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Copper- and vanadium-catalyzed asymmetric oxidations

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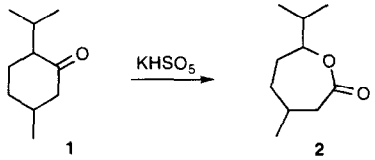
Abstract

Two asymmetric metal-catalyzed oxidations are discussed. Chiral copper complexes catalyze enantiospecific Baeyer–Villiger oxidations giving optically active lactones in up to 95% ee. Vanadium complexes have been used in enantioselective sulfide oxidations with hydrogen peroxide.

Keywords: Baeyer–Villiger oxidation; Asymmetric catalysis; Sulfide oxidation

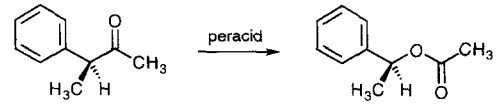
1. Introduction

In 1899 Baeyer and Villiger reported on a new transformation which allowed the synthesis of lactones from the corresponding cyclic ketones by regioselective oxygen insertion into a C–C-bond [1]. Thus, they found that ε-lactone **2** was formed as the major product when menthone (**1**) was treated with Caro's reagent ($KHSO_5$):



1 **2**

In a number of syntheses Baeyer–Villiger oxidations have been used as key-steps giving the desired intermediates with great reliability (for recent reviews, see [2]). The migratory aptitude of various groups adjacent to the carbonyl has been determined [3] and stereochemical and isotopic labeling results revealed that the migration occurs with retention of configuration at the migrating carbon. For example, Mislow and Brenner obtained ester (*S*)-**4** upon treatment of ketone (*S*)-**3** with peracid [4]:



(S)-**3** *(S)*-**4**

Until recently, asymmetric Baeyer–Villiger oxidations using racemic or prochiral ketones for the synthesis of optically active lactones or esters remained a domain of biocatalysis [5]. In 1994, we [6] and others [7] reported on the first enantiospecific *metal-catalyzed* Baeyer–Villiger-type oxidations.

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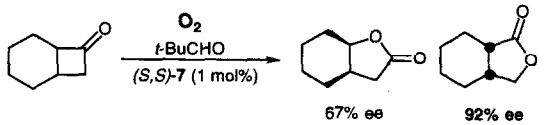
2. Results and discussion

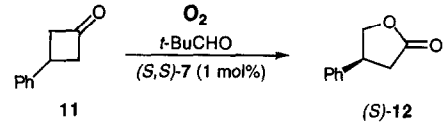
With 1 mol% of copper catalyst (*S,S*)-**7** aerobic oxidation (in the presence of pivaldehyde as coreducing agent) of racemic 2-arylcyclohexanones afforded the corresponding lactones with enantioselectivities of up to 69% ee (Scheme 1) [6].

Oxidation of chiral cyclobutanones such as *rac*-**8** gave optically active butyrolactones [8]. With 1 mol% of (*S,S*)-**7** enantioselectivities of up to 95% ee have been achieved:

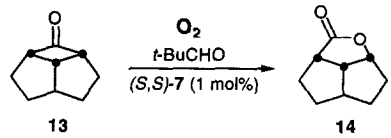


The oxidation proceeded in an enantiodivergent manner and two isomeric lactones were obtained which differed in three major aspects: (1) they resulted from oxygen insertion at either side of the carbonyl group, (2) their enantiomeric excesses were different, and (3) both lactones resulted from enantiomeric ketones. This behavior is reminiscent of the results reported earlier for microbiological transformations [9] (for reviews, see [10]).

In all Baeyer–Villiger-type reactions described above *racemic* ketones were used as starting materials giving optically active lactones via *stereospecific* oxidations. The *stereoselectivity* of the copper catalyst was demonstrated by asymmetric oxidations of *prochiral* cyclobutanones. In our first attempt using **11** as substrate and 1 mol% of (*S,S*)-**7** as catalyst the asymmetric induction remained low and the enantiomeric excess of butyrolactone (*S*)-**12** was only 44% [11]:

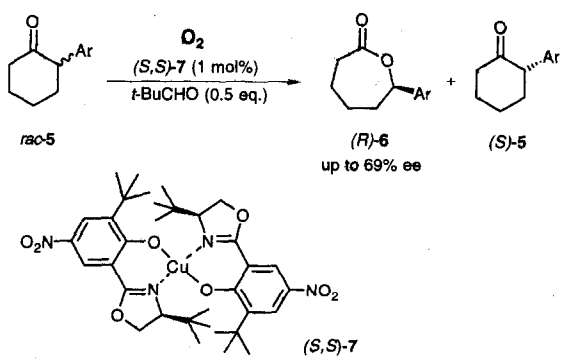


Assuming that a more defined transition state and a higher diastereofacial control in the formation of intermediates would improve the performance of the catalyst we investigated the Baeyer–Villiger oxidation of tricyclic ketone **13**. Previously, **13** had elegantly been used by Kelly et al. in enzymatic Baeyer–Villiger oxidations for mapping of the functional active site of Baeyer–Villigerases [12]. Supporting our model, we found that 1 mol% of (*S,S*)-**7** indeed did catalyze the formation of lactone **14**, now affording the product with 91% ee [11]:



Currently, we are investigating the use of other metal catalysts to improve the enantioselectivity in the asymmetric Baeyer–Villiger oxidation of prochiral cycloalkanones with more general structures.

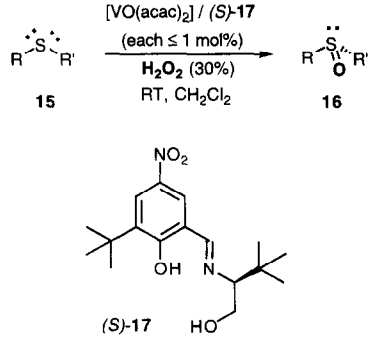
In the copper catalysis described above, dioxygen in combination with pivaldehyde as coreducing agent was used to oxidize the substrate. In a vanadium catalysis hydrogen peroxide could be used as the oxidant. A readily available vanadium complex prepared in-situ from $VO(acac)_2$ and Schiff-bases, such as (*S*)-**17** catalyzes the enantioselective oxidation of sulfides with H_2O_2 ($ee_{max} = 85\%$) (Scheme 2) [13].



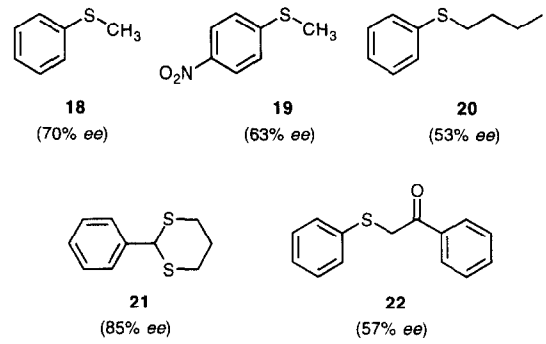
Scheme 1.

This transformation is remarkable for a number of reasons: (1) aqueous hydrogen peroxide is the most efficient oxidizing agent. Other vanadium catalysts, which often use *tert*-butylhydroperoxide as the oxygen source, are inhibited by the presence of water or other donor ligands. (For an excellent study of a related *achiral* vanadium catalyst which uses *tert*-butylhydroperoxide as the oxygen source in epoxidations, see [14].) (2) Compared to other asymmetric sulfide oxidations (reviews: [15]) this vanadium system is very efficient. Even with 0.01 mol% of the catalyst, enantioselective sulfoxide formation is achieved. (3) The reaction condition is unusually simple. The oxidation may be performed in open vessels, since oxygen and water do not affect the outcome. (4) The ligands are readily available from salicylaldehydes and amino alcohols and a number of compounds are known. (5) The reaction is ligand-accelerated [16]. Thus, the enantioselectivity is not or only slightly affected by the presence of achiral vanadium species.

Various sulfides have been oxidized with this chiral vanadium/H_2O_2 catalyst system and the influence of the ligand structure on the enantioselectivity in the sulfoxide formation has been studied. The best results were obtained with ligands derived from *tert*-leucinol. Furthermore, the substituents at C-4 and C-6 of the ligand aryl group have an influence on the asymmetric induction. Aryl alkyl sulfides give the corresponding sulfoxides in 53–70% ee. The highest



Scheme 2.



Scheme 3.

enantioselectivity (85% ee) was observed in the case of thioacetal **21**. Functionalized sulfides such as **22** can also be converted into the corresponding optically active sulfoxides (Scheme 3).

^{51}V-NMR spectroscopic studies of mixtures containing [VO(acac)$_2$], the ligand, and H_2O_2 showed that several species of vanadium with higher oxidation states are formed. Currently, we are investigating which vanadium-containing intermediate is responsible for the reaction behavior and the obtained enantioselectivities.

3. Experimental

3.1. General

Reactions under anhydrous conditions were performed in flame-dried glassware under Ar. The solvents were dried and distilled prior to use. Commercially available reagents were used as received without any further purification. The products were isolated by flash chromatography: ICN (Silitech, 0.032–0.063 mm). Ee-determination was done by HPLC (Merck-Hitachi; UV–VIS detector L-4250; pump L-6200A; integrator D-2500) and GC (Hewlett-Packard Series II 5890; integrator HP 3396), using chiral columns (for details see [11,13]). Optical rotations were measured with a Perkin-Elmer 141 polarimeter. ^{1}H- and ^{13}C-NMR spectroscopy was performed with a Bruker AC-300 or Varian-Gemini-300 spectrometer.

3.2. Asymmetric Baeyer–Villiger oxidation

A solution of the ketone (1 mmol) and the catalyst (10 μmol) in 2.5 ml of water-saturated benzene was treated with pivaldehyde (0.5 mmol) followed by the addition of 100 μl of water. The mixture was stirred under an atmosphere of oxygen for 16–20 h, diluted with 150 ml of diethyl ether, and washed with 50 ml of a saturated aqueous solution of $NaHCO_3$. After drying of the organic phase over Na_2SO_4 the solvent was removed and the crude product was chromatographed on silica gel. The enantiomeric excesses were determined by HPLC and GC [6,11]. In the oxidations of the cyclobutanone derivatives the use of water-saturated benzene resulted in lower chemical yields of lactones. Thus, in these cases dried benzene was used as solvent.

3.3. Asymmetric sulfide oxidation

The ligand (0.015 mmol) and $VO(acac)_2$ (2.6 mg, 0.01 mmol) were dissolved in 2 ml of dichloromethane. After stirring for 5 min the sulfide (1 mmol) was added followed by the dropwise addition of 30% H_2O_2 (1.1 mmol). The mixture was stirred for 16 h at ambient temperature. After separation of the aqueous layer the solvent was removed from the remaining mixture. The crude product was chromatographed on silica gel and — if necessary — purified by Kugelrohr distillation under high vacuum. The enantiomeric excesses were determined by HPLC [13].

Acknowledgements

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References

[1] A. Baeyer and V. Villiger, Ber. 32 (1899) 3625.
[2] G.R. Krow, Org. React. 43 (1993) 251; G.R. Krow, in: Comprehensive Organic Synthesis, B.M. Trost and I. Fleming (Eds.), Vol. 7 (Pergamon, Oxford, 1991) p. 671.
[3] R. Noyori, T. Sato and H. Kobayashi, Bull. Chem. Soc. Jpn. 56 (1983) 2661, and references therein.
[4] K. Mislow and J. Brenner, J. Am. Chem. Soc. 75 (1953) 2318.
[5] S.M. Roberts, N.J. Turner and A.J. Willetts, Chimia 47 (1993) 85; R. Azerad, Bull. Chem. Soc. Ft. 132 (1995) 17; K. Faber, Biotransformations in Organic Chemistry (Springer-Verlag, Heidelberg, 1992); K. Drauz and H. Waldmann (Eds.), Enzyme Catalysis in Organic Synthesis (VCH, Weinheim, 1995).
[6] C. Bolm, G. Schlingloff and K. Weickhardt, Angew. Chem. 106 (1994) 1944; Angew. Chem. Int. Ed. Engl. 33 (1994) 1848; C. Bolm, G. Schlingloff and K. Weickhardt, Tetrahedron Lett. 34 (1993) 3405.
[7] A. Gusso, C. Baccin, F. Pinna and G. Strukul, Organometallics 13 (1994) 3442.
[8] C. Bolm and G. Schlingloff, J. Chem. Soc. Chem. Commun. (1995) 1247.
[9] F. Petit and R. Furstoss, Tetrahedron: Asymmetry 4 (1993) 1341; V. Alphand and R. Furstoss, J. Org. Chem. 57 (1992) 1306; S.C. Lemoult, P.F. Richardson and S.M. Roberts, J. Chem. Soc. Perkin Trans. 1 (1995) 89; M.J. Taschner and L. Peddada, J. Chem. Soc. Chem. Commun. (1992) 1384; G. Grogan, S.M. Roberts and A.J. Willetts, J. Chem. Soc. Chem. Commun. (1993) 699; O. Abril, C.C. Ryerson, C. Walsh and G.M. Whitesides, Bioorg. Chem. 17 (1989) 41.
[10] C.T. Walsh and Y.- C.J. Chen, Angew. Chem. 100 (1988) 342; Angew. Chem. Int. Ed. Engl. 27 (1988) 333, and references therein.
[11] G. Schlingloff, Ph.D. thesis, University of Marburg, 1995.
[12] D.R. Kelly, C.J. Knowles, J.G. Mahdi, I.N. Taylor and M.A. Wright, J. Chem. Soc. Chem. Commun. (1995) 729; D.R. Kelly, C.J. Knowles, J.G. Mahdi, M.A. Wright, I.N. Taylor, D.E. Hibbs, M.B. Hursthouse, A.K. Mish'al, S.M. Roberts, P.W.H. Wan, G. Grogan and A.J. Willetts, J. Chem. Soc. Perkin Trans 1 (1995) 2057.
[13] C. Bolm and F. Bienewald, Angew. Chem. 107 (1995) 2883; Angew. Chem. Int. Ed. Engl. 34 (1995) 2640.
[14] H. Mimoun, M. Mignard, P. Brechot and L. Saussine, J. Am. Chem. Soc. 108 (1986) 3711.
[15] H.B. Kagan, in: Catalytic Asymmetric Synthesis, I. Ojima (Ed.) (VCH, New York, Weinheim, 1993) p. 203; H.B. Kagan and F. Rebiére, Synlett (1990) 643.
[16] D.J. Berrisford, C. Bolm and K.B. Sharpless, Angew. Chem. 107 (1995) 1159; Angew. Chem. Int. Ed. Engl. 34 (1995) 1059.