of one or several days are common. Overall, efficient oxidizing agents need to be developed.[2] As highlighted in a recent review,[1a] H_2O_2 has several advantages as an oxidant: Reactions are simple and the only by-product is water, there is no need for the addition of buffers, the active oxygen content is high, and the cost is low. However, H_2O_2 alone is rarely sufficient to achieve the conversion, and catalysts capable of activating it (enhancing its nucleophilic properties) are highly desirable. Although Baeyer−Villiger reactions catalysed by microorganisms (whole cells or purified enzymes) are well established,[3] little is known about metal-catalysed alternatives, despite the great industrial demand for them.[4] Several transition metals can activate H_2O_2 and catalyse oxidation reactions, particularly some acidic metal oxides such as OsO_4, MoO_3, Cr_2O_3, V_2O_5, TiO_2, and SeO_2,[5] but few systems have been found which can catalyse the Baeyer−Villiger oxidation. Examples[6] are $[MoO(\eta^2\text{-}O_2)_2(pic)]^-$, $[MoO(\eta^2\text{-}O_2)(dipic)]$ (pic = picolinate anion, dipic = dipicolinate anion), $(Ph_3P)_2Pt(\eta^2\text{-}O_2)$, $[(dppe)Pt(CF_3)(CH_2Cl_2)]^+[BF_4]^-$, $[(dppb)Pt(\mu\text{-}OH)]_2(BF_4)_2$ [dppe = 1,2-bis(diphenylphosphanyl)ethane, dppb = *o*-bis(diphenylphosphanyl)benzene] and Pt complexes modified with chiral diphosphanes. Since 1994 there have been a few reports of metal-catalysed asymmetric Baeyer−Villiger reactions,[7] as for instance through the activation of molecular oxygen, but this is still a limited area. In 1994 it was also found that $MeReO_3$ (MTO) is a very efficient catalyst for the Baeyer−Villiger reaction.[2] In the oxidation of cyclobutanone, the MTO/H_2O_2 system is more active than the most frequently used reagents (CF_3CO_3H, MCPBA, CH_3CO_3H, HCO_3H); the turnover frequency (200 min^{-1}) was comparable to the activities of the known metal-based catalysts and in some cases better. This reaction has not yet been explored much. Besides the successful oxidation of cyclopentanone, cyclohexanone, and 1-methylcyclohexanone[2] reported at the time, there has been only one other study of the potential of this catalytic system[8] in the Baeyer−Villiger oxidation, in which β-diketones were converted into carboxylic acids in high yields. Not only because γ-butyrolactones are very useful intermediates in synthesis,[1] but also because of the unexpected capability of MTO to catalyze both electrophilic and nucleophilic reactions of peroxides, we decided to explore the usefulness of this system further and study the regio- and chemoselectivity of the reaction.

Results and Discussion

The substrates were prepared according to known procedures.[9] The catalytic reactions were conducted as indicated in Scheme 1[2] and monitored by GC-MS. The results are presented in Table 1.[10] There was complete conversion of the starting material in all cases except **6** of which after 24 h, 6% had not yet reacted and even after 46 h about 2% remained in solution. The chromatographically pure products were identified by GC-MS, DEPT, ^{1}H-NMR, ^{13}C-NMR, and IR spectroscopy.



Scheme 1

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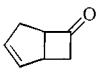
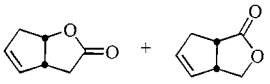
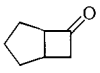
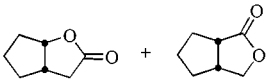
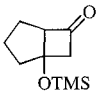
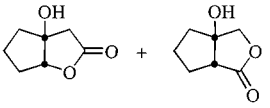
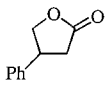
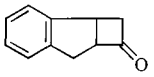
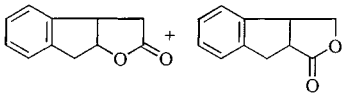
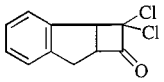
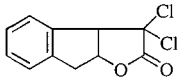
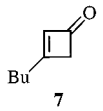
Table 1. Baeyer−Villiger oxidation of cyclobutanones

Entry	Ketone	Entry	Products	Ref.	Ratio[a] a : b	Reaction Time [h]	Yield[b] [%]
1		1a + 1b		10a	87 : 13	5	63
2		2a + 2b		10b	94 : 6	1	80
3		3a + 3b			96 : 4	1	70
4		4a		10c		7.5	68
5		5a + 5b		10d	87 : 13	2.5	76
6		6a				24	69

[a] Determined from the ratio of peak heights in ^{1}H-NMR spectra. − [b] The yields given are for isolated products after flash chromatography; for **6a**, the yield refers to the conversion after 24 h, calculated from the ratio of areas in GC-MS, relative to the starting material.

Lactone **6a** seemed to decompose partially during chromatography, since the amounts isolated were always low and small amounts of other unidentified products were also eluted. The yields of the oxidations indicated in Table 1 were good, and the best were generally associated with the fastest reactions. In Baeyer−Villiger reactions there is preferential migration of the most substituted (most electron-rich) carbon atom. In the examples studied two regioisomers formed, and migration of the most substituted carbon atom predominated. The regioselectivities obtained compare favourably with those of many Baeyer−Villiger oxidants.[11] To examine the possibility of using this method to prepare unsaturated lactones, cyclobutenone **7** was also prepared.[12] Under oxidation conditions it was converted completely after 4 h, but a large mixture of products was obtained.

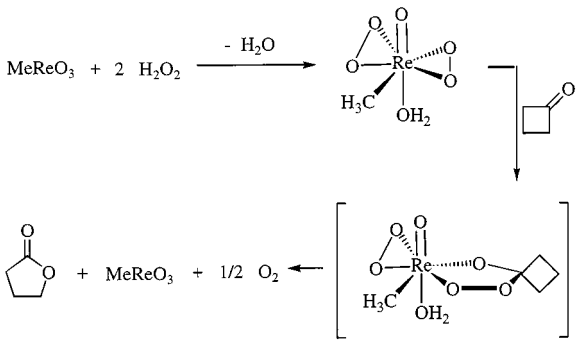


7

MTO is known to catalyse the oxidation of many classes of compounds[13] such as alkenes, alkynes, aromatic compounds, sulphur-containing compounds, phosphanes, arsanes, stibines , amines and other nitrogen-containing compounds, and halide ions. It also catalyses oxygen insertion into C−H bonds. Hence, it was of interest to study the chemoselectivity of the reaction. As shown in Table 1, the bicyclic and tricyclic compounds reacted faster, probably due to the increased ring strain. The only exception was **6**. It is known that electron-withdrawing groups retard the Baeyer−Villiger oxidation, and that oxygen insertion usually occurs between the carbon atom which is not substituted by the electron-withdrawing groups and the carbonyl group.[1] This effect has been used in synthesis to obtain a desired regioisomer with high selectivity.[14] With α,α-dichloro substitution only one regioisomer, **6a**, was isolated. To our knowledge this compound has not been described before, although some 3-substituted indenobutyrolactones have been patented as herbicides.[15]

In the oxidation of bicycloheptanone **1**, in which epoxidation of the double bond could compete with the Baeyer−Villiger oxidation, no by-product formed in excess of 5%, as indicated by the GC-MS data of the crude reaction mixture. Bicyclic lactones **1a** and **2a** are important synthons in the synthesis of prostaglandins and nucleosides.[16] The chemoselectivity observed in the oxidation of **1** was unexpected and remarkable because MTO is known to be a very efficient catalyst for olefin epoxidation. Indeed, this ability of MTO to favour lactonization over epoxidation, although normal for the uncatalyzed peracid oxidations, is unusual in metal-catalyzed Baeyer−Villiger reactions.[1a] Examples are the unselective oxidation of **1** to a mixture of products by the Cu/O_2 systems,[7b] and the predominant epoxidation of the exocyclic double bond of carvone over the corresponding lactonization in a 95:5 ratio.[1a,1b] So far, this result is the best illustration of the dual nature of the peroxide activation induced by MTO as discussed by Espenson.[8]

Scheme 2 illustrates the mechanistic pathway that has been proposed for the oxidation of cyclobutanones catalysed by MTO.[1a,2,8] The oxidation of the analogue **3a**, substituted at the bridgehead by the trimethylsiloxy group, proceeded with high regioselectivity and concomitant hydrolysis of the substituent in the presence of excess H_2O_2. The resulting alcohol is a highly functionalized molecule, which may be used as a building block for the construction of more elaborate molecules. To our knowledge there has also been no previous report of this compound.



Scheme 2. Mechanistic pathway for the Baeyer−Villiger oxidation catalysed by MTO

Conclusion

The activation of H_2O_2 by $MeReO_3$ provides a useful catalytic system for the synthesis of substituted γ-butyrolactones. The Baeyer−Villiger oxidations studied gave high yields of products (63−80%) and were highly regioselective. The reactions were generally fast with complete conversions taking place in 1−8 h at room temperature. α,α-Dichloro substitution was found to retard the reaction considerably, but only one regioisomer was produced. Double-bond epoxidation or aromatic oxidation did not compete favourably under the reaction conditions, but the oxidation of a cyclobutenone was not selective. A trimethylsilyl-substituted ketone was converted directly into the hydroxylated γ-butyrolactone with high regioselectivity.

Experimental Section

General Procedures and Materials: ^{1}H-NMR and ^{13}C-NMR spectra were recorded with a Bruker 300-MHz spectrometer in $CDCl_3$ at 300 MHz. Chemical shifts are reported in parts per million using TMS or chloroform as internal standard. − GC-MS spectra were obtained with a Shimadzu QP-5000 GC-MS spectrometer, with a DB-1701P fused silica capillary column (l = 30 m, i.d. = 0.25 mm, thickness of film: 0.3 μm). − IR spectra were recorded with a Unicam Mattson 7000 FTIR spectrometer. − Melting points were obtained with a Büchi 530 melting point apparatus and are uncorrected. − For flash chomatography Silica Gel 60 (0.063−0.200 mm) from Merck was used. − The solvents were dried according to standard procedures. − Methyltrioxorhenium was prepared by a known method,[17] from Re_2O_7, $(Cl_3CCO)_2O$, and $SnMe_4$. The hydrogen peroxide solution was prepared according to ref.[18] by mixing 30% H_2O_2 and diethyl ether and drying with anhydrous sodium sulphate. − Ketone **1** was purchased from Merck−Schuchardt. Ketone **2** was prepared by catalytic reduction (H_2, 12 atm, 5% Pd/C, CH_2Cl_2). To prepare **3**, the silyl enol ether of cyclopentanone was obtained either by formation of the enolate with LDA at low temperature, then quenching with TMSCl,[9a] or at reflux (cyclopentanone, Et_3N, TMSCl, DMF).[9a,9b] Cycloaddition to dichloroketene (generated in situ from dichloroacetyl chloride and Et_3N)[9c] and dechlorination (Bu_3SnH, AIBN)[9d] gave ketone **3**. Ketones **4**, **5**, and **6** were prepared by the cycloaddition of dichloroketene (generated in situ from trichloroacetyl chloride, Zn/Cu, $POCl_3$),[9e,9f] to the corresponding olefins and, in the case of **4** and **5**, by further dechlorination (Zn, HOAc).[9g,9h] The compounds were characterized by GC-MS, DEPT, ^{1}H-NMR, ^{13}C-NMR, and IR spectroscopy and by comparison with those described in the literature. References are given in Table 1.

General Procedure for the Catalytic Reactions: $MeReO_3$ (0.03 mmol) was dissolved in diethyl ether/H_2O_2 (3 mol L^{-1}, 7.2 mL), the solution was cooled to 12−15°C, and kept under nitrogen while the liquid or solid ketone was added (10 mmol). The solution was then stirred at room temperature for the times indicated in Table 1. The reaction was very exothermic, and in most cases the solvent started to reflux within 10 min. When the reaction was complete, the remaining H_2O_2 was destroyed by the addition of a catalytic amount of MnO_2 (0.5 mmol). The solution was filtered through Celite, then through anhydrous $MgSO_4$, and the solvent was evaporated. The products were isolated by flash chromatography.

3a-Hydroxyhexahydro-2*H*-cyclopenta[*b*]furan-2-one (3a+3b): Purified by flash chromatography (ethyl acetate/methanol, 7:3) to yield 70% of a clear, colourless oil, consisting of two unseparable isomers.

Major Isomer 3a: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50−2.08 (m, 6 H), 2.77 (AB system, 2 H, J = 18.6 Hz, $-CH_2-O-CO$), 4.65 (d, 1 H, J = 6 Hz, $-CH-O-CO$). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 23.3 (CH_2), 31.6 (CH_2), 40.6 (CH_2), 43.1 (CH_2), 83.4 (C_q), 91.6 (CH), 176.2 (C_q). − IR ($CDCl_3$): $\tilde{\nu}$ = 1767 (s, C=O). − MS (70 eV); *m*/*z*: 142 [M^+], 114, 86,71,70, 58, 57, 55, 44, 43, 42, 41, 39, 29, 28, 27.

Minor Isomer 3b: Distinguished by some of the chemical shifts. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.24 (AB system, J = 9 Hz, $-CH_2-O-CO-$). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 78.7 (CH_2). − MS (70 eV); *m*/*z*: 142 [M^+], 111, 84, 83, 57, 56, 55, 43, 42, 41, 39, 32, 29, 28, 27.

3,3′-Dichloro-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan-2-one (6a): Purified by flash chromatography (ethyl acetate/dichloromethane, 1:1), to yield a white crystaline solid, m.p. 129−130°C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.00−3.39 (m, 2 H, Ar−CH_2−), 4.42 (d, 1 H, J = 4.5 Hz, $-CH-CCl_2$), 5.39 (m, 1 H, $-CH-O-CO-$), 7.07−7.35 (m, 3 H, Ar−H), 7.61 (d, 1 H, J = 7.2 Hz, Ar−H).− IR (KBr): $\tilde{\nu}$ = 1788 (s, C=O). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 37.5 (CH_2), 61.5 (CH), 80.7 (C_q), 82.4 (CH_2), 125.4 (CH), 127.4 (CH), 128.5 (CH), 129.6 (CH), 134.9 (C_q), 140.9 (C_q), 167.3 (C_q). − MS (70 eV); *m*/*z* (%): 246 (3) [M + 4], 244 (15) [M + 2], 242 (23) [M^+], 200 (15), 198 (23), 165 (34), 164 (15), 163 (100), 162 (12), 129 (13), 128 (89), 127 (75), 116 (18), 115 (63), 104 (32), 89 (19), 82 (10), 81 (21), 77 (10), 75 (12), 64 (18), 63 (45), 62 (10), 57 (12), 51 (21), 50 (16), 39 (21).

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