

# Ruthenium-mediated amidation of saturated C–H bonds and crystal structure of a bis(tosyl)amidoruthenium(III) complex of 1,4,7-trimethyl-1,4,7-triazacyclononane

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A bis(tosyl)amidoruthenium(III) complex of 1,4,7-trimethyl-1,4,7-triazacyclononane ( $\text{Me}_3\text{tacn}$ ) is prepared, and its crystal structure revealed the two tosylamido ligands in a *cis* configuration; the  $[\text{Ru}^{\text{III}}(\text{Me}_3\text{tacn})(\text{NHTs})_2(\text{OH})] + \text{Ag}(\text{I})$  or PhINTs' protocol can effect amidation of saturated C–H bonds, and an electrophilic tosylimidoruthenium intermediate is implicated based on Hammett correlation studies and trapping experiments.

Amidation of saturated C–H bonds is an appealing route to amides and amines.<sup>1</sup> To our knowledge, only a handful of catalytic systems involving [*N*-(toluene-*p*-sulfonyl)imino]phenylidodane (PhINTs) as a nitrogen source have been reported for this transformation,<sup>2</sup> and a highly reactive metal tosylimido ( $\text{M}=\text{NTs}$ ) species is usually postulated to be the active intermediate. To date, few  $\text{M}=\text{NTs}$  complexes are known to react with saturated C–H bonds.<sup>3</sup> We reason that those  $\text{M}=\text{NTs}$  species capable of acting on saturated C–H bonds would be highly oxidizing and react readily with organic solvents rendering their isolation and/or investigation difficult. A way to tackle this problem would be to prepare structurally characterized metal-tosylamido complexes. Through proton-coupled oxidations, either chemically<sup>4</sup> or electrochemically,<sup>5</sup> it may be feasible to *in situ* generate and study the highly reactive  $\text{M}=\text{NTs}$  species from its tosylamido precursor. Herein is described the first tosylamidoruthenium(III) complex that can mediate amidation of saturated C–H bonds.

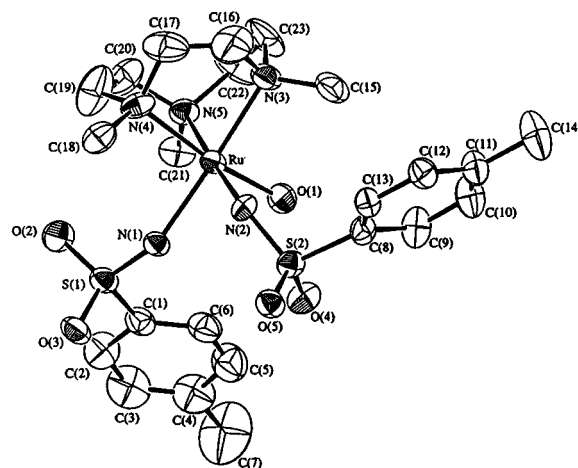
$[\text{Ru}^{\text{III}}(\text{Me}_3\text{tacn})(\text{NHTs})_2(\text{OH})]$  (**1**;  $\text{Me}_3\text{tacn}$  = 1,4,7-trimethyl-1,4,7-triazacyclononane) was prepared by reacting  $[(\text{Me}_3\text{tacn})\text{Ru}^{\text{III}}\text{Cl}_3]^6$  (0.1 g, 0.26 mmol) with  $\text{TsNHNa}$  (0.4 g, 2.1 mmol) in methanol (20  $\text{cm}^3$ ) at room temperature for 3 hours and was isolated as a yellow crystalline solid.† Magnetic susceptibility measurement gave  $\mu_{\text{eff}} = 1.8 \mu_{\text{B}}$ , consistent with a Ru(III) formulation. The infrared spectrum of **1** shows the N–H stretch at  $3400 \text{ cm}^{-1}$ . Fig. 1 shows the structure of complex **1** established by X-ray crystallography.‡ The two tosylamido ligands are in a *cis* configuration [N–Ru–N bond angle =  $80.4(2)^\circ$ ]. The Ru–N(tosylamido) distances of 2.072(5) and 2.140(5) Å are in between the related values of 2.025(1) Å in  $[\text{Ru}^{\text{IV}}(\text{Por})(\text{NHTs})(\text{pz})]$  (Por = porphyrinato ligand; pz = pyrazolate)<sup>7</sup> and 2.21(1) Å in  $[\text{Ru}^{\text{III}}(\text{Et}_2\text{dtc})(\text{PPh}_3)_2(\text{CO})(\text{NH}_2\text{SO}_2\text{C}_6\text{H}_2\text{Pr}^3\text{-}2,4,6)]$  ( $\text{Et}_2\text{dtc}$  = *N,N'*-diethyldithiocarbamate).<sup>8</sup> The observed Ru–OH distance of 1.947(4) Å is comparable to the related value of 1.904(2) Å found for  $[\text{Ru}^{\text{III}}(\text{N}_2\text{O}_2)(\text{O}-\text{H}_2)(\text{OH})](\text{ClO}_4)_2$  ( $\text{N}_2\text{O}_2$  = 6,7,8,9,10,11,17,18-octahydro-6,10-dimethyl-5*H*-dibenzo[*e,n*][1,4,8,12]dioxadiazacyclopentadecine).<sup>9</sup> The Ru–N–S angles of  $144.3(3)^\circ$  and  $132.3(3)^\circ$  suggest that the nitrogen atom is  $\text{sp}^2$  hybridized.

We found that addition of weakly oxidizing  $\text{AgClO}_4$  to **1** in acetonitrile gave a red species ( $\lambda_{\text{max}} = 480 \text{ nm}$ ), which would react with  $\text{PPh}_3$  to produce  $\text{TsN}=\text{PPh}_3$  and  $[\text{Ru}^{\text{II}}(\text{Me}_3\text{tacn})(\text{MeCN})_3](\text{ClO}_4)_2$  quantitatively. Likewise, other oxidants such as  $\text{PhI}(\text{OAc})_2$  and  $(\text{CPh}_3)(\text{PF}_6)$  are equally effective for this transformation. On the other hand, (1-cyclohexenyloxy)trimethylsilane was found to be converted to  $\alpha$ -*N*-tosylamino-cyclohexanone§ under '**1** +  $\text{AgClO}_4$ ' conditions comparable to the related transformations by the ' $[(\text{L})\text{Mn}^{\text{V}}\equiv\text{N}] + (\text{CF}_3\text{CO})_2\text{O}$ '

(L = Schiff base)<sup>10a</sup> and ' $\text{Cu}(\text{I}) + \text{PhINTs}$ '<sup>10b</sup> systems. These findings imply that a reactive Ru=NTs species might have been generated upon chemical oxidation of **1** presumably *via* oxidative deprotonation of the coordinated amido ligands. Although attempts to isolate and characterize the Ru=NTs species of  $\text{Me}_3\text{tacn}$  have proved futile, the '**1** +  $\text{Ag}(\text{I})$ ' protocol was found to carry out facile C–H amidation of allylic and aromatic hydrocarbons to afford the corresponding tosylamides (RNHTs).




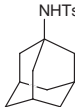



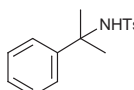




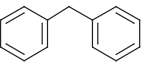
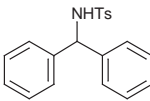
When cyclohexene (1 mmol) was treated with **1** (0.16 mmol) and  $\text{AgClO}_4$  (0.2 mmol) in acetonitrile (5  $\text{cm}^3$ ), a red solution resulted. The red color slowly disappeared upon stirring for 3 h at room temperature to form a yellow to brown solution with metallic silver deposited at the bottom of the reaction vessel. After GLC analysis, allylic toluene-*p*-sulfonamide was produced in 63% yield based on the Ru complex (Table 1). Ethylbenzene, cumene, indane and tetralin also reacted similarly to afford the corresponding benzyl tosylamide derivatives in 41–75% yield. It is noteworthy that adamantane can also be converted to 1-adamantane tosylamide selectively in 59% yield by the **1**/ $\text{AgClO}_4/\text{MeCN}$  system. In all cases,  $\text{TsNH}_2$  was detected as well, and the ' $\text{RNHTs} + \text{TsNH}_2$ ' production reached a total of 200% for two tosylamido moieties per ruthenium complex.

The effect of *para*-substituents (*p*-Y- $\text{C}_6\text{H}_4\text{CH}_2\text{CH}_3$ ; Y = MeO, Me, H, F, Cl) on the amidation of ethylbenzene by employing **1**/ $\text{AgClO}_4$  conditions has been studied. The relative rates ( $k_{\text{rel}}$ ) were established under competitive conditions where equimolar amounts of ethylbenzene and its substituted derivatives were used. We found that both electron-donating and -withdrawing substituents can promote the reaction, and a straight line ( $R = 0.99$ ) results using Jiang's  $\sigma_{\text{JJ}}$ <sup>11</sup> and



**Fig. 1** Molecular structure of  $[\text{Ru}^{\text{III}}(\text{Me}_3\text{tacn})(\text{NHTs})_2(\text{OH})]$  and atom-numbering scheme. Significant bond distances (Å) and angles ( $^\circ$ ): Ru–N(1) 2.072(5), Ru–N(2) 2.134(5), Ru–O(1) 1.949(4), Ru–N(3) 2.131(5), Ru–N(4) 2.190(5), Ru–N(5) 2.129(5), N(1)–S(1) 1.549(5), N(2)–S(2) 1.566(5); N(1)–Ru–N(2)  $80.2(2)$ , O(1)–Ru–N(2)  $92.0(2)$ , O(1)–Ru–N(1)  $96.2$ , O(1)–Ru–N(3)  $90.7(2)$ , N(2)–Ru–N(4)  $96.5(2)$ , N(1)–Ru–N(5)  $102.6(2)$ , Ru–N(1)–S(1)  $144.6(3)$ , Ru–N(2)–S(2)  $132.5(3)$ .

**Table 1** Ruthenium amidation of saturated C–H bonds

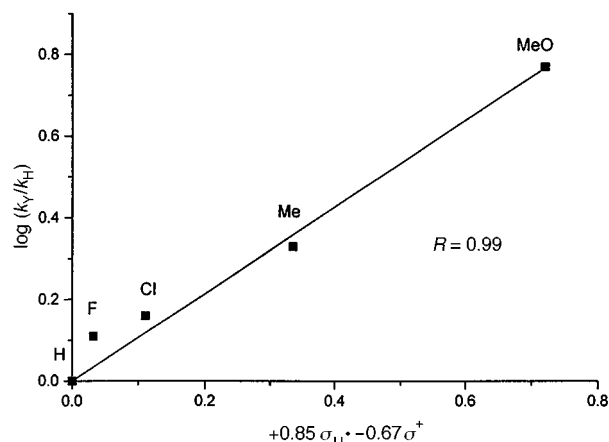
Entry	Substrate	Product	'1 + Ag(I)' '1 + PhINTs'	
			Yield (%) <sup>a,b</sup>	Yield (%); turnover number <sup>c,d</sup>
1			63	52; 29
2			59	50; 25
3			75	72; 48
4			41	30; 23
5			60	49; 25
6			52	45; 25
7			65	55; 37

<sup>a</sup> Reaction conditions: to an acetonitrile suspension (5 cm<sup>3</sup>) containing hydrocarbon substrate (1 mmol) and **1** (0.16 mmol) was added AgClO<sub>4</sub> (0.2 mmol); the resulting red solution was stirred for 3 h at room temperature. Aliquots were analyzed by GLC for product identification and quantification. <sup>b</sup> Yields are based on the amount of Ru complex used. <sup>c</sup> Reaction conditions: an acetonitrile mixture (10 cm<sup>3</sup>) of hydrocarbon substrate (1 mmol) and **1** (2 mol%) was treated with PhINTs (6 mmol), and the reddish brown solution was stirred at room temperature for 12 h. After rotary evaporation to dryness, the amide product was extracted with diethyl ether. Aliquots were taken from the organic extracts and analyzed by GLC for product identification and quantification. <sup>d</sup> Yields are based on the amount of PhI formed.

Hammett  $\sigma^+$  substituent constants, and  $\rho_{H^*} = +0.85$  and  $\rho^+ = -0.67$  ( $|\rho_{H^*}/\rho^+| = 1.27$ ) are obtained (Fig. 2). The correlation suggests that the ruthenium-mediated amidation reaction should involve a benzylic radical intermediate produced by H-atom abstraction of ethylbenzene. The negative  $\rho^+$  value is indicative of an electrophilic nature of the active ruthenium species. The results of the correlation studies and the trapping experiments imply that a highly oxidizing Ru=NTs species was generated upon oxidation of complex **1**.

The amidation reaction can become catalytic when PhINTs was utilized as the terminal nitrogen source and **1** as the catalyst in acetonitrile at room temperature (see Table 1). The reaction of hydrocarbon substrates with PhINTs in the presence of 2 mol% of **1** in acetonitrile afforded the corresponding amides in moderate to good yields. Up to 75 turnovers could be achieved for the amidation of ethylbenzene when a lower catalyst loading (**1** : PhINTs : ethylbenzene = 1 : 100 : 200) was employed.

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**Fig. 2** Dual-parameter Hammett correlation studies for the ruthenium-mediated amidation of *para*-substituted ethylbenzenes.

## Notes and references

† Characterization data for **1**. UV–VIS [ $\lambda_{\max}/\text{nm}$  ( $\log \epsilon_{\max}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ )] (CH<sub>3</sub>CN): 222 (4.26), 286 (3.59), 400 (3.35). Infrared (Nujol mull)/cm<sup>-1</sup>: 3400 ( $\nu_{\text{N-H}}$ ). FAB-MS:  $m/z$  613 [M – OH]<sup>+</sup>, 460 [M – NHTs]<sup>+</sup>, 443 [M – OH – NHTs]<sup>+</sup>. Anal. Calc. for C<sub>23</sub>H<sub>38</sub>N<sub>5</sub>O<sub>5</sub>RuS<sub>2</sub>: C, 43.87; H, 6.08; N, 11.12. Found: C, 43.9; H, 6.09; N, 11.15%.

‡ Crystal data for **1**: C<sub>23</sub>H<sub>38</sub>N<sub>5</sub>O<sub>5</sub>RuS<sub>2</sub>,  $M = 629.77$ , monoclinic, space group  $P2_1/n$  (no. 14), crystal dimensions 0.25 × 0.20 × 0.10 mm,  $a = 12.129(2)$ ,  $b = 15.696(3)$ ,  $c = 16.202(3)$  Å,  $\beta = 108.49(2)^\circ$ ,  $U = 2976.1(10)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.405 \text{ g cm}^{-3}$ ,  $\mu = 7.06 \text{ cm}^{-1}$ ,  $F(000) = 1308$ . Intensity data were collected at 301 K on a MAR diffractometer with graphite monochromatized Mo-K $\alpha$  radiation ( $\lambda = 0.71073$  Å). A total of 5144 unique reflections were obtained from a total of 26480 reflections ( $R_{\text{int}} = 0.058$ ) and 2741 with  $I > 3\sigma(I)$  were used in the structural analysis;  $R = 0.047$ ,  $R_w = 0.051$  with a goodness-of-fit of 1.62. The final Fourier difference map showed residual extrema in the range 0.90 to 0.46 e Å<sup>-3</sup>. CCDC 182/1060. See <http://www.rsc.org/suppdata/cc/1998/2677> for crystallographic files in .cif format.

§  $\alpha$ -*N*-Tosylaminocyclohexanone: yield = 48%, see also ref. 10(b).

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