

## Aziridination and amidation catalyzed by polymer-supported metalloporphyrins with $\text{PhI}(\text{OAc})_2$ and $\text{TsNH}_2$

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### Abstract

Manganese and ruthenium 5, 10, 15-tris(tolyl)-20-(4-hydroxyphenyl)porphyrins covalently attached to Merrifield's peptide resin(MPR) were prepared respectively. The catalysts efficiently catalyzed the aziridination/amidation of simple hydrocarbons and  $\Delta^5$ -steroid derivatives with  $\text{PhI}(\text{OAc})_2$  and  $\text{TsNH}_2$ . Moderate to excellent yields were obtained under mild reaction conditions. The catalysts **3a** and **3b** exhibit different diastereoselectivities towards the  $\Delta^5$ -steroid derivatives, the former shows  $\alpha$ -selectivity and the later shows  $\beta$ -selectivity under certain reaction conditions.

**Keywords:** Aziridination, amidation,  $\Delta^5$ -steroid derivatives, polymer-supported porphyrins

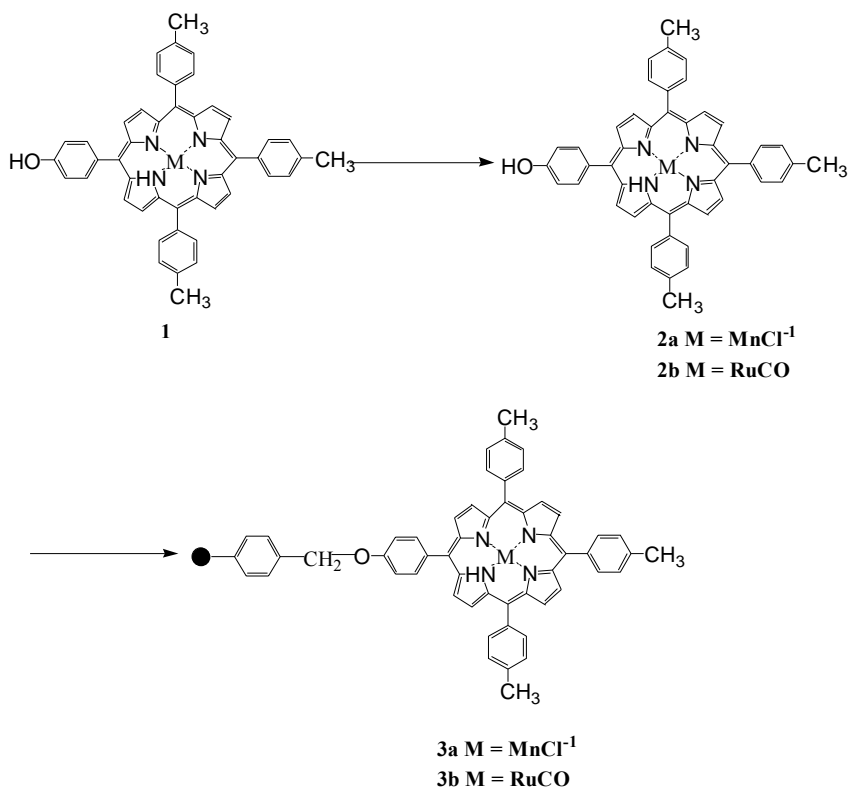
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### Introduction

Metal-mediated aziridination/amidation of hydrocarbons offers useful means for the synthesis of aziridines, amides and amines.<sup>1</sup> Metalloporphyrin catalysts as their special high selectivity and catalyst turnover number attract considerable interest in recent years.<sup>2</sup> However, the expensive price of these catalysts hinders their application. In the early 1980s, aziridination of alkenes and amidation of saturated C-H bonds catalyzed by a simple metalloporphyrin with (N-(p-tolylsulfonyl)imino) phenyliodinane (PhINTs) were firstly reported by Mansuy<sup>3</sup> and Breslow<sup>4</sup> respectively. Since then, a number of nonchiral<sup>2f, 5</sup> and chiral metalloporphyrin<sup>2a, 2e, 2i, 6</sup> catalysts have been developed and some progress has been made. In fact, most of the studies focused on the corresponding catalytic efficiency, or the promising application of these catalytic systems.<sup>2a, 2b, 2e, 2i</sup>

We found that ruthenium<sup>7</sup> and manganese porphyrins<sup>8</sup> attached to Merrifield's peptide resin (MPR) show high diastereoselectivity and high stability in epoxidation of glycol and 5-cholest-ene derivatives. Our interest in aziridination/amination reactions has prompted us to survey their efficiency in these reactions. Previous works focused on the aziridination of alkenes and amidation of C-H bond of alkanes with PhINTs catalyzed by various simple

metalloporphyrins. In this paper the results indicated that these polymer-supported porphyrins are also high efficient catalysts for the same aziridination or amidation with  $\text{PhI}(\text{OAc})_2$  and  $\text{TsNH}_2$ . This method for aziridination/amination of hydrocarbons is very convenient and inexpensive.



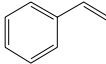
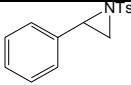
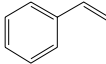
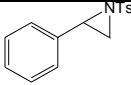

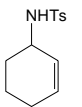

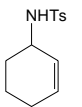
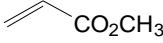
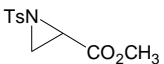
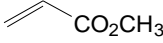
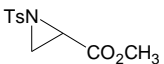
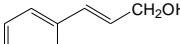
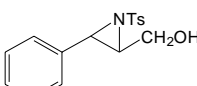
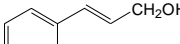
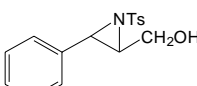

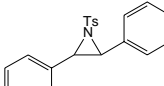

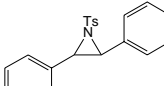
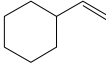
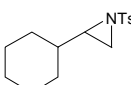
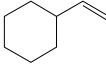
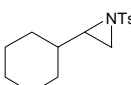
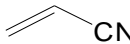
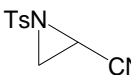
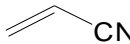
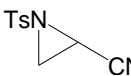
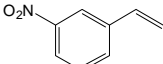
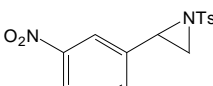
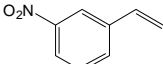
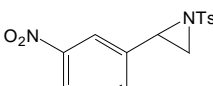
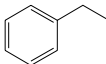
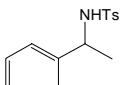
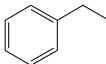
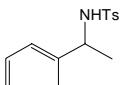
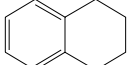
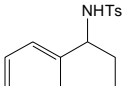
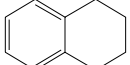
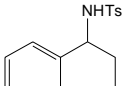
**Scheme 1.** Metalloporphyrins covalently immobilized onto Merrifield peptide resin.

## Results and Discussion

### Aziridination/amidation of hydrocarbons catalyzed by polymer-supported metalloporphyrins 3a and 3b

Polymer-supported aziridination/amidation catalysts are less developed previously. Che and coworkers reported the aziridination of hydrocarbons by porphyrin catalyst attached onto polyethylene glycol (PEG) in 76%-88% aziridine yields.<sup>9</sup> Herein, the aziridination/amidation of hydrocarbons with  $\text{PhI}(\text{OAc})_2$  and  $\text{TsNH}_2$  catalyzed by MPR-supported porphyrins were firstly reported. All reactions were carried out in a sealed flask under nitrogen atmosphere with dichloromethane as solvent. The results were summarized in **Table 1**. The yields of aziridination/amidation products range from 20% to 85% with substrate conversions of 12%-53% as shown in **Table 1**. The main product in the aziridination of cyclohexene was the allylic N-tosylamides (entry 2).

**Table 1.** Aziridination/amidation of hydrocarbons with “PhI(OAc)<sub>2</sub>+ TsNH<sub>2</sub>” catalyzed by **3a** and **3b**<sup>[a]</sup>

Entry	Substrate	Product	Catalyst	Conversion	Yields
				[%]	[%] <sup>[b]</sup>
1			<b>3a</b>	53	20
2			<b>3b</b>	44	28
3			<b>3a</b>	33	75 <sup>[c]</sup>
4			<b>3b</b>	27	65 <sup>[c]</sup>
5			<b>3a</b>	30	44
6			<b>3b</b>	26	32
7			<b>3a</b>	35	52
8			<b>3b</b>	25	65
9			<b>3a</b>	20	15
10			<b>3b</b>	12	45
11			<b>3a</b>	38	68
12			<b>3b</b>	32	72
13			<b>3a</b>	41	63
14			<b>3b</b>	26	85
15			<b>3a</b>	43	32
16			<b>3b</b>	35	26
17			<b>3a</b>	33	25
18			<b>3b</b>	24	28
19			<b>3a</b>	33	38
20			<b>3b</b>	23	45

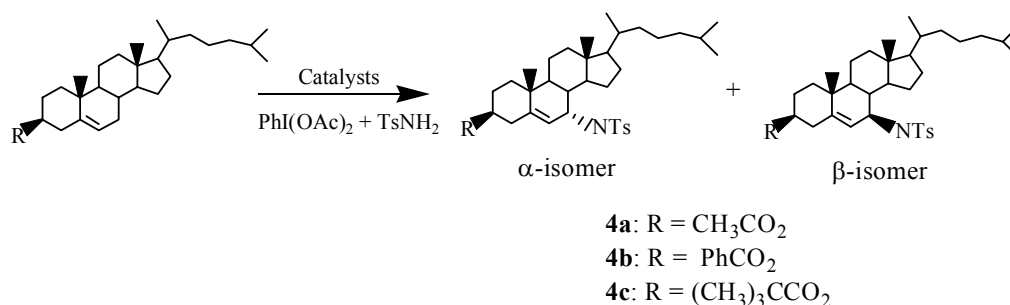
<sup>[a]</sup> Reaction conditions: CH<sub>2</sub>Cl<sub>2</sub>, 40 °C, 6h; **3a** : substrate : PhI(OAc)<sub>2</sub> : TsNH<sub>2</sub> (molar ratio) = 1 : 2500 : 3150 : 3750; **3b** : substrate : PhI(OAc)<sub>2</sub> : TsNH<sub>2</sub> (molar ratio) = 1 : 3000 : 3750 : 4500.

<sup>[b]</sup> Yields of isolated product based on the substrate used. <sup>[c]</sup> The aziridination product has also been detected.<sup>10</sup>

### Amidation of Δ<sup>5</sup>-steroids derivatives catalyzed by **3a** and **3b**

Amino steroids show a noteworthy biological activity. However the catalytic synthesis of this

substance remains sparse. Dodd and Dauban<sup>11</sup> demonstrated the copper-catalyzed aziridination of 1-pregnene-3, 20-dione in 53% yield with PhI=NSes (Ses = 2-(trimethylsilyl) ethanesulfonyl). Breslow<sup>12</sup> reported the amidation of equilenin acetate with PhI=NTs catalyzed by [Mn (TPFPP) Cl] (TPFPP = meso-tetrakis (pentafluorophenyl)porphyrinato dianion) in 47% yield. Che recently reported the amidation of chlosteryl acetate catalyzed by a chiral Ru(II)-salen complex<sup>13</sup> and a chiral Mn porphyrin<sup>2i</sup> with high diastereoselectivities. Herein, we studied the amidation of  $\Delta^5$ -steroids derivatives catalyzed by MPR-supported porphyrins with commercially available reagents PhI(OAc)<sub>2</sub> and TsNH<sub>2</sub>. We found two catalysts show moderate diastereoselectivity in the amidation (**Table 2**). It demonstrated that **3a** is  $\beta$ -selective (entries 1, 3 and 5) and **3b** is  $\alpha$ -selectivity (entries 2, 4 and 6) at 40 °C for 6h. The stereoselectivity together with the amide selectivity was investigated according to previously literature.<sup>2i, 13</sup>



**Scheme 2.** Amidation of  $\Delta^5$ -steroid derivatives with “PhI(OAc)<sub>2</sub> + TsNH<sub>2</sub>” catalyzed by polymer-supported metalloporphyrins **3a** and **3b**.

**Table 2.** The results of catalytic amidation of  $\Delta^5$ -steroid derivatives with “PhI(OAc)<sub>2</sub> + TsNH<sub>2</sub>” by polymer-supported metalloporphyrins **3a** and **3b**

Entry	Catalyst	Product <sup>[a]</sup>	Conversion [%]	Yield [%] <sup>[b]</sup>	Ratio of $\alpha/\beta$ <sup>[c]</sup>
1	<b>3a</b>	<b>4a</b>	28	40	1:1.6
2	<b>3b</b>	<b>4a</b>	42	69	1.5:1
3	<b>3a</b>	<b>4b</b>	26	53	1:1.2
4	<b>3b</b>	<b>4b</b>	35	56	1.4:1
5	<b>3a</b>	<b>4c</b>	32	43	1:1.8
6	<b>3b</b>	<b>4c</b>	46	62	2.2:1

<sup>[a]</sup> Reaction conditions: 40 °C, 6h; **3a** : Substrate : PhI(OAc)<sub>2</sub> : TsNH<sub>2</sub> (molar ratio) = 1 : 2500 : 3150 : 3750; **3b**: Substrate: PhI(OAc)<sub>2</sub> : TsNH<sub>2</sub> (molar ratio) = 1 : 3000 : 3750 : 4500 . <sup>[b]</sup>Yields of isolated product based on the amount of substrate consumed. <sup>[c]</sup> Determined by <sup>1</sup>H NMR spectroscopy according to literature method.<sup>15</sup>

## Experimental Section

**General Procedures.** Merrifield's peptide resin (Aldrich, 2% cross-linked, 200-400 mesh, 2mmol Cl/g),  $\text{Mn}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{PhI}(\text{OAc})_2$  (Acros),  $\text{TsNH}_2$  (Aldrich) and  $\text{Ru}_3(\text{CO})_{12}$  (Strem) were used as received. All alkenes of the highest quality available from commercial were purified as literature.<sup>2d</sup> The  $\Delta^5$ -steroid derivatives were commercially available from Sigma and Aldrich. All reaction solvents were AR grade and distilled before use according to standard procedures. 5, 10, 15-Tris (4-tolyl)-20-(4-hydroxyphenyl) porphyrin (**1**) was synthesized as reported procedures.<sup>14</sup> **2a**, **2b**, **3a** and **3b** were synthesized according to our previous reports.<sup>7,8</sup>

<sup>1</sup>H NMR spectra were measured on Varian INOVA-400 spectrometer (400 MHz) by using tetramethylsilane (TMS) as an internal standard. UV-Vis spectra were measured on a Shimadzu UV-240 spectrophotometer. The metal contents were determined on a Thermo Elemental IRIS-Adv ICP spectrometer. Elemental analyses were performed by using a Carlo-Elba 1106 elemental analytical instrument.

**5,10,15-Tris(4-tolyl)-20-(4-hydroxyphenyl)porphyrin (1).** Yield 14.3%; blue purple crystal, mp>300 °C; IR(KBr,  $\text{cm}^{-1}$ ): 3420, 3310, 3019, 2908, 2846, 1607, 1508, 1471; UV( $\text{CHCl}_3$ , nm)  $\lambda_{\text{max}}$  416.5 (Soret), 517.5, 553.5, 591.5, 648.0; Anal. Calcd. for  $\text{C}_{47}\text{H}_{36}\text{N}_4\text{O}$ : C, 83.93; H, 5.36; N, 7.96. Found: C, 83.32; H, 5.16; N, 7.93.

**Manganese 5,10,15-tris(4-tolyl)-20-(4-hydroxyphenyl)porphyrin chloride (2a).** Yield 86%, red purple crystal, mp>300 °C. UV( $\text{CHCl}_3$ , nm):  $\lambda_{\text{max}}$  480 (Soret).

**Ruthenium 5,10,15-tris(4-tolyl)-20-(4-hydroxyphenyl)porphyrin carbonyl (2b).** Yield, 83%, mp>300 °C. UV( $\text{CHCl}_3$ , nm):  $\lambda_{\text{max}}$  418 (Soret), 530. IR(KBr,  $\text{cm}^{-1}$ ): 1941(CO); FAB-MS: m/z 800( $\text{M}^+$ ), 772( $[\text{M}^+ - \text{CO}]$ ).

**Polymer-supported manganese porphyrin (3a).** Green solid, Mn content: 0.13 mmol/g.

**Polymer-supported ruthenium porphyrin (3b).** Red solid, Ru content: 0.083 mmol/g.

### General procedure for aziridination/amidation of simple hydrocarbons with “ $\text{PhI}(\text{OAc})_2 + \text{TsNH}_2$ ” catalyzed by complex **3a** and **3b**

To a well stirred suspension of molecular sieves (4Å, 50 mg) in dry dichloromethane (4mL) containing catalyst **3a** (Mn:  $1.0 \times 10^{-4}$  mmol) or **3b** (Ru:  $0.83 \times 10^{-4}$  mmol) at room temperature, the substrate (0.25 mmol) was added by means of a syringe. After 10 min,  $\text{TsNH}_2$  (0.37 mmol) and  $\text{PhI}(\text{OAc})_2$  (0.31 mmol) were added quickly and the mixture were stirred at 40 °C for 6h. The solution was then filtered and the products were purified by column chromatography on silica gel with n-hexane/ethyl acetate (6/1, v/v) as eluent. The products were analyzed by GC-MS and their <sup>1</sup>H NMR spectra were consistent with the known structures.<sup>2f, 15</sup>

### General procedure for amidation of $\Delta^5$ -steroids derivatives with “ $\text{PhI}(\text{OAc})_2 + \text{TsNH}_2$ ” catalyzed by catalyst **3a** and **3b**

In the same manner as described above,  $\Delta^5$ -steroid derivatives were converted into the amidation

products. The ratios of  $\alpha/\beta$ -isomers were determined by the  $^1\text{H}$  NMR spectra of  $\alpha/\beta$ -isomers mixture as in literature.<sup>2i, 15</sup>

## Acknowledgements

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