

Nanocrystalline zinc peroxide mediated unprecedented nitrene transfer: an expeditious access to *N*-tosylaziridines†

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An unprecedented zinc peroxide (ZnO_2) assisted synthetic strategy is reported for the synthesis of *N*-tosylaziridines from alkenes by using *N*-tosyliminotriphenylphosphorane ($\text{Ph}_3\text{P}=\text{NTs}$) as a nitrene transfer reagent under mild reaction conditions. The reaction of zinc peroxide with $\text{Ph}_3\text{P}=\text{NTs}$ yielded a zinc oxaziridine intermediate which subsequently reacts with alkenes to give corresponding *N*-tosylaziridines in high to excellent yields.

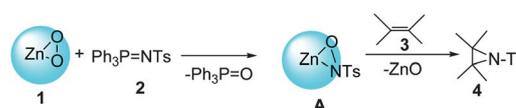
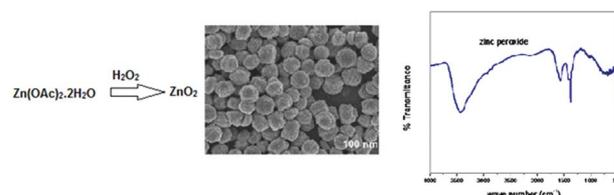
Aziridines are immensely important synthetic intermediates that are widely used as chiral auxiliaries or ligands in asymmetric synthesis, and are also present as important structural motifs in many biologically and pharmaceutically interesting compounds.¹ Among the known synthetic strategies, transition metal complex mediated aziridination of alkenes with a nitrene source is considered to be the most promising approach for the construction of the aziridine ring.² In this regard, [*N*-(*p*-toluenesulfonyl)imino]phenyl iodine ($\text{PhI}=\text{NTs}$) has been extensively used as a nitrene precursor for metal catalyzed aziridination of alkenes.³ Alternative nitrene sources such as *N*-halo-sulfonamides,⁴ organic azides⁵ have also been developed for this transformation. Several transition metal based catalysts including copper,⁶ ruthenium,⁷ cobalt,⁸ iron,⁹ manganese,¹⁰ gold,¹¹ rhenium¹² and silver¹³ have been used to catalyze aziridination of alkenes with these nitrene precursors.

Nowadays, there has been a growing interest in developing nanosized materials which often have novel physical and chemical properties differing from those of the corresponding bulk materials and therefore open up new avenues for their wide applications.¹⁴ Inorganic nanoperoxide materials such as ZnO_2 , CaO_2 and MgO_2 have gained considerable interest as they possess fascinating capabilities for oxygen storage, delivery, and generation when they are hydrolyzed or pyrolyzed in aqueous or

hot environment. We presumed that, analogous to the oxidation reaction, it should be possible to transfer the active oxygen of ZnO_2 to $\text{Ph}_3\text{P}=\text{NTs}$ to give corresponding zinc oxaziridine intermediate along with the liberation of triphenylphosphine oxide (**A**; Scheme 1). Accordingly, we planned this work and report herein an expeditious noncatalytic synthesis of *N*-tosylaziridines in the presence of nanocrystalline zinc peroxide, as synthesized by following the procedure given in this paper, directly from olefins with $\text{Ph}_3\text{P}=\text{NTs}$ as a nitrene source (Scheme 1).‡

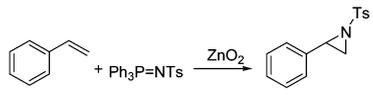
During the present investigation, nanocrystalline zinc peroxide **1** was successfully synthesized *via* hydrothermal methods (see ESI†) by using zinc acetate and hydrogen peroxide as oxidant (Scheme 2).¹⁵ The as synthesized nanocrystalline zinc peroxide powder was washed thoroughly with distilled water, methanol and dried under vacuum for 3 days at 60 °C. The synthesized nanocrystalline zinc peroxide was characterized by several techniques including FTIR, XRD, SEM and XPS. The detailed synthesis and characterization of **1** is given in the ESI.†

Further the desired *N*-tosyliminotriphenylphosphorane was synthesized by the reaction of *N*-tosyliminophenyl iodine

Scheme 1 ZnO_2 -assisted nitrene transfer.Scheme 2 Synthesis of nanocrystalline ZnO_2 **1**.

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Table 1 Optimization of reaction parameters^a


Entry	Temp. (°C)	Solvent	Yield ^b (%)
1	r.t.	CH ₃ CN	15
2	50	CH ₃ CN	85
3	65	CH ₃ CN	91
4	80	CH ₃ CN	80
5	65	ClCH ₂ CH ₂ Cl	54
6	65	EtOAc	62

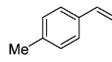
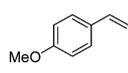
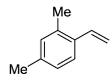
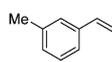
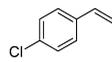
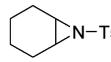
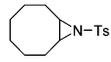
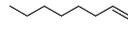
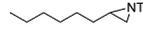
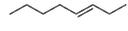
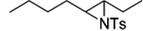
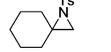
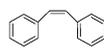
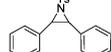
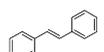
^a Reaction conditions: styrene (1.0 mmol), ZnO₂ (1.2 mmol), Ph₃P=NTs (1.2 mmol), solvent (5 mL) under nitrogen atmosphere for 12 h.
^b Isolated yields.

(PhI=NTs) and triphenylphosphine as following the literature procedure.¹⁶

As per the planned objective, at first we performed the reaction between Ph₃P=NTs (1.2 eq.), styrene (1 eq.) and as synthesized ZnO₂ (1.2 eq.) in acetonitrile at 65 °C for 12 h under nitrogen atmosphere. The progress of the reaction was monitored by TLC (SiO₂). After completion, the precipitated ZnO was separated by filtration and the resulting filtrate was subjected to usual work-up to give corresponding *N*-tosylaziridine in 92% yield. In order to find out the best reaction conditions, we have investigated the effect of reaction parameters such solvent and temperature on the product yield. The results of these experiments are summarized in Table 1. As shown, the reaction was found to be very slow at room temperature and afforded poor yield of expected product after 12 h of reaction (Table 1, entry 1). The reaction was found to increase with increasing the temperature and 65 °C was found to be optimum for this transformation. Further investigation on the effect of solvent, acetonitrile was found to be a solvent of choice whereas the use of dichloroethane and ethyl acetate as solvent provided the moderate yield of the desired product as 54% and 62% respectively (Table 1, entry 5 and 6).

After optimizing the reaction conditions, the reaction was extended to a variety of olefins and the results of these experiments are summarized in Table 2. Initially we studied the aziridination of various styrenes under described experimental conditions. As shown in Table 2, various styrenes bearing functional groups either electron donating or electron withdrawing reacted smoothly and efficiently to give the corresponding aziridine in high yields. In addition, both acyclic and cyclic aliphatic alkenes such as cyclohexene, cyclooctene, 1-hexene and 3-hexene could be successfully aziridinated under the described reaction conditions (Table 2, entry 8–11). The aziridination of *cis*- and *trans*-2-hexene yielded corresponding *cis*- and *trans*-aziridines exclusively (Table 1, entry 12 and 13), confirming the stereospecificity as well as concerted addition of the intermediate nitrene to the alkene. Other alkenes such as methylenecyclohexane, *cis*- *trans*-stilbene, α -methyl styrene

Table 2 ZnO₂-assisted aziridination of alkenes using Ph₃P=NTs as nitrene precursor^a

Entry	Substrate	Product	Yield ^b (%)
1			92
2			93
3			92
4			89
5			90
6			82
8			86
9			75
10			62
11			58
12			62 ^c
13			65 ^c
14			65
15			87
16			85
17			88

^a Reaction conditions: alkene (1 mmol), Ph₃P=NTs (1.2 mmol), ZnO₂ (1.2 mmol) and dry CH₃CN (5 mL) at 65 °C under nitrogen atmosphere for 12 h. ^b Isolated yields. ^c Stereospecificity determined by ¹H NMR.

could also be successfully aziridinated to afford the desired aziridines in good to moderate yields (Table 2, 14–17).

In a controlled blank experiment, no reaction could take place between styrene and Ph₃P=NTs in the absence of nanocrystalline ZnO₂ under similar reaction conditions (Table 2, entry 1).

The exact mechanism of the reaction remains to be resolved in detail. In analogy to the metal oxo and/or peroxy complex

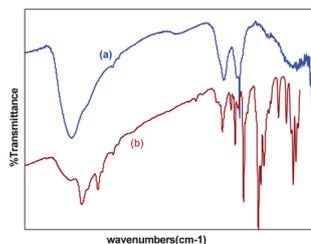


Fig. 1 FTIR spectra of (a) ZnO_2 ; (b) Zn-imido complex.

assisted aziridination of olefins,¹⁷ we assume the transfer of an oxygen from peroxide **1** to **2** which led to the formation of a 3-membered zinc-oxaziridine intermediate **A** and $\text{Ph}_3\text{P}=\text{O}$. This intermediate **A** could then react with olefins to form aziridines as shown in Scheme 1. To confirm the formation of the zinc-oxaziridine intermediate **A**, we have carried out a controlled blank experiment in the absence of alkene. A reaction mixture containing $\text{Ph}_3\text{P}=\text{NTs}$ (1.2 equiv.) and ZnO_2 (1.2 equiv.) was heated in dry acetonitrile at 65 °C for 15 h. On cooling, the precipitated solid was collected by filtration and analyzed by elemental analysis. The values obtained in elemental analysis (found: C, 33.48; H, 2.52; N, 5.52%) matches well with the calcd values for $\text{C}_7\text{H}_7\text{NO}_3\text{SZn}$, verified the formation of intermediate **A** during the reaction. In addition the appearance of characteristic bands of phenyl C–H stretching vibrations at ca. 3063 and 3028 cm^{-1} and sulfonyl ($-\text{SO}_2-$) moieties at 1171 cm^{-1} and 1309 cm^{-1} suggested the formation of expected intermediate **A** (Fig. 1). Furthermore, the exclusive isolation of *trans*- and *cis*-aziridines from *trans*- and *cis*-2-hexene respectively (Table 1, entry 12 and 13) supports the formation of nitrene intermediate and its concerted stereospecific addition to the alkene to give corresponding aziridine.

In conclusion, we have demonstrated a unique nanocrystalline zinc peroxide assisted approach for the non-catalytic direct generation of sulfonyl nitrene from $\text{Ph}_3\text{P}=\text{NTs}$ which was further reacted with alkene to form the corresponding aziridine. The key advantages such as facile synthesis of ZnO_2 , mild reaction conditions and higher product yields make this method as a superior and better alternative of the existing catalytic routes for the aziridination of alkenes.

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Notes and references

† Synthesis of nanocrystalline zinc peroxide: a solution of $\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$ (1 g) in deionized water (50 mL) was added H_2O_2 (5 mL, 30 wt%). The resulting mixture was stirred overnight at room temperature and then separated by filtration. The resulting fine powder was washed thoroughly with deionized water, alcohol to remove unreacted substrate and dried at 60 °C for 3 days to afford nanocrystalline ZnO_2 . The obtained product was fully characterized by several techniques including FTIR, XRD, SEM and XPS. The characterization data of the as synthesized ZnO_2 is given in ESI. General methods for the preparation of aziridines: zinc peroxide (1.2 mmol) was added to the mixture of olefin (1.0 mmol) $\text{Ph}_3\text{P}=\text{NTs}$ (1.2 mmol) in dry acetonitrile (5.0 mL) under nitrogen atmosphere at 65 °C. Progress of the reaction was monitored by TLC. After completion, the reaction mixture was filtered and the resulting organic layer was concentrated under reduced pressure.

The crude product was purified with column chromatography (SiO_2) using ethyl acetate–hexane (1 : 9) as eluent. The selectivity and conversion were determined by high resolution GC-MS analysis; however the identity of the products was confirmed by comparing their physical and spectral data with the known compounds.

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