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# Oxidation of Substituted Spiro[bicyclo[n.1.0]alkane-2,2'-[1,3]dioxolanes]. Formation of Substituted Lactones.

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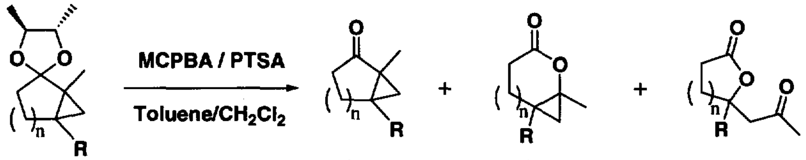
**Abstract:** 5-(Aryl)-1,4',5'-trimethylspiro[bicyclo[3.1.0]hexane-2,2'-[1,3]dioxolanes] are transformed to substituted ketolactones by treatment with *m*-chloroperbenzoic acid in the presence of *p*-toluenesulfonic acid.

*Keywords*: lactones; ketals; oxidation; cyclopropanes.

Ketals can be transformed into lactones by treatment with peracids in acidic conditions. [1] We have found that treatment of compounds of type **1** [2] with *m*-chloroperbenzoic acid (MCPBA) [3] in the presence of *p*-toluenesulfonic acid (PTSA) can lead to lactones of type **3** or **4** depending on the nature of substituent R and on the ring size of the spiroketal. Ketones of type **2** can also be isolated as minor products.



$1_{A\text{-}E}$ $2_{A\text{-}E}$ $3_{A\text{-}E}$ $4_{A\text{-}E}$

When $\mathbf{1_A}$ was treated with MCPBA (2.5 eq) in the presence of PTSA (1.0 eq) lactone $\mathbf{3_A}$ was obtained with high regioselectivity and in good yield (62%); ketone $\mathbf{2_A}$ was also isolated as a minor product (17%). Treatment of $\mathbf{1_B}$ in the same conditions led to ketone $\mathbf{2_B}$ (30% yield) and lactone $\mathbf{3_B}$ (40% yield) with no trace of lactone $\mathbf{4_B}$.[4] On the contrary, when $\mathbf{1_C}$, $\mathbf{1_D}$, and $\mathbf{1_E}$ were treated for several days with MCPBA (2.5 eq) and PTSA (1.0 eq), only traces of lactones $\mathbf{3_C}$-$\mathbf{3_D}$ were detected by GC/MS and ketolactones $\mathbf{4_C}$, $\mathbf{4_D}$ and $\mathbf{4_E}$ were respectively isolated as major products (~ 40% yield). Ketones $\mathbf{2_C}$-$\mathbf{2_E}$ were also formed as side-products and were isolated in low yields (1% - 25%). The results are summarized in the Table.

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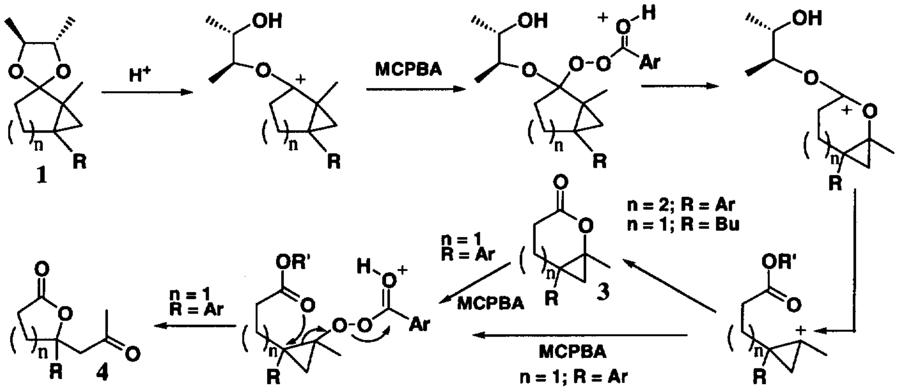
Table: Oxidation of lactones $1_A$ – $1_E$ by MCPBA/PTSA [a]

| Starting material<br>1 | time | Products (yield % [b])<br>2 | <br>3 | <br>4 |
|---|---|---|---|---|
| $1_A$ n = 1 ; R = butyl | 12 h | (17) | (62) | (-) |
| $1_B$ n = 2 ; R = *p*-methoxyphenyl | 7 d | (30) | (40) | (-) |
| $1_C$ n = 1 ; R = phenyl | 7 d | (20) | (-) | (41) |
| $1_D$ n = 1 ; R = *p*-tolyl | 3 h<br>7 d | (24)<br>(10) | (70)<br>(-) | (-)<br>(35) |
| $1_E$ n = 1 ; R = *p*-methoxyphenyl | 7 d | (traces) | (-) | (40) |

[a] The reactions were performed at rt in toluene/$CH_2Cl_2$ (1/1) at 0.1 M in $1_A$-$1_E$ ; MCPBA (2.5 eq) ; PTSA (1.0 eq). [b] Isolated products, after purification by flash-chromatography.

Variation of the aromatic substituent in ketals $1_C$-$1_E$ suggests that the yield of ketolactone $4_C$-$4_E$ (~ 40%) is almost unaffected by increasing electron density in the cyclopropane. When ketals $1_C$-$1_E$ were treated for several days with an excess of MCPBA or with MCPBA in the presence of $NaHCO_3$, they were recovered in 70% yield and ketones $2_C$-$2_E$ were isolated (5 – 10%). No lactones $3_C$-$3_E$ or $4_C$-$4_E$ were then detected. We have to point out that treatment of ketones $2_C$-$2_E$ with MCPBA and PTSA led only to degradation. Treatment of lactone $3_D$ with MCPBA (1.2 eq) and PTSA (1.0 eq) (7 days) furnished ketolactone $4_D$ (40%). When lactone $3_D$ was treated either with MCPBA alone or with PTSA alone, only traces of ketolactone $4_D$ were detected (~ 4 %) and the starting lactone was recovered. Therefore, it appears that the transformation of ketals $1_C$-$1_E$ to ketolactones $4_C$-$4_E$ implies the protonation of the ketal by PTSA. (Scheme)



By applying a simple procedure, 5-(aryl)-1,4',5'-trimethylspiro[bicyclo[3.1.0]hexane-2,2'-[1,3]dioxolanes] can thus be transformed easily into γ-disubstituted γ-lactones (aryl, acetonyl) in moderate yields.

## References and notes

1. Sugimura, T.; Fujiwara, Y.; Tai, A. *Tetrahedron Lett.* **1997**, *38*, 6019-6022 and references therein.
2. Compounds of type **1** were prepared by treatment of the corresponding ketone with (±)-2,3-butanediol.
3. Commercially available from ACROS (70-75%).
4. The presence of lactone $4_B$ was not detected in the crude reaction mixture by GC/MS or in the $^1H$ NMR spectra.