Formation of Enamines via Catalytic Dehydrogenation by Pincer-Iridium Complexes

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ABSTRACT

Efficient pincer-ligated iridium catalysts are reported for the dehydrogenation of simple tertiary amines to give enamines, and for the dehydrogenation of β-functionalized amines to give the corresponding 1,2-difunctionalized olefins. Experimentally determined kinetic isotope effects in conjunction with DFT-based analysis support a dehydrogenation mechanism involving initial pre-equilibrium oxidative addition of the amine α-C-H bond followed by rate-determining elimination of the β-C-H bond.
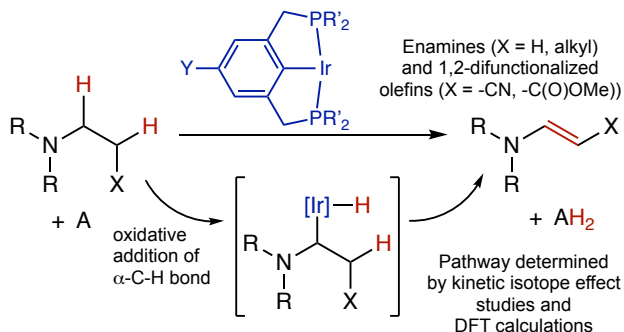
1. INTRODUCTION

The ability to effect selective catalytic conversions of typically unreactive C-H bonds has emerged as one of the major frontiers in organic chemistry in recent years, offering the promise of simple atom-economical methods for the synthesis of valuable functionalized organic compounds.[1] Pincer-ligated iridium complexes have been studied intensively in this context,[2] mostly as highly active and robust catalysts for the dehydrogenation of alkanes, but also for the dehydrogenation of aliphatic C-C linkages in molecules other than alkanes. We have previously reported[3] the synthesis of enamines via dehydrogenation of the corresponding tertiary amines catalyzed by (^{tBu4}PCP)Ir (**1**, ^{R4}PCP = κ^3-C$_6$H$_3$-2,6-(CH$_2$PR$_2$)$_2$),[4] using a sacrificial hydrogen acceptor (Scheme 1). Enamines are highly valuable synthons, used extensively as nucleophiles for the selective formation of C-C bonds by Michael reactions, as Diels-Alder dienophiles, and in a wide range of other reactions.[5]

**Scheme 1. Reported Synthesis of Enamines via Catalytic Dehydrogenation**
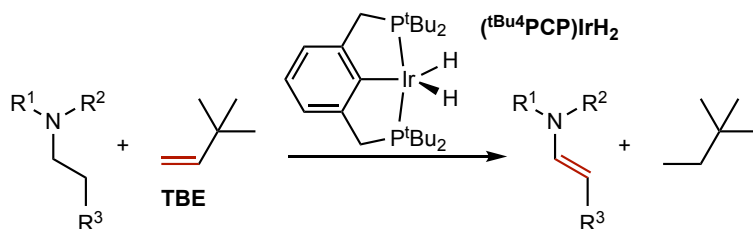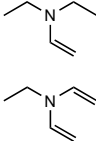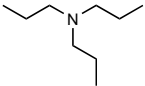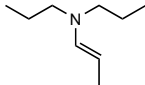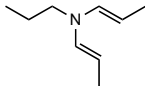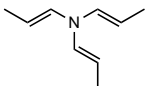
Subsequent to the early pincer-Ir dehydrogenation work with precursors of (^{tBu4}PCP)Ir,[4,6] it was found that precursors of (^{iPr4}PCP)Ir (**2**) and derivatives are often catalytically more active.[7,8] In this article we report that (^{iPr4}PCP)IrH$_n$ (n = 2, 4),[8-9] and the corresponding *p*-methoxy-substituted derivative (MeO-^{iPr4}PCP)IrH$_n$ (**3**)[10] are significantly more effective than (^{tBu4}PCP)IrH$_2$ as catalysts for dehydrogenation of tertiary amines to enamines. We also report that with these sterically much less demanding catalysts we are able to dehydrogenate crowded 1,2-difunctionalized saturated C-C linkages. This represents a novel approach to the corresponding 1,2-difunctionalized olefins, which are attractive precursors for further functionalization reactions such as cycloadditions, leading to building blocks that cannot be efficiently synthesized via known methods.

2. RESULTS AND DISCUSSION

2.1. Dehydrogenation of Tertiary Amines. In our previous report of the transfer-dehydrogenation of tertiary amines catalyzed by (^{tBu4}PCP)IrH$_n$,[3] we found that a relatively high catalyst loading was generally required to obtain good yields. With (^{iPr4}PCP)IrH$_n$ and the same substrates investigated previously, using NBE as hydrogen acceptor, satisfactory yields were generally achieved with a catalyst loading of only 2%, although higher temperatures and somewhat longer reaction times were generally required (Table 1). Note that with these same higher reaction temperatures and longer times, with (^{tBu4}PCP)IrH$_n$ (as opposed to (^{iPr4}PCP)IrH$_n$) the yields of the reactions were actually lowered, not increased. The need for higher temperature with (^{iPr4}PCP)IrH$_n$ is likely a consequence of stronger binding of olefin (either H-acceptor or enamine) to the sterically less-demanding catalyst. Very high yields obtained with (^{iPr4}PCP)IrH$_n$, much higher than with (^{tBu4}PCP)IrH$_n$, have also been reported for alkane transfer-dehydrogenation using the strongly-binding hydrogen acceptors ethylene and propylene; in this case too the optimal temperatures (>200 °C) are significantly higher than are found for (^{tBu4}PCP)IrH$_n$.[7c]

Table 1. Dehydrogenation of Tertiary Amines Catalyzed by (MeO-[iPr4]PCP)IrH$_n$ (with Previously Reported[3] Results Obtained with ([tBu4]PCP)IrH$_2$ Shown for Comparison)[a]

			(MeO-[iPr4]PCP)IrH$_2$		([tBu4]PCP)IrH$_2$[3]	
Entry	Substrate (0.1 M)	Product	Conditions (120 °C)	Yield (%)	Conditions (90 °C)	Yield (%)
1			48 h, 2 equiv NBE, 1% cat.	90	5 h, 2 equiv TBE, 10% cat.	98
					24 h, 2 equiv TBE, 2% cat.	65
2			32 h, 2 equiv NBE, 2% cat.	95	24 h, 2 equiv TBE, 10 % cat.	65
3			32 h, 4 equiv NBE, 2% cat.	53	24 h, 3 equiv TBE, 10% cat.	25
				40		75
4			32 h, 4 equiv NBE, 2% cat.	40	24 h, 2 equiv TBE, 10 % cat.	43
				38		11
				6		-
5			32 h, 2 equiv NBE, 2% cat.	39	24 h, 2 equiv TBE, 10 % cat.	10
6			48 h, 2 equiv NBE, 2% cat.	90	24 h, 3 equiv TBE, 10% cat.	67
					24 h, 2 equiv NBE, 10% cat.	92
7			48 h, 2 equiv NBE, 2% cat.	N.R.	24 h, 2 equiv TBE, 10 % cat., 110 °C	N.R.

a) All reactions were conducted with 0.1 M amine substrate in *p*-xylene-d$_{10}$ solvent and were monitored by ^{31}P NMR and ^{1}H NMR spectroscopy over the course of the reaction. Yields were determined by ^{1}H NMR spectroscopy.

In general, the same reactivity patterns were observed with (MeO-[iPr4]PCP)Ir as with ([tBu4]PCP)Ir. This includes complete selectivity for dehydrogenation of an N-ethyl group versus a N-*i*-propyl group (entry 1) and the failure to dehydrogenate the piperidine ring in either N-

methylpiperidine or N-ethylpiperidine. The greater effectiveness of (MeO-[iPr4]PCP)Ir as compared with ([tBu4]PCP)Ir, however, was much more marked for the dehydrogenation of *n*-propyl groups (entry 4) and the *i*-propyl group (entry 5). This is likely attributable to lesser crowding at the metal center of (MeO-[iPr4]PCP)Ir being particularly favorable, relative to ([tBu4]PCP)Ir, for dehydrogenation of C-C linkages more crowded than the ethyl group.

As was observed with ([tBu4]PCP)Ir-catalyzed reactions, all of the enamine products degraded, usually within several hours, after being isolated from the catalyst (via vacuum transfer of enamine and solvent); this behavior is consistent with the known instability of simple enamines.[5a,11] Thus it is remarkable that the enamines are stable at the high temperature (120 °C) at which they are formed. In view of that stability at elevated temperatures, however, it is not surprising that the enamines are indefinitely stable – while still in the presence of the Ir complex – at room temperature. As previously proposed, it seems probable that the Ir complex inhibits chain reactions leading to loss of the enamine.[3]

2.2 Dehydrogenation to Afford 1,2-Difunctional Olefins. 1,2-Difunctional olefins are of great interest as versatile intermediates in organic synthesis for various cycloadditions.[12] Electron-rich 1,2-difunctional olefins in particular can undergo useful [2+1] cycloadditions (cyclopropanation, Simmons-Smith type reaction),[13] [2+2],[14] [3+2][15] and [4+2][16] cycloadditions, to afford various compounds that serve as novel building blocks for organic synthesis.

In this context, and that of tertiary amine dehydrogenation, we considered the dehydrogenation of β-functionalized tertiary amines. We first attempted the catalytic dehydrogenation of the relatively sterically hindered diamine substrate, *N,N,N',N'*-tetramethyl-ethane-1,2-diamine (tetramethylethylenediamine; TMEDA) (eq 1). Various conditions were screened, including the use of NBE, TBE and camphene as hydrogen acceptors (Scheme 2); significant yields of the desired product were achieved only with NBE.[17]

$$\text{(1)}$$
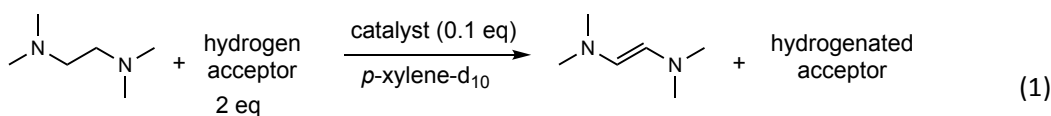
Scheme 2. Pincer-iridium catalysts screened
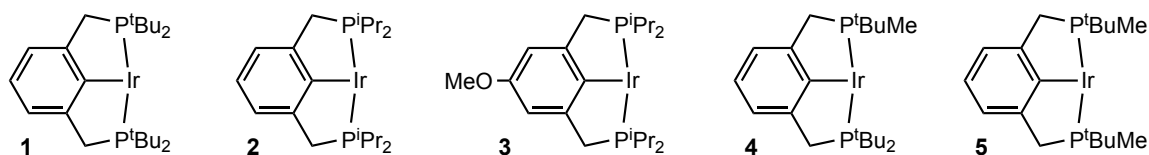
Catalysts **1**-**5** (Scheme 3) were screened for the reaction outlined in eq 1; among these catalysts, **2** and **3** proved to be similarly effective. Catalyst **1** gave no observable product, presumably highlighting the importance of steric factors for dehydrogenation of this sterically

hindered substrate (TMEDA). Catalyst **4** gave some product, but less than **2** or **3**. Catalyst **5** apparently polymerized the hydrogen acceptor (NBE)[18] and the desired dehydrogenation products were not detected.
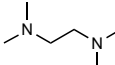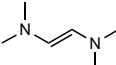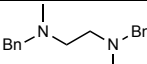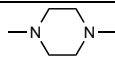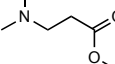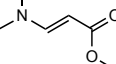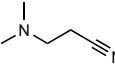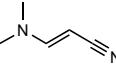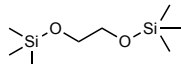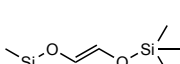
Other 1,2-difunctionalized ethane derivatives were investigated. Vinyl acrylates have been found to form stable, catalytically inactive, adducts with (tBu4PCP)Ir.[19] We were therefore pleasantly surprised that some, albeit limited, catalytic dehydrogenation of methyl 3-(dimethylamino)propanoate (entry 4) was achieved, likely due to steric hindrance preventing the formation of such inactive adducts. Relatedly, nitriles appear to coordinate fairly strongly to (RPCP)Ir fragments, yet a very good yield (84%) was obtained with the substrate 3-(dimethylamino)propanenitrile (entry 5).

Our previous attempts to dehydrogenate ethers have for the most part been unsuccessful apparently due to the formation of vinyl ether adducts. Some success has been achieved with ether dehydrogenation.[20] Most notably in the context of this work, Brookhart and co-workers found that (iPr4PCP)Ir could effect dehydrogenation of acyclic ethers,[21] and Huang and co-workers reported[22] dehydrogenation of cyclic amines and ethers with the related (iPr4PSCOP)Ir species. Inspired by the success noted above with 1,2-difunctionalized substrates such as TMEDA, we attempted dehydrogenation of a bulky bis(trimethylsilyl)diether substrate (entry 6), and were pleased to obtain excellent yields.

Entries 1, 4, 5, and 6 in Table 2 represent new chemical transformations. Only a single isomer (*E*) was obtained from each of the four reactions, as indicated in Table 2.

N,N'-Dimethyl-N,N'-dibenzyl-ethylene-1,2-diamine) did not undergo any reaction (entry 2), which is likely attributable to steric hindrance by the benzyl substituents as compared with the methyl groups. 1,4-dimethylpiperazine did not undergo dehydrogenation (entry 3) in accord with the failure, reported above, to dehydrogenate N-methyl and N-ethyl piperidine at the ring position.

Table 2. Dehydrogenation Reactions Catalyzed by (^{iPr4}PCP)Ir (**2**) with NBE as Hydrogen Acceptor [a]

Entry	Substrate	Product	Conditions	Yield (%)
1			**A** **B**	64% 98%
2			**A**	N.R.
3			**A**	N.R.
4			**A** (110 °C/55 h)	27
5			**A**	84
6			**A** (110 °C/40 h) (110 °C/70 h)	96 E/Z = 6.5/1 100 E/Z = 10/1

(a) All reactions were run in p-xylene-d_{10} and NBE was used as hydrogen acceptor. All yields were determined by ^{1}H NMR spectroscopy. **A**: 0.05 mmol substrate (0.1 M), 2.3 eq (0.115 mmol) NBE, 15 mol% (4.0 mg) **2**, 143 °C, 45 h, unless noted otherwise. **B**: 0.05 mmol substrate (0.1 M), 2.0 eq (0.10 mmol) NBE, 25 mol% (6.6 mg) **2**, 143 °C, 24 h.

2.3. Mechanistic studies. The apparently high reactivity of the acyclic amine substrates, indicated by the good product yields, was confirmed in a competition experiment between N,N-di(isopropyl)ethylamine (60 mM) and cyclooctane (COA; 600 mM).[23] The latter substrate is frequently used in alkane dehydrogenation studies because of its anomalously low enthalpy of dehydrogenation.[2,4,6]

Scheme 3. Competition Experiment to Determine Relative Reactivity of COA vs. ^{i}Pr$_2$NEt
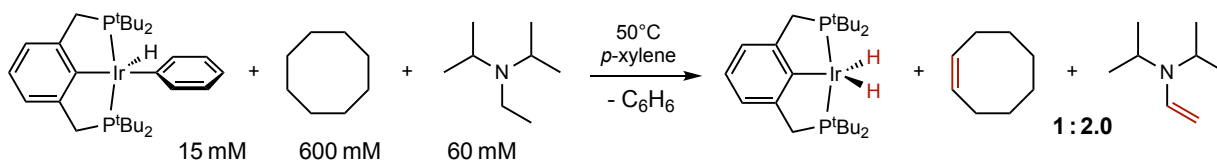
The reaction was conducted as a stoichiometric competition of (^{tBu4}PCP)Ir(H)(Ph) (which is known to act as an effective precursor of the fragment (^{tBu4}PCP)Ir even at or below room temperature[24]), in the absence of hydrogen acceptor, in order to facilitate characterization by ^{1}H NMR at the lowest possible concentrations of dehydrogenated substrate, and shortest possible times. This approach minimized the likelihood that the observed cyclooctene: vinylamine ratio would reflect thermodynamics rather than kinetics. The ratio of cyclooctene to N,N-di(isopropyl)vinylamine product remained roughly constant at 1:2.0, even from the earliest

reaction times, indicating a kinetic rather than a thermodynamic product distribution. Dehydrogenation of the ^{i}Pr$_2$NEt ethyl group is thus found to be 20 times more rapid than dehydrogenation of COA on a per mol basis; on a per C-C bond basis the ratio is therefore 160.

Competition experiments between N,N-di(alkyl)ethylamines reveal that the rate of dehydrogenation of the N-ethyl group is dependent upon the ancillary N-alkyl group as follows: i-propyl > ethyl > methyl in the ratio of ca. 140:7:1. The trend is opposite what would be expected based on consideration of steric factors. It is not obvious how this trend would be reconciled with the generally accepted reaction pathway for alkanes which proceeds via oxidative-addition followed by β-hydrogen elimination.[2,25] More generally, the origin of the much greater reactivity of amines compared with alkanes is not obvious in the context of such a mechanism. We therefore considered that alternative pathways might be operative, proceeding, for example, via radicals or via electron-transfer.

To address this fundamental mechanistic question we first conducted a series of kinetic isotope effect (KIE) experiments. N,N-di(isopropyl)ethylamine isotopologues ^{i}Pr$_2$N(CD$_2$CD$_3$), ^{i}Pr$_2$N(CD$_2$CH$_3$), and ^{i}Pr$_2$N(CH$_2$CD$_3$) were synthesized. In a competitive catalytic reaction (90° C), (^{tBu4}PCP)IrH$_n$ (10.2 mM), TBE (250 mM), ^{i}Pr$_2$N(C$_2$H$_5$) (30.7 mM) and ^{i}Pr$_2$N(C$_2$D$_5$) (61.4 mM) were allowed to react ; k_{C2H5}/k_{C2D5} was found to be 7.0. A stoichiometric competition reaction with (^{tBu4}PCP)Ir(H)(Ph), conducted in analogy with the above-described experiment with COA (Scheme 2), with ^{i}Pr$_2$N(C$_2$H$_5$) (146 mM) and ^{i}Pr$_2$N(CH$_2$CD$_3$) (291 mM) gave a KIE of k_{C2H5}/k_{CH2CD3} = 3.7. In another such stoichiometric competition reaction, the reaction of (^{tBu4}PCP)Ir(H)(Ph) with ^{i}Pr$_2$N(C$_2$H$_5$) (146 mM) and ^{i}Pr$_2$N(CD$_2$CH$_3$) (291 mM), the value of k_{C2H5}/k_{CD2CH3} was found to be 2.0. Thus k_{C2H5}/k_{C2D5} (7.0) is approximately equal to the product of the KIE values k_{C2H5}/k_{CH2CD3} (3.7) and k_{C2H5}/k_{CD2CH3} (2.0).

The results of these isotope effect experiments clearly imply that cleavage of both α- and β-C-H bonds occurs during or preceding the rate-determining step. Thus they argue against a mechanism proceeding via rate-determining electron-transfer or abstraction of an H atom from the amine.

The value of 2.0 for k_{C2H5}/k_{CD2CH3} is consistent with an equilibrium isotope effect (preceding a rate-determining step) for a reaction in which H is transferred from carbon to a metal atom, while the value of 3.7 for k_{C2H5}/k_{CH2CD3} indicates a rate-limiting kinetic isotope effect.[26] These isotope effects are thus consistent with a pathway featuring reversible oxidative addition of the α-C-H bond followed by rate-determining β-H-elimination (Scheme 4). It is still not obvious however, why such a mechanism would favor amines over alkanes. In this context we conducted a computational study to elucidate the detailed energetics of this putative reaction mechanism.

Scheme 4. Pathway for Amine Dehydrogenation by 1 Consistent with Observed Isotope Effects
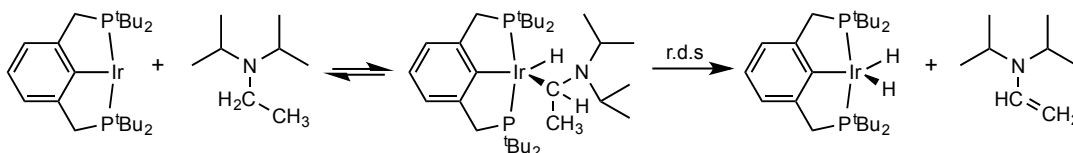
2.4. Computational Studies. A series of electronic structure calculations based on density functional theory (DFT; see Computational Details) were conducted for dehydrogenation pathways proceeding through oxidative addition of an aminoethyl C-H bond of $^iPr_2NEt$ or Me_2NEt to $(^{tBu4}PCP)Ir$, followed by β-H elimination to give the corresponding vinyl amines. We also calculated, for comparison, the energy profiles of pathways for dehydrogenation of COA, *n*-butane, and for the alkanes that are isostructural with $^iPr_2NEt$ and Me_2NEt, namely 3-ethyl-2,4-dimethylpentane and isopentane, respectively (corresponding products shown in Scheme 5). For all of these substrates except COA, two distinct dehydrogenation pathways of this type are possible, and both were investigated computationally (Scheme 6): pathway **a**, oxidative addition of a primary C-H bond followed by β-H-elimination of the adjacent secondary C-H bond, and pathway **b**, oxidative addition of the secondary C-H bond followed by β-H-elimination of the adjacent primary C-H bond.

Scheme 5. Products of Dehydrogenation of Various Substrates for which Dehydrogenation Pathways were Calculated
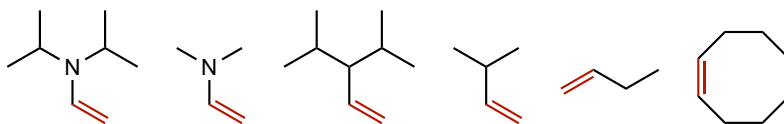
Scheme 6. Putative Pathways for Dehydrogenation of Amines and Alkanes Examined by DFT Calculations
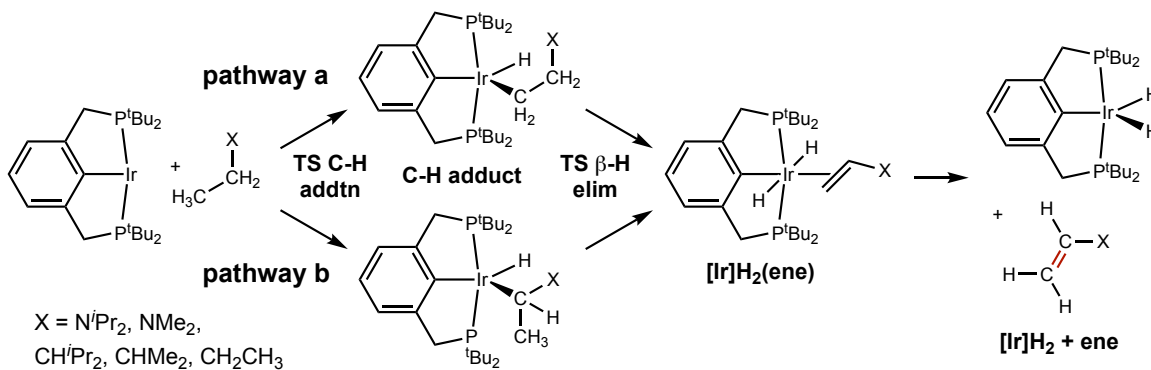
For all substrates and for either pathway, the energy of the TS for the second step, β-H elimination, is higher than that for the first C-H activation step. Thus β-H-elimination is calculated to be the rate-determining step for the formation of *trans*-(^{tBu4}PCP)IrH$_2$(olefin) (**[Ir]H$_2$(ene)**). The Gibbs free energies (relative to (^{tBu4}PCP)Ir plus free substrate) for the TS for C-H addition, the C-H addition intermediate, the TS for β-H-elimination, the intermediate *trans*-(^{tBu4}PCP)IrH$_2$(olefin), and the free olefin product plus (^{tBu4}PCP)IrH$_2$, are given in Table 3.

Table 3. Calculated Gibbs Free Energies (kcal/mol; 50°C; 1.0 M Substrate) of Key Intermediates and TSs for Dehydrogenation of Various Substrates via Pathways **a** and **b** Outlined in Scheme 6.

Substrate	Pathway	TS CH-addtn	C-H adduct	TS β-H-elim	IrH$_2$(ene)	IrH$_2$ + ene
^{i}Pr$_2$NEt	a	20.1	14.2	**31.4**	20.0	7.1
^{i}Pr$_2$NEt	b	29.9	29.1	**32.6**	20.0	7.1
Me$_2$NEt	a	19.5	13.2	**30.8**	20.9	6.0
Me$_2$NEt	b	25.0	23.9	**32.0**	20.9	6.0
COA		27.2	23.4	**34.9**	28.0	3.7
n-butane	a	22.0	16.1	**35.2**	28.2	12.3
n-butane	b	29.3	20.9	**36.8**	28.2	12.3
^{i}Pr$_2$CHEt	a	20.7	17.2	**36.3**	22.5	11.6
^{i}Pr$_2$CHEt	b	30.3	30.0	**32.9**	22.5	11.6
Me$_2$CHEt	a	22.8	14.6	**34.5**	22.3	12.4
Me$_2$CHEt	b	27.5	27.8	**36.7**	22.3	12.4

The calculated free energies shown in Table 3 can be considered in the context of the experimental observations described above. Relative rates for all substrates are determined by the free energy of the TS for β-H-elimination (**TS β-H-elim**); these TS energies are lowest for the amines, consistent with the qualitative observation that the amines are more reactive than alkanes. More quantitatively, as described above, in the competition experiment between ^{i}Pr$_2$NEt and COA, a relative rate factor of 160 per C-C bond favoring the amine was determined, which corresponds to $\Delta\Delta G^{\ddagger}_{50°C}$ = 3.3 kcal/mol. The calculated values of $\Delta\Delta G^{\ddagger}_{50°C}$, 3.5 kcal/mol and 2.2 kcal/mol for pathways **a** and **b** respectively, are both in good agreement with this value.

KIEs were calculated for dehydrogenation of the ^{i}Pr$_2$NEt isotopologues that were experimentally investigated. For pathway **a**, at 50 °C, the KIE was calculated to be 2.5 for the terminal position of the aminoethyl group of ^{i}Pr$_2$NEt ($k_{C_2H_5/CH_2CD_3}$) and 5.2 for the methylene group ($k_{C_2H_5/CD_2CH_3}$); for full isotopic substitution of the ethyl group $k_{C_2H_5/C_2D_5}$ = 13.1 at 50 °C and 9.9 at 90 °C. For pathway **b**, the calculated values are $k_{C_2H_5/CH_2C\mathbf{D_3}}$ = 3.5, $k_{C_2H_5/C\mathbf{D_2}CH_3}$ = 2.9, and $k_{C_2H_5/C_2D_5}$ = 10.1 (50 °C) and 7.8 (90°C). The experimental KIEs, discussed above, are $k_{C_2H_5/CH_2CD_3}$ = 3.7, $k_{C_2H_5/CD_2CH_3}$ = 2.0 (50 °C), and $k_{C_2H_5/C_2D_5}$ = 7.0 (90 °C). The experimental values are clearly inconsistent with the values calculated for pathway **a**. Conversely, they are in good agreement

with the calculations for pathway **b**; we believe this agreement offers very strong support for this pathway.

The difference in barrier heights computed for pathways **a** and **b** is, however, small in all cases (1-3 kcal/mol; Table 3), testing the reliability of the computational methods. Indeed, for ^{i}Pr$_2$NEt pathway **a** is calculated to have a Gibbs free-energy barrier that is 1.3 kcal/mol lower than pathway **b** (Table 3). We consider the magnitude of this discrepancy to be well within the overall limits of uncertainty for the applied computational methods. In particular, dispersion interactions are not accommodated well by the calculations, and therefore the slightly too high energy predicted for the more crowded TS obtained for ^{i}Pr$_2$NEt dehydrogenation along pathway **b** is not completely unexpected.[27,28] Very similarly, the slightly higher calculated barriers for dehydrogenation of ^{i}Pr$_2$NEt vs. Me$_2$NEt ($\Delta\Delta G^{\ddagger}_{50\,°C}$ = ca. 0.6 kcal/mol for either pathway **a** or **b**) may be attributed to a similarly poor treatment of dispersive interactions for ^{i}Pr$_2$NEt.
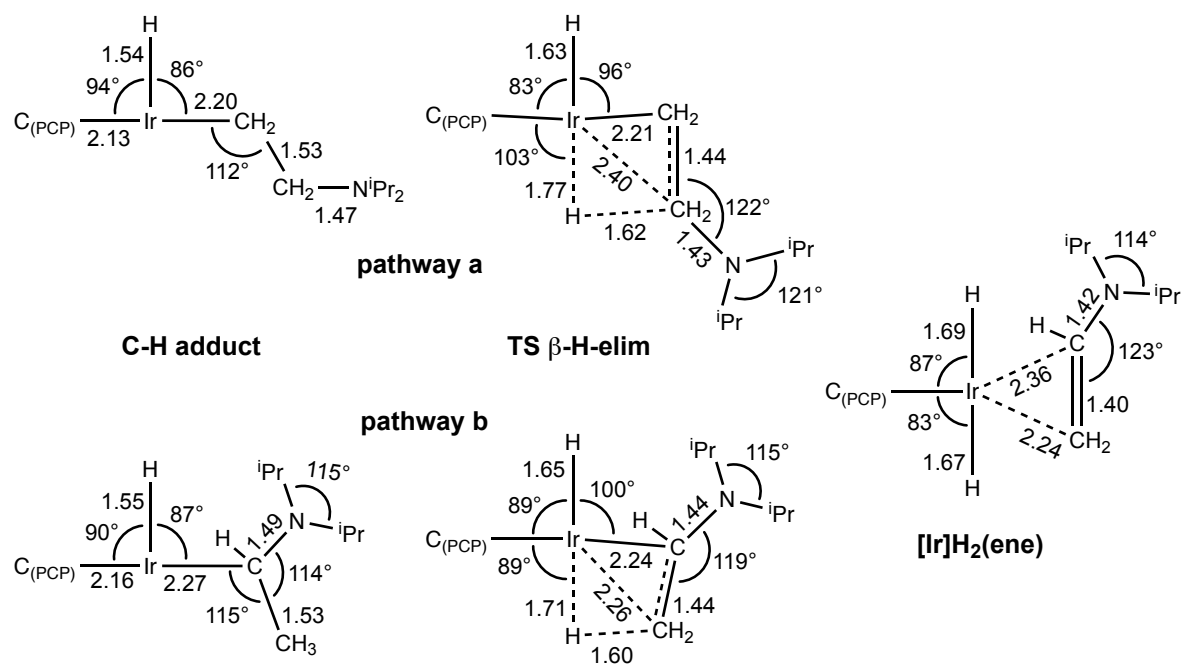
Figure 1. Selected metric parameters (bond distances in Å) for the products of C-H bond addition (**C-H adduct**), the TSs for β-H elimination (**TS β-H-elim**), and the resulting intermediate, **[Ir]H$_2$(ene)**, for the reaction of (^{tBu4}PCP)Ir with ^{i}Pr$_2$NEt via **pathway a** and **pathway b**.

The calculations offer a straightforward explanation for the selectivity for dehydrogenation of amines compared with alkanes. The energies of the C-H addition products and their barriers to β-H-elimination vary greatly between substrates and pathways. In contrast, the energies of the transition states **TS β-H-elim** (particularly for pathway **b**) correlate fairly well with the energies of the intermediates to which they connect, the β-H-elimination products, **[Ir]H$_2$(ene)**. In particular the intermediates resulting from amine dehydrogenation are the lowest in free

energy of those in Table 3, as are the corresponding transition states **TS β-H-elim**. Consistent with this correlation of free energies, the geometries of the transition states **TS β-H-elim** are notably similar to those of the intermediates **[Ir]H$_2$(ene)** as shown in Figure 1 for dehydrogenation of ^{i}Pr$_2$NEt. The product-like nature of **TS β-H-elim** also helps rationalize why the free energy of this TS is very similar for pathways **a** and **b** despite the fact that the different TSs are derived from C-H addition products which have very different free energies in the two pathways.

If the variations in the energies of **TS β-H-elim** can be rationalized in terms of the energies of the intermediates, **[Ir]H$_2$(ene)**, this raises the question as to what may explain the variations in energies of these intermediates. Comparison between the amines and the isostructural alkanes is probably most informative in this context. We note that the difference between the relative energies of the amine dehydrogenation intermediates and the isostructural alkane dehydrogenation intermediates, **[Ir]H$_2$(ene)**, is ca. 2 kcal/mol (Table 3). This compares with a difference of ca. 5 kcal/mol for the relative energies of the free enamine and alkene products, attributable to conjugation between the amino group and the C-C π-system. We presume that the lower energy of the **[Ir]H$_2$(ene)** amine dehydrogenation products simply reflects the lower energy of the free dehydrogenated species (with the difference mitigated by stronger binding of the enamine); this same effect is therefore ultimately responsible for the faster kinetics of dehydrogenation of amines compared with alkane.

3. CONCLUSIONS

Precursors of (^{iPr4}PCP)Ir and (MeO-^{iPr4}PCP)Ir are efficient catalysts for dehydrogenation of simple tertiary amines to give enamines, and for dehydrogenation of β-functionalized tertiary amines to give the corresponding 1,2-difunctionalized olefins which are of interest for further chemical manipulations such as cycloaddition reactions.[12-16] Combined mechanistic and computational studies indicate that the amine dehydrogenations proceed via C-H oxidative addition at the N-bound carbon, followed by rate-limiting β-H elimination.

4. EXPERIMENTAL SECTION

4.1. General Information. All reactions, recrystallizations and routine manipulations were conducted under an inert atmosphere using an argon-filled glove box or by using standard Schlenk techniques under argon atmosphere. J-Young NMR tubes were used for catalytic dehydrogenation reactions. Reagent grade solvents were used and dried according to established methods, then degassed with argon. All NMR solvents were dried, vacuum-transferred, and stored in an argon-filled glove box.

^{1}H, ^{31}P{^{1}H} and ^{13}C{^{1}H} NMR spectra were obtained on Varian 300-, 400- or 500-MHz spectrometers. ^{1}H and ^{13}C NMR chemical shifts are reported in ppm downfield from tetramethylsilane and were referenced to residual protiated (^{1}H) or deuterated solvent (^{13}C). Catalysts **1-H$_n$,**[4] **2-H$_n$,**[7a] **3-H$_n$,**[10] **4-H$_n$,**[7b] and **5-H$_n$,**[7b] and (^{tBu4}PCP)Ir(H)Ph[24] were prepared as

described in the literature. Simple amines were purchased from Sigma-Aldrich. *N,N*-diisopropylpropylamine, and isotopically labeled N, N-diisopropylethylamines *i*-Pr$_2$N(C$_2$D$_5$), *i*-Pr$_2$N(CD$_2$CH$_3$), and *i*-Pr$_2$N(CH$_2$CD$_3$) were synthesized according to a literature procedure.[29] All amines were purified by treating with Na/K alloy, followed by vacuum distillation. All substrates were stored over molecular sieves before use.

4.2. General Procedure for Catalytic Dehydrogenation. All substrates, hydrogen acceptors, catalysts, and solvents were loaded into a J-Young NMR tube in a glovebox under argon atmosphere. A ^{1}H NMR spectrum was acquired at time zero (t$_0$) and the NMR tube was heated in an oil bath. The reaction progress was monitored by ^{1}H NMR spectroscopy. Yields were calculated based on relevant peak areas in the ^{1}H NMR spectrum.

N, N-di(isopropyl)vinylamine. Colorless oil, ^{1}H NMR (300 MHz, *p*-xylene-*d$_{10}$*) δ = 6.10 (dd, 15.6 Hz, 9.2 Hz, 1H), 3.83 (d, 9.2 Hz, 1H), 3.82 (d, 15.6 Hz, 1 H), 3.41 (m, 6.5 Hz, 2H), 1.03 (d, 6.5 Hz, 12H). MS (EI) *m/z*: 127(parent), 112, 99, 70, 56.

N, N-dimethylvinylamine. Colorless oil, ^{1}H NMR (300 MHz, *p*-xylene-*d$_{10}$*) δ = 6.01 (dd, J_{HH} = 15.2 Hz, 8.4 Hz, 1 H), 3.84 (d, J_{HH} = 8.4 Hz, 1H), 3.74 (d, J_{HH} = 15.2 Hz, 1H), 2.39 (s, 6H). MS (EI) *m/z*: 71(parent), 58, 56, 44.

N, N-diethylvinylamine. Colorless oil, ^{1}H NMR (300 MHz, *p*-xylene-*d$_{10}$*) δ = 6.03 (dd, J_{HH} = 15.2 Hz, 9.2 Hz, 1H), 3.78(d, J_{HH} = 9.2 Hz, 1H), 3.75(d, J_{HH} = 15.2 Hz, 1H), 2.81(q, J_{HH} = 7.0 Hz, 4H), 1.05(t, J_{HH} = 7.0 Hz, 6H). MS (EI) *m/z*: 99(parent), 84, 73, 71, 56.

N, N-divinylethylamine. Colorless oil, ^{1}H NMR (300 MHz, *p*-xylene-*d$_{10}$*) δ = 6.00 (dd, J_{HH} = 15.6 Hz, 9.0 Hz, 2 H), 3.93 (d, J_{HH} = 15.6 Hz, 2 H), 3.86 (d, J_{HH} = 9.0 Hz, 2H), 3.14 (q, J_{HH} = 7.0 Hz, 2H), 1.02 (t, J_{HH} = 7.0 Hz, 3 H). MS (EI) *m/z*: 97(parent), 83, 70, 56.

N, N-dipropyl-(*E*)-1-propenylamine. Colorless oil, ^{1}H NMR (300 MHz, *p*-xylene-*d$_{10}$*) δ = 5.89 (dd, J_{HH} = 13.5 Hz, 1.5 Hz, 1H), 4.18 (qd, J_{HH} = 6.3 Hz, 13.5 Hz, 1 H), 2.75 (t, J_{HH} = 7.2 Hz, 4H), 1.85 (dd, J_{HH} = 6.3 Hz, 1.5 Hz, 3H), 1.48 (tq, J_{HH} = 7.2 Hz, 7.2 Hz, 4H), 0.98 (t, J_{HH} = 7.2 Hz, 6H).

N, N-di-(E)-1-propenylpropylamine. Colorless oil, ^{1}H NMR (300 MHz, *p*-xylene-*d$_{10}$*) δ = 5.91 (d, J_{HH} = 13.6 Hz, 2 H), 5.38 (m, J_{HH} = 13.6 Hz, 6.4 Hz, 2 H), 3.04 (t, J_{HH} = 7.6 Hz, 2 H), 1.75 (d, J_{HH} = 6.4 Hz, 6 H), 1.31 (m, 2H), 1.01 (t, J_{HH} = 6.8 Hz, 3 H). MS(EI) *m/z*: 139(parent), 124, 110, 98, 70.

N-vinylpiperidine. Colorless oil, ^{1}H NMR (300 MHz, *p*-xylene-*d$_{10}$*) δ = 5.99 (dd, J_{HH} = 15.3 Hz, 8.7 Hz, 2H), 3.90 (d, J_{HH} = 15.3 Hz, 1H), 2.88(d, J_{HH} = 8.7 Hz, 1H), 2.68 (t, J_{HH} = 5.3 Hz, 4H), 1.60 (m, 6H).

(E)-N,N,N',N'-tetramethylethylene-1,2-diamine: ^{1}H NMR (400 MHz, *p*-xylene-*d$_{10}$*) δ = 5.44 (s, 2H), 2.5 (s, 12H).

(E)-3-(dimethylamino)acrylonitrile: ^{1}H NMR (400 MHz, *p*-xylene-*d$_{10}$*) δ = 3.49 (d, J = 13.6Hz, 1H), 6.34 (d, J = 13.6 Hz, 1H), 2.60 (s, 6H).

Methyl (E)-3-(dimethylamino)acrylate: ^{1}H NMR (500 MHz, *p*-xylene-*d$_{10}$*) δ = 7.52 (d, J = 13.0 Hz, 1H), 4.80 (d, J = 13.0 Hz, 1H), 3.88 (s, 3H), 3.02 (s, 6H).

(E)-2,2,7,7-tetramethyl-3,6-dioxa-2,7-disilaoct-4-ene: ^{1}H NMR (300 MHz, *p*-xylene-*d$_{10}$*) δ = 5.65 (s, 2H), 0.35 (s, 18H).

5. COMPUTATIONAL METHODS.

All calculations employed density functional theory (DFT)[30] as implemented in the GAUSSIAN 16 series of computer programs.[31] We applied the M06 functional in the majority of calculations,[32] along with the SDD effective core potential and associated valence basis set for the Ir atom;[33] all other atoms (N, C, H) were assigned all-electron 6-31G(d,p) basis sets.[34] Interactions with bulk solvent were simulated using the SMD dielectric continuum solvation model[35] and *p*-xylene as the model solvent. Normal mode analysis was performed for stationary points and thermal energy corrections were evaluated using standard statistical mechanical expressions and unscaled vibrational frequencies.[36] Computed Gibbs free energies were adjusted to a temperature of 50 °C for comparison with experimental data.

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Notes
The authors declare no competing financial interest.

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work, the KIEs calculated by this method for pathway **b** (and not for pathway **a**) are consistent with the experimental results. Specifically k(C_2H_5)/k(CH_2CD_3) = 3.5, k(C_2H_5)/k(CD_2CH_3) = 2.8 (50 °C), and k(C_2H_5)/k(C_2D_5) = 7.7 (90°C) as compared with respective experimental values of 3.7, 2.0, and 7.0. (For pathway **a**, the respective calculated KIEs are 2.5, 4.7, and 8.9.) While the calculated difference, $\Delta\Delta G^{\ddagger}$ = 0.5 kcal/mol favoring pathway **b**, is in the direction consistent with experiment, the magnitude is too small to explain all experimental results since it would imply (if taken at face value) that the reaction would operate through both pathways at comparable rates (with pathway **b** predominating by a factor of only 2.2). However, even a difference of only 1.0 kcal/mol would result in one pathway predominating by a factor of 5.

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