Aziridination and amidation catalyzed by polymer-supported metalloporphyrins with PhI(OAc)2 and TsNH2

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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 Δ^5-steroid derivatives with $PhI(OAc)_2$ and $TsNH_2$. Moderate to excellent yields were obtained under mild reaction conditions. The catalysts **3a** and **3b** exhibit different diasteroselectivities towards the Δ^5-steroid derivatives, the former shows α-selectivity and the later shows β-selectivity under certain reaction conditions.

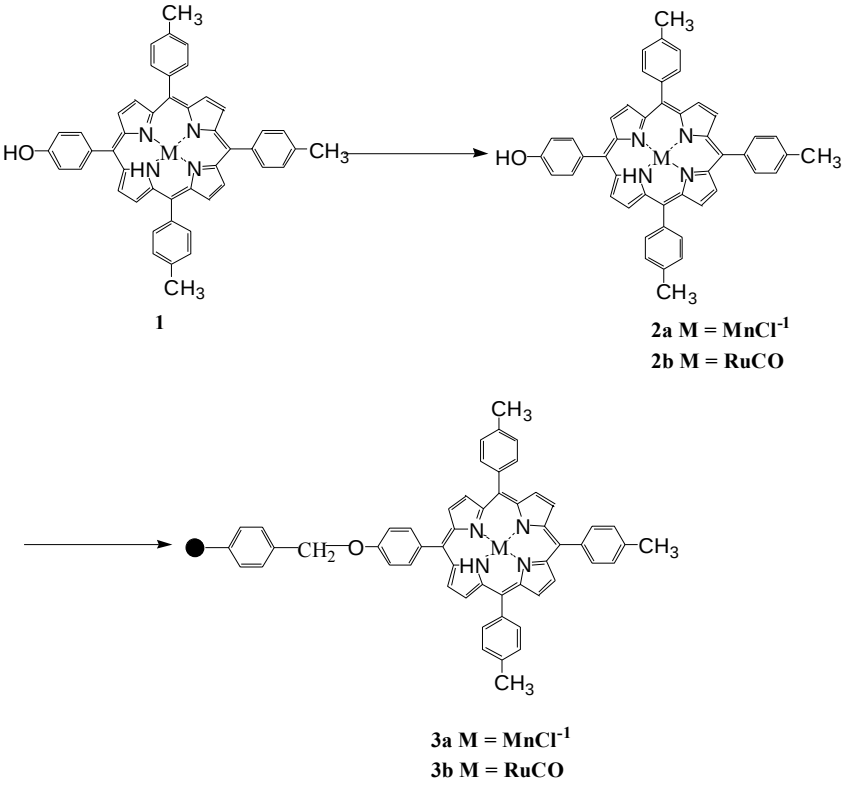
Keywords: Aziridination, amidation, Δ^5-steroid derivatives, polymer-supported porphyrins

Introduction

Metal-mediated aziridination/amidation of hydrocarbons offers useful means for the synthesis of aziridines, amides and amines.[1] Metalloporphyrin catalysts as their special high selectivity and catalyst turnover number attract considerable interest in recent years.[2] 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[3] and Breslow[4] respectively. Since then, a number of nonchiral[2f, 5] and chiral metalloporphyrin[2a, 2e, 2i, 6] 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.[2a, 2b, 2e, 2i]

We found that ruthenium[7] and manganese porphyrins[8] attached to Merrifield's peptide resin (MPR) show high diastereoselectivity and high stability in epoxidation of glycal 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 $PhI(OAc)_2$ and $TsNH_2$. This method for aziridination/amination of hydrocarbons is very convenient and inexpensive.



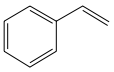
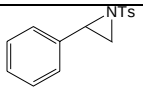
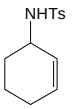
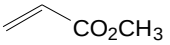
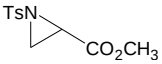
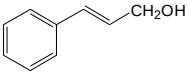
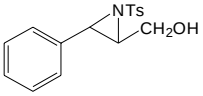
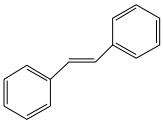
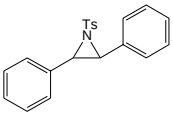
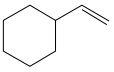
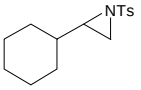
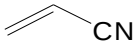
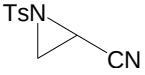
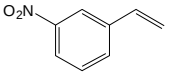
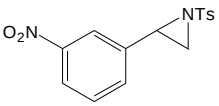
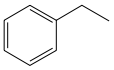
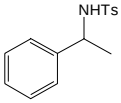
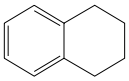
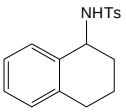
Scheme 1. Metalloporphyrins covalently immobilized onto Merrifield peptide resin.

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.[9] Herein, the aziridination/amidation of hydrocarbons with $PhI(OAc)_2$ and $TsNH_2$ 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 "$PhI(OAc)_2$+ $TsNH_2$" catalyzed by **3a** and **3b**[a]

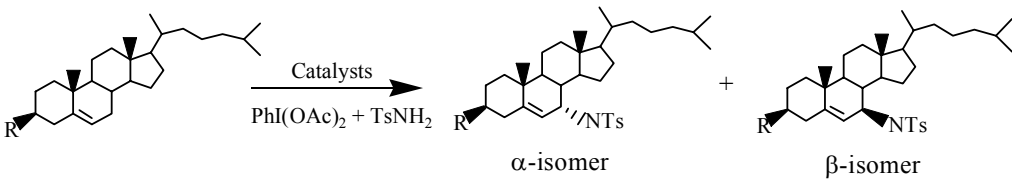
Entry	Substrate	Product	Catalyst	Conversion [%]	Yields [%][b]
1			**3a**	53	20
2			**3b**	44	28
3			**3a**	33	75[c]
4			**3b**	27	65[c]
5			**3a**	30	44
6			**3b**	26	32
7			**3a**	35	52
8			**3b**	25	65
9			**3a**	20	15
10			**3b**	12	45
11			**3a**	38	68
12			**3b**	32	72
13			**3a**	41	63
14			**3b**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

[a] Reaction conditions: CH_2Cl_2, 40 °C, 6h; **3a** : substrate : $PhI(OAc)_2$: $TsNH_2$ (molar ratio) = 1 : 2500 : 3150 : 3750; **3b** : substrate : $PhI(OAc)_2$: $TsNH_2$ (molar ratio) = 1 : 3000 : 3750 : 4500. [b]Yields of isolated product based on the substrate used. [c]The aziridination product has also been detected.[10]

Amidation of Δ^5-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[11] demonstrated the copper-catalyzed aziridination of 1-pregnene-3, 20-dione in 53% yield with PhI=NSes (Ses = 2-(trimethylsilyl) ethanesulfonyl). Breslow[12] 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[13] and a chiral Mn porphyrin[2i] with high diasteroselectivities. Herein, we studied the amidation of Δ^5-steroids derivatives catalyzed by MPR-supported porphyrins with commercially available reagents $PhI(OAc)_2$ and $TsNH_2$. We found two catalysts show moderate diastereoselectivity in the amidation (**Table 2**). It demonstrated that **3a** is β–selective (entries 1, 3 and 5) and **3b** is α–selectivity (entries 2, 4 and 6) at 40 °C for 6h. The stereoselectivity together with the amide selectivity was investigated according to previously literature.[2i, 13]



4a: R = CH_3CO_2
4b: R = $PhCO_2$
4c: R = $(CH_3)_3CCO_2$

Scheme 2. Amidation of Δ^5-steriod derivatives with "$PhI(OAc)_2$ + $TsNH_2$ " catalyzed by polymer-supported metalloporphyrins **3a** and **3b**.

Table 2. The results of catalytic amidation of Δ^5-steroid derivatives with "$PhI(OAc)_2$ + $TsNH_2$ " by polymer-supported metalloporphyrins **3a** and **3b**

Entry	Catalyst	Product[a]	Conversion [%]	Yield [%][b]	Ratio of α/β[c]
1	**3a**	**4a**	28	40	1:1.6
2	**3b**	**4a**	42	69	1.5:1
3	**3a**	**4b**	26	53	1:1:2
4	**3b**	**4b**	35	56	1.4:1
5	**3a**	**4c**	32	43	1:1.8
6	**3b**	**4c**	46	62	2.2:1

[a] Reaction conditions: 40 °C, 6h; **3a** : Substrate : $PhI(OAc)_2$: $TsNH_2$ (molar ratio) = 1 : 2500 : 3150 : 3750; **3b**: Substrate: PhI $(OAc)_2$: $TsNH_2$ (molar ratio) = 1 : 3000 : 3750 : 4500 . [b] Yields of isolated product based on the amount of substrate consumed. [c] Determined by ^{1}H NMR spectroscopy according to literature method.[15]

Experimental Section

General Procedures. Merrifield's peptide resin (Aldrich, 2% cross-linked, 200-400 mesh, 2mmol Cl/g), $Mn(OAc)_2 \cdot 4H_2O$, $PhI(OAc)_2$ (Acros), $TsNH_2$ (Aldrich) and $Ru_3(CO)_{12}$ (Strem) were used as received. All alkenes of the highest quality available from commercial were purified as literature.[2d] The Δ^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.[14] **2a, 2b, 3a** and **3b** were synthesized according to our previous reports.[7, 8]

^1H NMR spectra were measured on Varian INOVA-400 spectrometer (400 MHz) by using tetramethylsilane (TMS) as an internal standard. UV-Vis spectra were measureed 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 ^oC; IR(KBr, cm^{-1}): 3420, 3310, 3019, 2908, 2846, 1607, 1508, 1471; UV($CHCl_3$, nm) λ_{max} 416.5 (Soret), 517.5, 553.5, 591.5, 648.0; Anal. Calcd. for $C_{47}H_{36}N_4O$: 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 □. UV($CHCl_3$, nm): λ_{max} 480 (Soret).

Ruthenium 5,10,15-tris(4-tolyl)-20-(4-hydroxyphenyl)porphyrin carbonyl (2b). Yield, 83%, mp>300 ^oC. UV($CHCl_3$, nm): λ_{max} 418 (Soret), 530. IR(KBr, cm^{-1}): 1941(CO); FAB-MS: m/z 800(M^+), 772([M^+-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 "$PhI(OAc)_2$ + $TsNH_2$" 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: 1.0×10^{-4} mmol) or **3b** (Ru: 0.83×10^{-4} mmol) at room temperature, the substrate (0.25 mmol) was added by means of a syringe. After 10 min, $TsNH_2$ (0.37 mmol) and $PhI(OAc)_2$ (0.31 mmol) were added quickly and the mixture were stirred at 40 ^oC 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 ^1H NMR spectra were consistent with the known structures.[2f, 15]

General procedure for amidation of Δ^5-steroids derivatives with "$PhI(OAc)_2$ + $TsNH_2$" catalyzed by catalyst 3a and 3b

In the same manner as described above, Δ^5-steriod derivatives were converted into the amidation

products. The ratios of α/β–isomers were determined by the ^{1}H NMR spectra of α/β–isomers mixture as in literature.[2i, 15]

Acknowledgements

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