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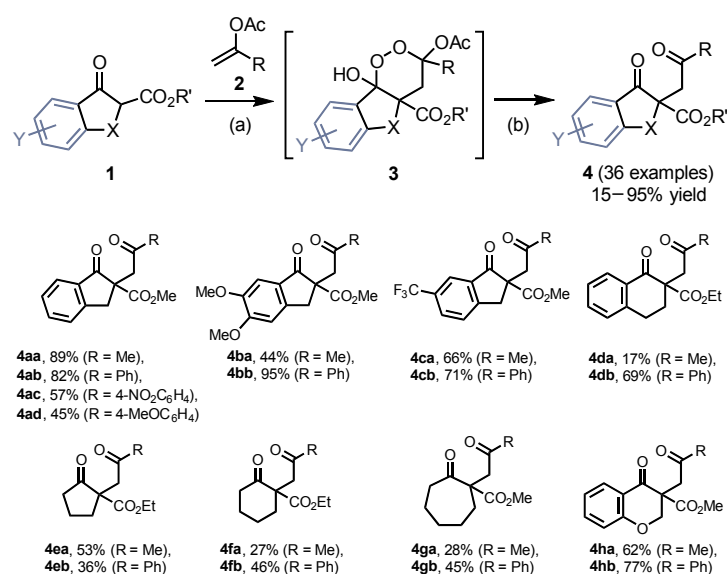
β -Oxo esters and enol acetates are coupled in a cerium-catalyzed, oxidative Umpolung reaction to furnish 1,4-diketones. Using α -aryl vinyl acetates the reaction is followed by a Baeyer-Villiger type rearrangement to provide lactones. Atmospheric oxygen is the oxidant in this process, which can be regarded as optimal from economic and ecological points of view. Further advantages of this new C–C coupling reaction are its operational simplicity and the application of nontoxic and inexpensive $\text{CeCl}_3 \cdot 7 \text{H}_2\text{O}$ as precatalyst.

Introduction

The δ -lactone unit is a widely spread structural motif in natural products and pharmaceutically active compounds, while 1,4-diketones are very attractive starting materials for the preparation of furan, thiophene and pyrrole derivatives. Commonly, the synthesis of 1,4-diketones requires an Umpolung strategy, for instance, the conjugated addition of acyl-anion equivalents to α,β -unsaturated ketones catalyzed by *N*-heterocyclic carbenes (Stetter reaction). On the other hand, the most powerful method to access δ -lactone derivatives is the Baeyer-Villiger oxidation of a cyclopentanone derivative, which is classically achieved by peroxyacetic acids. We present herein a new, cerium-catalyzed, oxidative Umpolung reaction to furnish 1,4-diketones and lactones.

Preparation of 1,4-Diketones^[1]

For the conversion of β -oxo esters **1** with enol acetates **2** and molecular oxygen (air) first suitable reaction parameters were identified: The use of 2,2,2-trifluoroethanol (TFE) as solvent and 2.5 mol% of the precatalyst $\text{CeCl}_3 \cdot 7 \text{H}_2\text{O}$ at 50°C gave complete conversion. The reaction proceeded *via* the 1,2-dioxane derivative **3** as intermediate product, which possesses two acetal functions (Scheme 1), so that acid-catalyzed hydrolysis upon workup was sufficient to achieve the 1,4-diketones **4**. The yields for benzoannulated oxo esters ranged from good to excellent (up to 95%), while monocyclic oxo esters gave lower yields (up to 53%).



Scheme 1. Synthesis of 1,4-diketones **4**. (a) 1.3–5.0 equiv. **2**, O_2 (air), 2.5 mol% $\text{CeCl}_3 \cdot 7 \text{H}_2\text{O}$, TFE, 50°C, 18 h; (b) acidic workup.

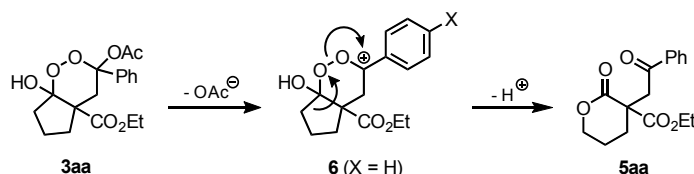
Preparation of δ -Lactones^[2]

In addition to the 1,4-diketones **4xy** the formation of δ -lactones **5xy** was observed when cyclopentanone-2-carboxylates **1x** were converted with α -aryl vinyl acetates **2y** under oxidative conditions (Table 1). Optimal results were obtained by lowering the amount of precatalyst (1 mol%) as well as the temperature (30°C). The δ -lactones **5xy** held a 1,4-dicarbonyl constitution and have a quaternary carbon center in their 2-position. The yields ranged from 74% with a donor substituted aromatic residue at enol ester **2c** (product **5bc**) to 38% with an electron deficient enol ester **2e** (product **5ae**); with a nitrophenyl-ring, the yields broke down (7% of product **5af**).

Table 1. Results for different oxo esters **1x** and enol acetates **2y**.

| Entry | 1x (n, R') | 2y (R) | Yields | |
|-------|----------------------------|---|------------|------------|
| | | | 4xy | 5xy |
| 1 | 1a (1, Et) | 2a (Ph) | 21% | 59% |
| 2 | 1a (1, Et) | 2b (4- BrC_6H_4) | 19% | 44% |
| 3 | 1a (1, Et) | 2c (4- MeOC_6H_4) | 15% | 66% |
| 4 | 1a (1, Et) | 2d [3,5-(CF_3) $_2\text{C}_6\text{H}_3$] | 21% | 47% |
| 5 | 1a (1, Et) | 2e (2,4- $\text{F}_2\text{C}_6\text{H}_3$) | 22% | 38% |
| 6 | 1a (1, Et) | 2f (4- $\text{NO}_2\text{C}_6\text{H}_4$) | 2% | 7% |
| 7 | 1a (1, Et) | 2g (2-thienyl) | 18% | 55% |
| 8 | 1a (1, Et) | 2h (2-furyl) | 20% | 55% |
| 9 | 1a (1, Et) | 2i (<i>N</i> -Tos-2-pyrrolyl) | 16% | 36% |
| 10 | 1b (1, <i>i</i> Bu) | 2a (Ph) | 29% | 64% |
| 11 | 1b (1, <i>i</i> Bu) | 2c (4- MeOC_6H_4) | 21% | 74% |
| 12 | 1c (2, Et) | 2a (Ph) | 41% | 9% |
| 13 | 1d (3, Me) | 2a (Ph) | 45% | 0% |

As a mechanistic rationale for the formation of a δ -lactone from endoperoxidic intermediate **3aa** we propose the loss of an acetate ion under formation of an oxycarbenium ion **6**. This species could actually decompose in analogy to a Baeyer-Villiger reaction pathway with the primary carbon atom migrating under ring expansion (Scheme 2).



Scheme 2. Mechanistic proposal for the formation of δ -lactones *via* oxycarbenium ion **6**.

[1] I. Geibel, J. Christoffers, *Eur. J. Org. Chem.* **2016**, 918–920.

[2] I. Geibel, A. Dierks, M. Schmidtman, J. Christoffers, *J. Org. Chem.* **2016**, doi: 10.1021/acs.joc.6b01441.