Enantioselective Aziridination and Amination Using *p*-Toluenesulfonyl Azide in the Presence of Ru(salen)(CO) Complex

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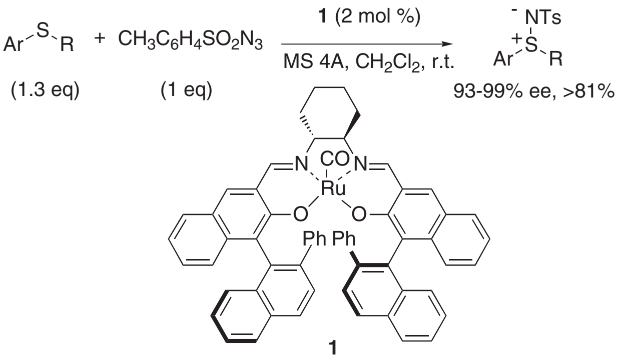
(*R*,*R*)-Ru(salen)(CO) complex (**1**) was found to catalyze enantioselective aziridination of conjugated terminal olefins and allylic C–H amination of conjugated olefins bearing geminal- and/or *trans*-substituent(s) in the presence of *p*-toluenesulfonyl azide.

Nitrene transfer is a fundamental C–N bond formation reaction. It is well known that many metal complexes catalyze the nitrene transfer reaction via a metal nitrenoide intermediate,[1] and much effort has been directed to development of metal-mediated asymmetric nitrene transfer reactions,[2] aziridination and C–H amination. Various chiral metal complexes such as metalloporphyrin,[3] metallosalen[4] [hereafter referred to as M(salen), M=Mn[4a-c] or Ru[4d]], Cu-bis(oxazoline),[5] Cu-bis(Schiff base),[6] Cu-axially chiral Schiff base,[7] and Cu-diamine complexes[8] have been introduced as catalysts for the asymmetric nitrene transfer reaction, and good to high enantioselectivity has been achieved. Most of these reactions use *N*-arylsulfonyliminophenyliodinanes as nitrene precursors, which are, however, not very efficient reagents in terms of atom economy. On the other hand, *N*-arylsulfonyl and *N*-carbamoyl azides are more atom-economic nitrene precursors. Jacobsen et al. reported that *N*-arylsulfonyl azide served as a nitrene precursor for asymmetric aziridination in the presence of copper ion under photo-irradiation, albeit with moderate enantioselectivity.[9] Back and Körber reported sulfimidation using *N-tert*-butoxycarbonyl azide as the precursor in the presence of $FeCl_3$.[10] Recently, we found that Ru(salen)(CO) (**1**) decomposed *N*-arylsulfonyl azides in the presence of various alkyl aryl sulfides to give the corresponding alkyl aryl sulfimides in a highly enantioselective manner, without photo-irradiation (Scheme 1).[11] We also expected that complex **1** would catalyze nitrene transfer reaction to alkenes of high nucleophilicity. Thus, we examined aziridination of conjugated olefins.



Scheme 1.

We first examined aziridination of conjugated terminal olefins (Table 1).[12] The reactions of all the substrates examined proceeded with high enantioselectivity, except that the reaction of 2-phenylbutadiene was very slow (entry 6). However, non-conjugated terminal olefins such as 1-octene underwent neither aziridination nor allylic C–H amination.

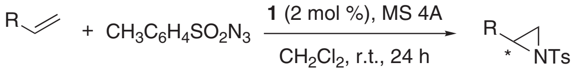


Table 1. Asymmetric aziridination of terminal conjugated olefins with complex **1** as catalyst

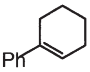
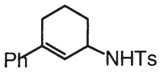
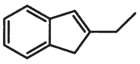
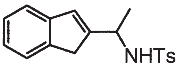
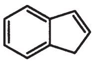
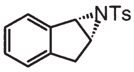
Entry	R	Yield/%[a]	% ee	Confign
1	C_6H_5	71	87[b]	*S*[c]
2	*p*-BrC_6H_4	87	90[d]	—
3	*p*-$O_2NC_6H_4$	98	92[e]	—
4	$C_6H_5C{\equiv}C$	85	95[f]	—
5	2-$C_{10}H_7$	86	87[g]	—
6	$H_2C{=}C(C_6H_5)$	7.3	90[h]	—

[a]Isolated yield. [b]Determined by HPLC using DAICEL CHIRALCEL OJ-H (hexane-*i*-PrOH=1:1). [c]Determined by comparison of the specific optical rotation with the reported value: $[\alpha]_D^{22}$ + 84.0 (*c* 0.63, $CHCl_3$); Lit.[13] $[\alpha]_D$ + 27.4 (*c* 1, $CHCl_3$) for (*S*)-isomer (28% ee). [d]Determined by HPLC using DAICEL CHIRALPAK AS-H (hexane-*i*-PrOH=2:1). [e]Determined by HPLC using DAICEL CHIRALPAK AD-H (hexane-*i*-PrOH=2:1). [f]Determined by HPLC using DAICEL CHIRALPAK AS-H (hexane-*i*-PrOH=7:3). [g]Determined by HPLC using DAICEL CHIRALCEL OF (hexane-*i*-PrOH=2:1). [h]Determined by HPLC using DAICEL CHIRALCEL OD-H (hexane-*i*-PrOH=1:1).

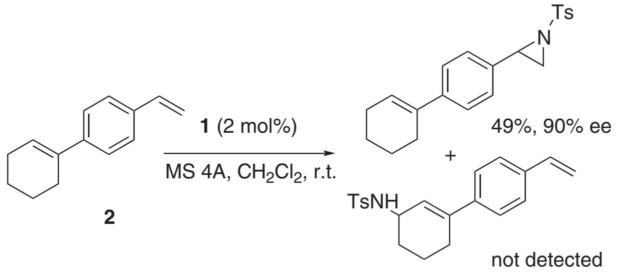
We next examined the reactions of di- and tri-substituted conjugated olefins under the same conditions (Table 2). Consumption rates of these olefins were slow but the reaction pathway varied with the substrate used.[14] When olefin possessed substituent(s) *trans* and/or geminal to the aryl substituent, allylic C–H amination occurred exclusively (entries 1-3). It is, however, noteworthy that C–H amination occurred at the *E*-substituent in preference to the geminal substituent (entry 2). On the other hand, inden underwent aziridination exclusively with high enantioselectivity, though the chemical yield was only modest. No C–H amination at C1 was observed. However, the reaction of dihydronaphthalene gave a trace amount (< 5%) of an allylic aminated product.

As expected from the above discussion, aziridination occurred at the mono-substituted double bond, when compound **2** bearing both mono- and tri-substituted double bonds was submitted to the present nitrene transfer reaction (Scheme 2). Neither aziridination of the trisubstituted olefin nor C–H amination was observed.

Table 2. Reactions of substituted conjugated olefins with toluenesulfonyl azide in the presence of complex **1**

Entry	Substrate	Product	Yield/%[ab]	% ee
1	Ph(CH$_3$)C=CH$_2$	Ph(TsNHCH$_2$)C=CH$_2$	18 (20)	
2			36 (36)	57[c]
3			17 (17)	80[d]
4			25 (26)	92[e]

[a]Isolated yield. [b]The number in the parentheses is the percent conversion of olefin, which was calculated by ^{1}H NMR analysis. [c]Determined by HPLC using DAICEL CHIRALCEL OD-H (hexane-*i*-PrOH=2:1). [d]Determined by HPLC using DAICEL CHIRALCEL OD-H (hexane-*i*-PrOH=1:1). [e]Determined by HPLC using DAICEL CHIRALPAK AD (hexane-*i*-PrOH=5:1). Absolute configuration was determined to be 1*S*,2*R* by comparison of the specific rotation: $[\alpha]_D^{22} + 27.7$ (*c* 0.13, CHCl$_3$); Lit.[13] $[\alpha]_D + 11.6$ (*c* 1, CHCl$_3$) for 1*S*,2*R*-isomer (52% ee).



Scheme 2.

These results suggest that olefins approach the Ru-nitrenoid species in a perpendicular or skewed-perpendicular manner which impedes interaction of the *Z*-substituent (R$_Z$) with the nitrene atom and the *Z*-substituent is reluctant to C–H amination (Figure 1).[15] The coefficient of the β-carbon of HOMO of the styrene derivative is larger than that of the α-carbon. Therefore, the allylic C–H bond on the *E*-substituent (R$_E$) is considered to be more activated than the allylic C–H bond on the geminal substituent (R$_G$). This explains why the *E*-substituent was aminated in preference to the geminal substituent (Table 2, entry 2).

In conclusion, we were able to demonstrate that Ru(salen)(CO) complex **1** served as the catalyst for enantioselective nitrene transfer reaction (aziridination or C–H amination) using *N*-toluenesulfonyl azide as the nitrene source and that the reaction pathway was strongly affected by the substitution pattern of the olefin used.

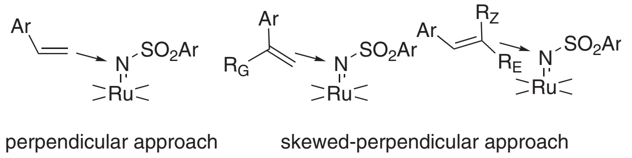


Figure 1. Proposal for substrate approach.

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12 Typical experimental procedure is exemplified by the aziridination of styrene: under nitrogen atmosphere, a toluene solution (0.25 mL) of complex **1** (1.9 mg, 2 μmol) was concentrated twice azeotropically in vacuo. MS 4A (20 mg) and styrene (10.4 mg, 0.1 mmol) were added to the residue. To the mixture was added dichloromethane (0.5 mL) and the resulting suspension was stirred for 0.5 h at room temperature. To the suspension was added *p*-toluenesulfonyl azide (15.5 μL, 0.1 mmol) and stirred for 24 h. The reaction mixture was directly chromatographed on silica gel using hexane and ethyl acetate (hexane:ethyl acetate = 1/0-19/1-8/2) to give the corresponding aziridine (19.4 mg) in 71% yield. The enantiomeric excess of the product was determined by HPLC analysis using DAICEL CHIRALCEL OJ-H (hexane:*i*-PrOH = 1:1).

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