Novel Asymmetric and Stereospecific Aziridination of Alkenes with a Chiral Nitridomanganese Complex**

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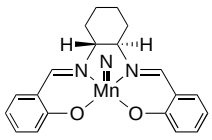
Optically active aziridines are useful building blocks for nitrogen-containing functional compounds.[1] They are also found in some natural and biologically active products such as mitomycins and azinomycins.[1, 2] Among the various routes that have been developed thus far to give chiral aziridines,[3] reagent-controlled asymmetric aziridinations of carbon–carbon double bonds are remarkable in terms of their simplicity and convenience as a synthetic procedure.[4] The chiral Cu^{I} or Mn^{III} complexes discovered by Evans,[4a,b] Jacobsen,[4c–e] and Katsuki[4f,g] represent efficient catalysts for such reactions when [*N*-(*p*-toluenesulfonyl)imino]phenyliodinane, PhI=NTs, is used as a nitrogen source. On the other hand, it is noteworthy that an approach for direct aziridination with nitrido(5,10,15,20-tetramesitylporphyrinato)manganese (TMPMnN) has been reported by Groves and Takahashi, but their study was restricted to the use of *cis*-cyclooctene as the alkene.[5] Recently this type of reaction was extended by Carreira and co-workers to the amination of silyl enol ethers and glycols with new types of nitridomanganese complexes.[6] An asymmetric version of this methodology, however, has not yet been achieved. This situation prompted us to investigate a novel chiral nitrido complex that would impart enantioselective aziridination. We report herein the first asymmetric and stereospecific aziridination of styrene derivatives by transfer of a nitrogen atom from a chiral nitridomanganese complex, wherein the additives play a key role in the performance of the reaction and its selectivity.

The chiral nitridomanganese complexes **1** and **2** were readily prepared from literature procedures,[7] including



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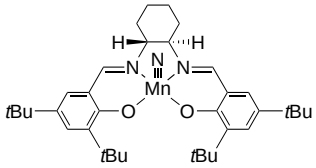

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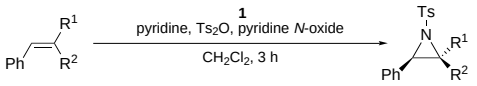
Carreira's method,[6a] by the treatment of chiral ligands with $Mn(OAc)_2$, NH_4OH, and NaOCl. An alternative procedure for the preparation of **1** was developed by us and consists of a reaction of a chiral Mn^{III} complex[8] with gaseous NH_3 and Chloramine-T as the oxidant in MeOH.[9]

Although trifluoroacetic anhydride (TFAA) was used by Groves as well as Carreira for the activation of their nitrido complexes, when we employed this reagent in the aziridination of unfunctionalized alkenes with the chiral nitridomanganese complex **1** no aziridine derivatives were obtained.[10] As a result we searched for another activating reagent and found *p*-toluenesulfonic anhydride (Ts_2O) to be effective for the aziridination of alkenes (Table 1). The reaction of the nitrido complex **1** with styrene (10 equiv) in methylene chloride at room temperature for 3 h in the presence of Ts_2O (1.2 equiv) and pyridine (1.5 equiv) gave the corresponding *N*-tosylaziridine in 49% yield based on **1**. The yield of aziridine increased up to 63% with a decrease in the amount of pyridine and with the enantiomeric excess (*ee*) of the product being 31%. The aziridination proceeded smoothly at 0 °C and retained both

Table 1. Asymmetric aziridination of styrene derivatives with the nitrido complex **1**[a]



Substrate R^1	Substrate R^2	Additive	T [°C]	Yield [%]	*ee* [%]
H	H	–	RT	63	31[b,c]
H	H	pyridine *N*-oxide	0	78	41[b,c]
Me	H	–	RT	60	73[d,e]
Me	H	pyridine *N*-oxide	0	72	85[d,e]
H	Me	–	RT	14	30[d,f]
H	Me	pyridine *N*-oxide	RT	34	25[d,f]
*n*Pr	H	pyridine *N*-oxide	0	66	90[b,f]
*i*Pr	H	pyridine *N*-oxide	0	53[g]	94[b,f]

[a] Reaction conditions: **1** (1 equiv), pyridine (0.5 equiv), Ts_2O (1.2 equiv), additive (1.2 equiv), alkene (10 equiv), 3 h, CH_2Cl_2. [b] The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralcel OJ column. [c] The absolute configuration was determined as *R* by comparison of the measured optical rotations with the reported values.[4b] [d] The enantiomeric excess was determined by ^1H NMR analysis with $[Eu(hfc)_3]$. [e] The absolute configuration was determined as (2*R*,3*R*) by comparison of the measured optical rotations with the reported values.[4b] [f] The absolute configuration was not determined. [g] The reaction was run for 5 h.

the yield and enantioselectivity. In order to obtain better enantioselectivity, we examined the reaction in the presence of pyridine *N*-oxide.[11] The addition of pyridine *N*-oxide at 0 °C gave the best result (78%, 41% *ee*). The aziridination proceeded even at −20 °C with 40% *ee*. Thus, the use of pyridine *N*-oxide improved not only the enantioselectivity but also the yield of the product. These results represent the first example of the aziridination of styrene and, in addition, the first asymmetric synthesis with a chiral nitridomanganese complex. When complex **2**, which bears Jacobsen's ligand, was tested under the best conditions the yield was very low (9%) but the enantioselectivity of the aziridine was moderate (50%).

The pronounced effect of pyridine *N*-oxide was also observed in the aziridination of *trans*-β-methylstyrene. Although *trans*-β-methylstyrene was not aziridinated below

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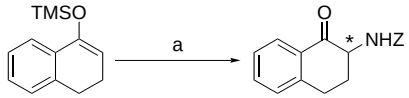
room temperature in the absence of pyridine *N*-oxide, the addition of the *N*-oxide to the reaction system resulted in a good yield and enantioselectivity (72%, 85% *ee*) even at 0 °C. In comparison, the aziridination of *cis*-β-methylstyrene was not observed at 0 °C in spite of the presence of pyridine *N*-oxide. In the absence of the *N*-oxide the desired *cis* aziridine was obtained in a poor yield and with a low *ee* value at room temperature. The addition of pyridine *N*-oxide improved the yield of aziridine, but a remarkable change in the *ee* value was not observed. The fact that the use of *trans*-β-methylstyrene resulted in high enantioselectivity encouraged us to investigate the asymmetric aziridination of other *trans*-disubstituted alkenes. The reaction of *trans*-1-phenyl-1-pentene with **1** under optimal conditions afforded the desired product in good yield (66%) and with high enantioselectivity (90% *ee*). Even better results were obtained when *trans*-3-methyl-1-phenyl-1-butene was utilized as the substrate. However, aziridination was not observed when a more bulky alkene, namely *trans* styrene with a *tert*-butyl substituent in the β position, was employed in the reaction. It is noteworthy that high stereospecificity was observed in all the aziridinations of *trans*- and *cis*-1,2-disubstituted alkenes, although such reactions in the presence of metal catalysts and PhI=NTs did not always show high streospecificity.[4] In addition, the allylic amination product was not produced in all the reactions.

The present reaction was applied with the aim of using the silyl enol ether to direct the asymmetric amination. The amination, which is presumed to take place via an aziridine intermediate,[6d, 12] proceeded smoothly to give the N-tosylated α-aminoketone in 76% yield and 48% *ee* (Scheme 1). When **1** was tested under Carreira's conditions[6a] the N-trifluoroacetylated α-aminoketone was obtained in moderate yield and *ee* (58%, 79% *ee*).[13] These results are of significance in that they suggest that additives such as Ts_2O and TFAA, which are used for the generation of the imido complex,[5a] might control the aziridination with **1**.



Z = Ts 76%, 48% *ee*
Z = CF_3CO 58%, 79% *ee*

Scheme 1. [a] Z = Ts: **1** (1 equiv), pyridine (0.5 equiv), Ts_2O (1.5 equiv), pyridine *N*-oxide (1.2 equiv), silyl enol ether (10 equiv), CH_2Cl_2, 0 °C, 6 h; Z = CF_3CO: **1** (2 equiv), pyridine (3 equiv), $(CF_3CO)_2O$ (2.4 equiv), silyl enol ether (1 equiv), CH_2Cl_2, −78 °C → RT, 3 h.

The aziridination of styrene derivatives proceeds with a chiral nitridomanganese complex **1** to give products in good yield and with excellent enantioselectivity. In addition, this methodology results in stereospecific aziridination. We also conclude that additives play an important role in the reaction; Ts_2O was the most effective reagent in the activation of **1**, and the use of pyridine *N*-oxide was necessary to obtain high enantioselectivity. Efforts to extend the scope of this process to other alkenes are currently in progress.

Experimental Section

General conditions for aziridination reactions: Pyridine (0.25 mmol), alkene (5.0 mmol), and a solution of *p*-toluenesulfonic anhydride (0.6 mmol) in CH_2Cl_2 (3 mL) were added to a solution of **1** (0.5 mmol) and pyridine *N*-oxide (0.6 mmol) in CH_2Cl_2 (2 mL) under nitrogen, and the mixture was stirred for 3 h. Pentane (15 mL), silica gel (400 mg), and celite (400 mg) were added and the mixture was stirred for 0.5 h. The reaction mixture was then passed through a 3-cm plug of silica gel with diethyl ether (5 × 15 mL) as eluent. The filtrate was concentrated in vacuo, and the residue purified by flash column chromatography on silica gel (EtOAc/hexane). Enantiomeric excesses of the aziridines were determined by chiral HPLC analysis (Daicel Chiralcel OJ) or by using the ^1H NMR chiral shift reagent [Eu(hfc)$_3$].

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[9] Treatment of the Mn^{III} complex[8] (35.6 mg, 0.09 mmol) with Chloramine-T (141 mg, 0.5 mmol) in MeOH (5 mL) at room temperature for 40 h afforded complex **1** in 84% yield.
[10] The use of trifluoromethanesulfonic anhydride or *p*-toluenesulfonyl chloride as an activator did not give good results relative to *p*-toluenesulfonic anhydride.
[11] Katsuki and his co-workers have reported that pyridine *N*-oxide is an effective additive for the asymmetric epoxidation catalyzed by salen–manganese(III) complexes, and they applied these findings to the asymmetric aziridination of alkenes with PhI=NTs: R. Irie, Y. Ito, T. Katsuki, *Synlett* **1991**, 265–266.
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[13] The chiral product could be purified to greater than 98% *ee* by recrystallization from benzene/hexane.

Sapphyrin Supramolecules through C–H···S and C–H···Se Hydrogen Bonds—First Structural Characterization of *meso*-Arylsapphyrins Bearing Heteroatoms**

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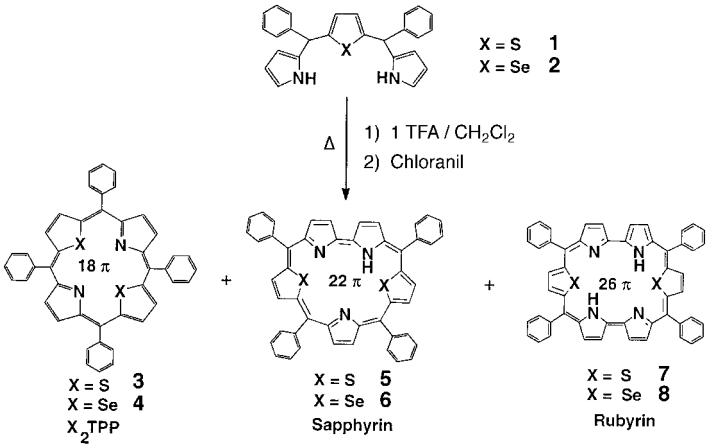
Dedicated to Professors C. N. R. Rao and Jean'ne M. Shreeve on the occasion of their 65th birthdays

Controlling the assembly of macromolecules in the solid state through weak interactions such as hydrogen bonding and van der Waals forces is currently being explored for the synthesis of functional materials for molecular recognition and catalysis.[1] Many supramolecules held together by weak C–H···O and C–H···N hydrogen bonds are known.[2] In contrast, molecules held together by C–H···S and C–H···Se hydrogen bonds are very rare, and to the best of our knowledge there are only three reports to date on such interactions.[3] Here we describe the first structural characterization of two core-modified sapphyrins synthesized by an unprecedented coupling of a modified tripyrrane. Sapphyrins have been shown to self-assemble in the solid state to form a supramolecular ladder held together by weak C–H···S or C–H···Se and C–H···N hydrogen-bonding interactions.

Literature methods for the synthesis of sapphyrins include a traditional [3+2] acid-catalyzed MacDonald-type condensation between the appropriate precursors, reaction of diformylbipyrrole with benzaldehyde and pyrrole under Lindsey conditions,[4] and an acid-catalyzed condensation of *a,c*-biladienes with pyrrole-2-carbaldehydes.[5] Recently, a *meso*-substituted sapphyrin was isolated as a side product in 1% yield in the Rothemund reaction of benzaldehyde and pyrrole.[6] In all these reactions at least two precursors are required for the condensation under different conditions. However, our reaction of the modified tripyrranes **1** and **2** in dichloromethane containing an appropriate acid catalyst gave 18π, 22π, and 26π macrocycles in moderate yields (Scheme 1). The product distribution and the yields of isolated products were dependent on the nature of the acid catalyst and its concentration. For S- and Se-containing tripyrranes at lower concentrations of trifluoroacetic acid (TFA), the major product was rubyrin, while at higher concentrations of TFA, sapphyrin and rubyrin were isolated in moderately good yields in addition to small amounts of X_2TPP (X = S or Se; TPP = tetraphenylporphyrin). The formation of **5** and **6** requires partial acidolysis of tripyrranes under the reaction conditions. We have observed that both **1** and **2** undergo acidolysis, and the extent of acidolysis is dependent on the TFA concentration. The higher yields of **5** and **6** at higher concentrations of TFA is consistent with this observation. For the formation of **7** and **8** we suggest an acid-catalyzed self-condensation of two tripyrrane units through an oxidative coupling,[7] forming a rubyrinogen intermediate which on dehydrogenation gives rubyrin.[8] Attempts to isolate the corresponding rubyrinogen proved futile because it oxidizes readily to the corresponding aromatic congener. The sole formation of rubyrins at the lower concentrations of TFA (0.1 equiv) at which acidolysis is minimal suggests that the self-coupling is preferred at this concentration.



Scheme 1. Synthesis of various sapphyrins and rubyrins from **1** and **2**.

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