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Oxidation of α,β-unsaturated carbonyl groups with ruthenium (III)-chloride and peracetic acid: a new access to α-oxo-ene-diols

Uwe Beifuss* and Andreas Herde

Institut für Organische Chemie der Georg-August-Universität Göttingen, Tammannstr. 2, D-37077 Göttingen, Germany

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Abstract

A one pot oxidation of cyclic unsaturated carbonyl and carboxylic compounds with ruthenium (III)-chloride and peracetic acid to the corresponding α-oxo-ene-diols (aci-reductones) has been developed.

Keywords: Oxidation; Ruthenium and compounds; Enols and derivatives.

Currently there is great interest in the development of lipophilic antioxidants in medicinal chemistry as active oxygen species play an important role in the development or exacerbation of various kinds of diseases [1]. In addition, new lipophilic antioxidants are needed for food protection and several technical applications [2]. Ascorbic acid is a well known natural antioxidant, and it is the 1-oxo-2-ene-2,3-diol (aci-reductone) structure element [3-5] which is responsible for its antioxidative effect [6]. Due to its strongly hydrophilic properties, ascorbic acid cannot be used as an antioxidant in lipophilic environment, though. This is why we set out to develop antioxidants with better lipophilic properties than ascorbic acid itself.

To study the antioxidative effect of the aci-reductone moiety as a function of the overall structure we were looking for a short and reliable method for the preparation of 1-oxo-2-ene-2,3-diols. For the synthesis of aci-reductones only a few general methods have been available so far, most of them requiring several steps [3-5]. One of the most useful procedures for the preparation of cyclic aci-reductones is based on the thermolysis of the corresponding 2-diazo-1,3-diketones, which in turn can be obtained from the parent 1,3-diketones [7].

It is known that α-hydroxy ketones with a α′-C=O-group are in equilibrium with the corresponding α-oxo-ene-diol [3-5]. This is why it should be possible to reduce the question of access to aci-reductones to the synthesis of α-hydroxy ketones with a α′-C=O-group [8].

Oxidation of cyclic α,β-unsaturated ketones like **1a-e** as well as the transformation of *N-n*-butylmaleimide **1f** with ruthenium (III)-chloride and peracetic acid led to the corresponding aci-reductones in yields between 45-58 % (Table). The carbocyclic products **2a-e** exclusively exist as their 1-oxo-2-ene-2,3-diol tautomers, while the oxidation product of **1f** is present as a

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mixture of **2f** and the corresponding 1,3-dioxo-2-hydroxy tautomer. The oxidation of the 4-alkyl substituted cyclohex-2-en-1-ones **1c-e** presents a simple access to lipophilic cyclic aci-reductones. As an example **2d** [1] was formed exclusively upon oxidation of **1d**.

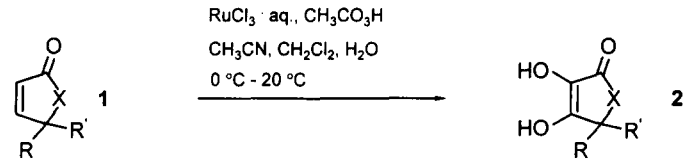

Table
Oxidation of **1** with $RuCl_3$·aq. and peracetic acid.

Entry	Substrate	X	R	R'	$RuCl_3$·aq. [mol %]	Product	Yield **2** [%]
1	**1a**	CH_2	H	H	1.8	**2a**	45
2	**1b**	$(CH_2)_2$	H	H	1.7	**2b**	58
3	**1c**	$(CH_2)_2$	H	$H_3CCH(CH_2)_3CH(CH_3)_2$	6.7	**2c**	50
4	**1d**	$(CH_2)_2$	H	*iso*-propyl	12.9	**2d**	49
5	**1e**	$(CH_2)_2$	H	cyclohexyl	10.3	**2e**	55
6	**1f**	*N*-*n*Bu	= O		3.2	**2f**	48

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[1] Preparation of **2d**: 450 mg (3.25 mmol) **1d** and 104 mg (0.42 mmol) $RuCl_3$ aq. were placed in a flask equipped with a septum and reflux condenser. 2.5 ml CH_3CN, 2.5 ml CH_2Cl_2 and 2.5 ml H_2O were added successively and the stirred reaction mixture was cooled. At 0 °C 2.01 g (10.3 mmol) CH_3CO_3H (39 %) was added dropwise during 40 min. The reaction mixture started boiling and was decolourized. After 15 h at room temp. 15 ml Na_2SO_3-solution (5 %) were added and the reaction mixture was extracted with CH_2Cl_2 (4 × 30 ml). The combined aqueous phases were extracted with Et_2O using a perforator. The combined organic phases were dried (Na_2SO_4) and evaporated in vacuo. Flash chromatography (Et_2O / petroleum ether = 1:2) yielded 276 mg (49 %) **2d**.
^1H NMR (300 MHz, $CDCl_3$): δ = 0.95, 0.97 (d, *J* = 6.5 Hz, 6 H, 2 × CH_3), 1.82 - 2.09 (m, 3H, 1'-H, 5-H_2), 2.12 - 2.22 (m, 1H, 4-H), 2.42 (m_c, 2H, 6-H_2), 5.50 - 6.70 (br, 2 H, 2-OH, 3-OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.71, 20.46 (2 x CH_3), 23.82 (C-5), 30.15 (C-1'), 32.28 (C-6), 51.62 (C-4), 179.50 and 181.53 (C-1, C-2 and C-3).