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The Asymmetric Kharasch Reaction. Catalytic Enantioselective Allylic Acyloxylation of Olefins with Chiral Copper(I) Complexes and tert-Butyl Perbenzoate

Merritt B. Andrus*, Ankush B. Argade, Xi Chen, and Michael G. Pamment
Purdue University, Department of Chemistry
1393 H.C. Brown Building, West Lafayette, IN 47907

Abstract: Olefins were treated with *tert*-butyl perbenzoate in the presence of chiral copper(I) triflate bisoxazoline complexes to give non-racemic allyl benzoates as products. The yields range from 34 to 62% and the enantiomeric excesses from 30 to 81%. A model for the selectivity is proposed.

Kharasch reported the allylic oxyacylation of olefins using *t*-butyl perbenzoate and a catalytic amount of copper salt in refluxing benzene.[1] Yields of allyl ester products are generally high and the regioselectivity is 9:1 for the internal secondary ester over the terminal primary isomer. After hydrolysis the process becomes an allyl alcohol synthesis. There are two previous attempts to develop asymmetric versions of the reaction using copper camphorate complexes as catalysts with cyclic olefins and copper salts with amino acids.[2] The selectivities were in general low with cyclohexene being the best at 30% ee determined using optical rotations. When compared to known methods such as enone reductions[3] and divinyl zinc addition to aldehydes,[4] allylic acyloxylation holds great potential as a non-racemic allyl alcohol synthesis and would nicely compliment other asymmetric olefin reactions, epoxidation[5] and dihydroxylation.[6]

The mechanism involves reductive homolysis of the perester oxygen-oxygen bond by copper(I) to give copper(II) benzoate and *t*-butoxy radical (fig. 1).[7] The *t*-butoxy radical abstracts an allylic hydrogen atom to give *t*-butanol and an allylic radical.[8] The next step is rapid addition of copper(II) to the allyl radical to generate copper(III) benzoate with the bound allyl fragment.[9] The geometry of the olefin is maintained by the allyl radical with internal olefins due to the high barrier to rotation (~20 kcal/mol).[10] The final step of the chain mechanism is rearrangement of the copper(III) intermediate to give the allylester product and the regenerated copper(I) catalyst. The final step accounts for the regiochemistry of the product. The

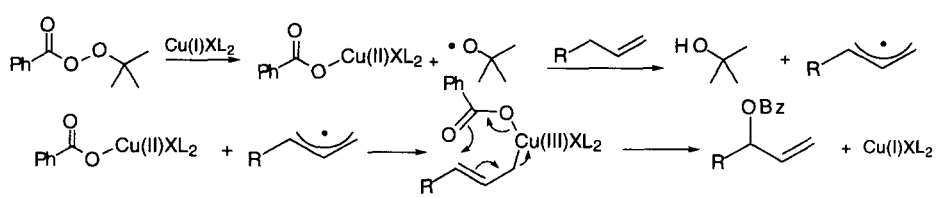
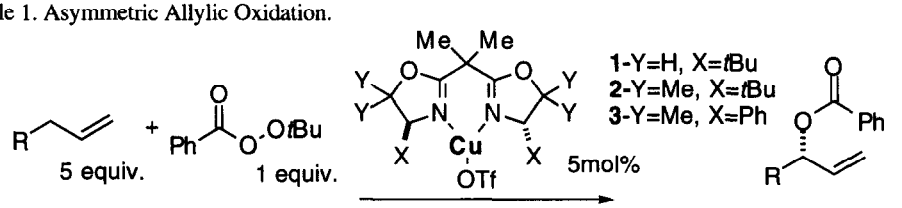
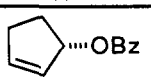
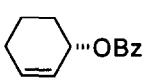
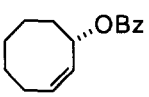
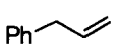
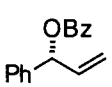
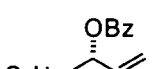


Figure 1. Mechanism of Allylic Olefin Oxidation With Cu(I) and Perester.

copper(II) intermediate attacks the allyl radical at the least hindered terminal position. Rearrangement then delivers the benzoate to the internal secondary position.[11] The potential for asymmetric synthesis depends on the use of a ligand (L) that can coordinate copper(III) and induce the asymmetric formation of the allyl benzoate product. Recently the use of bisoxazoline copper catalysts[12] for catalytic asymmetric cyclopropanation[13] and aziridination[14] have been reported with high selectivities. A catalytic cycle involving copper adding a stoichiometric reagent, increasing its oxidation state, and reacting with an olefin inspired our efforts to apply complexes of this type to the Kharasch reaction. The results are shown below in Table 1.

Table 1. Asymmetric Allylic Oxidation.



Entry[a]	Olefin	Product[b]	Catalyst	Solvent	Temp.[c]	%Yield[b]	%ee[d]
							
2	"	"	**1**	CH_3CN	-20°	44	70
3	"	"	**2**	"	-20°	41	42
4	"	"	**3**	"	-20°	49	**81**
							
5			**1**	CH_3CN	5°	62	67
6	"	"	**1**	"	-20°	43	**80**
7	"	"	**2**	"	-20°	49	67
8	"	"	**3**	"	5°	59	46
9	"	"	**3**	"	-20°	44	47
							
10			**1**	CH_3CN	-20°	44	13
11	"	"	**2**	"	-20°	43	0
							
12			**1**	PhH	55°	34	36
13	"	"	**1**	CH_3CN	5°	50	0
							
14			**1**	PhH	55°	50	30
15	"	"	**1**	CH_3CN	5°	13	0

[a] 0.5 mmol scale. [b] ^1H and ^{13}C NMR characterization. Isolated yields based on perester. [c] 5° C was maintained by a refrigerator. The freezer used for -20° C. [d] integration of ^1H NMR(500 MHz) signal for *o*-protons of the benzoate with chiral shift reagent Eu(hfc)$_3$ and compared to spectra of the racemic compound.

The reactions were performed by slowly adding one equivalent of *tert*-butyl perbenzoate, using a polypropylene tube, to a glass vial containing a degassed (N_2) acetonitrile (2 mL, benzene entries 12,14) solution at 0 °C (RT for 12,14) with five equivalents of olefin (0.5 mmol) and five mol% of copper(I) triflate-bisoxazoline. The reaction was allowed to proceed with stirring for five days (2 days 12,14) at the indicated temperature. The allyl benzoate products were isolated by silica gel chromatography and the selectivities were determined by ^{1}H NMR using Eu(hfc)$_3$ chiral shift reagent. Acetonitrile, acetic acid mixtures were used as solvent for the reaction, according to Kochi,[7] and finally acetonitrile alone was found to be the superior solvent for the reaction at lower temperatures. Selectivity for cyclopentene[15] was best, at 81% ee (enantiomeric excess, 90.5:9.5 ratio) using catalyst **3** that contains the gem-dimethyloxazolines.[16] The ligand from catalyst **3** can be recovered from the reaction mixture and recycled. With cyclohexene the highest selectivity 80% ee was obtained using **1** as catalyst.[17] In this case the gem-dimethyls and phenyl in place of *tert*-butyl on the ligand erode the selectivity (**1** vs **3**). Similar results have been recently observed by Pfaltz with cyclohexene and cyclopentene using catalyst **1**.[18] The bisoxazoline ligand from **1** has not been recovered from the reactions due to apparent decomposition. The gem-dimethyl ligands (**2** and **3**) were investigated to avoid oxidation α-to oxygen on the ligand and improve catalyst stability. Cyclooctene reacts at a much slower rate and with lower selectivities. Acyclic olefins have been found to react with good yields in acetonitrile at low temperatures, but low selectivities (entries 12-15). Surprisingly, at higher temperatures in benzene the selectivities are raised to 36 and 30% ee for allylbenzene and 1-octene.[19] Cyclohexene at 55 °C in benzene gave a 82% yield in one day but in only 16% ee. The ligands in all cases were derived from (*S*)-amino acids and the indicated isomers were obtained as the major enantiomers, (*S*)- for cyclopentene, cyclohexene, and 1-octene and (*R*) for allylbenzene.

A model is proposed to account for the stereoinduction in figure 2. The favored transitions states are depicted with the allyl and benzoate ligands positioned to minimize interaction with the flanking *tert*-butyl groups the bisoxazoline ligand. The copper (III) intermediate will adopt a distorted square

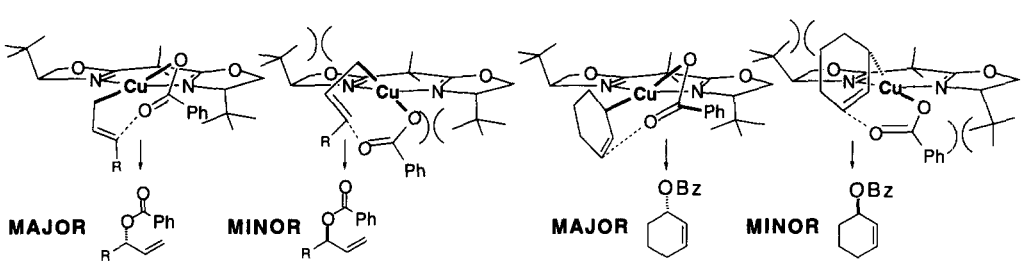


Figure 2. Selectivity Model.

geometry placing the allyl and benzoate groups above or below the plane of copper-bisoxazoline ring. The rearrangement then delivers the benzoate to the internal position of the acyclic olefin or the distal position of the cyclic olefin. With cyclic olefins the initial attack of copper(II) on the allyl radical can initially produce two diastereomeric allyl adducts. The selectivity of the reaction then arises from a preferred pathway for allyl radical attack or equilibration of the intermediate copper (III)-allyl adducts prior to rearrangement leading to

product. The lower selectivities for the acyclic olefins can be accounted for by the model in that an extra degree of freedom is present allowing for rotation and attack on the opposite olefin face.

While the yields reported here are low, being based on the perester, the initial goal of finding a selective catalyst for the reaction has been met. Efforts are in progress to increase catalyst turnover numbers, reactivity, and extend the reaction to other useful substrates.

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References

1. Kharasch, M. S.; Sosnovsky, G.; Yang, N. C. *J. Am. Chem. Soc.* **1959**, *81*, 5819.
2. Denney, D.B.; Napier, R.; Cammarata, A. *J. Org. Chem.* **1965**, *30*, 3151-3153. Muzart, J. *J. Mol. Catal.* **1991**, *64*, 381-384.
3. Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551-5553. Corey, E. J.; Link, J. O. *Tetrahedron Lett.* **1989**, *30*, 6275-6278.
4. Oppolzer, W.; Radinov, R.N. *Tetrahedron Lett.* **1988**, *29*, 5645-5648.
5. Hoft, E. *Top. Curr. Chem.* **1993**, *164*, 63-77.
6. Kolb, H.C.; Andersson, P.G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1994**, *116*, 1278-1291.
7. Kochi, J. K. *J. Am. Chem. Soc.* **1962**, *84*, 774. Kochi, J. K.; Bemis, A. *Tetrahedron* **1968**, *24*, 5099.
8. Walling, C.; Zavitsas, A. A. *J. Am. Chem. Soc.* **1963**, *85*, 2084-2090. Walling, C; Thaler, W. *J. Am. Chem. Soc.* **1961**, *83*, 3877. Walling, C. In "Free Radicals in Solution" J. Wiley and Sons, 1957, New York. Small, R. D.; Scaiano, J. C.; Patterson, L.K. *Photochem. Photobiol.* **1979**, *29*, 49.
9. Kochi, J. K.; Subramanian, R. V. J. *J. Am. Chem. Soc.* **1965**, *87*, 4866.
10. Beckwith, A. L. J.; Zavitsas, A. A. *J. Am. Chem. Soc.* **1986**, *108*, 8230-8234. Kochi, J. K.; Krusic, P. J. *J. Am. Chem. Soc.* **1968**, *90*, 7157-7159. Bennett, J. E.; Brown, D. M.; Mile, B. *Trans. Faraday Soc.* **1970**, *66*, 386-397.
11. Walling, C.; Thaler, W. *J. Am. Chem. Soc.* **1961**, *83*, 3877.
12. The aminoacid was reduced with $NaBH_4$ and I_2, acylated with dimethylmalonyl chloride, then converted to the dichloride with $SOCl_2$, and cyclization with NaOMe. The bisoxazoline was then complexed with $CuOTf{\bullet}PhH_{1/2}$
13. Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726-728. Lowenthal, R. E.; Masamune,S. *Tetrahedron Lett.* **1991**, *32*, 7373-7376. Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339-345.
14. Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742-2753.
15. (*S*)-1-cyclopenten-1-ol obtained from hydrolysis (NaOH) $[\alpha]_D$ -101.2° ($CHCl_3$, c 0.23), lit.: $[\alpha]_D$ -105.8° Toshio, S.; Goto, Y.; Wakabayashi, Y.; Fujisawa, T. *Tetrahedron Lett.* **1983**, *24*, 4123-4126.
16. Corey, E. J.; Ishihara, K. *Tetrahedron Lett.* **1992**, *33*, 6807-6810. The N-BOC amino acid was converted to the methyl ester, reacted with excess methyl magnesium bromide, then TMSOTf and lutidine to remove the BOC group. Treatment with dimethylmalonylchloride followed by cyclization using CaH_2 under Dean-Stark conditions gave the bis(gem-dimethylbisaxazoline).
17. (*S*)-1-cyclohexen-1-ol obtained from hydrolysis (NaOH) $[\alpha]_D$ -88.8° ($CHCl_3$, c 0.198), lit.: $[\alpha]_D$ -112° ref.15.
18. Pfaltz, A. (U. of Basel) cyclic olefins in the 60 to 80% ee range, personal communication. *Tetrahedron Lett.* (submitted)
19. (*R*)-1-phenyl-1-hydroxy-2-propene from hydrolysis (NaOH) $[\alpha]_D$ +4.28° ($CHCl_3$, c 0.187), lit.: $[\alpha]_D$ +3.0° ($CHCl_3$, c 5.17) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129-6139.

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