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Tertiary Carbinamine Synthesis by Rhodium-Catalyzed [3+2] Annulation of N-Unsubstituted Aromatic Ketimines and Alkynes

Zhong-Ming Sun, Shuo-Ping Chen, and Pinjing Zhao*[a]

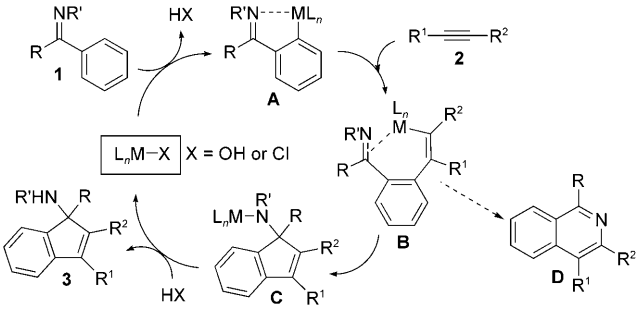
Abstract: A convenient and waste-free synthesis of indene-based tertiary carbinamines by rhodium-catalyzed imine/alkyne [3+2] annulation is described. Under the optimized conditions of 0.5–2.5 mol% [{(cod)Rh(OH)}$_2$] (cod = 1,5-cyclooctadiene) catalyst, 1,3-bis(diphenylphosphanyl)propane (DPPP) ligand, in toluene at 120°C, N-unsubstituted aromatic ketimines and internal alkynes were coupled in a 1:1 ratio to form tertiary 1*H*-inden-1-amines in good yields and with high selectivities over isoquinoline products. A plausible catalytic cycle involves sequential imine-directed aromatic C–H bond activation, alkyne insertion, and a rare example of intramolecular ketimine insertion into a Rh^{I}–alkenyl linkage.

Keywords: alkynes · carbinamines · C–H activation · ketimines · rhodium

Introduction

Transition-metal-catalyzed tandem reaction sequences have become a powerful strategy for the rapid assembly of complex structures with simple substrates.[1] Over the past decade, catalytic activation of C–H bonds has increasingly been exploited in various tandem reaction sequences.[2] This approach towards reactive organometallic intermediates through C–H bond activation provides an eco-friendly alternative to conventional methods, for example, transmetalation with main-group organometallic reagents, or oxidative addition with organic halides and pseudohalides. Herein, we report a catalytic C–H bond activation/C–C bond formation tandem process for the construction of indene-based tertiary carbinamines by a 1:1 coupling of aromatic ketimines with alkynes.

We envision a catalytic cycle that is initiated by the well-documented heteroatom-directed C–H bond activation (Scheme 1).[2] In particular, imine-directed *ortho*-C–H bond activation with aromatic ketimine **1** would form a cyclometalated aryl complex **A**.[3a] Insertion of alkyne **2** into the metal–aryl linkage would generate an imine-chelated metal–alkenyl intermediate **B**. Ring closure by an intramolecular ketimine insertion into the metal–alkenyl linkage would form an indene-based amido complex **C**.[3b] Subsequent proton exchange would release the *tert*-carbinamine product **3** and regenerate the catalyst, which reacts with the ketimine substrate to complete the catalytic cycle. This formal [3+2] annulation would provide a convenient and waste-free complement to current synthetic routes towards tertiary carbinamines.[4]



Scheme 1. A proposed catalytic cycle for the transition-metal-catalyzed [3+2] annulation of aromatic ketimines and alkynes.

A key step in our design is the generation of a nucleophilic transition-metal–alkenyl intermediate **B** that is reactive towards intramolecular ketimine addition. Analogous late-transition-metal–alkenyl and aryl nucleophiles have been successfully accessed in catalytic tandem sequences initiated by other types of elementary reactions.[5] For example, the groups of Yamamoto and Lu have reported Pd-catalyzed in-

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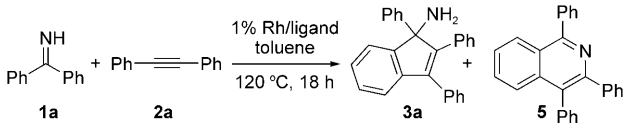
tramolecular ketone arylations initiated by oxidative additions with aryl bromides or transmetalation with arylboronic acids.[5a–d] Very recently, Lautens and co-workers have demonstrated the control over the electrophilic/nucleophilic dual reactivity of arylpalladium species generated by oxidative additions with aryl halides.[6] When such tandem sequences are initiated by C–H bond activations, however, formation of nucleophilic organometallic intermediates appears to be much more challenging.[7] In particular, aromatic ketones and imines are known to undergo catalytic tandem C–H bond activation and addition with alkynes (or olefins) without formation of carbocycles through intramolecular nucleophilic additions.[2,8] In contrast, the formation of heterocycles is more commonly observed in tandem sequences initiated by heteroatom-directed C–H bond activation.[9] For example, Satoh, Miura, and co-workers have developed the Rh-catalyzed oxidative coupling of benzoic acids with alkynes and olefins to form isocoumarin and phthalide derivatives.[10] Analogous syntheses of N-heterocycles have also been reported by several groups.[11] In particular, a very recent report by Satoh, Miura, and co-workers has shown that a Rh^{III}-based catalyst promoted indenone–imine formation by oxidative coupling of *N*-arylbenzaldimines and alkynes in the presence of stoichiometric $Cu(OAc)_2$. However, the use of ketimine substrates led to isoquinoline formation.[11i] Therefore, a major challenge for our design is the selective cyclization through intramolecular ketimine addition instead of the formation of isoquinoline-type products (Scheme 1, compound **D**).[5,11a,g–i] Recently, Kuninobu, Takai, and co-workers have developed Re-based catalysts for a variety of [3+2] annulations by a tandem sequence that is analogous to the catalytic cycle shown in Scheme 1.[12] In particular, imine- or ketone-directed aromatic C–H bond activation, followed by alkyne or acrylate insertion, generated organorhenium nucleophiles that underwent intramolecular ketone or ketimine additions. Notably, except for one reported example of *N*-benzyl *tert*-carbinamine,[12d] this rhenium catalysis did not form isolatable tertiary carbinol or carbinamine products due to the rapid loss of H_2O/amine under the reaction conditions. Thus, another challenge here is to retain the newly formed tertiary carbinamine functionality, which provides the opportunity to develop relevant asymmetric catalysis.[6]

For the current study, we initially focused our attention on relatively less studied, N-unsubstituted diaryl ketimine substrates with the following considerations: First, diaryl ketimines can be prepared conveniently by Grignard reactions by using readily available aryl halides and aryl cyanides.[13] This modular synthetic approach would also allow us to explore reactivity dependence on various aromatic substituents (see below). Second, [3+2] annulations with N-unsubstituted diaryl ketimines would be operationally simple and without the need for additional deprotection procedures. Third, reactions with diaryl ketimines will avoid potential interference by imine/enamine tautomerization. It is noteworthy, however, that the relatively weak ketimine N–H linkage could lead to formation of metal–iminyl complexes. These late metal iminyl species are known to undergo a number of elementary organometallic reactions that could compete against the desired [3+2] annulations.[14–16]

Results and Discussion

We began our investigation by studying catalytic reactions between benzophenone imine (**1a**) and diphenylacetylene (**2a**) (Table 1). Special attention was paid to rhodium-based catalysts due to their successful applications in catalytic C–H activations and C–C bond formations.[2a,17] The desired [3+2] product, 1-phenyl-*1H*-inden-1-amine (**3a**), was formed by using catalysts generated from [{(cod)Rh(OH)}$_2$] (**4**; cod = 1,5-cyclooctadiene) and phosphane ligands. An isoquinoline byproduct **5** was also detected,[11i] and reaction conditions were screened to improve the yield of **3a**. Under the optimized conditions of **4** (0.5 mol %) and DPPP ligand (1.2 mol %), in dry toluene at 120 °C, the 1:1 reaction of **1a**

Table 1. Development of the catalytic conditions.[a]



	Rh Catalyst	Ligand[b]	Yield [%][c] **3a+5**	**3a/5**
1	[{(cod)Rh(OH)}$_2$] (**4**)	none	<5	1:5
2	**4**	PEt_3	0	–
3	**4**	PCy_3	30	1:2.2
4	**4**	$PtBu_3$	0	–
5	**4**	PPh_3	69	1:1.5
6	**4**	PPh_3	57	1:50[d]
7	**4**	DPPM	0	–
8	**4**	DIPHOS	25	5:1
9	**4**	DPPP	98	50:1
10	**4**	DPPB	58	10:1
11	**4**	DPPpent	0	–
12	**4**	DPPF	10	2.5:1
13	**4**	XANTPHOS	0	–
14	**4**	BIPHEP	40	1:1
15	**4**	(*rac*)-BINAP	23	2:1
16	**4**	(*R*,*R*)-DIOP	75	7:1[e]
17	$RhCl_3 \cdot x H_2O$	DPPP	0	–
18	[{(coe)$_2$Rh(Cl)}$_2$]	DPPP	0	–
19	[Rh(cod)$_2$]BF_4	DPPP	0	–

[a] Reaction conditions: **1a** (0.23 mmol), **2a** (1.05 equiv), Rh catalyst (0.01 equiv Rh), phosphane (0.03 equiv for monophosphanes, 0.012 equiv for chelating phosphanes), toluene (1.0 mL), 120 °C, 18 h. [b] DPPM = bis(diphenylphosphanyl)methane, DIPHOS = 1,2-bis(diphenylphosphanyl)ethane, DPPP = 1,3-bis(diphenylphosphanyl)propane, DPPB = 1,4-bis(diphenylphosphanyl)butane, DPPpent = 1,5-bis(diphenylphosphanyl)-pentane, DPPF = 1,1′-bis-(diphenylphosphanyl)ferrocene, XANTPHOS = 4,5-bis(diphenylphosphanyl)-9,9-dimethylxanthene, BIPHEP = 2,2′-bis(diphenylphosphanyl)-1,1′-biphenyl, BINAP = 2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl, (*R*,*R*)-DIOP = (4*R*,5*R*)-(−)4,5-bis(diphenylphosphanylmethyl)-2,2-dimethyl-1,3-dioxolane, COE = cyclooctene. [c] The combined yields of **3a** and **5** were determined by GC. [d] This reaction was carried out in DMF and product **5** was isolated in 50 % yield. [e] This reaction was carried out with 2.5 mol % of **4**. Product **3a** was isolated in 65 % yield and 51 % *ee* (see the Supporting Information for HPLC analysis).

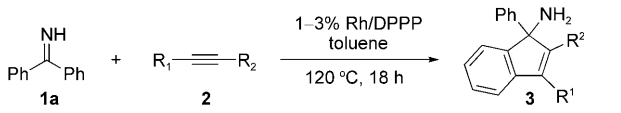
and **2a** gave a near-quantitative yield and over 50:1 selectivity of **3a** versus **5** (Table 1, entry 9). The overall yield and selectivity was significantly influenced by various factors, such as rhodium precursor, phosphane ligand, and solvent polarity. In particular, monophosphane ligands (Table 1, entries 2–5) and polar solvents, such as DMF, CH_3CN, and *t*-amyl alcohol, led to lower yields and significantly lower selectivities of **3a** versus **5**. The high efficiency of this catalyst system encouraged us to attempt the enantioselective formation of **3a** and up to 51% *ee* was achieved by using (*R*,*R*)-DIOP as the chiral ligand (Table 1, entry 16). This preliminary result will serve as a proof-of-principle for the future development of relevant processes in asymmetric catalysis.[6]

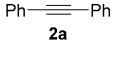
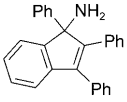
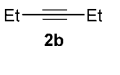
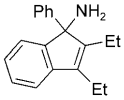
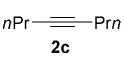
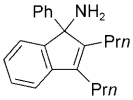
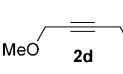
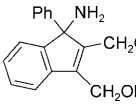
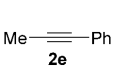
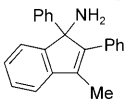
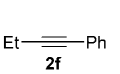
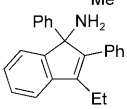
Notably, formation of **5** represents an isoquinoline synthesis that draws parallels to recent studies by the groups of Fagnou, Satoh, Miura, and others.[11] This formally dehydrogenative [4+2] annulation could be improved by using PPh_3 ligand and DMF solvent. However, several unidentified byproducts were also detected and **5** was isolated in 50% yield despite a near-quantitative conversion and very high selectivity of [4+2] versus [3+2] annulation (Table 1, entry 6).[18]

With the standard reaction conditions established, various alkyne substrates were studied for Rh-catalyzed [3+2] annulation with **1a** (Table 2). Compared with diphenylacetylene (**2a**), ethyl- and *n*-propyl-substituted alkynes **2b**, **2c**, and **2f** were slightly less reactive and required higher catalyst loadings (1.0–1.5 mol% of **4**) to give the annulation products in high yields. In contrast, reactivities of methoxymethyl- and methyl-substituted alkynes **2d** and **2e** were similar to that of **2a**. Nonsymmetric alkynes **2e** and **2f** reacted with high regioselectivities to form the 2-phenyl-3-alkyl regioisomers in >30:1 ratios. Among other alkyne substrates that have been reported for catalytic C–H alkenylations, terminal alkynes (e.g., phenylacetylene) and trialkylsilyl-substituted alkynes (e.g., bis(trimethylsilyl)acetylene and 1-phenyl-2-trimethylsilylacetylene) were unreactive.[19] Carboxy alkynes, such as dimethyl- and diethyl acetylenedicarboxylates, decomposed under the current reaction conditions.[20]

A series of diaryl ketimine substrates were studied for the catalytic [3+2] annulation with **2a** and the results are summarized in Table 3. Diaryl ketimines with electron-withdrawing F and CF_3 groups at the *para* positions (**1b**, **1c**, **1f**, **1g**) were slightly less reactive than **1a**, giving the [3+2] products in high yields with 1.0 mol% loading of catalyst **4**. Similar reactivities were observed with substrates modified by *para*-methoxy and *meta*-CF_3 substituents (**1h**, **1i**). However, 3,3′-bis(CF_3)- and 4,4′-bis(OMe)-substituted **1d** and **1e** suffered low reactivity in toluene due to limited solubility, giving <10% GC yields with standard reaction conditions. Switching the solvent to DMF allowed **1d** and **1e** to give good yields of [3+2] products with 1.5 mol% loading of **4**, although small amounts (<10%) of the isoquinoline byproducts were also detected. Nonsymmetrical, monosubstituted ketimines **1f–i** reacted with moderate regioselectivities (≈2–3:1) favoring coupling at the phenyl groups functionalized with *para*-F/CF_3/methoxy and *meta*-CF_3 groups. Notably, the reaction was severely inhibited by *ortho* substituents: no reactions occurred with 2-methoxybenzophenone imine or 2,6-difluorobenzophenone imine, whereas *ortho*-fluorinated **1j** reacted reluctantly with higher catalyst loading (55% yield with 2.5 mol% of **4**). Interestingly, compound **1j** reacted with reversed regioselectivity that favored coupling at the unsubstituted phenyl in a 2:1 ratio.

Table 2. Scope of alkyne substrates for catalytic [3+2] annulation.[a]

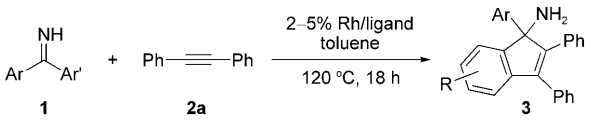


	Alkyne	Product	Rh loading [%]	Yield [%][b]
1	 **2a**	 **3a**	1	94
2	 **2b**	 **3b**	2	88
3	 **2c**	 **3c**	3	83
4	 **2d**	 **3d**	1	90
5	 **2e**	 **3e**	1	88[c] (>50:1)
6	 **2f**	 **3f**	2	96[c] (>30:1)

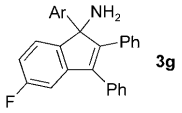
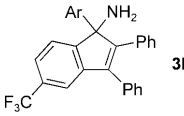
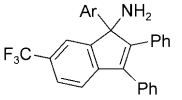
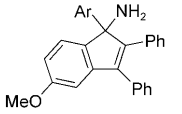
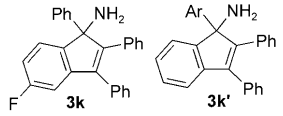
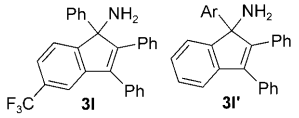
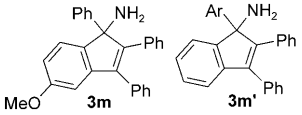
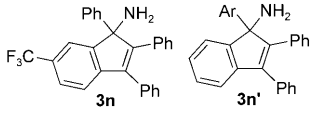
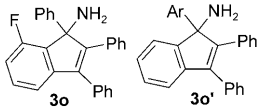
[a] Reaction conditions: **1a** (0.45 mmol), **2** (1.05 equiv), **4** (0.005–0.015 equiv), DPPP (1.2 equiv per Rh), toluene (1.0 mL), 120°C, 18 h. [b] Averaged yield of the isolated product from two runs. [c] Only the major regioisomer was shown. The selectivity was determined by NMR spectroscopic analysis.

Current results on the substrate scope and effects of aromatic substituents provided the following mechanistic insights into the proposed catalytic cycle (Scheme 1): First, high regioselectivities for the incorporation of nonsymmetric alkynes supported the proposed C–H alkenylation via an arylrhodium(I) intermediate, **A**. As observed with products **3e** and **3f**, alkyne insertion into the Rh^I–aryl linkage placed the Rh center preferentially at the benzylic position in the alkenylrhodium(I) intermediate, **B** (Scheme 1, **A**→**B**, R^1=alkyl, R^2=Ar).[21] Second, alkyne insertion into a metal–hydrocarbyl linkage is expected to be facilitated by π conjugation and inhibited by steric hindrance. Therefore, the observed higher overall reactivity with phenyl-substituted **2a** and the less sterically demanding alkynes **2d** and **2e** was consistent with a rate-limiting alkyne insertion step. However, the reactivity differences were not significant enough for a solid conclusion. Third, moderate regioselectivities with nonsymmetrical ketimines **1f**, **1g**, and **1i** argued against an electro-

Table 3. Scope of ketimine substrates for catalytic [3+2] annulation.[a]



1 2a 3

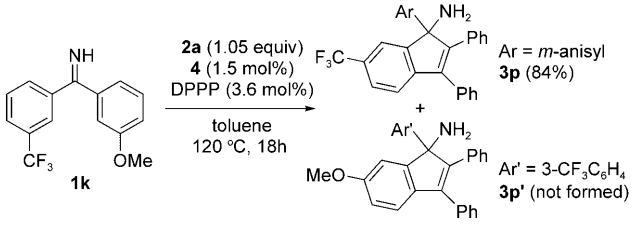
	Ketimine	Product	Yield [%][b]
1	Ar, Ar′ = 4-FC_6H_4 (**1b**)	 **3g**	94
2	Ar, Ar′ = 4-$CF_3C_6H_4$ (**1c**)	 **3h**	83
3	Ar, Ar′ = 3-$CF_3C_6H_4$ (**1d**)	 **3i**	74[c]
4	Ar, Ar′ = *p*-anisyl (**1e**)	 **3j**	82[c]
5	Ar = 4-FC_6H_4; Ar′ = Ph (**1f**)	 **3k** **3k'**	96 (2.4:1)
6	Ar = 4-$CF_3C_6H_4$; Ar′ = Ph (**1g**)	 **3l** **3l'**	89 (3.2:1)
7	Ar = *p*-anisyl; Ar′ = Ph (**1h**)	 **3m** **3m'**	95 (1.9:1)
8	Ar = 3-$CF_3C_6H_4$; Ar′ = Ph (**1i**)	 **3n** **3n'**	92 (2.0:1)
9	Ar = 2-FC_6H_4; Ar′ = Ph (**1j**)	 **3o** **3o'**	55[d] (1:2)

[a] Reaction conditions: **1** (0.45 mmol), **2a** (1.05 equiv), **4** (0.010 equiv), DPPP (1.2 equiv/Rh), toluene (1.0 mL), 120 °C, 18 h. [b] Averaged yield of isolated product from two runs. The selectivity of **3**/**3′** was determined by NMR spectroscopy and X-ray analysis (see the Supporting Information). [c] With **4** (0.015 equiv) in DMF (1.0 mL) to improve solubility. [d] With **4** (0.025 equiv) and in toluene (1.5 mL).

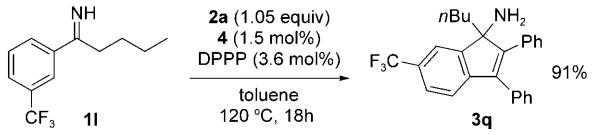
Besides diaryl ketimines, several types of structurally relevant substrates were also explored for the catalytic [3+2] annulation with alkynes. N-Unsubstituted monoaryl ketimines appeared to be less reactive than the diaryl analogues. For example, valerophenone imine (Ph(*n*Bu)C(=NH))[9] was inert towards **2a** with the current catalyst system. In contrast, *meta*-CF_3-substituted valerophenone imine **1l** reacted smoothly with **2a** to give the corresponding [3+2] product **3q** in 91% yield (Scheme 3).[23] Reactions with several aromatic ketones and N-substituted aromatic imines were also studied, but none of them gave detectable amounts of [3+2] products.[24]

The apparent lack of [3+2] reactivity with aromatic ketones and N-substituted imines was quite intriguing, since these substrates have been reported to undergo several catalytic tandem C–H bond activation/alkyne insertion processes.[2,25–27] This seemingly unique reactivity of N-unsubstituted ketimines could result from facile formation of a ketimine–Rh^I σ complex,[28] or from formation of a Rh^I–iminyl complex. Either complex may serve as a reactive intermediate to facilitate the activation of aromatic C–H bonds. To explore such possibilities, we have sought to prepare Rh^I–imine and –iminyl complexes and study their potential roles in the proposed catalytic cycle. Attempted reactions between a DPPP-ligated rhodium(I) hydroxide and **1a** failed to form any detectable rhodium complexes (Scheme 4). In

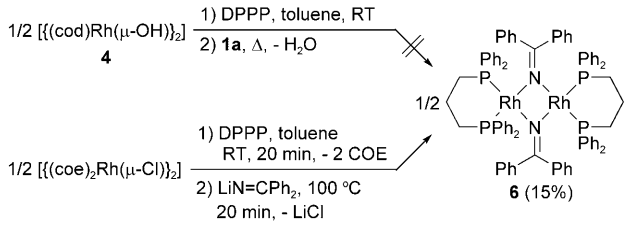
philic substitution pathway for the aromatic C–H activation step, which would prefer alkenylation at electron-neutral phenyl groups over ones with electron-withdrawing F and CF_3 substituents. As an additional mechanistic probe, we synthesized **1k** and studied its reaction with **2a** (Scheme 2). Consistent with a non-electrophilic substitution pathway,[22] the C–H activation occurred exclusively at the *meta*-CF_3-substituted phenyl. Finally, the significantly reduced reactivity and reversed regioselectivity with *ortho*-fluorinated **1j** was consistent with involvement of the cyclometalated intermediate **A**, which would be destabilized by *ortho* substituents due to steric hindrance.[2h]



Scheme 2. Reaction of imine **1k** with **2a**.

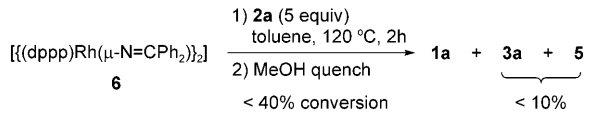


Scheme 3. Reaction of *meta*-CF_3-substituted valerophenone imine **1l** with **2a**.



Scheme 4. Attempted reaction between a DPPP-ligated rhodium(I) hydroxide and **1a**.

contrast, metathesis between a DPPP-ligated rhodium(I) chloride and the lithiated imine $LiN{=}CPh_2$ did form a discrete dimeric Rh^I–iminyl complex,[14] [{(dppp)Rh(μ-N=CPh_2)}$_2$] (**6**), in 15% yield.[29] Complex **6** was fully characterized by NMR spectroscopy and single-crystal X-ray diffraction,[30] which supported a "bent-dimer" structure that was commonly observed with dinuclear square planar complexes of d^8 metal centers.[31] Complex **6** showed high thermal stability upon heating at 120°C in toluene and no product from *ortho* C–H activation was detected by ^{31}P NMR. Furthermore, compound **6** decomposed very slowly with added alkyne **2a** (5 equiv) upon heating at 120°C in toluene (Scheme 5). Roughly 40% conversion was achieved after



Scheme 5. Stability of **6** at 120°C in the presence of **2a**.

2 h, and only trace amounts of **3a** and **5** were formed according to NMR spectroscopy and GC analysis.[32] Therefore, the preliminary mechanistic results are most consistent with a catalytic cycle that does not directly involve the Rh^I–iminyl intermediate **6**, and a more systematic mechanistic investigation will be a focus for our future research.

Conclusion

A new method of Rh-catalyzed [3+2] annulation of N-unsubstituted aromatic ketimines and internal alkynes has been developed based on imine-directed aromatic C–H bond activation and a rare example of intramolecular ketimine insertion into a Rh^I–alkenyl linkage. Current efforts are focused on further mechanistic studies that would lead to improvement of the catalyst efficiency for broader synthetic applications and for asymmetric catalysis.

Experimental Section

General: Unless otherwise noted, all manipulations were carried out under a nitrogen atmosphere by using standard Schlenk-line or glove box techniques. All glassware was oven-dried for at least 1 h prior to use. THF, diethyl ether, toluene, benzene, hexane, and pentane were degassed by purging with nitrogen for 45 min and dried with a solvent purification system (MBraun MB-SPS). $CDCl_3$ and [D_8]THF were degassed by purging with nitrogen and dried over activated 3 Å molecular sieves. N-Unsubstituted diaryl ketimines were synthesized by Grignard reactions based on a literature procedure.[13a] Other reagents and substrates were purchased from commercial vendors and were used as received. TLC plates were visualized by exposure to ultraviolet light or by exposure to I_2 sealed in a bottle at room temperature. Organic solutions were concentrated by rotary evaporation at ≈10 torr. Flash column chromatography was performed with 32–63 micron silica gel.

GC analyses were carried out on Shimadzu GC-2010 with *n*-dodecane as the internal standard. ^1H NMR spectra were obtained on a 400 MHz spectrometer and chemical shifts were recorded relative to residual protiated solvent. ^{13}C NMR spectra were obtained at 100 MHz and chemical shifts were recorded relative to the solvent resonance. Both ^1H and ^{13}C NMR chemical shifts were reported in parts per million downfield from tetramethylsilane ($\delta = 0$ ppm). ^{31}P NMR spectra were obtained at 121.5 MHz and chemical shifts were reported in parts per million downfield of 85% H_3PO_4 ($\delta = 0$ ppm). ^{19}F NMR spectra were obtained at 282.4 MHz and all chemical shifts were reported in parts per million upfield of CF_3COOH ($\delta = -78.5$ ppm). HRMS were obtained on a Bruker Daltronics BioTOF HRMS. HPLC analyses were carried out on a Waters 515 HPLC pump and a 2487 dual absorbance detector connected to a PC with Empower workstation. Single-crystal X-ray diffraction data sets were collected on a Bruker single-crystal X-ray diffractometer with a SMART CCD 1 K area detector at 293 K with $Mo_{K\alpha}$ radiation. Crystals were selected in paratone oil, mounted on a crystal loop, and positioned in the diffractometer. The structure was solved and refined (on F^2) by using the SHELXL-97 package.[33] Please refer to the Supporting Information for detailed results of single-crystal X-ray diffraction analysis on compounds **3a**, **3e**, **3k**/**3k′**, **5**, and the rhodium(I) iminyl complex **6**. CCDC-743084, 743085, 743086, and 743088 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Preparation of 3-trifluoromethylvalerophenone imine (1l):[8] 3-Trifluoromethylbenzonitrile (621 mg, 3.63 mmol, 1.0 equiv) in THF (25 mL) was added to a 100 mL round-bottomed flask equipped with a magnetic stirrer bar. The resulting solution was sealed and cooled to −78°C; a balloon filled with argon was fixed on the flask to balance the pressure. *n*BuLi (3.3 mL, 1.6 M in THF, 5.4 mmol, 1.4 equiv) was added dropwise at a rate of 0.1 mL min^{-1} (a syringe pump was applied), resulting in a red/brown solution throughout the reaction. The solution was stirred at −78°C for one hour and an additional hour at room temperature and then treated with small portions of $Na_2SO_4{\cdot}10H_2O$ (0.59 g, 1.82 mmol, 0.5 equiv). The mixture was stirred for 30 min during which time the color changed to light yellow. The solvents were removed by rotary evaporation and the residue was dissolved in 50 mL of EtOAc/Hexane (1:3) and then filtered through Celite to remove inorganic salts. Crude yellow/brown oil (680 mg, 82% yield) was obtained after removal of the solvents; further purification by vacuum distillation gave **1l** as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 9.40$ (very broad s, 1H), 8.01 (s, 1H), 7.92 (d, J = 6.0 Hz, 1H), 7.65 (d, $J = 7.6$ Hz, 1H), 7.50 (t, $J = 8.0$ Hz, 1H), 2.71 (t, J = 7.6 Hz, 2H), 1.58 (m, 2H), 1.35 (m, 2H), 0.95 ppm (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 177.7$, 139.9, 130.0, 129.31 (q, J = 25.9 Hz), 129.18, 127.0, 124.1 (q, $J = 267$ Hz), 123.7, 37.5, 28.1, 22.4, 14.0 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): $\delta = -63.3$ ppm (s).

General procedure for Rh-catalyzed [3+2] imine/alkyne annulations

Method A: The alkyne substrate (0.88 mmol, 1.0 equiv), imine substrate (1.05 equiv), and a stock solution of Rh/DPPP in toluene (1.5 mL, containing $[\{(cod)Rh(OH)\}_2]$ (0.005 equiv) and DPPP (0.012 equiv)) were added to a 4 mL screw-cap vial equipped with a magnetic stirrer bar. The vial was sealed with a silicone-lined screw cap, transferred out of the glove box, and stirred at 120 °C for 18 h. This reaction temperature and reaction time was the same for Methods B–D. After the reaction mixture was cooled to room temperature, all volatile materials were removed under reduced pressure. Further purification was achieved by flash column chromatography. Yields of the isolated products are based on the average of two runs under identical conditions.

Method B: Imine (0.68 mmol, 1.0 equiv), alkyne (1.05 equiv), $[\{(cod)Rh(OH)\}_2]$ (0.01 equiv), and DPPP (0.024 equiv).

Method C: Imine (0.45 mmol, 1.0 equiv), alkyne (1.05 equiv), $[\{(cod)Rh(OH)\}_2]$ (0.015 equiv), and DPPP (0.036 equiv).

Method D: Reactions were performed in DMF (1.0 mL) with imine (0.30 mmol, 1.0 equiv), alkyne (1.05 equiv), $[\{(cod)Rh(OH)\}_2]$ (0.015 equiv), and DPPP (0.036 equiv). The reaction mixture was cooled and quenched with H_2O (30 mL). The residue was extracted into CH_2Cl_2 (3×30 mL), washed with brine (3×20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. Further purification was achieved by flash column chromatography.

1,2,3-Triphenyl-1*H*-inden-1-ylamine (3a): Compound **3a** was prepared from **2a** and **1a** by using Method A. Chromatography (1:4 ethyl acetate/hexane, $R_f=0.35$) gave **3a** as a white solid (210.0 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.60$–7.52 (m, 2H), 7.46–7.00 (m, 15H), 6.90–6.82 (m, 2H), 1.98 ppm (s, -NH_2); ^{13}C NMR (126 MHz, [D$_8$]THF: $\delta=154.3$, 151.8, 143.8, 143.0, 139.2, 135.7, 135.2, 129.9, 129.6, 128.6, 128.3, 127.7, 127.5, 127.2, 126.9, 126.5, 126.4, 125.9, 123.2, 120.6, 72.1 ppm; HRMS: *m*/*z* calcd for $C_{27}H_{19}^+$ (loss of -NH_2 group): 343.1481; found: 343.1475.

2,3-Diethyl-1-phenyl-1*H*-inden-1-ylamine (3b): Compound **3b** was prepared from **2b** and **1a** by using Method B. Chromatography (1:2 ethyl acetate/hexane, $R_f=0.30$) gave **3b** as a colorless oil (157 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.35$ (dt, $J_1=6.8$, $J_2=0.8$ Hz, 2H), 7.30–7.16 (m, 5H), 7.12–7.05 (m, 2H), 2.66–2.50 (m, 2H), 2.34–2.10 (m, 2H), 1.76 (brs, 2H; -NH_2), 1.27 (t, $J=7.2$ Hz, 3H), 0.89 ppm (t, $J=7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.9$, 151.6, 143.9, 142.9, 138.2, 128.2, 127.4, 126.7, 125.9, 125.5, 122.2, 118.8, 71.2, 18.8, 18.4, 14.7, 13.6 ppm; HRMS: *m*/*z* calcd for $C_{19}H_{19}^+$ (loss of -NH_2 group): 247.1481; found: 247.1480.

1-Phenyl-2,3-dipropyl-1*H*-inden-1-ylamine (3c): Compound **3c** was prepared from **2c** and **1a** by using Method C. Chromatography (1:2 ethyl acetate/hexane, $R_f=0.35$) gave **2c** as a colorless oil (109 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.31$ (d, $J=6.8$ Hz, 2H), 7.28–7.12 (m, 5H), 7.05 (m, 2H), 2.49 (t, $J=8.4$ Hz, 2H), 2.30–2.14 (m, 1H), 2.14–1.98 (m, 1H), 1.76 (brs, 2H; -NH_2), 1.74–1.60 (m, 2H), 1.42–1.22 (m, 1H), 1.20–1.05 (m, 1H), 1.02 (t, $J=7.2$ Hz, 3H), 0.82 ppm (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.9$, 150.9, 144.1, 142.9, 137.0, 128.2, 127.4, 126.7, 125.9, 125.5, 122.2, 119.0, 71.2, 28.0, 27.8, 23.1, 22.1, 14.9, 14.6 ppm; HRMS: *m*/*z* calcd for $C_{21}H_{23}^+$ (loss of -NH_2 group): 275.1794; found: 275.1783.

2,3-Bis-methoxymethyl-1-phenyl-1*H*-inden-1-ylamine (3d): Compound **3d** was prepared from **2d** and **1a** by using Method A. Chromatography (3:2 ethyl acetate/hexane, $R_f=0.35$) gave **3d** as a colorless oil (265 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.45$ (dt, $J_1=7.6$, $J_2=0.8$ Hz, 1H), 7.36–7.10 (m, 8H), 4.52 (s, 2H), 4.25 (d, $J=12.4$ Hz, 1H), 3.97 (d, $J=12.4$ Hz, 1H), 3.42 (s, 3H), 3.23 (s, 3H), 2.03 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.0$, 149.4, 142.3, 142.1, 136.7, 128.6, 128.0, 127.1, 127.0, 125.9, 122.8, 121.1, 71.5, 67.0, 66.3, 58.6, 58.5 ppm; HRMS: *m*/*z* calcd for $C_{19}H_{21}O_2NNa^+$: 318.1465; found: 318.1455.

3-Methyl-1,2-diphenyl-1*H*-inden-1-ylamine (3e): Compound **3e** was prepared from **2e** and **1a** by using Method A. Chromatography (1:3 ethyl acetate/hexane, $R_f=0.40$) gave **3e** as a white solid (227 mg, 87%). The assigned structure of **3e** was confirmed by X-ray crystallography (please see the Supporting Information for details). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.80$–6.80 (m, 14H), 2.20 (s, 3H), 1.75 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.0$, 150.4, 144.2, 142.8, 135.1, 134.6, 129.4, 128.5, 128.3, 127.8, 127.4, 126.8, 126.6, 125.8, 122.7, 119.6, 71.8, 11.9; HRMS: *m*/*z* calcd for $C_{22}H_{17}^+$ (loss of -NH_2 group): 281.1325; found: 281.1319.

3-Ethyl-1,2-diphenyl-1*H*-inden-1-ylamine (3f): Compound **3f** was prepared from **2f** and **1a** by using Method B. Chromatography (1:3 ethyl acetate/hexane, $R_f=0.40$) gave **3f** as a white solid (199 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.48$–7.10 (m, 12H), 6.94–6.88 (m, 2H), 2.58 (m, 2H), 1.75 (s, -2H; NH_2), 1.26 ppm (t, $J=7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.4$, 150.3, 143.2, 142.5, 140.4, 135.2, 129.3, 128.4, 128.2, 127.7, 127.4, 126.8, 126.4, 125.9, 123.0, 120.0, 71.8, 19.5, 13.9 ppm; HRMS: *m*/*z* calcd for $C_{23}H_{19}^+$: 295.1481; found: 295.1480.

5-Fluoro-1-(4-fluoro-phenyl)-2,3-diphenyl-1*H*-inden-1-ylamine (3g): Compound **3g** was prepared from **2a** and **1b** by using Method C. Chromatography (1:3 ethyl acetate/hexane, $R_f=0.35$) gave **3g** as a white solid (167 mg, 94%). This compound displayed the spectral patterns of unsymmetrical phenyls due to limited bond rotations. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.50$ (dd, $J_1=8.4$, $J_2=5.2$ Hz, 2H), 7.44–7.28 (m, 5H), 7.20–7.02 (m, 4H), 6.98 (t, $J=8.4$ Hz, 3H), 6.85 (d, $J=7.2$ Hz, 3H), 1.81 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=163.2$ (d, J(C,F)=242.7 Hz), 162.1(d, J(C,F)=244.1 Hz), 152.8, 148.2, 144.9 (d, $J=8.1$ Hz), 138.6, 138.3, 134.4, 134.0, 132.6 (d, $J=8.1$ Hz), 129.6, 129.4, 128.9, 128.2, 128.0, 127.7, 127.3 (d, $J=8.1$ Hz), 124.2 (d, $J=9.5$ Hz), 115.7, 115.5, 113.4, 113.1, 108.7, 108.5, 70.9 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): $\delta=-115.4$ (t, $J=9.3$ Hz), -116.8 ppm (t, $J=5.9$ Hz); HRMS: *m*/*z* calcd for $C_{27}H_{19}NF_2Na^+$: 418.1378; found: 418.1389; calcd for $C_{27}H_{17}F_2^+$ (loss of -NH_2 group): 379.1293; found: 379.1300.

2,3-Diphenyl-5-trifluoromethyl-1-(4-trifluoromethylphenyl)-1*H*-inden-1-ylamine (3h): Compound **3h** was prepared from **2a** and **1c** by using Method C. Chromatography (1:3 ethyl acetate/hexane, $R_f=0.30$) gave **3h** as a light yellow solid (185 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.69$ (dd, $J_1=8.4$, $J_2=0.4$ Hz, 2H), 7.56 (m, 3H), 7.50–7.32 (m, 6H), 7.28 (dd, $J_1=8.0$, $J_2=0.4$ Hz, 1H), 7.20–7.02 (m, 3H), 6.84 (dd, $J_1=7.2$, $J_2=0.4$ Hz, 2H), 1.89 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=155.8$, 152.1, 146.4, 143.6, 139.2, 134.0, 133.5, 130.77 (q, $J=32.4$ Hz), 129.75 (q, $J=32.0$ Hz), 129.60, 129.4, 129.2, 128.43, 128.37, 128.0, 126.09, 125.99 (q, $J=4.0$ Hz), 124.39 (q, $J=273.9$ Hz), 124.29 (q, $J=273.0$ Hz), 124.1 (q, $J=4.0$ Hz), 123.5, 118.1 (q, $J=4.0$ Hz), 71.6 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): $\delta=-62.65$ (s), -62.97 ppm (s); HRMS: *m*/*z* calcd for $C_{29}H_{17}F_6^+$: 479.1229; found: 479.1241.

2,3-Diphenyl-6-trifluoromethyl-1-(3-trifluoromethylphenyl)-1*H*-inden-1-ylamine (3i): Compound **3i** was prepared from **2a** and **1d** by using Method D. Chromatography (1:3 ethyl acetate/hexane, $R_f=0.30$) gave **3i** as a light yellow solid (165 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.94$ (s, 1H), 7.63 (d, $J=7.6$ Hz, 1H), 7.53 (dd, $J_1=8.0$, $J_2=0.8$ Hz, 2H), 7.50–7.30 (m, 8H), 7.20–7.00 (m, 3H), 6.82 (dd, $J_1=7.2$, $J_2=1.2$ Hz, 2H), 1.90 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=153.3$, 152.8, 146.4, 143.3, 139.3, 134.2, 133.6, 131.4 (q, $J=32.4$ Hz), 129.6, 129.52, 129.47, 129.3, 129.09, 129.02 (q, $J=32.0$ Hz), 128.5, 128.3, 128.1, 125.8 (q, $J=4.1$ Hz), 124.5 (q, $J=4.1$ Hz), 124.51 (q, $J=272.0$ Hz), 124.32 (q, $J=272.7$ Hz), 122.6 (q, $J=4.0$ Hz), 121.5, 120.2 (q, $J=4.1$ Hz), 71.7 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): $\delta=-62.3$ (s), -63.0 ppm (s); HRMS: *m*/*z* calcd for $C_{29}H_{17}F_6^+$: 479.1229; found: 479.1228; calcd for $C_{29}H_{19}NF_6Na^+$: 518.1314; found: 518.1309.

5-Methoxy-1-(4-methoxy-phenyl)-2,3-diphenyl-1*H*-inden-1-ylamine (3j): Compound **3j** was prepared from **2a** and **1e** by using Method D. Chromatography (1:2 ethyl acetate/hexane, $R_f=0.40$) gave **3j** as a white solid (102.6 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.60$–7.25 (m, 7H), 7.20–7.00 (m, 4H), 6.95–6.80 (m, 5H), 6.71 (dd, $J_1=8.0$, $J_2=0.8$ Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 1.85 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=160.0$, 158.7, 152.6, 145.6, 144.4, 139.0, 135.20, 135.13, 134.7, 129.9, 129.6, 128.8, 128.2, 127.7, 127.4, 126.9, 123.9, 114.7, 111.7, 107.5, 70.9, 55.7, 55.4 ppm; HRMS: *m*/*z* calcd for $C_{29}H_{23}O_2$: 403.1693; found: 403.1697.

5-Fluoro-1,2,3-triphenyl-1*H*-inden-1-ylamine (3k) and 1-(4-fluoro-phenyl)-2,3-di-phenyl-1H-inden-1-ylamine (3k′): Compound **3k** was prepared from **2a** and **1f** by using Method C. Chromatography (1:4 ethyl acetate/hexane, $R_f=0.30$) gave a mixture of **3k** and **3k′** as a white solid

(170 mg, 96%). Compounds **3k** and **3k′** could not be separated by chromatography. Based on the analyses of single-crystal X-ray diffraction (see the Supporting Information for details) and ^{19}F NMR spectroscopy, **3k** and **3k′** have a ratio of 71 to 29%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–6.80 (m, 18H), 1.86 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.3 (d, J = 242.8 Hz), 162.2 (d, J = 244.2 Hz), 153.2, 153.0, 151.0, 148.54, 148.51, 145.1 (d, J = 8.1 Hz), 142.8, 142.7, 139.6, 138.73, 138.70, 135.1, 134.7, 134.5, 134.3, 132.7 (d, J = 8.1 Hz), 129.8, 129.6, 129.5, 128.99, 128.97, 128.86, 128.3, 128.1, 127.9, 127.7, 127.58, 127.56 (d, J = 8.1 Hz), 127.3, 127.0, 125.7, 124.4 (d, J = 9.5 Hz), 123.3, 121.3, 115.8, 115.53, 113.4, 113.2, 108.7, 108.5, 71.5, 71.4 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = −114.8 (t, J = 9.0 Hz), −116.3 ppm (t, J = 9.0 Hz); HRMS: m/z calcd for $C_{27}H_{18}F^+$ (loss of -NH_2 group): 361.1387; found: 361.1367.

1,2,3-Triphenyl-5-trifluoromethyl-1*H*-inden-1-ylamine (3l) and 2,3-diphenyl-1-(4-trifluoromethylphenyl)-1*H*-inden-1-ylamine (3l′): Compound **3l** was prepared from **2a** and 4-trifluoromethyl-benzophenone imine (**1g**) by using Method C. Chromatography (1:4 ethyl acetate/hexane, R_f = 0.40) gave a mixture of **3l** and **3l′** as a white solid (171 mg, 89%). Compounds **3l** and **3l′** could not be separated by chromatography. Based on the analysis by ^{19}F NMR spectroscopy, **3l** and **3l′** have a ratio of 76 to 24%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, 1H, J = 8.0 Hz), 7.64–7.50 (m, 3H), 7.48–7.00 (m, 12H), 6.94–6.80 (m, 2H), 1.87 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 152.8, 143.7, 141.8, 138.7, 134.4, 134.0, 130.40 (q, J = 32.5 Hz), 129.8, 129.7, 129.6, 129.5, 129.12, 129.08, 128.9, 128.3, 128.2, 128.0, 127.9 (d, J = 33.7 Hz), 127.7 (d, J = 29.7 Hz), 127.1, 126.2, 125.9 (q, J = 4.0 Hz), 125.7, 124.0 (q, J = 4.6 Hz), 123.6, 123.3, 121.5, 117.9 (q, J = 4.6 Hz), 71.8 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = −62.7 (s), −63.0 ppm (s); HRMS: m/z calcd for $C_{28}H_{18}F_3^+$ (loss of -NH_2 group): 411.1355; found: 411.1381.

5-Methoxy-1,2,3-triphenyl-1*H*-inden-1-ylamine (3m) and 1-(4-methoxyphenyl)-2,3-diphenyl-1*H*-inden-1-ylamine (3m′): Compound **3m** was prepared from **2a** and **1h** by using Method C. Chromatography (1:1 ethyl acetate/hexane, R_f = 0.35) gave a mixture of **3m** and **3m′** as a white solid (166 mg, 95%). Compounds **3m** and **3m′** could not be separated by chromatography. Based on the analyses by ^{1}H NMR spectroscopy, **3m** and **3m′** have a ratio of 65 to 35%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.56 (m, 2H), 7.54–7.02 (m, 12H), 7.00–6.84 (m, 3H), 6.73 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.4 Hz), 3.80, 3.79 (s, 3H), 1.93 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 158.6, 153.3, 152.4, 151.1, 145.3, 144.3, 143.2, 142.7, 139.1, 135.2, 135.0, 134.6, 134.5, 132.6, 131.9, 129.72, 129.68, 129.5, 128.71, 128.67, 128.0, 127.66, 127.60, 127.32, 127.25, 126.86, 126.81, 126.75, 125.6, 123.8, 123.1, 121.0, 114.1, 113.6, 111.6, 107.4, 71.3, 71.1, 55.6, 55.2 ppm; HRMS: m/z calcd for $C_{28}H_{21}O^+$ (loss of -NH_2 group): 373.1587; found: 373.1590.

1,2,3-Triphenyl-6-trifluoromethyl-1*H*-inden-1-ylamine (3n) and 2,3-diphenyl-1-(3-trifluoromethylphenyl)-1*H*-inden-1-ylamine (3n′): Compound **3n** was prepared from **2a** and **1i** by using Method C. Chromatography (1:4 ethyl acetate/hexane, R_f = 0.40 for **3n**, R_f = 0.30 for **3n′**) gave **3n** (65 mg), **3n′** (31 mg), and **3n**+**3n′** (80 mg) as white solids (total yield: 92%, **3n**/**3n′** = 2:1). **3n**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.44 (m, 4H), 7.44–7.22 (m, 10H), 7.16–7.02 (m, 3H), 6.86 (m, 2H), 1.88 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, [D_8]THF): δ = 155.1, 154.7, 146.9, 142.3, 138.2, 134.8, 134.5, 129.8, 129.4, 128.7, 128.5, 128.05 (quartet, J = 32 Hz), 127.78, 127.70, 127.4, 127.0, 125.8, 125.0 (q, J = 273 Hz), 124.7 (q, J = 4.6 Hz), 120.8, 119.8 (q, J = 3.0 Hz), 72.2 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = −62.6 ppm (s). **3n′**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (s, 1H), 7.84–7.00 (m, 15H), 6.84 (s, 2H), 1.90 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, [D_8]THF): δ = 153.6, 151.0, 145.6, 142.8, 139.8, 135.3, 134.7, 130.45 (q, J = 31.9 Hz), 129.8, 129.7, 129.4, 128.9, 128.6, 127.8, 127.59, 127.56, 127.1, 126.6, 123.4 (q, J = 3.8 Hz), 123.1, 122.8 (q, J = 4.6 Hz), 120.9, 71.9 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = −63.4 ppm (s); HRMS: m/z calcd for $C_{28}H_{18}F_3^+$ (loss of -NH_2 group): 411.1355; found: 411.1376.

7-Fluoro-1,2,3-triphenyl-1*H*-inden-1-ylamine (3o) and 1-(2-fluorophenyl)-2,3-diphenyl-1*H*-inden-1-ylamine (3o′): Compound **3o** was prepared from **2a** and **1j** by using Method C with 5% Rh catalyst. Chromatography (1:4 ethyl acetate/hexane, R_f = 0.40 for **3o**, R_f = 0.30 for **3o′**) gave **3o** (22 mg), **3o′** (36 mg), and **3o**+**3o′** (38 mg) as white solids (total yield: 55%, **3o**:**3o′** = 1:2). HRMS: m/z calcd for $C_{27}H_{18}F^+$ (loss of -NH_2 group): 361.1387; found: 361.1397. **3o**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, 1H), 7.42–7.16 (m, 12H), 7.10 (d, J = 6.4 Hz, 1H), 7.08 (s, 1H), 7.04 (d, J = 6.4 Hz, 1H), 6.98–6.88 (m, 2H), 2.07 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.3 (d, J(F,C) = 248.2 Hz), 151.7, 146.2, 141.1, 139.2, 138.1, 134.8, 134.1, 129.9, 129.7, 128.8, 128.7, 128.1, 128.0, 127.7, 127.4, 125.8, 122.6, 117.3, 114.4 (d, J = 20.2 Hz), 71.4 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = −123.3 ppm (s). **3o′**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (t, J = 8.0 Hz, 1H), 7.60–6.80 (m, 17H), 1.94 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.5 (d, J(F,C) = 248.2 Hz), 151.3, 149.2, 143.6, 139.6, 135.4, 134.8, 129.7, 129.6, 129.2, 129.1, 128.9 (d, J = 2.7 Hz), 128.7, 128.2, 125.1, 127.7, 127.4, 126.8, 124.4, 122.6, 121.2, 116.2 (d, J = 20.5 Hz), 69.5 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = −113.7 (s).

1-(3-Methoxy-phenyl)-2,3-diphenyl-6-trifluoromethyl-1*H*-inden-1-ylamine (3p): Compound **3p** was prepared from **2a** and **1k** by using Method C. Chromatography (1:4 ethyl acetate: hexane, R_f = 0.30) gave **3p** as a white solid (173 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.45 (m, 2H), 7.42–7.30 (m, 6H), 7.30–7.16 (m, 2H), 7.14–7.06 (m, 4H), 6.89 (dt, J_1 = 6.0, J_2 = 1.2 Hz, 2H), 6.82 (dq, J_1 = 8.0, J_2 = 0.8 Hz, 1H), 3.78 (s, 3H), 1.85 ppm (s, 2H; -NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.3, 153.7, 153.4, 146.4, 143.5, 138.7, 134.6, 133.9, 130.1, 129.8, 129.5, 129.0, 128.72 (q, J = 31.2 Hz), 128.33, 128.16, 127.9, 125.4 (q, J = 4.1 Hz), 124.6 (q, J = 272.7 Hz), 121.2, 120.1 (q, J = 4.1 Hz), 118.0, 112.6, 111.8, 71.8, 55.4 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = −62.2 ppm (s); HRMS: m/z calcd for $C_{29}H_{20}OF_3^+$: 441.1461; found: 441.1478.

1-Butyl-2,3-diphenyl-6-trifluoromethyl-1*H*-inden-1-ylamine (3q): Compound **3q** was prepared from **2a** and **1l** by using Method C. Chromatography (1:4 ethyl acetate/hexane, R_f = 0.40) gave **3q** as a light yellow solid (167 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (q, J = 0.8 Hz, 1H), 7.53 (dq, J_1 = 8.0, J_2 = 0.8 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.32–7.20 (m, 10H), 2.08–1.80 (m, 2H), 1.64 (s, 2H), 1.24–1.04 (m, 4H), 0.76 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 151.3, 146.9, 138.9, 135.2, 134.4, 129.62, 129.51, 128.66, 128.51, 128.35 (q, J = 31.9 Hz), 127.85, 127.79, 124.9 (q, J = 272.7 Hz), 125.2 (q, J = 4.0 Hz), 120.8, 118.9 (q, J = 4.0 Hz), 69.9, 38.2, 26.0, 22.9, 14.0 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ = −62.1 ppm (s); HRMS: m/z calcd for $C_{26}H_{22}F_3^+$: 391.1668; found: 391.1694; calcd for $C_{26}H_{24}NF_3Na^+$: 430.1753; found: 430.1778.

1,3,4-Triphenylisoquinoline (5): Compound **5** was prepared from **2a** and **1a** by using Method D with PPh_3 as the ligand (benzophenone (0.88 mmol), 1% Rh, PPh_3/Rh (3 equiv)). Chromatography (1:4 ethyl acetate/hexane, R_f = 0.50) gave **5** as a light yellow solid (157 mg, 50% yield). Crude **5** (60 mg) and Et_2O (1 mL) were placed into a vial. The mixture was sealed and heated at 80°C for approximately 10 min until completely dissolved. After cooling to room temperature, colorless crystals were observed on the vial wall. Suitable crystals were selected under a microscope for single-crystal X-ray diffraction (see the Supporting Information for details). ^{1}H and ^{13}C NMR spectroscopy results were in agreement with literature data.[11a]

Synthesis and crystallization of [{(dppp)Rh(N=CPh$_2$)}$_2$] (6): [{(coe)$_2$Rh-(μ-Cl)}$_2$] (60 mg, 0.0837 mmol, 1.0 equiv), DPPP (72.5 mg, 0.176 mmol, 2.10 equiv), and toluene (3 mL) were added to a 4 mL vial (A), equipped with a magnetic stirrer bar. The mixture was stirred for 20 min at RT to form a red solution of [{(dppp)Rh(μ-Cl)}$_2$]. LiN($SiMe_3$)$_2$ (30.9 mg, 0.185 mmol, 2.20 equiv), **1a** (31.8 mg, 0.175 mmol, 2.10 equiv), and toluene (3 mL) were added to a 20 mL scintillation vial (B) equipped with a magnetic stirrer bar. The mixture was stirred for 20 min at RT to form a yellow solution of LiN=CPh_2. [{(dppp)Rh(μ-Cl)}$_2$] in vial A was added dropwise into vial B and then heated at 100°C for 20 min, at which time >95% conversion was achieved based on ^{31}P NMR spectroscopic analysis. After filtration through Celite, the solution was concentrated to 2.5 mL under reduced pressure and layered by hexane (3.5 mL). Red/brown block crystals were obtained on the vial wall after 3 d (25 mg, 18% yield based on Rh). ^{31}P NMR (121.5 MHz, toluene): δ = 21.71 (d, J_{Rh-P} = 159.7 Hz). This complex is extremely air sensitive and satisfactory element analysis could not be obtained.

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[1] L. F. Tietze, G. Brasche, K. Gericke, *Domino Reactions in Organic Synthesis*, Wiley, New York, **2006**.

[2] For recent reviews, see: a) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2009**, DOI:10.1021/cr900005n; b) T. Kitamura, *Eur. J. Org. Chem.* **2009**, 1111–1125; c) F. Kakiuchi, T. Kochi, *Synthesis* **2008**, 3013–3039; d) B.-J. Li, S.-D. Yang, Z.-J. Shi, *Synlett* **2008**, 949–957; e) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174–238; f) T. Satoh, M. Miura, *Top. Organomet. Chem.* **2008**, *24*, 61–84; g) Y. J. Park, C.-H. Jun, *Bull. Korean Chem. Soc.* **2005**, *26*, 871–877; h) F. Kakiuchi, S. Murai, *Acc. Chem. Res.* **2002**, *35*, 826–834; i) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev.* **2002**, *102*, 1731–1769; j) G. Dyker, *Angew. Chem.* **1999**, *111*, 1808–1822; *Angew. Chem. Int. Ed.* **1999**, *38*, 1698–1712; k) Y. Guari, S. Sabo-Etienne, B. Chaudret, *Eur. J. Inorg. Chem.* **1999**, 1047–1055.

[3] a) This transformation from the catalyst ("L_nM-X") to intermediate **A** is shown in Scheme 1 as a single step, generating one equivalent of HX. Such a one-step process is often used to describe an electrophilic substitution pathway for C–H bond activation. However, we would like to clarify that the current one-step transformation is a simplified description and does not imply an electrophilic substitution pathway (see the Results and Discussion for details). b) The proposed intramolecular imine coordination in intermediate **B** is likely to occur through a π complexation by the C=N moiety. As one of the reviewers kindly pointed out, the alternative coordination mode, σ complexation by the nitrogen atom, would limit the rotation of the electrophile (C=N moiety). This would disturb the orbital interaction that is necessary for the proposed intramolecular imine insertion and, as a result, inhibit the formation of the carbocycle. For a related example with intramolecular coordination by the imine nitrogen that led to the heterocycle formation, please see reference [11e].

[4] For recent progress towards *tert*-carbinamines with catalytic or stoichiometric use of organometallic reagents, see: a) G. K. Friestad, A. K. Mathies, *Tetrahedron* **2007**, *63*, 2541–2569; b) M. Shibasaki, M. Kanai, *Chem. Rev.* **2008**, *108*, 2853–2873; c) S. Kobayashi, H. Konishi, U. Schneider, *Chem. Commun.* **2008**, 2313–2315; d) P. Fu, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2008**, *130*, 5530–5541; e) A. D. Dilman, D. E. Arkhipov, V. V. Levin, P. A. Belyakov, A. A. Korlyukov, M. I. Struchkova, V. A. Tartakovsky, *J. Org. Chem.* **2008**, *73*, 5643–5646; f) G. T. Notte, J. L. Leighton, *J. Am. Chem. Soc.* **2008**, *130*, 6676–6677; g) A. M. Johns, Z. Liu, J. F. Hartwig, *Angew. Chem.* **2007**, *119*, 7397–7399; *Angew. Chem. Int. Ed.* **2007**, *46*, 7259–7261.

[5] For late-metal-catalyzed intramolecular ketone additions, see: a) L. G. Quan, V. Gevorgyan, Y. Yamamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3545–3546; b) L. G. Quan, M. Lamrani, Y. Yamamoto, *J. Am. Chem. Soc.* **2000**, *122*, 4827–4828; c) L. Zhao, X. Lu, *Angew. Chem.* **2002**, *114*, 4519–4521; *Angew. Chem. Int. Ed.* **2002**, *41*, 4343–4345; d) G. Liu, X. Lu, *J. Am. Chem. Soc.* **2006**, *128*, 16504–16505; e) T. Nishimura, Y. Yasuhara, T. Hayashi, *J. Am. Chem. Soc.* **2007**, *129*, 7506–7507; f) T. Miura, M. Murakami, *Chem. Commun.* **2007**, 217–224.

[6] For an example of diastereoselective intramolecular *N*-sulfinyl ketimine insertion into a Pd–aryl linkage, see: Y.-B. Zhao, B. Mariampillai, D. A. Candito, B. Laleu, M. Li, M. Lautens, *Angew. Chem.* **2009**, *121*, 1881–1884; *Angew. Chem. Int. Ed.* **2009**, *48*, 1849–1852.

[7] Mn-mediated stoichiometric intramolecular ketone and ketimine additions have been observed, for examples, see: a) L. S. Liebeskind, J. R. Gasdaska, J. S. McCallum, *J. Org. Chem.* **1989**, *54*, 669–677; b) M. B. Dinger, L. Main, B. K. Nicholson, *J. Organomet. Chem.* **1998**, *565*, 125–134.

[8] For a recent example, see: T. Katagiri, T. Mukai, T. Satoh, K. Hirano, M. Miura, *Chem. Lett.* **2009**, *38*, 118–119.

[9] For recent examples of heterocycle formation through Pd-catalyzed domino sequences initiated by oxidative additions with aryl halides, see reference [5] and D. A. Candito, M. Lautens, *Angew. Chem.* **2009**, *121*, 6841–6844; *Angew. Chem. Int. Ed.* **2009**, *48*, 6713–6716.

[10] a) K. Ueura, T. Satoh, M. Miura, *Org. Lett.* **2007**, *9*, 1407–1409; b) T. Satoh, K. Ueura, M. Miura, *Pure Appl. Chem.* **2008**, *80*, 1127–1134; c) M. Shimizu, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2009**, *74*, 3478–3483.

[11] a) S.-G. Lim, J. H. Lee, C. W. Moon, J.-B. Hong, C.-H. Jun, *Org. Lett.* **2003**, *5*, 2759–2761; b) D. A. Colby, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2006**, *128*, 5604–5605; c) D. A. Colby, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2008**, *130*, 3645–3651; d) N. Umeda, H. Tsurugi, T. Satoh, M. Miura, *Angew. Chem.* **2008**, *120*, 4083–4086; *Angew. Chem. Int. Ed.* **2008**, *47*, 4019–4022; e) L. Li, W. W. Brennessel, W. D. Jones, *J. Am. Chem. Soc.* **2008**, *130*, 12414–12419; f) D. R. Stuart, M. Bertrand-Laperle, K. M. N. Burgess, K. Fagnou, *J. Am. Chem. Soc.* **2008**, *130*, 16474–16475; g) N. Guimond, K. Fagnou, *J. Am. Chem. Soc.* **2009**, *131*, 12050–12051; h) K. Parthasarathy, M. Jeganmohan, C.-H. Cheng, *Org. Lett.* **2008**, *10*, 325–328; i) T. Fukutani, N. Umeda, K. Hirano, T. Satoh, M. Miura, *Chem. Commun.* **2009**, 5141–5143.

[12] a) Y. Kuninobu, A. Kawata, K. Takai, *J. Am. Chem. Soc.* **2005**, *127*, 13498–13499; b) Y. Kuninobu, Y. Tokunaga, A. Kawata, K. Takai, *J. Am. Chem. Soc.* **2006**, *128*, 202–209; c) Y. Kuninobu, Y. Nishina, M. Shouho, K. Takai, *Angew. Chem.* **2006**, *118*, 2832–2834; *Angew. Chem. Int. Ed.* **2006**, *45*, 2766–2768; d) Y. Kuninobu, Y. Nishina, K. Okaguchi, M. Shouho, K. Takai, *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1393–1401.

[13] a) Y. Dejaegher, S. Mangelinckx, N. De Kimpe, *Synlett* **2002**, 0113–0115; b) G. Hou, F. Gosselin, W. Li, J. C. McWilliams, Y. Sun, M. Weisel, P. D. O'Shea, C.-Y. Chen, I. W. Davies, X. Zhang, *J. Am. Chem. Soc.* **2009**, *131*, 9882–9883.

[14] For examples of β-carbon eliminations from Rh^{I}– and Pd^{II}–iminyl species, see: a) T. Nishimura, S. Uemura, *J. Am. Chem. Soc.* **2000**, *122*, 12049–12050; b) P. Zhao, C. D. Incarvito, J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 3124–3125; c) P. Zhao, J. F. Hartwig, *Organometallics* **2008**, *27*, 4749–4757.

[15] For examples of C–N bond formation through reductive eliminations from arylpalladium(II) iminyls, see: a) J. F. Hartwig, *Acc. Chem. Res.* **1998**, *31*, 852–860; b) J. Barluenga, F. Aznar, C. Valdés, *Angew. Chem.* **2004**, *116*, 347–349; *Angew. Chem. Int. Ed.* **2004**, *43*, 343–345.

[16] For proposed C–N bond formation through olefin insertions into a Pd–iminyl linkage, see: a) S. Zaman, M. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1055–1062; b) S. Zaman, M. Kitamura, A. D. Abell, *Aust. J. Chem.* **2007**, *60*, 624–626.

[17] a) *Modern Rhodium-Catalyzed Organic Reactions* (Ed.: P. A. Evans), Wiley-VCH, Weinheim, **2005**; b) K. Fagnou, M. Lautens, *Chem. Rev.* **2003**, *103*, 169–196.

[18] It is likely that the low yields resulted from competitive pathways mediated by rhodium hydride species. However, attempted reactions with various added hydrogen acceptors did not give improved yields.

[19] It is likely that terminal alkynes formed unproductive rhodium–alkynyl complexes, although detection of such species was not attempted. The lack of reactivity of trialkylsilyl-substituted alkynes could result from the steric hindrance or electronic effects from the silyl functionality.

[20] Styrene and *n*-butyl acrylate were also tested as olefin substrates, but neither showed any reactivity with the current catalyst system.

[21] An alternative and common C–H alkenylation mechanism involves generation of an arylrhodium(III) hydrido intermediate, followed by alkyne insertion into the Rh^{III}–hydride linkage and subsequent C–C reduction elimination, see references [2a,h] for detailed discussions.

[22] Plausible pathways for the directed C–H bond activation include oxidative addition and σ-bond metathesis. In particular, C–H oxidative addition of "L_nM-X" would generate a Rh^{III} intermediate; subse-

quent loss of HX through reductive elimination would generate the proposed arylrhodium(I) intermediate **A** as shown in Scheme 1 (see ref. [2] for detailed discussions). For a recent mechanism study, see: L. Li, W. W. Brennessel, W. D. Jones, *Organometallics* **2009**, *28*, 3492–3500.

[23] The CF_3-induced rate enhancement could result from the higher reactivity of C–H activation with an electron-poor aryl, or from the higher reactivity of intramolecular addition to an electron-poor imine electrophile.

[24] Attempted substrates include acetophenone, benzophenone, *N*-phenyl benzophenone imine, *N*-*tert*-butyl benzaldimine, and benzophenone *O*-pentafluorobenzoyl oxime.

[25] a) U. R. Aulwurm, J. U. Melchinger, H. Kisch, *Organometallics* **1995**, *14*, 3385–3395; b) C.-H. Jun, J.-B. Hong, Y.-H. Kim, K.-Y. Chung, *Angew. Chem.* **2000**, *112*, 3582–3584; *Angew. Chem. Int. Ed.* **2000**, *39*, 3440–3442; c) H. Werner, N. Mahr, J. Wolf, A. Fries, M. Laubender, E. Bleuel, R. Garde, P. Lahuerta, *Organometallics* **2003**, *22*, 3566–3576; d) S.-G. Lim, J.-A. Ahn, C.-H. Jun, *Org. Lett.* **2004**, *6*, 4687–4690; e) K. Tsuchikama, Y. Kuwata, Y.-K. Tahara, Y. Yoshinami, T. Shibata, *Org. Lett.* **2007**, *9*, 3097–3099.

[26] a) For Rh-catalyzed *ortho*-arylation of N-unsubstituted benzophenone imine with $NaBPh_4$ through imine-directed C–H bond activation, see: K. Ueura, T. Satoh, M. Miura, *Org. Lett.* **2005**, *7*, 2229–2231; b) see reference [8] for a comparison of the reactivity of N-unsubstituted ketimines and N-silyl analogues.

[27] Lewis acidic metal complexes may also promote the cyclization of *ortho*-alkenyl aromatic imine intermediates. However, the lack of reactivity with Lewis acidic Rh^{I} or Rh^{III} precursors argued against this possibility (Table 1, entries 17–19). For a toluene sulfonic acid (TsOH)-catalyzed cyclization of *ortho*-alkenyl aromatic ketones, see: P. W. R. Harris, P. D. Woodgate, *Synth. Commun.* **1997**, *27*, 4195.

[28] a) M. B. Ezhova, B. O. Patrick, B. R. James, *Organometallics* **2005**, *24*, 3753–3757; b) M. L. Buil, M. A. Esteruelas, E. Goni, M. Olivan, E. Onate, *Organometallics* **2006**, *25*, 3076–3083; c) for an example of an aromatic ketone–rhodium(I) complex, see: C. P. Lenges, M. Brookhart, *J. Am. Chem. Soc.* **1999**, *121*, 6616–6623.

[29] This preparation proceeded with high chemical yields (>80%); the low yield of the isolated product reflected the solubility issue during crystallization.

[30] See the Supporting Information for details.

[31] a) M. A. Esteruelas, F. J. Lahoz, M. Olivan, E. Onate, L. A. Oro, *Organometallics* **1994**, *13*, 3315–3323; b) G. Aullón, S. Alvarez, *Inorg. Chem.* **2001**, *40*, 4937–4946; c) W. J. Marshall, G. Aullon, S. Alvarez, K. D. Dobbs, V. V. Grushin, *Eur. J. Inorg. Chem.* **2006**, 3340–3345.

[32] GC analysis was carried out after the reaction was quenched with dry MeOH. The major product was the recovered benzophenone imine **1a**.

[33] G. M. Sheldrick, Crystallographic Software Package, SHELXTL, version 5.1, Bruker-AXS, Madison, WI, **1998**.

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