Non-heme iron(II) complexes are efficient olefin aziridination catalysts†

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Iron(II) complexes of polydentate nitrogen donor ligands catalyze the rapid aziridination of olefins by PhINTs.

Metal-mediated syntheses of nitrogen-containing organic compounds are the focus of continuing investigation in contemporary inorganic and organometallic chemistry. The aziridination of olefins by *N*-tosyliminophenyliodinane (PhINTs), mediated by discrete copper or rhodium complexes, is a well-established protocol for the formation of aziridines from diverse aromatic and aliphatic olefins.[1] Olefin aziridination catalysts derived from other transition metals, including cobalt,[2] silver,[3] and gold,[4] have been described recently. Related iron complexes have received sparse attention as potential catalysts for olefin aziridination. Latour and Avenier demonstrated that a mixed-valent diiron complex reacts with PhINTs and large excesses of olefins (>25 equiv. *vs.* PhINTs) over several hours to generate *N*-tosylaziridines in 42–69% yields.[5] Hossain and co-workers reported that an organometallic iron(II) complex can mediate the aziridination of styrene by PhINTs in 85% yield when the catalyst is present in a 10 mol% (*vs.* PhINTs) amount.[6] Iron–porphyrin and iron–corrole complexes have been shown to mediate the aziridination of olefins by PhINTs, chloramine-T, or bromamine-T.[7] Herein, we illustrate the utility of mononuclear non-heme iron(II) complexes as catalysts for the aziridination of olefins by PhINTs. These systems provide aziridines in moderate to good yields, require only small excesses of olefins for optimum reactivity, and feature reaction rates that are markedly faster than previously reported iron catalysts.

In this study, we examined the reactivity of iron(II) complexes supported by the linear triamine ligand 1,1,4,7,7-pentamethyldiethylenetriamine (Me$_5$dien) as well as the related macrocyclic ligand 1,4,7-triisopropyl-1,4,7-triazacyclononane (iPr$_3$TACN). The reaction of Me$_5$dien with Fe(CF$_3$SO$_3$)$_2$·2CH$_3$CN in THF provides colorless crystals of [(Me$_5$dien)Fe(O$_3$SCF$_3$)$_2$] (**1**) in 62% yield. The solid state structure of **1** was established from X-ray crystallography (Fig. 1).‡ Complex **1** features a square-pyramidal iron(II) center with the tridentate ligand bound in a meridional fashion, as well as two monodentate triflate ligands. The overall structure of **1** is similar to that of the previously reported copper(II)-triflate complex of Me$_5$dien.[8] The iron–ligand bond lengths are entirely consistent with the presence of a high-spin (S = 2) Fe(II) center in the complex, which was confirmed from a solid state magnetic susceptibility measurement (μ_{eff} = 4.97 μ_{B}). The ^{1}H NMR spectrum of **1** consists of a single set of seven paramagnetically shifted and broadened resonances (CD$_3$CN; δ 138.6 (6H), 123.4 (2H), 107.9 (6H), 92.4 (3H), 81.0 (2H), 80.2 (2H), 59.0 (2H) ppm) that confirm the solution integrity of the complex and also demonstrate that the approximate C_s symmetry of the complex is retained in solution. As reported elsewhere, the reaction of iPr$_3$TACN with Fe(CF$_3$SO$_3$)$_2$·2CH$_3$CN provides [(iPr$_3$TACN)Fe(O$_3$SCF$_3$)$_2$] (**2**) which contains a square-pyramidal high-spin Fe(II) center bound by a facial N$_3$-macrocyclic ligand and a pair of *cis* triflate co-ligands.[9] Complex **2** exhibits a set of three paramagnetically shifted and broadened resonances in its ^{1}H NMR spectrum (CD$_3$CN; δ 50.4 (12H), 21.2 (3H), −2.6 (18H) ppm), demonstrating the integrity of the complex in solution and revealing the approximate C_3 symmetry of the complex in a coordinating solvent. We have previously demonstrated that a copper(II) complex of iPr$_3$TACN is a potent olefin aziridination catalyst.[10]

The abilities of **1** and **2** to mediate the aziridination of olefins by PhINTs were examined under a standard set of conditions (Scheme 1), and compared to the catalytic reactivity of Fe(CF$_3$SO$_3$)$_2$·2CH$_3$CN in the same process.§ As shown in

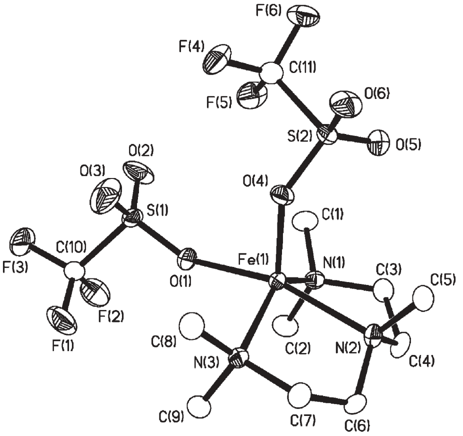

Fig. 1 Thermal ellipsoid representation (35% probability boundaries) of the X-ray crystal structure of **1**. Significant interatomic distances (Å) and angles (°) include: Fe1–O1, 2.114(3); Fe1–O4, 2.028(3); Fe1–N1, 2.145(4); Fe1–N2, 2.236(4); Fe1–N3, 2.152(3); O1–Fe1–O4, 94.4(1); O1–Fe1–N1, 89.3(1); O1–Fe1–N2, 160.2(2); O1–Fe1–N3, 94.1(1); O4–Fe1–N1, 119.5(2); O4–Fe1–N2, 105.4(2); O4–Fe1–N3, 103.4(2); N1–Fe1–N2, 81.1(2); N1–Fe1–N3, 136.6(2); N2–Fe1–N3, 81.4(2).

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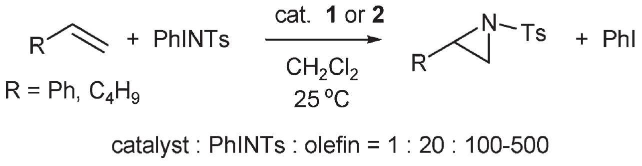
† Electronic supplementary information (ESI) available: Synthetic details and characterization data for **1**. See DOI: 10.1039/b700493a



Scheme 1 Iron-mediated aziridination of olefins by PhINTs.

Table 1 Olefin aziridination mediated by iron(II) complexes[a]

Substrate	Equiv *vs.* PhINTs	1	2	$Fe(CF_3SO_3)_2\cdot 2CH_3CN$
Styrene	25	>95	>95	—
	10	70	62	<5
	5	68	65	<5
1-Hexene	5	30	26	19

[a] Individual entries reflect % yields of the aziridine products relative to the molar amount of PhINTs present in the reaction mixture. Reactions were conducted in CH_2Cl_2 at ambient temperature with a catalyst : PhINTs ratio of 1 : 20. Products were identified and quantified by GC-MS.

Table 1, both **1** and **2** are competent catalysts for the aziridination of styrene by PhINTs. Essentially quantitative yields of 2-phenyl-*N*-tosylaziridine are obtained when using large excesses of the substrate styrene,[5] while reasonable yields of this aziridine are still generated when using 5–10 equivalents of styrene relative to PhINTs. Under identical conditions and reaction times, $Fe(CF_3SO_3)_2\cdot 2CH_3CN$ is a much less active catalyst for the aziridination of styrene. We note that the reactions of styrene with PhINTs in the presence of **1** or **2** are quite rapid; reactions are complete (as judged by the dissolution of PhINTs) in one minute or less, while reactions mediated by $Fe(CF_3SO_3)_2\cdot 2CH_3CN$ require hours to proceed to completion. Aliphatic olefins such as 1-hexene undergo aziridination by PhINTs in the presence of **1** or **2** as well, albeit in reduced yields and with less distinction between the activities of **1** and **2** and that of $Fe(CF_3SO_3)_2\cdot 2CH_3CN$.

The stabilities of the catalytically active species derived from **1** and **2** were examined by sequential addition of aliquots of PhINTs to reaction mixtures containing either **1** or **2** and styrene after an initial portion of the iodinane had reacted (initial catalyst : PhINTs : styrene ratio = 1 : 20 : 500). Samples of the reaction mixtures were analyzed after each aliquot of PhINTs was consumed, and aziridine yields were quantified by GC analysis. The results of these experiments are summarized in Fig. 2. Under these conditions, a catalyst with unlimited stability would exhibit 100% conversion of PhINTs to aziridine (20 productive turnovers) for each aliquot of the iodinane added (Fig. 2, dashed line). While complexes **1** and **2** do not behave in this ideal manner, both complexes do exhibit continued catalytic reactivity as additional aliquots of PhINTs are introduced into their respective reaction mixtures. The yield of 2-phenyl-*N*-tosyl aziridine stops increasing after a third aliquot of PhINTs is added to the catalytic mixture containing complex **1**, while the mixture containing complex **2** consumes an additional aliquot of PhINTs and therefore provides a higher overall aziridine yield and a greater number of productive turnovers. After a total of 4 aliquots of PhINTs is added, the reaction mixture containing **1** affords an overall aziridine yield of 42% (34 total turnovers), while the parallel reaction mediated by **2** provides the aziridine in 70% overall yield (56 total turnovers). The measurably greater yields of aziridine derived from complex **2** over complex **1** after the second, third, and fourth aliquots of PhINTs are added suggest that the active catalyst derived from **2** is more robust under the reaction conditions than is the active catalyst derived from **1**. This behaviour may reflect the stabilizing effect of the macrocyclic ligand iPr_3TACN that is present in **2** over the linear triamine Me_5dien found in **1**.

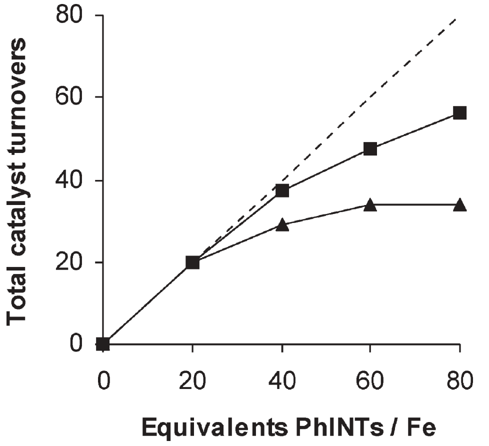


Fig. 2 Production of 2-phenyl-*N*-tosylaziridine by sequential addition of PhINTs to a CH_2Cl_2 solution containing **1** (▲) or **2** (■) and styrene (1 : 500 ratio). Ideal catalyst behaviour (complete conversion of PhINTs to aziridine) is represented by the dashed line.

Having established that **1** and **2** mediate the aziridination of styrene by PhINTs, we sought to examine the electronic and structural factors that influence the reactivity of these complexes. Cyclic voltammograms of **1** and **2** were recorded in CH_2Cl_2 to assess the redox behaviour of the catalysts (Table 2). While the oxidation of **1** is completely irreversible, complex **2** exhibits quasi-reversible redox behaviour, albeit at a significantly higher potential. Of note is that the oxidation potentials of **1** and **2** span an ~500 mV range, which suggests that a precisely tuned redox potential is not a strict requirement for catalytic reactivity within this group of complexes.

One structural property which may influence the abilities of these complexes to mediate the aziridination of olefins by PhINTs is the distribution of the labile coordination sites within the coordination spheres of the iron centers. Complexes **1** and **2** each contain at least one pair of *cis* labile coordination sites. To determine if these *cis* labile sites are required for efficient catalytic

Table 2 Comparative redox potentials and aziridination reactivity for iron(II) complexes

Complex	$E_{1/2}$ (mV) *vs.* Fc/Fc^{+a}	Aziridine yield (%)[b]
1	+330[c]	>95
2	+831[d]	>95
$[TPAFe(CH_3CN)_2]OTf_2$	+536	80
$[L^8py_2FeOTf]OTf$	+694[e]	26
$[N4pyFe(CH_3CN)]OTf_2$	+580[f]	16

[a] Determined at room temperature in CH_2Cl_2 containing 1 mM complex and 0.1 M Bu_4NClO_4. [b] Reactions conducted in CH_2Cl_2 with a catalyst : PhINTs : substrate ratio of 1 : 20 : 200–500. [c] Irreversible oxidation with E_{pa} = +330 mV. [d] Quasi-reversible with i_{pc}/i_{pa} = 0.61. [e] Quasi-reversible with i_{pc}/i_{pa} = 0.51. [f] From reference 14.

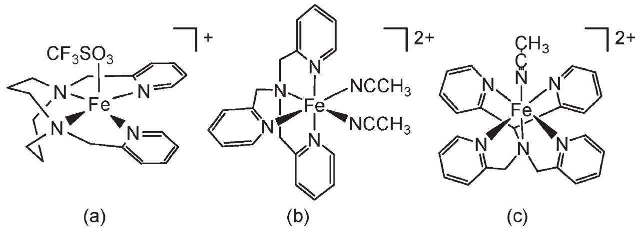


Fig. 3 Structures of the cations in [L^{8}py$_2$FeOTf]OTf (a), [TPAFe (CH$_3$CN)$_2$]OTf$_2$ (b), and [N4pyFe(CH$_3$CN)]OTf$_2$ (c).

aziridination reactivity, we examined the abilities of a set of closely related non-heme iron(II) complexes, which feature differing numbers and distributions of labile coordination sites, to mediate the aziridination of styrene by PhINTs. These previously reported complexes include [L^{8}py$_2$FeOTf]OTf,[11] [TPAFe(CH$_3$CN)$_2$]OTf$_2$,[12] and [N4pyFe(CH$_3$CN)]OTf$_2$ (Fig. 3).[13] Of these three complexes, only the complex with a pair of *cis* labile coordination sites, [TPAFe(CH$_3$CN)$_2$]OTf$_2$, serves as an effective catalyst for the aziridination of styrene by PhINTs (Table 2), providing the appropriate aziridine in 80% yield. The other two complexes, which contain either a pair of *trans* labile sites ([L^{8}py$_2$FeOTf]OTf) or a single labile site ([N4pyFe(CH$_3$CN)]OTf$_2$), provide significantly lower yields of aziridines under parallel reaction conditions. The divergent reactivity of these three complexes is controlled neither by spin state ([L^{8}py$_2$FeOTf]OTf contains a high-spin iron(II) ion, while [TPAFe(CH$_3$CN)$_2$]OTf$_2$ and [N4pyFe(CH$_3$CN)]OTf$_2$ contain low-spin iron(II) centers) nor by redox potential, as the potentials of all three complexes (Table 2) fall within the window of potentials established between **1** and **2**. These observations suggest that a pair of *cis* labile coordination sites on the iron center, such as those found in **1**, **2**, and [TPAFe(CH$_3$CN)$_2$]OTf$_2$, may indeed be required for efficient catalytic olefin aziridination reactivity. This structural property would thus parallel the requirements previously defined for efficient iron(II)-catalyzed *cis*-dihydroxylation of olefins by H_2O_2.[15]

Herein, we have demonstrated that simple non-heme iron complexes serve as effective catalysts for the aziridination of olefins by PhINTs. Optimum yields of aziridine products are obtained rapidly and require only a small excess of olefin substrate. These non-heme iron complexes retain their abilities to mediate olefin aziridination for multiple turnovers, with maximum turnover numbers observed for a complex supported by a macrocyclic ligand. By consideration of both the electronic and structural properties of the iron-containing catalyst, it may be possible to develop potent, long-lived catalysts for the aziridination of both aliphatic and aromatic olefins. Efforts to develop such complexes and to probe the mechanism of the iron-mediated olefin aziridination reaction are underway in our laboratories.

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Notes and references

‡ X-Ray crystallographic data for **1**, $C_{11}H_{23}F_6FeN_3O_6S_2$, M = 527.29, monoclinic, a = 13.312(2) Å, b = 10.946(2) Å, c = 15.148(3) Å, β = 110.86(2)°, V = 2062.7(6) Å^3, T = 173 K, space group Cc, Z = 4, μ(Mo Kα) = 1.020 mm^{-1}, 2329 reflections collected, 2329 unique, 2251 having $I > 2\sigma(I)$. Least-squares refinement was performed with SHELXL V6.10.[16] The final residuals for data with $I > 2\sigma(I)$ refined against 263 variable parameters were $R1$ = 0.0420 and w$R2$ = 0.1056; Flack parameter = −0.01(2). CCDC 634112. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b700493a

§ Standard procedure for the aziridination of styrene by PhINTs in the presence of **1**: in an inert atmosphere glovebox, a mixture of PhINTs (0.130 g, 0.349 mmol) and styrene (200 μL, 1.75 mmol) in CH_2Cl_2 (3 ml) was treated with solid **1** (0.0092 g, 0.0174 mmol). The mixture immediately turned golden brown in color, and the insoluble iodinane dissolved completely within one minute. After this time, the clear brown solution was passed through a column of alumina and eluted with EtOAc (10 ml). The combined eluates were evaporated, and the resulting residue diluted to a known volume and analyzed using GC-MS. Products were identified from their mass spectra and from comparison of the retention times to those of known samples, and the aziridines were quantified through the use of calibration curves that relate detector response to aziridine concentration in solution. This procedure resulted in a final aziridine yield of 0.237 mmol, or 68% of the theoretical amount based on the molar amount of PhINTs used. For comparisons to $Fe(CF_3SO_3)_2\cdot 2CH_3CN$: parallel, concurrent aziridinations of styrene by PhINTs were examined, with one reaction mediated by **1** (or **2**) and a second reaction mediated by $Fe(CF_3SO_3)_2\cdot 2CH_3CN$. The aziridinations were initiated at the same time, and the reactions were quenched (by filtering through an alumina column) when the iodinane had completely dissolved in the reaction mixture containing **1** (or **2**). Workup and product identification and quantitation continued as above.

1 For reviews, see: H. Lebel, O. Leogane, K. Huard and S. Lectard, *Pure Appl. Chem.*, 2006, **78**, 363; J. A. Halfen, *Curr. Org. Chem.*, 2005, **9**, 657; P. Müller and C. Fruit, *Chem. Rev.*, 2003, **103**, 2905.

2 G.-Y. Gao, J. D. Harden and X. P. Zhang, *Org. Lett.*, 2005, **7**, 3191.

3 Y. Cui and C. He, *J. Am. Chem. Soc.*, 2003, **125**, 16202.

4 Z. Li, X. Ding and C. He, *J. Org. Chem.*, 2006, **71**, 5876.

5 F. Avenier and J.-M. Latour, *Chem. Commun.*, 2004, 1544.

6 B. D. Heuss, M. F. Mayer, S. Dennis and M. M. Hossain, *Inorg. Chim. Acta*, 2003, **342**, 301.

7 J.-P. Mahy, G. Bedi, P. Battioni and D. Mansuy, *J. Chem. Soc., Perkin Trans. 2*, 1988, 1517; R. Vyas, G.-Y. Gao, J. D. Harden and X. P. Zhang, *Org. Lett.*, 2004, **6**, 1907; L. Simkhovich and Z. Gross, *Tetrahedron Lett.*, 2001, **42**, 8089.

8 M. J. Scott, S. C. Lee and R. H. Holm, *Inorg. Chem.*, 1994, **33**, 4651.

9 A. Diebold, A. Elbouadili and K. S. Hagen, *Inorg. Chem.*, 2000, **39**, 3915.

10 J. A. Halfen, J. K. Hallman, J. A. Schultz and J. P. Emerson, *Organometallics*, 1999, **18**, 5435.

11 M. R. Bukowski, H. L. Halfen, T. A. van den Berg, J. A. Halfen and L. Que, Jr., *Angew. Chem., Int. Ed.*, 2005, **44**, 584.

12 Y. Zang, J. Kim, Y. Dong, E. C. Wilkinson, E. H. Appelman and L. Que, Jr., *J. Am. Chem. Soc.*, 1997, **119**, 4197.

13 G. Roelfes, M. Lubben, K. Chen, R. Y. N. Ho, A. Meetsma, S. Genseberger, R. M. Hermant, R. Hage, S. K. Mandal, V. G. Young, Jr., Y. Zang, H. Kooijman, A. L. Spek, L. Que, Jr. and B. L. Feringa, *Inorg. Chem.*, 1999, **38**, 1929.

14 M. J. Collins, K. Ray and L. Que, Jr., *Inorg. Chem.*, 2006, **45**, 8009.

15 K. Chen, M. Costas, J. Kim, A. K. Tipton and L. Que, Jr., *J. Am. Chem. Soc.*, 2002, **124**, 3026.

16 G. M. Sheldrick, *SHELXTL V6.10*, Bruker Analytical X-Ray Systems, Madison, WI, 2000.