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Amidation of Unfunctionalized Hydrocarbons Catalyzed by Ruthenium Cyclic Amine or Bipyridine Complexes

Sze-Man Au, Jie-Sheng Huang, Chi-Ming Che,* and Wing-Yiu Yu

Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong

cmche@hku.hk

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Selective amidation of simple hydrocarbons with pre-isolated and in-situ formed iminoiodanes catalyzed by ruthenium complexes $[Ru^{III}(Me_3tacn)(CF_3CO_2)_3{\cdot}H_2O]$ (**2b**, Me_3tacn = *N*,*N*′,*N*″-trimethyl-1,4,7-triazacyclononane) and *cis*-$[Ru^{II}(6,6'\text{-}Cl_2bpy)_2Cl_2]$ (**3**, 6,6′-Cl_2bpy = 6,6′-dichloro-2,2′-bipyridine) was investigated. With PhI=NTs as nitrogen source, both catalysts efficiently promote the amidation of adamantane, cyclohexene, ethylbenzene, cumene, indan, tetralin, and diphenylmethane to afford N-substituted sulfonamides in 80−93% yields with high selectivity. Competitive amidations of para-substituted ethylbenzenes and kinetic isotope effect for the amidation of cyclohexene/cyclohexene-d_{10} suggest that the amidation processes probably proceed via the hydrogen abstraction by a reactive Ru=NTs species to form a carboradical intermediate. The amidation with $PhI(OAc)_2/TsNH_2$ gave results comparable to those obtained with PhI=NTs. Extension of the "$PhI(OAc)_2/TsNH_2$ + catalyst **2b** or **3**" protocol to $MeSO_2NH_2$ and $PhCONH_2$ with ethylbenzene as substrate produced the corresponding N-substituted amides in up to 89% yield.

Introduction

The selective amination of *unfunctionalized* hydrocarbons in the presence of metal catalysts constitutes an appealing route for the synthesis of amines.[1] However, so far only a few such aminations are known, including the allylic amination of alkenes with "ArNHOH + iron or molybdenum catalysts"[2] and "$ArNO_2$/CO + ruthenium or iron catalysts",[3] which are proposed to proceed via an ene-like reaction featuring alkene double bond transposition[2,3b] or involve a metal−alkene complex as active species.[3a] The metal-mediated direct amination of hydrocarbons via alkyl- or arylimido insertion into saturated C−H bonds, a nitrogen analogue of hydroxylation via oxo group transfer process, would serve as another attractive methodology but as yet remains unrealized.[4] Notably, direct amidations of hydrocarbons with "PhI=NTs + manganese porphyrin catalysts"[5] or "PhI=NNs + dirhodium catalysts"[6] have been achieved.[7,8] These putative sulfonylimido group transfer processes provide a unique approach to N-substituted sulfonamides that could be desulfonylated by hydrolytic[9] or reductive[10] methods to amines or used directly as well-protected amines for further functionalizations.

Our quest for ruthenium amination or amidation catalysts was based on the well-documented oxidation chemistry of high-valent ruthenium−oxo complexes.[11] We envisaged that the ruthenium−imido analogues should also exhibit rich oxidation chemistry that has potential application in the C−H bond functionalization. Upon isolation of several imido ruthenium(VI) porphyrins,[12] we found that the bis(tosylimido) complexes **1a**,**b** can undergo stoichiometric amidation with a variety of hydrocarbons.[12b,d] In particular, the amidation of 2-ethylnaphthalene by complex **1b** with a chiral porphyrinato ligand

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(1) (a) Roundhill, D. M. *Chem. Rev.* **1992**, *92*, 1. (b) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675. (c) Johannsen, M.; Jϕrgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689.

(2) (a) Srivastava, A.; Ma, Y.-A.; Pankayatselvan, R.; Dinges, W.; Nicholas, K. M. *J. Chem. Soc., Chem. Commun.* **1992**, 853. (b) Johannsen, M.; Jϕrgensen, K. A. *J. Org. Chem.* **1994**, *59*, 214. (c) Srivastava, R. S.; Nicholas, K. M. *Tetrahedron Lett.* **1994**, *35*, 8739. (d) Srivastava, R. S.; Nicholas, K. M. *Chem. Commun.* **1996**, 2335.

(3) (a) Cenini, S.; Ragaini, F.; Tollari, S.; Paone, D. *J. Am. Chem. Soc.* **1996**, *118*, 11964. (b) Srivastava, R. S.; Nicholas, K. M. *Chem. Commun.* **1998**, 2705.

(4) Some zirconium bisamides, $Cp_2Zr(NHR)_2$, are known to catalyze the hydroamination of alkynes and allene to form enamines and imines via zirconium alkyl- or arylimido intermediates, see for example: (a) Walsh, P. J.; Baranger, A. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 1708. (b) Baranger, A. M.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 2753. These processes are characteristic of the [2 + 2] cycloaddition of Zr=NR multiple bonds with C≡C or C=C bonds, and result in a reduction of the alkynes or allene, unlike the direct insertion of imido groups into saturated C−H bonds. Stoichiometric C−H bond activation of an alkane or arene can be effected by transient $Ti{=}NSiBu^t_3$ species via the 1,2-addition of the C−H bond across the Ti=N multiple bond (Cummins, C. C.; Baxter, S. M.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1988**, *110*, 8731) but such a reaction does not result in imido group transfer to the hydrocarbon.

(5) (a) Breslow, R.; Gellman, S. H. *J. Chem. Soc., Chem. Commun.* **1982**, 1400. (b) Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1983**, *105*, 6728. (c) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. *Tetrahedron Lett.* **1988**, *29*, 1927. (d) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. *New J. Chem.* **1989**, *13*, 651. (e) Yang, J.; Weinberg, R.; Breslow, R. *Chem. Commun.* **2000**, 531.

(6) (a) Müller, P.; Baud, C.; Jacquier, Y.; Moran, M.; Nägeli, I. *J. Phys. Org. Chem.* **1996**, *9*, 341. (b) Nägeli, I.; Baud, C.; Bernardinelli, G.; Jacquier, Y.; Moran, M.; Müller, P. *Hel. Chim. Acta* **1997**, *80*, 1087.

(7) For related amidation with chloramine-T trihydrate ($TsNClNa{\cdot}3H_2O$) catalyzed by copper complex, see: Albone, D. P.; Aujla, P. S.; Taylor, P. C.; Challenger, S.; Derrick, A. M. *J. Org. Chem.* **1998**, *63*, 9569.

(8) For related amidation with alkyl peroxycarbamate ($Bu^tOOCONHTs$) catalyzed by copper complexes, see: Kohmura, Y.; Kawasaki, K.-i.; Katsuki, T. *Synlett* **1997**, 1456.

(9) Roemmele, R. C.; Rapoport, H. *J. Org. Chem.* **1988**, *53*, 2367.

(10) Fleming, I.; Frackenpohl, J.; Ila, H. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1229, and many references therein.

(11) For reviews, see: (a) Griffith, W. P. *Chem. Soc. Rev.* **1992**, *21*, 179. (b) Che, C.-M.; Yam, V. W. W. *Adv. Inorg. Chem.* **1992**, *39*, 233.

(12) (a) Huang, J. S.; Che, C.-M.; Poon, C.-K. *J. Chem. Soc., Chem. Commun.* **1992**, 161. (b) Au, S.-M.; Huang, J.-S.; Yu, W.-Y.; Fung, W.-H.; Che, C.-M. *J. Am. Chem. Soc.* **1999**, *121*, 9120. (c) Huang, J.-S.; Sun, X.-R.; Leung, S. K.-Y.; Cheung, K.-K.; Che, C.-M. *Chem. Eur. J.* **2000**, *6*, 334. (d) Zhou, X.-G.; Yu, X.-Q.; Huang, J.-S.; Che, C.-M. *Chem. Commun.* **1999**, 2377.

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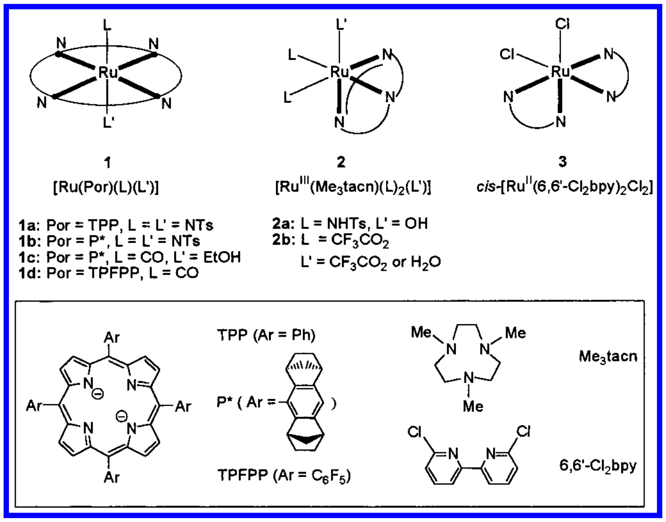
results in the highest enantiocontrol yet obtained for a metal-mediated asymmetric amidation of saturated C−H bonds.[12d] On the basis of these findings, catalytic amidations with "PhI=NTs + ruthenium porphyrin **1c** or **1d**" were eventually developed.[12d,13] However, isolated high-valent ruthenium−imido complexes without porphyrin auxiliaries are extremely rare,[14] and none of them have been reported to undergo amidation reactions with a hydrocarbon.

The present work deals with the PhI=NTs amidation of hydrocarbons catalyzed by ruthenium *non-porphyrin* complexes **2** and **3**,[15] which proceeds probably via sulfonylimido insertion into saturated C−H bonds. Moreover, like electron-deficient manganese porphyrin [Mn(TPFPP)Cl],[13] complexes **2b** and **3** can catalyze the amidation directly with commercially available $PhI(OAc)_2/TsNH_2$ without the necessity to pre-isolate PhI=NTs.[16] The "$PhI(OAc)_2/TsNH_2$ + **2b** or **3**" protocol can be extended to $MeSO_2NH_2$ and $PhCONH_2$, in which cases the corresponding iminoiodanes are either explosive ($PhI{=}NSO_2Me$) or unknown (PhI=NCOPh).[16] This significantly increases the types of amides that can be prepared via ruthenium-catalyzed amidations. Especially, the amidation of ethylbenzene with "$PhI(OAc)_2/PhCONH_2$ + **2b** or **3**" provides *the first access to an N-substituted amide of carboxylic acid via metal-catalyzed amidation of saturated C−H bonds.*



Results and Discussion

Catalyst Development. We previously demonstrated that the ligands *N*,*N*′,*N*″-trimethyl-1,4,7-triazacyclononane (Me_3tacn) and 6,6′-dichloro-2,2′-bipyridine (6,6′-Cl_2bpy) are well suited for accessing highly oxidizing and sterically bulky ruthenium-oxo complexes.[17] Both ligands exhibit a remarkable capability of stabilizing *cis*-dioxo functional groups, contrary to the *trans*-dioxo groups constrained by the porphyrin ligands.[18] In addition, by employing the Ru−Me_3tacn complex **2b** as a catalyst, the *tert*-butyl hydroperoxide epoxidation of alkenes[19] and oxidation of alcohols[20] were found to be highly chemoselective.

To uncover efficient non-porphyrin ruthenium amidation catalysts, we screened a variety of ruthenium complexes with tetra-, tri-, and bidentate ligands, of which those containing Me_3tacn (complexes **2a**,**b**) and 6,6′-Cl_2bpy (complex **3**) gave the best results.[21] Catalysts **2** and **3** have several features in common. One is that they are more easily accessible than the porphyrin catalysts **1c**,**d**. Further, they bear neutral chelating ligands that are robust toward oxidation,[17] with the coordination atoms arranged in a facial or helical geometry, in contrast to the planar coordination mode of the porphyrinato dianions in **1c**,**d**. Finally, they might be converted preferentially to *cis*-bis(imido) species, as in the case of the *cis*-dioxo analogues mentioned above, which contrasts with the *trans*-bis(imido) active species in **1c**- or **1d**-catalyzed amidations.[12d,13] These features may cause the catalytic activity or selectivity of the non-porphyrin complexes **2** and **3** to be different from that of the porphyrin complexes. With regard to catalysts **2a**[15] and **2b**, the former was found to be rather moisture sensitive. Consequently, catalyst **2b**, which is stabler to moisture yet effects the amidation more rapidly, was used throughout this work.

Complex 2b- or 3-Catalyzed Amidation with PhI=NTs. (i) Substrate Scope. Both complexes **2b** and **3** are efficient catalysts for the PhI=NTs amidation of various hydrocarbons from adamantane to allylic or benzylic alkenes. The amidations were generally conducted at room temperature for 3 h by employing 2 mol % catalysts (relative to the starting PhI=NTs) and a slight excess of hydrocarbon substrates. This contrasts with catalyst **2a**[15] and other non-porphyrin amidation catalysts,[6−8] which require much longer time (12 h for **2a** and 15−72 h for the others) to reach completion and often employ larger excess of substrates. The results obtained for **2b** or **3**-catalyzed amidations of adamantane, cyclohexene, ethylbenzene, cumene, indan, tetralin, and diphenylmethane in acetonitrile (**2b**) or dichloromethane (**3**) are summarized in Table 1. In all cases the unsubstituted sulfonamide ($TsNH_2$) was observed to be a major byproduct, with the total moles of $TsNH_2$ and the desired N-substituted amide close to those of starting PhI=NTs. Since excess substrates were used in the amidation

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[13] Yu, X.-Q.; Huang, J.-S.; Zhou, X.-G.; Che, C.-M. *Org. Lett.* **2000**, *2*, 2233.

[14] (a) Redshaw, C.; Clegg, W.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1992**, 2059. (b) Danopoulos, A. A.; Wilkinson, G.; Hussain-Bates, B.; Hursthouse, M. B. *Polyhedron* **1992**, *11*, 2961.

[15] The stoichiometric amidation by complex **2a**/$AgClO_4$ and the PhI=NTs amidation catalyzed by complex **2a** were preliminarily reported elsewhere: Au, S.-M.; Zhang, S.-B.; Fung, W.-H.; Yu, W.-Y.; Che, C.-M.; Cheung, K.-K. *Chem. Commun.* **1998**, 2677.

[16] The known iminoiodanes, such as PhI=NTs and PhI=NNs, were all prepared from the reactions between $PhI(OAc)_2$ and the corresponding amides under basic conditions, see: Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123 and the references therein.

[17] (a) Che, C.-M.; Leung, W.-H. *J. Chem. Soc., Chem. Commun.* **1987**, 1376. (b) Wong, K.-Y.; Lee, W.-O.; Che, C.-M.; Anson, F. C. *J. Electroanal. Chem.* **1991**, *319*, 207. (c) Cheng, W.-C.; Yu, W.-Y.; Cheung, K.-K.; Che, C.-M. *J. Chem. Soc., Dalton Trans.* **1994**, 57. (d) Cheng, W.-C.; Yu, W.-Y.; Cheung, K.-K.; Che, C.-M. *J. Chem. Soc., Chem. Commun.* **1994**, 1063.

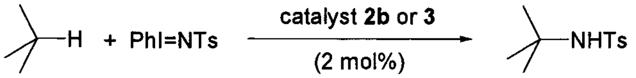
[18] Selected examples: (a) Groves, J. T.; Quinn, R. *Inorg. Chem.* **1984**, *23*, 3844. (b) Leung, W.-H.; Che, C.-M. *J. Am. Chem. Soc.* **1989**, *111*, 8812. (c) Ho, C.; Leung, W.-H.; Che, C.-M. *J. Chem. Soc., Dalton Trans.* **1991**, 2933.

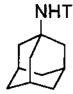
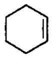
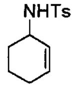
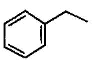
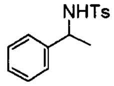
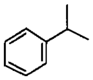
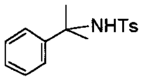
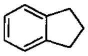
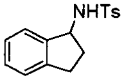
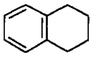
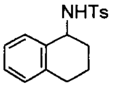
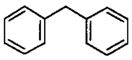
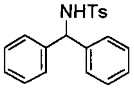
[19] Cheng, W.-C.; Fung, W.-H.; Che, C.-M. *J. Mol. Catal. A* **1996**, *113*, 311.

[20] Fung, W.-H.; Yu, W.-Y.; Che, C.-M. *J. Org. Chem.* **1998**, *63*, 2873.

[21] Other ruthenium complexes screened include [Ru^{II}(salen)(PPh_3)$_2$] (prepared as in: Bhowon, M. G.; Wah, H. L. K.; Narain, R. *Polyhedron* **1999**, *18*, 341, salen = 1,2-bis(3,5-dichlorosalicylideneamino)ethane dianion), [Ru^{II}(Tp)(PPh_3)$_2$Cl] (prepared as in: Alcock, N. W.; Burns, I. D.; Claire, K. S.; Hill, A. F. *Inorg. Chem.* **1992**, *31*, 2906, Tp = hydrotris(pyrazol-1-yl)borate), [Ru^{II}(COD)Cl_2]$_n$ (95%, Aldrich, COD = η^4-1,5-cyclooctadiene), and $RuCl_3 \cdot xH_2O$ (Aldrich). These complexes were found to be poor catalysts for the amidation reactions.

Table 1. Amidation of Saturated C−H Bonds with PhI=NTs Catalyzed by Complex 2b or 3[a]



Entry	Substrate	Product	Catalyst	Conversion (%)	Yield (%)[b]
1			**2b**	57	87
2			**3**	52	86
3			**2b**	57	90
4			**3**	58	92
5			**2b**	79	93
6			**3**	70	90
7			**2b**	38	80
8			**3**	40	90
9			**2b**	53	85
10			**3**	49	81
11			**2b**	57	86
12			**3**	50	84
13			**2b**	61	90
14			**3**	58	89

[a] Reaction conditions: 25 °C, 3 h, catalyst:(PhI=NTs):substrate mole ratio = 1:50:60, MeCN (**2b**) or CH_2Cl_2 (**3**). [b] GC yield based on the amount of substrate consumed.

processes, the substrate conversions obtained are rather good, the best (79%, entry 5) of which is close to the quantitative value of ~83%.

The amidation of adamantane (entries 1 and 2) selectively occurred at the tertiary C−H bonds, with the corresponding amide formed in ~87% yields (based on the amount of adamantane consumed). Such tertiary C−H bond selectivity has been observed in the amidations of the same substrate involving complexes **1a**,[12b] **1d**,[13] and **2a**.[15] However, the PhI=NNs amidation of adamantane catalyzed by previously reported dirhodium catalyst took place at both tertiary and secondary C−H bonds, affording a mixture of the corresponding amides in a 71:5 ratio.[6b]

With cyclohexene as substrate, both catalysts **2b** and **3** resulted in allylic amidations to form *N*-(cyclohex-2-en-1-yl)tosylamide in excellent yields (entries 3 and 4). Interestingly, no aziridine was detected in the reaction although many metal-catalyzed aziridinations of unfunctionalized alkenes with PhI=NTs have been known.[22] In contrast, the amidation of cyclohexene in other nonporphyrin amidation systems including "PhI=NNs + $Rh_2(OAc)_4$"[6] and "TsNClNa + copper catalyst"[7] did afford a mixture of the corresponding amide and aziridine. The "$Bu^tOOCONHTs + Cu(OTf)_2$" system was not reported to produce the aziridine but the yield of the desired amide was rather low (27%).[8]

Of the amidation results in Table 1, the best were achieved for the benzylic substrate ethylbenzene (entries 5 and 6), whose amidation was directed toward the saturated C−H bonds of the benzyl moiety to form the corresponding amide in 93 (**2b**) and 90% (**3**) yields with good to excellent substrate conversions. Extension of such a benzylic amidation to other substrates, including cumene (entries 7 and 8), indan (entries 9 and 10), tetralin (entries 11 and 12), and diphenylmethane (entries 13 and 14) gave comparable results but the substrate conversions were considerably lower. It is astonishing that diphenylmethane is a good substrate for complex **2** or **3**-catalyzed amidation,[23] which is superior to other benzylic hydrocarbons examined in this work except ethylbenzene. Previously, only dirhodium acetate was reported to effect the iminoiodane amidation of diphenylmethane;[6b] however, in that case the yield of the corresponding amide was much lower than those obtained for other benzylic hydrocarbons such as indan and tetralin.

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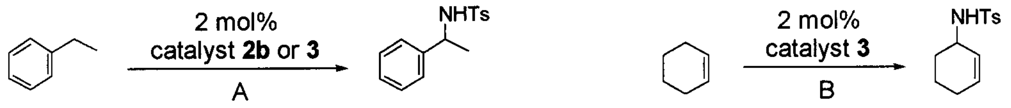
[22] Representative examples: (a) Mansuy, D.; Mahy, J.-P.; Dureault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc., Chem. Commun.* **1984**, 1161. (b) O'Connor, K. J.; Wey, S.-J.; Burrows, C. J. *Tetrahedron Lett.* **1992**, *33*, 1001. (c) Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326. (d) Noda, K.; Hosoya, N.; Irie, R.; Ito, Y.; Katsuki, T. *Synlett* **1993**, 469. (e) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742.

[23] For related complex **2a**-catalyzed amidations, see ref 15.

Table 2. Effects of Solvent, Temperature, Nitrogen Source, and Catalyst Loading in Amidation of Ethylbenzene and Cyclohexene Catalyzed by Complex 2b or 3



entry	reaction	nitrogen source	solvent	T (°C)	conversion (%)	yield[a] (%)
1	A (**2b**)	PhI=NTs	toluene	25	49	75
2	A (**2b**)	PhI=NTs	CH_2Cl_2	25	69	82
3	A (**2b**)	PhI=NTs	MeCN	25	79	93
4	A (**2b**)	PhI=NTs	MeCN	82	63	79
5	A (**2b**, 1 mol %)	PhI=NTs	MeCN	25	60	89
6	A (**2b**)	$PhI(OAc)_2 + TsNH_2$	MeCN	25	76	90
7	A (**3**)	PhI=NTs	CH_2Cl_2	25	70	90
8	A (**3**)	PhI=NTs	CH_2Cl_2	40	73	85
9	B	PhI=NTs	acetone	25	25	81
10	B	PhI=NTs	MeCN	25	31	85
11	B	PhI=NTs	CH_2Cl_2	25	58	92
12	B	PhI=NTs	CH_2Cl_2	40	63	92
13	B	$PhI(OAc)_2 + TsNH_2$	CH_2Cl_2	25	55	89

[a] GC yield based on the amount of substrate consumed.

(ii) Effect of Solvent, Temperature, and Catalyst Loading. While we preliminarily reported the complex **2a**-catalyzed amidations,[15] the reactions were all conducted in acetonitrile at room temperature with 2 mol % catalyst. To ascertain how solvent, temperature and catalyst loading affect the amidation efficiency of this class of ruthenium catalyst, we carried out the amidation reactions of ethylbenzene in various solvents, including toluene, dichloromethane and acetonitrile at different temperatures by employing the more reactive catalyst **2b**. The results are shown in entries 1−4 in Table 2. Evidently, acetonitrile is the solvent of choice, which results in a considerably higher yield of the amide than either toluene or dichloromethane at room temperature. With acetonitrile as solvent, increasing temperature to 82 °C led to a significant decrease of both the substrate conversion and amide selectivity (cf. entries 3 and 4 in Table 2). This might be ascribed to the thermal decomposition of PhI=NTs in this solvent. Not surprisingly, reducing the loading of **2b** from 2 to 1 mol % caused a considerable decrease of the substrate conversion but with a slight decerease in the amide selectivity (cf. entries 3 and 5).

The effects of solvent and temperature were also inspected in the case of complex **3**-catalyzed amidation of ethylbenzene and cyclohexene (entries 7−12 in Table 2). Unlike the case of catalyst **2b**, of the solvents (dichloromethane, acetone, and acetonitrile) investigated in the **3**-catalyzed amidation at room temperature, dichloromethane, rather than acetonitrile, is clearly the superior one (cf. entries 9−11). Moreover, in contrast with the deleterious effect of higher temperature on the **2b**-catalyzed amidation of ethylbenzene in acetonitrile, elevation of temperature in the **3**-catalyzed amidation of either ethylbenzene or cyclohexene in dichloromethane resulted in slightly higher substrate conversion with little or no loss of amide selectivity (cf. entries 7 and 8; 11 and 12).

(ii) Mechanistic Aspects. Metal-catalyzed amidations of hydrocarbons with iminoiodanes such as PhI=NTs are generally proposed to involve metal−imido active species.[5,6,12d] However, only in the case of ruthenium porphyrin catalyst was an imido intermediate isolated.[12d] By analogy with iron- or manganese porphyrin-catalyzed alkene hydroxylations with PhIO, the PhI=NTs allylic amidations catalyzed by manganese porphyrins are postulated to proceed via hydrogen atom abstraction by a high-valent Mn=NTs intermediate.[5c] Mechanistic studies on the dirhodium-catalyzed amidations[6b] reveal that either a direct insertion or hydrogen abstraction/radical recombination mechanism must be operative.

Table 3. Relative Rates (k_{rel}) for the PhI=NTs Amidation of Ethylbenzenes (p-X-$C_6H_4CH_2CH_3$) Catalyzed by Complex 2b or 3

entry	X	k_{rel}	
		catalyst **2b**	catalyst **3**
1	MeO	4.65	5.66
2	Me	2.09	1.88
3	Cl	1.39	1.29
4	F	1.09	1.12
5	H	1	1

To help elucidate the mechanism of complex **2b** or **3**-catalyzed amidations, we performed competition experiments for the catalytic PhI=NTs amidation of para-substituted ethylbenzenes. The measured relative amidation rates, k_{rel}, of p-X-$C_6H_4CH_2CH_3$ (X = MeO, Me, Cl, F) against that of ethylbenzene for both catalysts are summarized in Table 3. It is evident from the table that either electron-donating or -withdrawing para-substituents promote the amidation processes. This contrasts with the dirhodium-catalyzed PhI=NNs amidations of ethylbenzenes which are retarded by electron-withdrawing, although promoted by electron-donating para-substituents.[6b] However, the results in Table 3 are parallel to those obtained for the stoichiometric amidation of the same substituted ethylbenzenes by bis(tosylimido) ruthenium(VI) porphyrin **1a**[12b] or the non-porphyrin complex **2a**/$AgClO_4$.[15]

In the case of either catalyst **2b** or **3**, plotting the log(k_{rel}) against the Hammett constant σ of the para-substituent resulted in a concave instead of a straight line, suggesting the intervention of a radical intermediate in the amidation processes.[24] Consequently, the log(k_{rel}) was plotted against a carboradical parameter, TE,[25] as

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(24) Groves, J. T.; Gross, Z.; Stern, M. K. *Inorg. Chem.* **1994**, *33*, 5065.

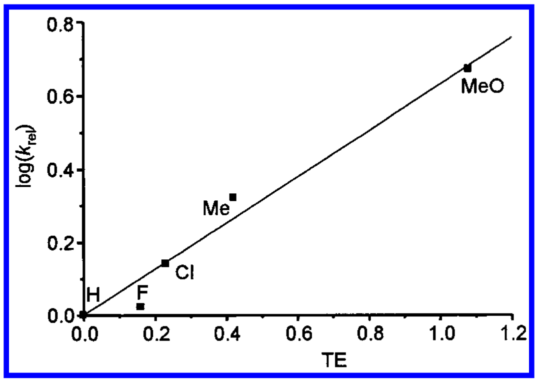

Figure 1. Log(k_{rel}) vs TE plot for the **2b**-catalyzed amidation of para-substituted ethylbenzenes p-X-$C_6H_4CH_2CH_3$ with PhI=NTs.

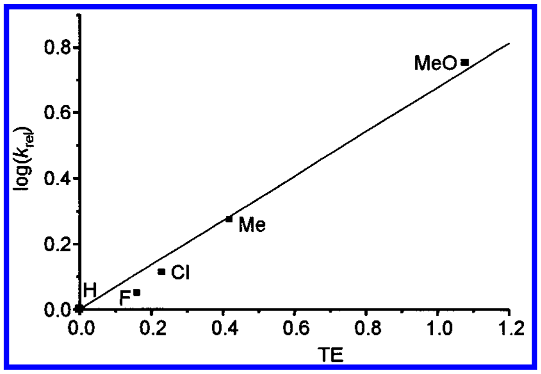

Figure 2. Log(k_{rel}) vs TE plot for the **3**-catalyzed amidation of para-substituted ethylbenzenes p-X-$C_6H_4CH_2CH_3$ with PhI=NTs.

previously done for the stoichiometric amidation by complex **1a**.[12b] Interestingly, the log(k_{rel}) vs TE plots for catalysts **2b** and **3** both exhibit a good linearity, as shown in Figures 1 and 2. The slopes of the plots ($\rho_{TE}^{\bullet}$) were determined to be 0.63 (catalyst **2b**) and 0.68 (catalyst **3**), which are similar to the $\rho_{TE}^{\bullet}$ (0.62) obtained for the stoichiometric amidation by complex **1a**.[12b] We previously reported[15] that plotting log(k_{rel}) against another radical parameter, $\sigma_{JJ}^{\bullet}$,[26] for the stoichiometric amidation by complex **2a**/$AgClO_4$ gave rise to a good linearity. To compare this stoichiometric amidation with the closely related catalytic amidation of **2b**, we also plotted the log(k_{rel}) of **2a**/$AgClO_4$ against TE and obtained an excellent linearity with $\rho_{TE}^{\bullet}$ of 0.72, a value comparable to that obtained for the **2b**-catalyzed amidation. These observations indicate that the active species in these ruthenium-mediated amidations should be similar. Therefore, the PhI=NTs amidations of ethylbenzenes catalyzed by complex **2b** or **3** most probably involve a benzylic radical intermediate generated via the hydrogen atom abstraction by a high-valent Ru=NTs species. To provide further evidence for this mechanism, we inspected the kinetic isotope effect for either **2b** or **3**-catalyzed amidation of cyclohexene and cyclohexene-d_{10}. These systems were found to exhibit a primary kinetic isotope effect, with k_H/k_D of 6.5 (catalyst **2b**) and 6.1 (catalyst **3**). The k_H/k_D values are similar to that determined for the stoichiometric amidation of the same substrates by complex **1a** (6.1),[12b] and are not inconsistent with a hydrogen abstraction process.

Although the amidations catalyzed by complex **2b** and **3** likely involve high-valent Ru=NTs intermediates, attempts to isolate these species in the catalytic reactions were unsuccessful. In fact, isolable high-valent ruthenium imido complexes without porphyrin ligands are extremely rare,[14] as mentioned earlier. The possibility of generating Ru=NTs species bearing a Me_3tacn ligand has been discussed before.[15] In this work, we examined the behavior of complex **3** toward the attack by PhI=NTs and observed that treating a solution of **3** in dichloromethane with PhI=NTs (~2 equiv) resulted in a color change to brown accompanied by the disappearance of the MLCT band of **3** in the UV−visible spectrum. Investigation of the reaction by electrospray mass spectrometry gave an intense peak at m/z 756 which can be ascribed to the $[Ru(6,6'\text{-}Cl_2bpy)_2(NTs)Cl]^+$ species. Efforts are underway to isolate and fully characterize the intriguing new ruthenium complex.

Complex 2b- or 3-Catalyzed Amidation with PhI(OAc)$_2$/RNH$_2$ (R = Ts, MeSO$_2$, and PhCO). A major drawback of the amidation with PhI=NR lies in the rather limited types of the iminoiodanes currently attainable.[16,27] It would be interesting if the precursors to PhI=NR, namely $PhI(OAc)_2$ and RNH_2, can be directly used in the amidation reactions to allow the iminoiodanes formed in-situ immediately amidate hydrocarbons in the presence of a metal catalyst. In this manner, the preparation of N-substituted amides through amidation of hydrocarbons for the R groups whose corresponding PhI=NR's are unstable or unknown could be realized.

We initially explored the possibility of directly using commercially available $PhI(OAc)_2/TsNH_2$ instead of PhI=NTs as the nitrogen source. The results achieved for **2b**-catalyzed amidation of ethylbenzene and **3**-catalyzed amidation of cyclohexene are shown in Table 2 (entries 6 and 13), which are fairly similar to those obtained for the corresponding amidations with PhI=NTs (cf. entries 6 and 3; entries 13 and 11). This encouraged us to attempt extension of the "$PhI(OAc)_2/TsNH_2$ + **2b** or **3**" protocol to $MeSO_2NH_2$, the corresponding iminoiodane of which has never been used as the nitrogen source in the amidations probably owing to its unstable and explosive nature.[16] Table 4 (entries 2 and 11) shows the results obtained for the amidation of ethylbenzene with "$PhI(OAc)_2/MeSO_2NH_2$ + **2b** or **3**". Notably, by employing either of the catalysts, the N-substituted methanesulfonamide was obtained in 85% yield with ~50% substrate conversion.

Remarkably, the "$PhI(OAc)_2/RNH_2$ + **2b** or **3**" protocol is applicable to $PhCONH_2$. The results achieved for the amidation of ethylbenzene to form *N*-(1-phenylethyl)-benzamide are also shown in Table 4.[28] When the **2b**-catalyzed amidation of ethylbenzene was carried out in dichloromethane at room temperature for 12 h with **2b**/ethylbenzene/$PhI(OAc)_2/PhCONH_2$ mole ratio of 1:60:50:

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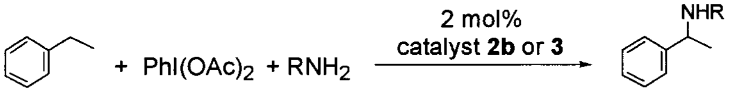
[25] Wu, Y.-D.; Wong, C.-L.; Chan, K. W. K.; Ji, G.-Z.; Jiang, X.-K. *J. Org. Chem*. **1996**, *61*, 746.

[26] Jiang, X.-K. *Acc. Chem. Res.* **1997**, *30*, 283.

[27] (a) Södergren, M. J.; Alonso, D. A.; Bedekar, A. V.; Andersson, P. G. *Tetrahedron Lett.* **1997**, *38*, 6897. (b) Dauban, P.; Dodd, R. H. *J. Org. Chem*. **1999**, *64*, 5304.

[28] We noted that *N*-(1-phenylethyl)benzamide could also be prepared, *in two steps*, via mercury-mediated addition of benzamide to styrene, see: (a) Barluenga, J.; Jiménez, C.; Nájera, C.; Yus, M. *J. Chem. Soc., Chem. Commun.* **1981**, 670. (b) Barluenga, J.; Jiménez, C.; Nájera, C.; Yus, M. *J. Chem. Soc., Perkin Trans. 1* **1983**, 591. These processes result in a reduction of the hydrocarbon and require the use of a stoichiometric amount of highly toxic mercury compounds.

Table 4. Amidation of Ethylbenzene with $PhI(OAc)_2/RNH_2$ Catalyzed by Complex 2b or 3[a]



entry	catalyst	RNH_2	solvent	additive	conversion (%)	yield[b] (%)
1	**2b**	$PhCONH_2$	CH_2Cl_2		63	89
2	**2b**	$MeSO_2NH_2$	CH_2Cl_2		51	85
3	**2b**	$PhCONH_2$	CH_2Cl_2	Im or py	36	83
4	**2b**	$PhCONH_2$	CH_2Cl_2	Lut	31	82
5	**2b**	$PhCONH_2$	CH_2Cl_2	2,6-Cl_2py	34	82
6	**2b**	$PhCONH_2$	CH_2Cl_2	K_2CO_3	47	85
7[c]	**2b**	$PhCONH_2$	CH_2Cl_2		19	80
8	**3**	$PhCONH_2$	CH_2Cl_2		59	87
9	**3**	$PhCONH_2$	MeCN		49	85
10	**3**	$PhCONH_2$	acetone		29	82
11	**3**	$MeSO_2NH_2$	CH_2Cl_2		46	85

[a] Reaction conditions: 25 °C, 12 h, catalyst/ethylbenzene/$PhI(OAc)_2/RNH_2$ mole ratio = 1:60:50:50. [b] GC yield based on the amount of substrate consumed. [c] NBS was used instead of $PhI(OAc)_2$.

50, the corresponding N-substituted benzamide was formed in 89% yield with 63% substrate conversion (entry 1). Similar results were achieved under the same conditions by employing catalyst **3** (entry 8). We found that the amidation of ethylbenzene with "$PhI(OAc)_2/PhCONH_2$ + **2b**" led to virtually indistinguishable results in dichloromethane and acetonitrile; however, a considerable solvent effect was observed for the "$PhI(OAc)_2/PhCONH_2$ + **3**" system, with the substrate conversion and the amide yield follow the order dichloromethane > acetonitrile > acetone (cf. entries 8−10).

It can be expected that the amidations with $PhI(OAc)_2/RNH_2$ would involve the formation of acetic acid. Accordingly, addition of bases to the amidation reactions may be beneficial to improving the catalyst efficiency. To our surprise, when organic bases such as imidazole (Im), pyridine (py), 2,6-dichloropyridine (2,6-Cl_2py), and 2,6-lutidine (Lut) were introduced in either catalytic or stoichiometric amounts to the amidation of ethylbenzene with "$PhI(OAc)_2/PhCONH_2$ + **2b**", the substrate conversions were approximately halved, accompanied by a slight decrease in the amide selectivity (cf. entry 1 and entries 3−5 in Table 4). Adding inorganic bases such as K_2CO_3 to the system also considerably reduced the substrate conversion, with the amide selectivity decreased slightly (cf. entries 1 and 6). On the other hand, although additives such as pyridine *N*-oxide or "pyridine *N*-oxide + pyridine" are reported to promote sulfonylimido group transfer to styrene in the "Ts_2O + nitrido manganese-salen" system,[29] introducing such additives to the reaction of ethylbenzene with $PhI(OAc)_2/PhCONH_2$ in the presence of catalyst **2b** or **3** made the catalyst completely loss their activity toward the amidation.

Note that in the case of $PhI(OAc)_2/TsNH_2$ amidations, the in-situ formed PhI=NTs is most probably responsible for the generation of active amidating species; however, it is not clear whether the unknown PhI=NCOPh is really involved in the $PhI(OAc)_2/PhCONH_2$ counterparts. Recognizing the oxidative nature of $PhI(OAc)_2$, we tried to replace $PhI(OAc)_2$ with other oxidants such as *N*-bromosuccinimide (NBS) and found that the "NBS/$PhCONH_2$ + catalyst **2b**" system could also amidate ethylbenzene to form *N*-(1-phenylethyl)benzamide in 80% yield but with a low substrate conversion (19%, entry 7 in Table 4).

Conclusion

Ruthenium complexes **2b** and **3** are efficient catalysts for the amidation of a series of unfunctionalized hydrocarbons with PhI=NTs. These catalytic amidation reactions exhibit high selectivity for adamantane (only the tertiary C−H bonds are amidated), cyclohexene (no aziridination was observed), ethylbenzene, cumene, indan, tetralin, and diphenylmethane (all result in the amidation of the benzylic C−H bond). Competition experiments on para-substituted ethylbenzenes reveal that both electron-donating and -withdrawing substituents promote the amidation processes, with $\log(k_{rel})$ vs TE (a carboradical parameter) plots exhibiting good linearity and having small $\rho_{TE}^{\bullet}$ values of 0.63 (catalyst **2b**) and 0.68 (catalyst **3**), which can accommodate a hydrogen abstraction mechanism involving a carboradical intermediate. Kinetic isotope effect measurements on the amidation of cyclohexene/cyclohexene-d_{10} give k_H/k_D values of 6.5 (catalyst **2b**) and 6.1 (catalyst **3**), consistent with the hydrogen abstraction mechanism. Both complexes **2b** and **3** can also efficiently catalyze the amidation of ethylbenzene or cyclohexene directly with commercially available $PhI(OAc)_2/TsNH_2$, demonstrating the feasibility of an amidation protocol "$PhI(OAc)_2/RNH_2$ + ruthenium catalyst". The amidation of ethylbenzene with "$PhI(OAc)_2/RNH_2$ + catalyst **2b** or **3**" affords the corresponding N-substituted amides in 85% yield with R = $MeSO_2$ and up to 89% yield with R = PhCO. The present work contributes the first metal-catalyzed amidation of saturated C−H bonds that forms an N-substituted amide of carboxylic acid.

Experimental Section

General Methods. Acetonitrile (predistilled from potassium permanganate), toluene, and cyclohexene were distilled from calcium hydride under nitrogen. Dichloromethane was purified as described previously.[12b] Adamantane was recrystallized from ethanol. Ethylbenzene and its para-substituted derivatives, cumene, tetralin, indan, and diphenylmethane, were purified by passing through a column of activated alumina. Complexes $[Ru^{III}(Me_3tacn)(CF_3CO_2)_3{\cdot}H_2O]$ (**2b**)[20] and

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[29] Minakata, S.; Ando, T.; Nishimura, M.; Ryu, I.; Komatsu, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3392.

cis-[$\mathrm{Ru^{II}}$(6,6′-$\mathrm{Cl_2bpy)_2Cl_2}$] (**3**)[17a,b] were prepared by the literature methods.

General Procedure for Complex 2b- or 3-Catalyzed Amidation with PhI═NTs. To a mixture of substrate (0.72 mmol), catalyst (0.012 mmol), and solvent (10 mL) was added PhI═NTs (0.6 mmol). The reaction mixture was stirred at room temperature for 3 h and then evaporated to dryness. The organic products were extracted with diethyl ether. Aliquots of the extract were then analyzed by GC. The reaction products were identified by comparing their retention times with those of authentic samples.[30] The quantities of the products and the consumed substrate were determined in the presence of an internal standard.

General Procedure for Complex 2b- or 3-Catalyzed Amidation with $\mathbf{PhI(OAc)_2/RNH_2}$. This procedure is identical with that described above except that $\mathrm{PhI(OAc)_2}$ and $\mathrm{RNH_2}$ (0.6 mmol each) were used instead of PhI═NTs and that the reaction mixture was stirred for 12 h rather than 3 h.[31]

Competitive PhI═NTs Amidation of Para-Substituted Ethylbenzenes or Cyclohexene/Cyclohexene-d_{10}. Complex **2b** or **3** (0.02 mmol) was added to a mixture of PhI═NTs (0.5 mmol) and ethylbenzene/*p*-X-$\mathrm{C_6H_4CH_2CH_3}$ or cyclohexene/cyclohexene-d_{10} (1 mmol each) in acetonitrile or dichloromethane (10 mL) containing 1,4-dichlorobenzene (1 mmol) as the internal standard. The mixture was stirred at room temperature for 3 h. The remaining quantities of ethylbenzene ($\mathrm{H_f}$) and *p*-X−$\mathrm{C_6H_4CH_2CH_3}$ ($\mathrm{X_f}$) or cyclohexene ($\mathrm{H_f}'$) and cyclohexene-d_{10} ($\mathrm{D_f}$) were determined by GC. The relative amidation rates k_{rel} of the ethylbenzenes and the kinetic isotope effects $k_{\mathrm{H}}/k_{\mathrm{D}}$ of cyclohexene were calculated from the following equations:[20]

$$k_{\mathrm{rel}} = \log(\mathrm{X_f}/\mathrm{X_i})/\log(\mathrm{H_f}/\mathrm{H_i})$$

$$k_{\mathrm{H}}/k_{\mathrm{D}} = \log(\mathrm{H_f}'/\mathrm{H_i}')/\log(\mathrm{D_f}/\mathrm{D_i})$$

where $\mathrm{X_i}$, $\mathrm{H_i}$, $\mathrm{H_i}'$, and $\mathrm{D_i}$ are the initial quantities of *p*-X-$\mathrm{C_6H_4}$-$\mathrm{CH_2CH_3}$, ethylbenzene, cyclohexene, and cyclohexene-d_{10}, respectively.

Acknowledgment. This work was supported by The University of Hong Kong and the Hong Kong Research Grants Council.

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[30] For preparation of authentic samples of the hydrocarbon amidation products, see: (a) Reference 12b (adamantane, cyclohexene, ethylbenzene, and cumene). (b) Reference 7 (indan). (c) Reference 8 (tetralin). (d) McFarland, J. W.; Schut, D.; Zwanenburg, B. *Tetrahedron* **1981**, *37*, 389 (diphenylmethane).

[31] For preparation of authentic samples of *N*-(1-phenylethyl)-methanesulfonamide and *N*-(1-phenylethyl)benzamide, see, respectively: (a) Kim, S. Y.; Sung, N.-D.; Choi, J.-K.; Kim, S. S. *Tetrahedron Lett.* **1999**, *40*, 117. (b) Reference 28.