Catalytic Epoxidation of Enones Mediated by Zinc Alkylperoxide/tert-BuOOH Systems

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ABSTRACT: The epoxidation of enones by zinc alkylperoxides is a challenging task receiving considerable attention in contemporary research; however, until now no well-defined zinc alkylperoxide based systems have been described. Here, a new catalytic method of epoxidation of enones in the presence of zinc alkylperoxides supported by N,N-bidentate ligands and tert-butyl hydroperoxide is reported. A new dimeric zinc alkylperoxide complex supported by an aminotropinominimidate ligand is also presented. The studied catalytic systems show high activity in the epoxidation of trans-chalcone, and in the case of a chiral catalyst with the (S,S)-N,N′-bis(1-phenylethyl)aminotropinominimidate ligand a moderate enantioselectivity was achieved.

O ver the last two decades, numerous efforts have been devoted to the development of efficient catalysts for the asymmetric epoxidation of electron-deficient olefins. A number of catalytic systems, including chiral metal complexes and organocatalysts, have been successfully established. In light of the increasing demand for green and sustainable chemistry, the development of environmentally friendly metal-based catalysts with considerable activity is highly desirable. In this regard, zinc complexes seem very promising reagents for this process. Nevertheless, the epoxidation of α,β-unsaturated ketones mediated by zinc complexes remains an underdeveloped field and only a few examples have been reported until now. In these works alkylperoxide zinc compounds acted as efficient epoxidizing reagents. Initially, Yamamoto and co-workers used R₂Zn/O₂ systems as the stoichiometric oxidant for the epoxidation of α,β-unsaturated ketones. In 1996, the first approach of the enantioselective epoxidation of enone derivatives that was based on stoichiometric quantities of diethylzinc and a chiral alcohol in the presence of dioxygen was reported.† Then Pu and co-workers reported the use of a chiral polyvinaphthyl in similar stoichiometric reactions as well as the development of a catalytic variant mediated by zinc species. In this catalytic process, oxygen was replaced as the oxidant by tert-butyl hydroperoxide (TBHP). It is worth stressing that all of the mentioned reaction systems were conducted without the use of well-defined zinc reagents, which were generated in situ. We have been systematically exploring the chemistry of well-defined organozinc complexes with a view toward the study of fundamental transformations involving dioxygen. In the course of these investigations we isolated and structurally characterized the first examples of zinc alkylperoxides. The resulting zinc alkylperoxide complex stabilized by a β-diketimine, [{EtOO}Zn(BDI)]₂ (1), showed very high activity in the epoxidation of enones in stoichiometric reactions. We envisioned that zinc alkylperoxides supported by unsaturated N,N-bidentate ligands might serve as platforms for a catalytic version of this reaction. The proof of this concept is reported herein. A number of examples demonstrate well that the structure and reactivity of RZn(N,N′)-type complexes depend on the identity of the N,N-bidentate ligands. In particular, supporting ligands play a crucial role in oxygenation processes. For the current study a β-diketiminate ligand and achiral and chiral aminotropinominimidate ligands were selected: N,N′-pent-2-en-2-yl-4-ylidenobis(2,6-disopropylamine)-bis(diketimine) (BDI), N-isopropyl-2-[(isopropylamino)tritropinominate (ATI-1), and (S,S)-N,N′-di-(1-phenylethyl)-aminotropinominimidate (ATI-2), which are capable of providing a range of electronic and steric environments (Scheme 1a). The desired zinc tert-butylperoxide complexes were synthesized in a two-step procedure according to Scheme 1b.

The syntheses and characterization of compound 1 have been reported elsewhere. The zinc alkylperoxides stabilized with ATI-1 and ATI-2 were prepared using a similar two-step synthetic procedure involving equimolar amounts of t-Bu₂Zn in toluene and the selected aminotropinominimidate proligand, followed by the addition of dioxygen at −20 °C.

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In the next step the resulting zinc alkylperoxides 1–3 were tested with respect to their catalytic activity in the epoxidation of enones with TBHP as an oxidant. trans-Chalcone was chosen as a model substrate for epoxidation, as it is a commonly used compound in similar reactions.2–5 Chalcone was dissolved in toluene under a nitrogen atmosphere, and then a tert-BuOOH/toluene solution and the corresponding catalyst were added at 0 °C and the reaction was conducted further at this temperature (Scheme 2). The conversion to epoxide was monitored by gas chromatography. The results are presented in Table 1. All of the tested catalytic systems involving zinc alkylperoxides in combination with TBHP allowed full conversion of trans-chalcone to 2-benzoyl-3-phenyloxirane within no more than 8 h at 0 °C.10 The most active proved to be compound 1, as it allowed 96% conversion after 3 h. The chiral catalyst 3 gave a similar result of 98% conversion after 4 h with 29% ee (the 2S,3R enantiomer was obtained).

Lowering the reaction temperature for 3 to −20 °C did not lead to an improvement of enantiomeric excess; in fact, both the conversion and ee after 24 h were decreased to only 20% and 17%, respectively. Strikingly, the lowest activity at 0 °C among the tested zinc alkylperoxides was exhibited by 2, as the reaction reached full conversion only after 8 h. The obtained reaction times for epoxidation of trans-chalcone place the investigated systems among the most active known catalysts for epoxidation of enones.2,4,11

It seems reasonable that the proposed catalytic reaction proceeds according to the mechanism shown in Scheme 3. The monomer–dimer equilibrium present in the solution of zinc tert-butyperoxide allows the coordination of the enone to the metal center of the monomeric complex, which is followed by epoxidation of the enone by the alkylperoxide moiety and formation of zinc tert-butoxide. The cycle is completed by oxidation of alkoxide to peroxide by TBHP. The comparison of reaction times needed to reach full conversion in each system allows conclusions to be drawn concerning the relative activities of the test systems. Catalytic systems involving compounds 1 and 3 as catalysts showed similar, high activity in the epoxidation of trans-chalcone. This observation indicates that the supporting ligand backbone does not essentially affect the catalytic activity of zinc alkylperoxides. Remarkably, compound 2 showed much lower activity. This differentiation of activity...
may be caused by noncovalent interactions between the supporting ligand and trans-chalcone. The presence of N-bonded benzylic phenyl rings in the AT2 ligand is likely to facilitate π–π interactions with phenyl rings of trans-chalcone, which may extend the time of contact between the catalyst active site and the substrate. Such interaction is not possible in the case of the AT1 ligand, which lacks phenyl rings. The low enantioslectivity of the 3/TBHP system may be caused by its high activity; it is, however, a promising result for future investigations on catalytic systems for epoxidation of enones.

In conclusion, we have described the first catalytic system based on well-defined zinc alkylperoxides supported by unsaturated N,N-bidentate ligands and tert-butyl hydroperoxide as the oxidant. The studied system shows higher activity than any organozinc-based system reported in the literature so far. Currently, a more detailed study is being undertaken to extend the present system to other metal alkylperoxides as well as to different chiral auxiliary N,N-ligands to improve the enantioselectivity.

**ASSOCIATED CONTENT**

2 Supporting Information

Text, figures, tables, and a CIF file giving synthetic procedures, characterization data, and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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**REFERENCES**


(10) In the control reaction of trans-chalcone and TBHP in the absence of catalyst unchanged substrate was recovered after 24 h.