

Amidation of Saturated C–H Bonds Catalyzed by Electron-Deficient Ruthenium and Manganese Porphyrins. A Highly Catalytic Nitrogen Atom Transfer Process

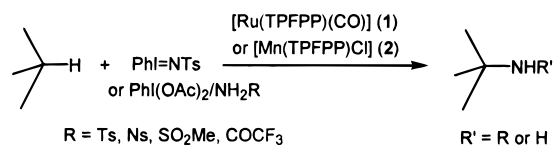
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ABSTRACT



Amidation of a variety of hydrocarbons with PhI=NTs catalyzed by ruthenium and manganese *meso*-tetrakis(pentafluorophenyl)porphyrins 1 and 2 afforded *N*-substituted amides in up to 92% yields with good to excellent substrate conversions. By employing catalyst 2, exceptionally high turnovers (up to 2600) were achieved, and the amidations can be effected by directly using PhI(OAc)₂/NH₂R as amidating reagents; in the case of R = COCF₃ a direct amination was realized in up to 90% yield.

Metal complex-catalyzed nitrogen atom transfer reactions are among the most attractive methodologies for the syntheses of aziridines,¹ amides,^{2–5} or amines.⁶ Despite encouraging advances, a conspicuous problem currently facing these

systems lies in their rather low catalyst turnovers (rarely >50). This contrasts with closely related epoxidation or hydroxylation processes via metal-mediated oxygen atom transfer reactions, for which thousands of catalyst turnovers are not uncommon.⁷ We report here the amidation of

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Table 1. Amidation of Saturated C–H Bonds with $\text{PhI}=\text{NTs}$ Catalyzed by $[\text{Ru}(\text{TPFPP})(\text{CO})]$ (**1**) or $[\text{Mn}(\text{TPFPP})\text{Cl}]$ (**2**)^a

entry	substrate	product	catalyst	conversion (%)	isolated yield (%) ^b
1			1	16	86
2			2	42	82
3			1	99	73
4			2	99	71
5			1	98	74
6			2	98	80
7			1	55	86
8			2	93	92
9			1	70	78
10			2	93	77
11			1	92	71
12			2	96	76
13			1	36	90
14			2	71	87
15			2	99	56
					23
16			1	32	70
17			2	69	48
			1		19
			2		13
			1		9
			2		12
18			1	43	59
19			2	95	81
20			1	42	83
21			2	74	71

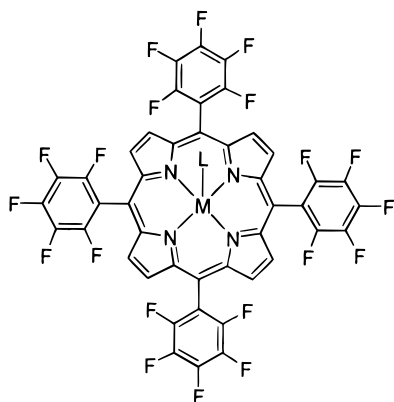
^a All reactions were performed in CH_2Cl_2 at 40 °C for 2 h with a catalyst:substrate:($\text{PhI}=\text{NTs}$) molar ratio of 1:75:150. ^b On the basis of the amount of substrate consumed.

saturated C–H bonds with $\text{PhI}=\text{NTs}$ catalyzed by electron-deficient ruthenium and manganese porphyrins (complexes **1** and **2**, respectively),⁸ which features exceptionally high turnovers (up to 2600 with **2** as catalyst) for a catalytic nitrogen atom transfer process.

The metal-mediated amidation of saturated C–H bonds with a nitrene source was pioneered in 1982 by Breslow and co-workers,^{2a} who successfully amidated cyclohexane with $\text{PhI}=\text{NTs}$ in the presence of iron or manganese porphyrins. Thereafter, Mansuy and co-workers demonstrated that iron and particularly manganese porphyrins can catalyze $\text{PhI}=\text{NTs}$ amidation of adamantane or allylic amidation of alkenes in up to 70% yields.³ Recent investigations by Müller⁴ and us⁵ revealed the efficacy of dirhodium and ruthenium catalysts, respectively, for the amidation of a series of hydrocarbons with $\text{PhI}=\text{NR}$ ($\text{R} = \text{Ns}$ (SO_2 -*p*- $\text{C}_6\text{H}_4\text{NO}_2$)⁴ and Ts ⁵). However, all these amidation systems require the presynthesis of a nitrene source from $\text{PhI}(\text{OAc})_2$ and NH_2R . In the present work, complex **2** also serves as a good catalyst for amidation of several hydrocarbons directly with commercially available $\text{PhI}(\text{OAc})_2$ and NH_2R ($\text{R} = \text{Ts}$, Ns , and

SO_2Me) as amidating reagents. Especially interesting is that in the case of $\text{R} = \text{COCF}_3$ a direct amination of indan was realized.

Complexes **1** and **2** each bear an electron-deficient porphyrin macrocycle—*meso*-tetrakis(pentafluorophenyl)porphyrinato dianion (TPFPP). Like their counterparts with other porphyrinato ligands,^{2,3,5c} both complexes are efficient catalysts toward $\text{PhI}=\text{NTs}$ amidation of a variety of hydrocarbons including ethylbenzene, indan, adamantane, cyclohexene, tetrahydrofuran, 1,2-dihydronaphthalene, 2-ethylnaphthalene, and 3-hexene. In contrast to previous amidation studies, which were usually carried out with up to a 100 fold-excess of substrates^{3–5} or in an equivolume mixture of substrate and solvent^{2a} to minimize catalyst decomposition,^{4b} complex **1** or **2**-catalyzed amidations can be performed efficiently by employing excess $\text{PhI}=\text{NTs}$ with substrates as limiting reagents. The results obtained for the reactions in dichloromethane at 40 °C with a catalyst:substrate:($\text{PhI}=\text{NTs}$) molar ratio of 1:75:150 are shown in Table 1. It can be seen from Table 1 that indan (entries 3 and 4), adamantane (entries 5 and 6), and 1,2-dihydronaphthalene (entries 11 and



1: M = Ru(II), L = CO
2: M = Mn(III), L = Cl

12) are superior substrates for the amidation reaction catalyzed by either complex **1** or **2**, with excellent conversions obtained for both catalysts. Note that for almost all the amidations shown in Table 1 complex **2** is a more efficient catalyst than complex **1**. With ethylbenzene (entries 1 and 2), tetrahydrofuran (entries 9 and 10), and 2-ethylnaphthalene (entries 13 and 14) as substrates, much higher conversions were obtained by using catalyst **2**. However, in these cases, the yields of *N*-substituted amides (relative to the amounts of substrates consumed) are slightly lower than those obtained for catalyst **1**. Of all the substrates examined, cyclohexene was amidated to the corresponding amide in the highest yield (92%) with a 93% conversion of the alkene (entry 8, catalyst **2**).

Note that the reactions of hydrocarbons allyl benzene, cyclooctene, and 1-octene with $\text{PhI}=\text{NTs}$ in the presence of

catalyst **1** or **2** generated aziridines instead of amides as the predominant products, as shown in entries 16–21 in Table 1. Again, complex **2** is a more efficient catalyst in these cases, catalyzing the aziridination of cyclooctene in 81% yield with 95% substrate conversion (entry 19). For the reactions using allyl benzene (entries 16 and 17) and 1-octene (entries 20 and 21) as substrates, although catalyst **2** resulted in higher conversions of the substrates and higher overall yields of aziridines, the aziridine selectivities were lower than those of catalyst **1**.

The solvent and temperature effects were examined by using indan as the substrate. It was found that dichloromethane was superior to acetonitrile or benzene, and with dichloromethane as solvent the amidations were best performed at 40 °C. For example, decreasing the temperature from 40 to 20 °C led to a decrease in the yield of *N*-tosyl-1-aminoindan (**3**) from 73 to 60% (catalyst **1**). In contrast to oxygen atom transfer reactions such as alkene epoxidations, which usually benefit from donating additives such as methylimidazole (MeIm) and pyridine *N*-oxide (pyO),⁹ introducing additives 1-MeIm, pyO, and 4-Ph-pyO to complex **2**-catalyzed amidation of indan led to a considerable decrease in the yield of amide **3**. For instance, when equimolar quantities of 1-MeIm and $\text{PhI}=\text{NTs}$ were used, only traces of **3** were obtained.

The effect of catalyst loading was inspected in the case of complex **2**-catalyzed amidation of indan. Remarkably, reducing the loading of **2** to 0.04 mol % (relative to starting $\text{PhI}=\text{NTs}$) caused almost no decrease in the yield of **3**, with turnovers increasing to 1600. When 0.013 mol % of **2** was used, turnovers as high as 2600 were achieved. Complex **2**

Table 2. Amidation of Saturated C–H Bonds with $\text{PhI}(\text{OAc})_2$ and NH_2R (R = Ts, Ns, SO_2Me) Catalyzed by Complex **2**^a

$\text{Cycloalkane-H} + \text{PhI}(\text{OAc})_2 + \text{NH}_2\text{R} \xrightarrow{\text{complex 2}} \text{Cycloalkane-NHR}$					
entry	substrate	R	product	conversion (%)	isolated yield (%) ^b
1		Ts		58	81
2		Ts		88	90
3		Ns		93	92
4		SO_2Me		94	81
5		Ts		36	72
6		Ts		86	83
7		Ts		91	85

^a All reactions were performed in CH_2Cl_2 at 40 °C for 2 h with a catalyst:substrate: $\text{PhI}(\text{OAc})_2$: NH_2R molar ratio of 1:100:125:150. ^b On the basis of the amount of substrate consumed.

is also a robust catalyst for alkene aziridination. For example, the $\text{PhI}=\text{NTs}$ aziridination of 1-octene catalyzed by **2** (0.019 mol %) gave rise to 1944 turnovers.

The amidations of ethylbenzene, indan, adamantane, cyclohexene, and tetrahydrofuran directly with $\text{PhI}(\text{OAc})_2$ and NH_2Ts as amidating reagents were explored by employing catalyst **2**. In dichloromethane at 40 °C, with a **2**:substrate: $\text{PhI}(\text{OAc})_2$: NH_2Ts molar ratio of 1:100:125:150, the corresponding *N*-substituted amides were obtained in 72–90% yields within 2 h with good to excellent substrate conversions (Table 2). A comparison of the data in Tables 1 and 2 reveals that the $\text{PhI}(\text{OAc})_2/\text{NH}_2\text{Ts}$ amidations result in comparable or even higher yields than their $\text{PhI}=\text{NTs}$ counterparts. However, the substrate conversions in the former cases are lower except that for ethylbenzene.

Attempts were made to extend the **2**/ $\text{PhI}(\text{OAc})_2$ / NH_2Ts system to other commercially available amides, such as NH_2R ($\text{R} = \text{Ns}$, SO_2Me) and NH_2COCF_3 . As shown in entries 3 and 4 in Table 2, the amidation of indan with $\text{PhI}(\text{OAc})_2/\text{NH}_2\text{R}$ ($\text{R} = \text{Ns}$ or SO_2Me) afforded excellent conversions of the substrate, with the corresponding *N*-substituted amides isolated in up to 92% yields. Remarkably, by employing $\text{PhI}(\text{OAc})_2/\text{NH}_2\text{COCF}_3$ as the amidating reagent, a direct amination of indan was achieved (entry 1 in Table 3). Addition of inorganic bases such as Na_2CO_3 and NaOH led to a significant increase in both the conversion of indan and the yield of 1-aminoindan (entries 2 and 3 in Table 3). For example, in the presence of NaOH , the complex **2**-catalyzed amination of indan with $\text{PhI}(\text{OAc})_2/\text{NH}_2\text{COCF}_3$ afforded 1-aminoindan in 90% isolated yield with good substrate conversion. However, addition of 1-MeIm instead of NaOH to the reaction rendered the catalyst almost completely inactive toward the amination (entry 4 in Table 3).

According to the recent discovery by Breslow and co-workers,⁸ the above-described protocol “complex **1** or **2**/ $\text{PhI}(\text{OAc})_2/\text{NH}_2\text{R}$ ” could offer a new entry for amidation of organic nature products such as aromatic steroid equilenin acetate, which may be important for developing novel types of biologically useful nitrogen-containing products.

Table 3. Amination of Indan with $\text{PhI}(\text{OAc})_2$ and NH_2COCF_3 Catalyzed by Complex **2**^a

entry	additive	conversion (%)	isolated yield (%) ^b
1		55	61
2	Na_2CO_3	69	88
3	NaOH	73	90
4	1-MeIm	trace	trace

^a Reaction conditions: identical with those in Table 2. ^b On the basis of the amount of substrate consumed.

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Supporting Information Available: Detailed experimental procedures and spectral data of the amidation products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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