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ABSTRACT: Reactions are described of the second-generation Hoveyda catalyst **HII** with amines, pyridine, and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), in the presence and absence of olefin substrates. These nitrogen bases have a profoundly negative impact on metathesis yields, but in most cases are innocuous toward the pre-catalyst. **HII** adducts were formed by primary and secondary amines (*n*-butylamine, *sec*-butylamine, benzylamine, pyrrolidine, morpholine), pyridine, and DBU at room temperature. No reaction was evident for NEt_3, even at 60 °C. On longer reaction at RT, unencumbered primary amines abstract the benzylidene ligand from **HII**. With 10 equiv $NH_2{}^nBu$, this process was complete in 12 h, affording $NH^nBu(CH_2Ar)$ (Ar = *o*-C_6H_4-O^iPr) and $[RuCl(H_2IMes)(NH_2{}^nBu)_4]Cl$. For benzylamine, benzylidene abstraction occurred over days at RT. No such reaction was observed for *sec*-butylamine, secondary amines, NEt_3, pyridine, or DBU. All of these bases, however, strongly inhibited metathesis of styrene by **HII**, with a general trend toward more deleterious effects with higher Bronsted basicity. Studies at 10 mol% **HII** and 10 equiv DBU, NEt_3, and pyrrolidine (60 °C, C_6D_6) indicated that the primary mechanism for decomposition involved base-induced deprotonation of the metallacyclobutane intermediate, rather than the Lewis base-mediated decomposition pathways previously established for the Grubbs catalysts. In the corresponding metathesis of ethylene, this decomposition process is rapid even at RT, highlighting the vulnerability of the monosubstituted metallacyclobutane.

Keywords. *homogeneous catalysis, olefin metathesis, amine, metallacyclobutane, decomposition, Hoveyda catalyst, Hoveyda-Grubbs catalyst*

Introduction

Olefin metathesis offers exceptional power and efficiency in the assembly of carbon-carbon bonds.[1] The development of readily-handled, highly active ruthenium catalysts (preeminently the second-generation Grubbs and Hoveyda catalysts **GII** and **HII**; Chart 1)[2,3] led to widespread uptake of these methodologies in organic synthesis. Notwithstanding the importance of metathesis in the synthesis of alkaloids and other nitrogen heterocycles,[4] however, compounds bearing sterically accessible nitrogen sites challenge the functional-group tolerance of these catalysts.[5-7]
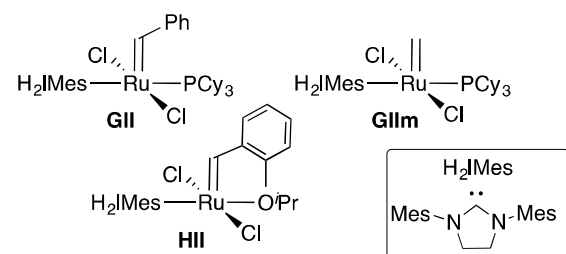
Chart 1. Metathesis Catalysts Discussed, and the Resting-State Methylidene Complex for GII

Reports from pharma highlight the destructive effect on metathesis of even traces of morpholine, DBU (1,8-diazabicyclo[5.4.0]-undec-7-ene), and other nitrogen bases.[8-10] Likewise, metathesis of amine-bearing substrates has long been known to require either *N*-protection,[11] or an adjacent substituent to block access to and/or withdraw electron density from the nitrogen site.[5-7] The Cossy group recently extended the latter strategy to metathesis of *N*-heteroaromatic compounds.[12] For protected amines, a survey of recent examples[13-21] illustrates moderate to excellent metathesis yields. Reaction is relatively slow even at high catalyst loadings, however, suggesting competing catalyst deactivation.

A clear understanding of the processes by which catalysts decompose is key to designing solutions.[22-24] The deleterious effect of sterically accessible amine and pyridine donors on metathesis is widely presumed to be due to their excellent Lewis basicity,[6,7,12] owing in large part to studies of the Grubbs catalysts.[25-28] Particularly damaging, even toward the robust precatalyst **GII**, are sterically ac-

cessible primary amines. We recently demonstrated that *n*-butylamine abstracts the benzylidene ligand from **GII** over several hours at room temperature (Scheme 1, top).[26,27,29] In contrast, secondary amines,[26] DBU,[26] and pyridine[30] form stable adducts with **GII**.

Much more vulnerable is the resting-state methylidene complex **GIIm**. Amines greatly accelerate decomposition of this species.[26,27] Such donors cause complete loss of the methylidene ligand over hours at RT, a process that requires days for **GIIm** at 55 °C in the absence of amine.[28] In both cases, decomposition occurs via dissociation of the PCy_3 ligand, which then abstracts the methylidene ligand. Consistent with the general pathway depicted in Scheme 1 (bottom), we recently intercepted and crystallographically characterized the σ-alkyl species **Ru-1** for the first-generation Grubbs catalyst $RuCl_2(PCy_3)_2(=CHPh)$ **GI**.[31]
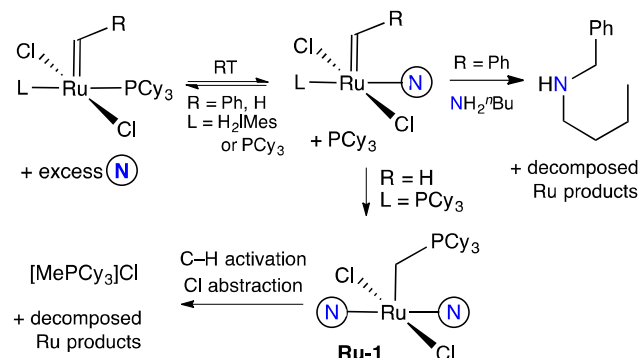
Scheme 1. Amine-Induced Deactivation of the Grubbs Catalysts.

While free PCy_3 plays a central role in this decomposition chemistry, a related pathway can be envisaged for phosphine-free catalysts: that is, attack on the methylidene ligand by nitrogen nucleophiles, in place of PCy_3. Despite the growing importance of **HII** and its congeners, the decomposition behavior of such phosphine-free catalysts has seen little attention.[32] In the present study, we examined the reactions of nitrogen bases with **HII** in the presence and absence of metathesis substrates. The bases selected for study (Chart 2) include examples highlighted in the literature as particularly deleterious, with the addition of others (NEt_3, NH_2CH_2Ph, $NH_2s^{ec}Bu$) designed to gauge the effect of amine bulk and basicity. Here we report that Bronsted basicity – specifically, proton abstraction from the metallacyclobutane intermediate – is the primary contributor to deactivation of **HII** during metathesis. Lewis basicity is found to play a significant role only for the smallest, most accessible primary amines.
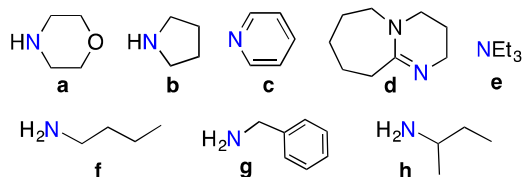
Results and Discussion

Prior to examining the impact of **a–f** on **HII** during catalysis, we established the reaction chemistry in the absence of substrate. These experiments are important to dissect out the respective roles of the metallacyclobutane or other intermediates, relative to **HII** itself. They carry further weight given that **HII** functions as not only the pre-catalyst, but also a key resting state during metathesis.[33] Despite the presence of the oxygen donor in the styrenyl ether ligand, the chemistry of **HII** itself was found to parallel that previously communicated[26] for reaction of **GII** with a subset of these donors.

Adduct formation on reaction of HII with *N*-donors. In a series of NMR experiments, **HII** was treated with a tenfold excess of **a–h** in C_6D_6, in the presence of an internal integration standard (TMB, trimethoxybenzene) to enable quantification of non-alkylidene Ru products. As shown in Scheme 2 and described below, stable adducts were observed for the secondary amines, pyridine, and DBU (**a–d**), while no reaction was evident for NEt_3 **e**, even at 60 °C.

For the adducts of **a–d**, a new singlet for the alkylidene proton was observed in the region 20.0–20.7 ppm (Table 1). Diagnostic for release of the chelated ether oxygen is the downfield location of this signal relative to that for **HII** at 16.72 ppm.[34] Release of the chelate is further supported by the upfield location of the C*H*Me₂ septet, for which the midpoint appears between 4.2-4.0 ppm, near that of the free styrenyl ether (4.15 ppm). In comparison, a midpoint of 4.48 ppm is found for this signal in **HII** itself. A through-space interaction between the isopropoxy C*H*Me₂ methine and the alkylidene proton was confirmed by NOE experiments with the pyrrolidine adduct **HIIb**. Control experiment showed no such NOE effect for **HII** itself, in which the position of the isopropoxy group is locked by chelation.
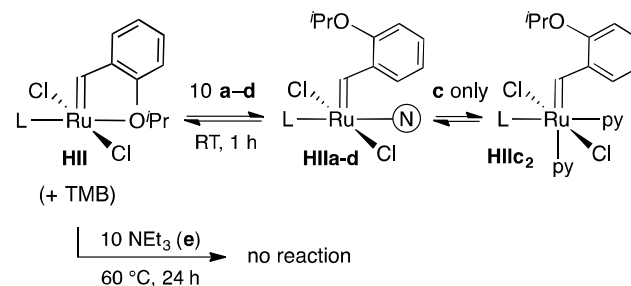
a L = H₂IMes. For primary amines **f–h**, see below.

Scheme 2. Reaction of HII with Di- or Trisubstituted *N*-Donors.[a]

Table 1. Key ¹H NMR Data and Equilibrium Yields for *N*-Adducts of HII and GII.[a]

N-donor	HII adducts δ_H (yield)	GII adducts[26] δ_H (yield)

|		
none	16.72	19.65
a: morpholine	20.39 (71)	19.73 (65)
b: pyrrolidine	20.25 (100)	19.67 (93)
c: pyridine	19.97 (100)[b,c]	19.83 (55)[b]
d: DBU	20.71 (74)	19.93 (75)
e: NEt$_3$	no reaction	no reaction
f: NH$_2$^{n}Bu	19.81 (95),[b] 18.58 (5)	19.56 (90)[b,d]
g: NH$_2$CH$_2$Ph	19.74 (78),[b] 18.84 (22)	not reported
h: NH$_2$^{sec}Bu	20.00 (100)[c]	not reported

[a]Chemical shift of [Ru]=CHAr (C$_6$D$_6$, 500 MHz). Equilibrium yields in brackets, exclusive of decomposition. [b]Assigned as bis(amine) adduct; see text. [c]Value at –20 °C in C$_7$D$_8$ (br s at RT). [d]Cf. value of 18.96 reported[25] for **GIId$_2$** at –30 °C in CD$_2$Cl$_2$.

The resulting adducts were thermally stable at 60 °C, showing no detectable decomposition after heating for 24 h. A dynamic equilibrium between the adducts and **HII** is operative, as indicated by ^{1}H EXSY experiments with **HIIb**, which exhibited a correlation cross-peak between the alkylidene signals for **HII** and **HIIb** (see S.I.) Partial reversion to **HII** was induced on exposure to vacuum, consistent with an equilibrium reaction.

In comparison, treating **HII** with *n*-butylamine **f** (Scheme 3) resulted in immediate formation of mono- and bis-amine adducts: no **HII** was visible, but 9% loss of alkylidene was evident at the time of the first NMR measurement (4 min), increasing to 15% at 15 min. The dominant product ([Ru]=CHAr δ_H 19.81 ppm) is assigned as bis-amine adduct **HIIf$_2$**, by analogy to the structure crystallographically established for **GIIf$_2$**.[25] Mono-amine derivative **HIIf** was present in minor amounts (δ_H 18.58 ppm, <5%). The analogous mono-amine complex was not observed for **GII**, but reportedly formed via loss of amine on drying **GIIf$_2$** under vacuum.[25,26]

Ensuing benzylidene abstraction by **f** was slightly faster than in the **GII** system.[26] Loss of alkylidene was complete after 12 h at RT (vs. 95% for **GII**), and the diagnostic methylene singlet for the amine product NH(^{n}Bu)(CH$_2$Ar) **1** (Ar = C$_6$H$_4$-*o*-O^{i}Pr) was evident at 3.93 ppm (0.8 equiv vs. starting **HII**).[35]

The corresponding reactions with benzylamine **g** proceeded similarly, affording mono- and bis-amine derivatives **HIIg** and **HIIg$_2$** (Scheme 3; Table 1). Decomposition was much slower, however, presumably reflecting the greater bulk and lower basicity[36] of the amine. Thus, after 96 h, the alkylidene signal for the **HIIg$_2$** adduct was still observable at 19.74 ppm (ca. 6%; cf. zero remaining **HIIf$_2$** after 12 h). A similar proportion of the amine derivative NH(CH$_2$Ph)(CH$_2$Ar) **1'** was observed.
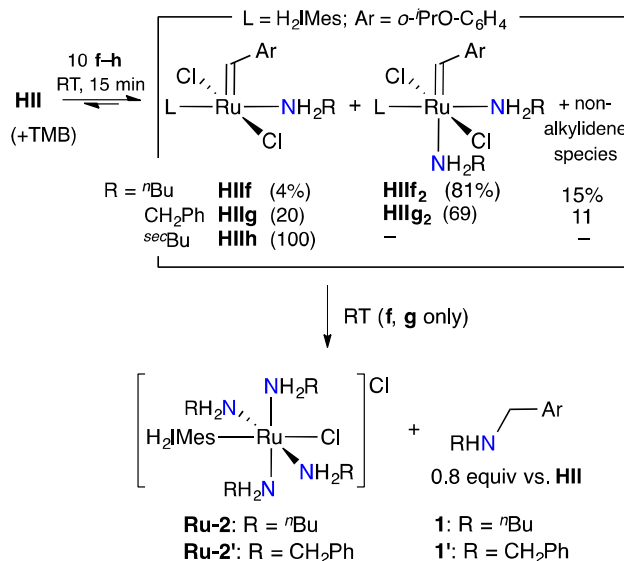
Scheme 3. Reaction of HII with Primary Amines.

In situ quantification of the ruthenium co-product is hampered by the excess amine present. We isolated the *n*-butylamine derivative **Ru-2** from both **HII** and **GII**, by addition of 10 equiv **f** at RT in benzene (Scheme 4). The yellow product precipitated over 24 h, and was purified by extracting with hexanes (81% isolated yield for **GII**; or 69% for the smaller-scale reaction with **HII**). This cationic complex is unstable in solution in the absence of excess amine, presumably because of competing coordination of the chloride counter-ion and displacement of bound NH$_2$^{n}Bu. Similar behavior, including a cascade of ensuing reactions associated with solvent-induced chlorination, was previously reported for nitrile derivatives of Ru(II).[37] The structure shown is supported by combustion analysis, and by NMR analysis in the presence of a small amount of added amine (1% v/v).[38]
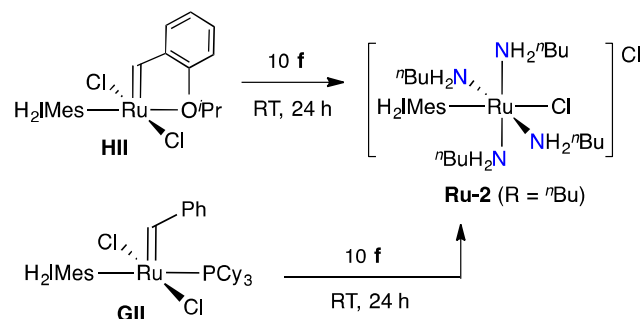
[a] Amine co-products (NH(^{n}Bu)(CH$_2$Ar) **1** or NH(^{n}Bu)(CH$_2$Ph) not shown.

Scheme 4. Isolation of Ru-2 from the Reaction of HII or GII with *n*-Butylamine.[a]

Notably, no benzylidene abstraction occurred in the corresponding reaction of **HII** with *sec*-butylamine **h**. Instead, mono-amine adduct **HIIh** was formed as the sole product, and this species resisted decomposition even after heating for 24 h at 60 °C. We infer that

disubstitution at the carbon α to the nitrogen atom is sufficient to block approach to the benzylidene ligand.

Consistent with this steric sensitivity is a mechanism involving benzylidene abstraction via nucleophilic attack at the [Ru]=CHAr carbon (Scheme 5).[39] Precedent for the σ-alkyl moiety in intermediate **A** is provided by structurally characterized **Ru-1** (Scheme 1) in the Grubbs system.[31] Elimination of the alkyl ligand – whether by a concerted pathway, as shown, or via a Ru-hydride intermediate – would liberate the secondary amine **1**.
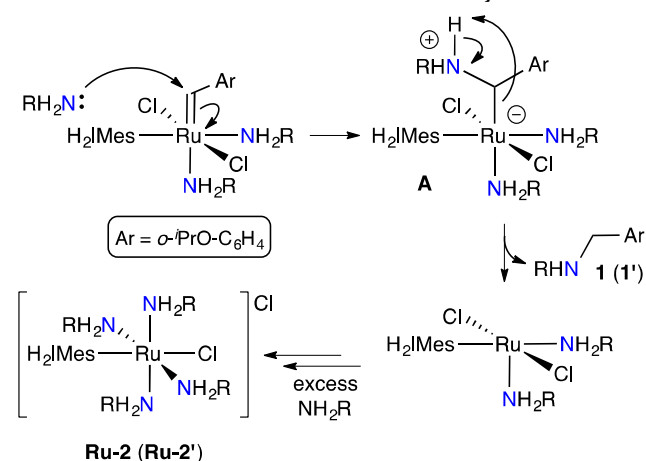
Scheme 5. Proposed Mechanism for Benzylidene Abstraction by Sterically Accessible Primary Amines.

The overall pattern of decomposition by primary amines outlines above indicates that a sharp decline in aggressiveness in the order NH$_2^n$Bu >> NH$_2$CH$_2$Ph, while attack by α-substituted NH$_2^{sec}$Bu is completely inhibited. **HII** is thus relatively tolerant toward amines or related nucleophiles for which benzylidene abstraction is curbed by bulk or limited basicity. Because ligation of these Lewis donors is readily reversible, their negative impact on the precatalyst (that is, **HII** itself) is better described as deactivation than decomposition. Very different results are found in the presence of olefin, as described in the next section.

Base-Induced Decomposition of HII and Its Active Species During Metathesis. We next examined the impact of base on the longevity and productivity of **HII** during metathesis. As a probe reaction, we chose the self-metathesis of styrene by **HII** (1 mol%) at 60 °C in benzene. The homodimerization of styrene to form stilbene is known to proceed in high yield, but at relatively slow rates even using 3-5 mol% Ru.[40-42] It thus provides a convenient model for assessing the detrimental effect of base.

In control reactions without added **a–f**, yields of stilbene reached ca. 80% after 2 h, and 94% after 24 h. In the presence of **a–f**, the maximum yield decreased in all cases (Figure 1). The impact of just one equivalent of amine per **HII** is offset by adduct formation. With 10 equiv **a–f**, however, metathesis activity is dramatically reduced, and a general trend toward lower CM yields with increasing Bronsted basicity is evident.[36] A minor anomaly with NH$_2^n$Bu **f** is attributed to the capacity of this sterically

accessible primary amine to abstract the alkylidene ligand from **HII**, as described above.

The negligible proportion of stilbene (<5%) formed with the stronger bases attests to the efficiency of decomposition. Perhaps most unexpected is the low CM yield observed in the presence of a tenfold excess of NEt$_3$ **e**. This is particularly important given the steric protection presumed for tertiary amine centers, as noted in the Introduction. A role for proton abstraction in catalyst deactivation is proposed below. *N*-binding (i.e. sequestration of amine by binding to the metal, as in Scheme 1) is presumed to compete with this pathway.
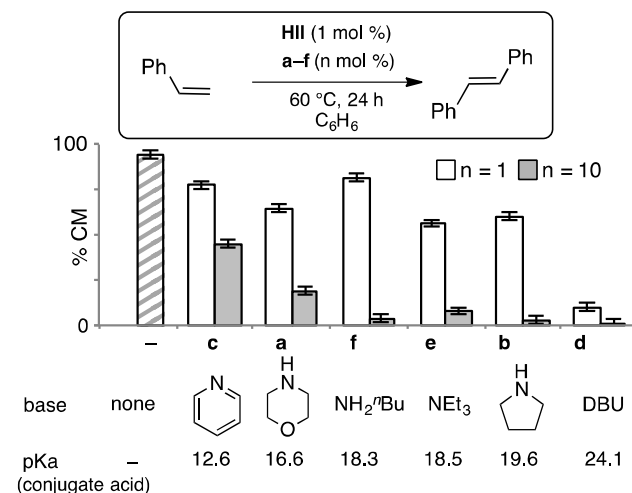

Figure 1. Impact of *N*–base on metathesis yields.[36]

Decomposition Pathway. To gain insight into the mechanism by which bases decompose the active catalyst, NMR experiments were carried out under the conditions above, but using 10 equiv each of styrene and amine. In this portion of the study, we focused on the three most deleterious bases, pyrrolidine **b**, DBU **d**, and NEt$_3$ **e**. (We omitted primary amine **f** in order to highlight decomposition that originates in the active species, as opposed to the precatalyst). For DBU and NEt$_3$, loss of all alkylidene species was complete within 30 min at 60 °C (Table 2); cf. 18 h for pyrrolidine **b**.

Unexpectedly, experiments directed at assessing temperature effects indicated that decomposition by NEt$_3$ **e** is fast even at RT, with complete loss of alkylidene by 1h. In comparison, ca. 90% loss is found with DBU after 10 h at RT. In all cases, the sole or principal organic decomposition product is (*E*)–PhCH=CHCH$_2$Ph **3**, irrespective of temperature. The identity of **3** was confirmed by MS and NMR analysis. The olefinic signals offer characteristic NMR values, in terms of both chemical shift and multiplicity: a doublet at 6.31 ppm ($^3J_{HH}$ = 16 Hz) for the Ph*H*C proton, and a doublet of triplets at 6.19 ppm ($^3J_{HH}$ = 16 Hz, $^3J_{HH}$ = 7 Hz) for the =C*H*CH$_2$Ph proton, in excellent agreement with literature values,[43] and with DEPT-135 and COSY data. Trans-selectivity is indicated by the magnitude of the $^3J_{HH}$ coupling constant (16 Hz). A minor co-product, observed in the control reaction without base, and in the presence of NEt$_3$, is the related species (*E*)-PhCH=CHCH$_3$ **3'**.[44] The

origin of these products, and the mechanistic implications thereof, are discussed below.

**Table 2. Decomposition Rates and Products on Reaction of HII with Styrene in the Presence of Amines.[a]**
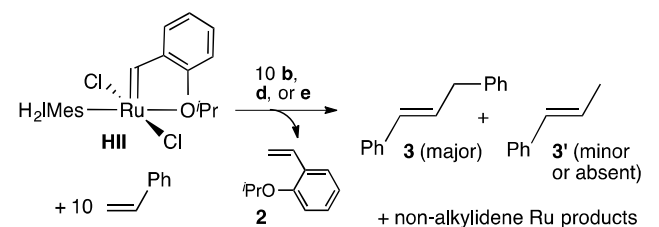
N-base	T (°C)	time (h)	% loss of [Ru]=CHR	% 3	% 3'
none	60	24	91	–	17
pyrrolidine b	60	10	90	72	–
		18	quant	81	–
DBU d	60	0.5	quant	88	–
NEt₃ e	60	0.5	quant	70	13
DBU d	21	18	quant	90	–
NEt₃ e	21	1	quant	74	9

[a]Conditions: 200 mM styrene, C_6D_6, J. Young tube. ¹H NMR integration vs. TMB; ±2.5% in replicate runs. Yields of **3** are based on starting **HII**. Yields of stilbene vs. starting styrene <4%.

These reactions proceed via initial cross-metathesis of **HII** with styrene, liberating isopropoxystyrene **2** in near-quantitative amounts (95% based on starting **HII**).[45] Complete, efficient uptake of the entire **HII** charge is indicated, notwithstanding the relatively small proportion of substrate present. This point is worth emphasis, as it contradicts the widespread view that **HII** initiates slowly: it is fully consistent, however, with the rapid turnon established for this catalyst in recent ¹³C-labelling studies.[33]

In the slower reaction with pyrrolidine **b**, we were able to observe the known adduct **GIIb**[26] (70% yield at 2 h, based on starting **HII**). This complex is formed by trapping of the four-coordinate benzylidene intermediate **Ru-3** (Scheme 6). While **GIIb** disappears relatively slowly, it does not successfully engage in metathesis. Decomposition accounts for the failure to observe **GIIb** and **HIIb** in the expected equilibrium ratio. Instead, the organic product of catalyst decomposition, PhCH=CHCH₂Ph **3**, accounts for 80-90% of the "missing" **HII** at any time (see conversion plot of Scheme 6).
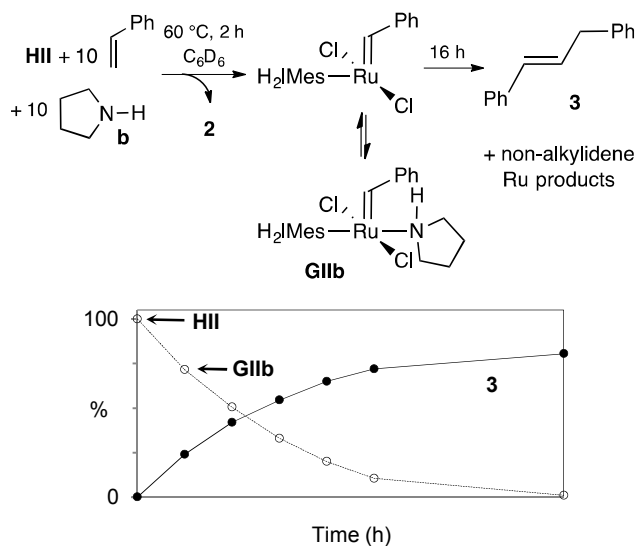
Scheme 6. Reaction of HII with Styrene and Pyrrolidine, and Rate Plot for Loss of Alkylidene.

The three-carbon backbone present in **3** is an important marker implicating attack of base on the metallacyclobutane intermediate (e.g. **Ru-4**; Scheme 7). Proton abstraction from the Cβ site is proposed to generate an anionic σ-alkyl complex such as **Ru-5**, the basicity of which enables E–H bond activation and ensuing elimination, as earlier established for σ-alkyl complex **Ru-1**.[46] Key to this pathway is poor steric protection of the kite-shaped[32b] metallacyclobutane ring, which permits approach of amine. Notably absent is the o-isopropoxyphenyl analog of **3** (i.e. PhCH=CHCH₂Ar). We infer that the increased bulk of the aryl substituent in **Ru-4"** impedes approach of base to Cβ, and hence inhibits deprotonation of this species.
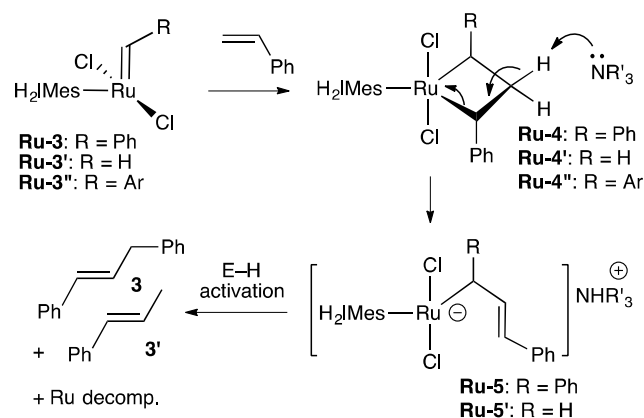
Scheme 7. Proposed Mechanism for Base-Induced Catalyst Decomposition During Metathesis.

Interestingly, on replacing pyrrolidine **b** with the bulkier, less basic amine NEt₃ **e**, 10–15% PhCH=CHMe **3'** is observed, depending on temperature. Formation of **3'** indicates that metathesis proceeds to the monosubstituted metallacyclobutane (MCB) **Ru-4'**, a reflection of the inability of NEt₃ to trap out the four-coordinate intermediate (see **Ru-3**, etc.) via adduct

formation. More extensive metathesis is inhibited by decomposition. The rapidity of decomposition even at RT, indicates that the transition state for β-elimination (i.e. transformation of **Ru-4** to **Ru-5**) is rather low in energy. The barrier appears to decline as MCB substitution decreases, as indicated by the very rapid degradation of **HII** in the presence of ethylene and base at RT; see below.

In the absence of base, catalyst decomposition during styrene metathesis was much slower, with 9% **HII** still present after 24 h at 60 °C. Stilbene was observed in ca. 70% yield. Of note, small amounts of PhCH=CHCH$_3$ **3'** and propylene (0.2 equiv vs. starting **HII**) were also evident, indicating decomposition via the monosubstituted MCB intermediate. MCB deprotonation can thus occur even without assistance by base. The Sasol group earlier reported evidence for β-hydride transfer from MCB intermediates as a key deactivation pathway for **GIIm** in the presence of ethylene.[47] Bespalova and co-workers subsequently invoked such a pathway to account for decomposition of **HII** and formation of propylene under ethylene.[32a]

Decomposition was much faster under ethylene atmosphere, even at RT. Exposing **HII** to ethylene in the presence of pyrrolidine **b** (Scheme 8) resulted in >90% loss of all alkylidene signals within 2 h. This should be compared with just 8% loss at 2 h under these conditions in the absence of base. Major products were ArCH$_2$CH=CH$_2$ **4** and its β-methylstyrene isomer ArCH=CHMe **4'**, formed in nearly 80% total yield relative to starting **HII**. Both originate in MCB **Ru-6**, consistent with the pathway shown for the analogous intermediate **Ru-4** in Scheme 7. Somewhat unexpectedly, no propylene was observed, in contrast to the pyrrolidine-free control reaction. This is certainly due in part to the efficiency of decomposition, which hampers the ensuing formation of the unsubstituted MCB **Ru-6**. We do not rule out, however, the possibility that the balance of decomposition (20%) occurs via this pathway, and that the propylene gas is lost in the headspace.
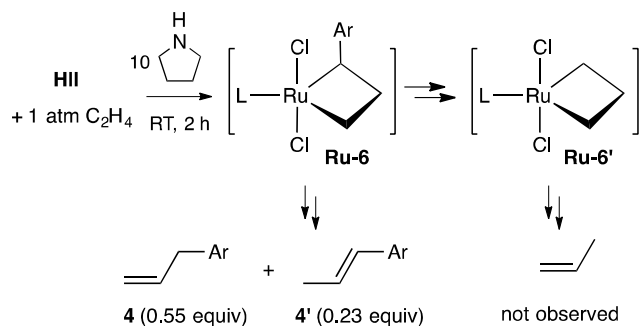
Scheme 8. Organic Products from Base-Induced Decomposition of HII During Ethylene Metathesis.

Accelerated catalyst decomposition during metathesis of ethylene, as compared with styrene, is consistent with the greater accessibility of the monosubstituted metallacyclobutane ring in **Ru-6**, relative to disubstituted **Ru-4**. This heightened vulnerability to base in the presence of ethylene is of particular interest from the perspective of "ethenolysis" reactions used to generate α-olefins from internal olefins, a subject of considerable interest in multiple contexts, including metathesis of renewable feedstocks.[48] More generally, it underscores the importance of efficiently sweeping ethylene out of metathesis reactions where amines or other Bronsted bases are present, as a means of minimizing catalyst decomposition. Decomposition via base-induced deprotonation of the unsubstituted MCB is thus expected to be particularly problematic during industrial processes involving **HII** and related catalysts, where mass transfer limitations apply; during synthetic reactions with limited headspace; and during NMR-tube or other sealed-tube experiments.

Conclusions

The foregoing represents the first study of the effect of additives on decomposition of the important Hoveyda catalyst **HII**. The precatalyst itself proved tolerant toward all but the most sterically accessible, unbranched primary amines. While the ether ligand is readily displaced by *N*-donors, in most cases this merely generates stable adducts, which exist in equilibrium with **HII**. Sterically unencumbered amines, however, attack the precatalyst and abstract the benzylidene moiety as NHR(CH$_2$Ar) (R = ^{n}Bu, CH$_2$Ph).

In the presence of substrate, the impact of base is much more dramatic. Metathesis yields are highly sensitive to the basicity of the amine, and even 1 equivalent of DBU causes almost complete loss of activity. In all cases, however, metathesis is sharply reduced by a stoichiometric excess of amine. Closer examination of the reactions with pyrrolidine, NEt$_3$ and DBU revealed attack on the key metallacyclobutane (MCB) intermediate, and indicated that decomposition was complete within ca. two cycles of metathesis. The organic products of decomposition were consistent with deprotonation of the metallacyclobutane by the Bronsted base to form a Ru-alkyl intermediate, and elimination via E–H activation pathways. The rapid deactivation by NEt$_3$ is particularly noteworthy, given the steric protection widely presumed for tertiary nitrogen centers.

Also of note is the dramatically higher vulnerability of the MCB intermediate formed in the presence of ethylene, which was rapidly decomposed in the presence of base even at ambient temperatures. These data suggest that, where basic substrates or contaminants are present, catalyst productivity will be highly sensitive to removal of ethylene, the usual coproduct of metathesis.

Experimental

General Procedures. Reactions were carried out using standard glovebox or Schenk techniques at ambient temperature, unless otherwise indicated. Dry, oxygen-free C$_6$H$_6$, CH$_2$Cl$_2$, and hexanes were obtained using a Glass Contour solvent purification system. C$_6$D$_6$, C$_7$D$_8$, and CD$_2$Cl$_2$ (Cambridge Isotopes) were degassed by five

consecutive freeze/pump/thaw cycles. All solvents were stored over 4Å molecular sieves under N_2 for at least 12 h prior to use. Decane and styrene (>99%, Sigma-Aldrich) were degassed as above and stored over 4 Å molecular sieves. DBU (98%, Acros), pyridine (>99%, Fisher) and NEt_3 (99%, Alfa Aesar) were distilled over CaH_2; morpholine (Sigma-Aldrich, >99.5%, packed under N_2) was used as received. All other amines (Sigma-Aldrich or Alfa Aesar; maximum grade, 99% or higher) were degassed immediately on receipt and stored under N_2. Amine purity was verified by ^1H NMR analysis prior to use. Ethylene (Linde grade 3.0), 1,3,5-trimethoxybenzene (>99%, Sigma-Aldrich) and potassium tris(pyrazolyl)borate (>97%, TCI) were used as received. Literature methods were used to prepare **GII**,[49] **HII**,[49] and 2-isopropoxybenzaldehyde.[50]

NMR spectra were recorded on Bruker Avance 300 and 500 spectrometers at 296 K, unless otherwise noted, and referenced to the residual proton or carbon signals of the deuterated solvent (^1H, ^{13}C). Signals are reported relative to TMS at 0 ppm. Metathesis conversions and yields were measured on a GC (Agilent 7890A) equipped with a flame ionization detector (FID) and polysiloxane column (Agilent HP-5) at an inlet split ratio of 10:1 and inlet temperature of 250 °C. Retention times were confirmed by comparison to pure samples. Styrene and stilbene were quantified from integrated peak areas vs. decane internal standard, corrected for response factors of decane and analyte. Calibration curves (peak areas vs. concentration) were constructed in the relevant concentration regime to account for the dependence on detector response for all analytes. GC-MS analysis was perfomed using an Agilent 5975B inert XL EI/CI instrument equipped with a polysiloxane column.

Stoichiometric Reactions of HII with Nitrogen Bases. To a solution of **HII** (15 mg, 0.024 mmol) in 1.00 mL C_6D_6 was added TMB (ca. 1 mg) as an internal integration standard. This solution was divided into two portions (0.012 mmol **HII**), half being treated with amine or pyridine, and the other half being used as a control reaction. In a screw-cap Rotoflo NMR tube, the initial ratio of **HII** : TMB was measured by integrating the ^1H NMR signals for the [Ru]=CH and TMB sp^2-CH protons. A solution of 12 μL $NH_2{}^nBu$ **f** (8.9 mg, 0.12 mmol, 10 equiv) in 80 μL C_6D_6 was injected using a gas-tight syringe. The pierced septum was immediately protected with Parafilm, a stopwatch was started, and the mixture was shaken vigorously for 30 s. The first ^1H NMR spectrum was collected within 4 min. Loss of the alkylidene signals was monitored at 20 min intervals over 12 h.

For the corresponding reaction of benzylamine **g**, the first spectrum was measured at 15 min and 24 h (ca. 50% loss in total alkylidene at 24 h). Spectra were measured at 24 h intervals for a further 72 h. For all other amines (morpholine **a**, pyrrolidine **b**, pyridine **c**, DBU **d**, NEt_3 **e**, sec-butylamine **h**), spectra were measured at 1 h and again at 24 h. For pyridine **c** and sec-butylamine **h**, spectra were recorded at –20 °C (C_7D_8) to reduce the breadth of the alkylidene signal. Reactions of **a–e** and **h**

showed no change after 24 h at RT, or after heating to 60 °C for an additional 24 h.

Confirmation of HII–HIIb Equilibrium. A sample was prepared as above, with collection of an ^1H NMR spectrum after 1 h. The sample was then dried under vacuum (ca. 50 mTorr) for 20 min, and re-dissolved for analysis. ^1H NMR (C_6D_6, 500.1 MHz): δ 20.25 (Ru=CHAr for **HIIb**, 53%), 16.72 (Ru=CHAr for **HII**, 47%).

Synthesis of [RuCl(H$_2$IMes)(NH$_2{}^n$Bu)$_4$]Cl (Ru-2). To a pink solution of **GII** (175 mg, 0.206 mmol) in 13 mL C_6H_6 was added $NH_2{}^nBu$ (0.200 mL, 2.02 mmol, 10 equiv). The solution turned green immediately, and yellow over 24 h. A pale yellow precipitate deposited over this time. The solvent was stripped off, and the residue was washed with hexanes (3 x 5 mL). Yield after drying under vacuum: 128 mg (81%). The corresponding reaction of **HII** likewise afforded **Ru-2**, in 69% isolated yield. ^1H NMR (CD_2Cl_2 + 1% $NH_2{}^nBu$, 500.1 MHz): δ 7.00 (s, 4H, m-CH of Mes), 3.96 (s, 4H, CH_2 of H$_2$IMes), 2.69–2.59 (m, 8H, NH_2), 2.56 (s, 12H, o-CH_3 of Mes), 2.29 (s, 6H, p-CH_3 of Mes), 1.99–1.88 (m, 8H, α-CH_2 of ^{n}Bu), 1.33 (t of t, $^3J_{HH}$ = 7 Hz, 8H, β-CH_2 of ^{n}Bu), 1.14 (q of t, $^3J_{HH}$ = 7 Hz, 8H, γ-CH_2 of ^{n}Bu), 0.86 (t, $^3J_{HH}$ = 7 Hz, 12H, CH_3 of ^{n}Bu). ^{13}C{^{1}H} NMR (CD_2Cl_2 + 1% $NH_2{}^nBu$, 125.8 MHz): δ 224.6 (C_{NHC} of H$_2$IMes), 139.9, 138.5, 137.7, 130.7 (m-CH of Mes), 53.6 (CH_2 of H$_2$IMes), 45.2 (α-CH_2 of ^{n}Bu), 35.8 (β-CH_2 of ^{n}Bu), 20.9 (p-CH$_3$ of Mes), 20.4 (γ-CH_2 of ^{n}Bu, detected from HMQC correlation with γ-CH_2 of ^{n}Bu), 20.3 (o-CH_3 of Mes), 14.0 (CH_3 of ^{n}Bu). IR (ATR, cm^{-1}): ν(N-H) 3361–3134. Anal. Calc'd. for $C_{37}H_{70}N_6Cl_2Ru$: C, 57.64; H, 9.15; N, 10.90. Found: C, 57.52; H, 9.00; N, 10.79. *Note*: The NH, β-CH_2, and CH_3 signals are obscured by added $NH_2{}^nBu$. The integration values and multiplicities for these signals were confirmed from the spectrum for the dominant species **Ru-2** in CD_2Cl_2 (see SI). The chemical shifts for β-CH_2, and CH_3 signals were confirmed by COSY correlation with γ-CH$_2$.

Preparation of NH(R)(CH$_2$Ar); Ar = o-C$_6$H$_4$-O^{i}Pr. Isopropoxy-substituted benzylamines were prepared by modification of a reported reductive amination procedure.[51] These reactions were carried out in air with non-dried solvents.

R = n-Bu (1). $NH_2{}^nBu$ (1.1 mL, 0.80 g, 11 mmol) and excess Na_2SO_4 (ca. 4 g) were added to a stirred, colorless solution of o-isopropoxybenzaldehyde (1.2 g, 7.1 mmol) in 30 mL THF. After 2 h, the mixture was filtered to remove excess Na_2SO_4. The filtrate was treated with sodium borohydride (1.1 g, 29 mmol) and 15 mL CH_3OH, and stirring was continued for 2 h. The reaction was then quenched with 20 mL saturated aq. NH_4Cl, extracted with CH_2Cl_2, washed with brine, dried with Na_2SO_4, and stripped of solvent. Chromatography on silica. gel (3% MeOH + 0.5% NH_4OH in CH_2Cl_2) afforded **1** as a colorless liquid. Yield 1.37 g (88%). Note: for compound numbering, see SI. ^1H NMR (C_6D_6, 300.3 MHz): δ 7.45 (dd, $^3J_{HH}$ = 7 Hz, $^4J_{HH}$ = 1 Hz, 1H, C$_3H$ of Ar), 7.11 (ddd, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 1 Hz, 1H, C$_5H$ of Ar), 6.90 (ddd, $^3J_{HH}$ = 7 Hz, $^4J_{HH}$ = 1 Hz, 1H, C$_4H$ of Ar), 6.65 (d, $^3J_{HH}$ = 8 Hz, 1H, C$_6H$ of Ar),

4.20 (septet, $^3J_{HH}$ = 6 Hz, 1H, CH of ^{i}Pr), 3.93 (s, 2H, ArCH_2N), 2.59 (t, $^3J_{HH}$ = 7 Hz, α-CH_2 of ^{n}Bu), 2.46 (br s, 1H, NH), 1.57–1.39 (m, 2H, β-CH_2 of ^{n}Bu), 1.37–1.20 (m, 2H, γ-CH_2 of ^{n}Bu), 1.10 (d, $^3J_{HH}$ = 6 Hz, 6H, CH_3 of ^{i}Pr), 0.85 (t, $^3J_{HH}$ = 7 Hz, CH_3 of ^{n}Bu). ^{13}C{^{1}H} NMR (C$_6$D$_6$, 75.53 MHz): δ 156.5 (C_1 of Ar), 130.4 (C_3H of Ar), 130.0 (C_2 of Ar), 128.1 (C_5H of Ar, by HMQC correlation with C$_5$$H$), 120.6 ($C_4$H of Ar), 112.9 ($C_6$H of Ar), 69.7 (CH of ^{i}Pr), 49.2 (ArCH$_2$N), 49.1 (α-CH$_2$ of ^{n}Bu), 32.5 (β-CH$_2$ of ^{n}Bu), 22.1 (CH$_3$ of ^{i}Pr), 20.8 (γ-CH$_2$ of ^{n}Bu), 14.2 (CH$_3$ of ^{n}Bu). GC-MS m/z: [M$^+$] calc'd for C$_{14}$H$_{23}$NO, 221.2; found, 221.2. IR (ATR, cm^{-1}): ν(N-H) 3365. Anal. Calc'd. for C$_{14}$H$_{23}$NO: C, 75.97; H, 10.47, 6.33. Found: C, 75.63; H, 10.20; N, 6.56.

R = CH$_2$Ph (1'). Synthesis as for **1**, using NH$_2$CH$_2$Ph in place of NH$_2$^{n}Bu. Yield: 61%. ^{1}H NMR (C$_6$D$_6$, 300.3 MHz): δ 7.37 (d, $^3J_{HH}$ = 8 Hz, 2H, o-Ph), 7.31 (dd, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, 1H, C$_3$$H$ of Ar), 7.20 (t, $^3J_{HH}$ = 8 Hz, 2H, m-Ph), 7.14–7.07 (overlapping m, 2H, p-Ph + C$_5$$H$ of Ar), 6.89 (ddd, $^3J_{HH}$ = 7 Hz, $^4J_{HH}$ = 1 Hz, 1 H, C$_4$$H$ of Ar), 6.64 (d, $^3J_{HH}$ = 8 Hz, 1H, C$_6$$H$ of Ar), 4.16 (septet, $^3J_{HH}$ = 6 Hz, 1H, CH of ^{i}Pr), 3.89 (s, 2H, NCH_2Ar), 3.71 (s, 2H, NCH_2Ph), 1.50 (br s, 1H, NH), 1.04 (d, $^3J_{HH}$ = 6 Hz, 6H, CH_3 of ^{i}Pr). ^{13}C{^{1}H} NMR (C$_6$D$_6$, 75.53 MHz): δ 156.4 (C_1 of Ar), 141.6 (ipso-Ph), 130.4 (C_3H of Ar), 130.3 (C_2 of Ar), 128.53, 128.52, 128.4, 127.0 (p-Ph), 120.6 (C_4H of Ar), 112.9 (C_6H of Ar), 69.7 (CH of ^{i}Pr), 53.4 (NCH$_2$Ph), 49.1 (NCH$_2$Ar), 22.1 (CH$_3$ of ^{i}Pr). GC-MS m/z: [M$^+$] calc'd for C$_{17}$H$_{21}$NO, 255.2; found, 255.2. IR (ATR, cm^{-1}): ν(N-H) 3337. Anal. Calc'd. for C$_{17}$H$_{21}$NO: C, 79.96; H, 8.29, 5.49. Found: C, 79.77; H, 8.09; N, 5.36.

Assessing Impact of Base on Maximum Turnover Numbers (TON) in Self-Metathesis of Styrene. A stock solution of styrene and decane was prepared (0.275 M and 0.215 M, respectively) and an aliquot (ca. 50 μL) was taken to measure the initial ratio of substrate to internal standard. A Schlenk tube equipped with a stir-bar was charged with 2.0 mL of this stock solution (0.55 mmol styrene, 0.43 mmol decane) and diluted to 4.9 mL with C$_6$H$_6$. Pyrrolidine **b** was then added (0.10 mL of a 0.55 M stock solution in C$_6$H$_6$; 0.055 mmol; 10 equiv vs. **HII**). Finally, **HII** (0.50 mL of a 0.011 M stock solution, 5.5 μmol) was added. Final volume: 5.5 mL C$_6$H$_6$, [styrene] = 100 mM, [base] = 10 mM, [**HII**] = 1 mM). The reaction vessel was transferred to a Schlenk line and heated to 60 °C within 10 min. After stirring for 24 h and 48 h, aliquots were removed against a flow of N$_2$, quenched with excess KTp (ca. 1 mg, >10 equiv vs. Ru) in 1 mL CH$_2$Cl$_2$, and analyzed by GC-FID. Values are averages of two independent trials (± 2.5%).

Identifying Catalyst Decomposition Products Formed by Metathesis in the Presence of Base.

(a) During Self-Metathesis of Styrene. A solution of **HII** (15 mg, 0.024 mmol) and TMB (ca. 1 mg, 0.006 mmol) was prepared in 1.20 mL C$_6$D$_6$. An aliquot (0.60 mL, 0.012 mmol **HII**) was transferred to a J-Young NMR tube. Pyrrolidine **b** (10 μL, 0.12 mmol, 10 equiv) was added, and a ^{1}H NMR spectrum was collected to determine the initial integration ratio of **HII** relative to TMB. Styrene (14 μL, 0.12 mmol, 200 mM, 10 equiv) was then added. The remaining solution was likewise treated with styrene, and used as a control reaction. Both reactions were heated to 60 °C, and monitored at 2 h intervals. At 10 h: 90% loss of alkylidene; 99% at 18 h. Additional experiments utilized 10 equiv DBU **d** or NEt$_3$ **e**. No alkylidene signals were evident for either of these bases after 30 min. For additional experiments at 21 °C: complete loss of alkylidene after 1h for NEt$_3$ **e**. With DBU **d**: 88% loss at 10 h, complete decomposition by 18 h. With pyrrolidine **b**: 78% loss of alkylidene at 7 d (NMR data collected at 24 h intervals). Under all conditions, <4% stilbene was formed (GC-FID analysis). The organic decomposition products were (E)–PhCH=CHCH$_2$Ph **3** (major) and (E)–PhCH=CHCH$_3$ **3'** (minor): proportions are given in Table 2. Alkylidene signal for **GIIb** intermediate): δ 19.6 7 ppm.

Characterization data for (E)–PhCH=CHCH$_2$Ph 3. ^{1}H NMR (C$_6$D$_6$, 500.1 MHz): δ 6.31 (d, $^3J_{HH}$ = 16 Hz, 1H, PhHC=), 6.19 (dt, $^3J_{HH}$ = 16 Hz, $^3J_{HH}$ 7 Hz, 1H, =CHCH$_2$Ph), 3.25 (d, $^3J_{HH}$ = 7 Hz, 2H, =CHCH_2Ph). ^{1}H and ^{13}C{^{1}H} NMR signals for the Ph group of **3** were incompletely resolved from those for styrene and styrenyl ether **2**. Key ^{13}C{^{1}H} NMR data (C$_6$D$_6$, 125.8 MHz): δ 131.5 (PhHC=), 129.4 (=CHCH$_2$Ph), 39.6 (=CHCH_2Ph). DEPT-135 experiments support assignment of the key olefin and methylene signals; ^{1}H-COSY experiments confirm connectivity (for spectra, see SI). GC-MS m/z: [M+] calc'd for C$_{15}$H$_{14}$, 194.1; found, 194.1. NMR[43] and EI-MS[52] data agree with literature values for **3**.

Characterization data for (E)–PhCH=CHCH$_3$ 3'. ^{1}H NMR (C$_6$D$_6$, 500.1 MHz): δ 6.29 (d, $^3J_{HH}$ = 16 Hz, 1H, PhHC=C), 6.03 (d of q, $^3J_{HH}$ = 16 Hz, $^3J_{HH}$ = 7 Hz, 1H, C=CHCH$_3$), 1.64 (d, $^3J_{HH}$ = 7 Hz, $^3J_{HH}$ = 3H, C=CHCH_3).

(b) During Degenerate Metathesis of Ethylene. A solution of **HII** (15 mg, 0.024 mmol) and TMB (ca. 2 mg, 0.012 mmol) was prepared in 1.20 mL C$_6$D$_6$. An aliquot (0.60 mL, 0.012 mmol **HII**) was transferred to a J-Young NMR tube, and pyrrolidine (10 μL, 0.12 mmol, 10 equiv) was added. The remaining solution was used as a control reaction. A ^{1}H NMR spectrum was collected to determine the integration ratio of **HII** relative to TMB. To saturate the solutions in ethylene, each sample was freeze-pump-thaw degassed (5 x), then thawed under static vacuum. 1 atm of C$_2$H$_4$ was introduced at RT, samples were shaken vigorously, and a timer was started. ^{1}H NMR spectra were collected after 2 h and 16 h (when full decomposition was evident). In situ yields of styrenyl ether **2**, ArCH$_2$CH=CH$_2$ **4**, and ArCH=CHCH$_3$ **4'** were quantified by integration of well-isolated olefinic signals relative to starting **HII** (normalized against TMB). Specific values: 6.10–6.00 (m, 1H, **4**), 6.21–6.13 (m, 1H, **4'**), 5.74 (dd, $^3J_{HH}$ = 10 Hz, $^2J_{HH}$ = 2 Hz, 1H, **2**). Values for **4** and **4'** agree with data previously reported.[53] GC-MS data collected after full decomposition.

Characterization data for ArCH$_2$CH=CH$_2$ 4. ^{1}H NMR (C$_6$D$_6$, 500.1 MHz): δ 6.09–5.97 (m, 1H, CH=CH$_2$), 5.12–5.00 (m, 2H, CH=CH_2), 4.24–4.13 (m, 1H, CH_3 of ^{i}Pr, overlaps with **4'**), 3.48 (d, $^3J_{HH}$ = 6 Hz, 2H, ArCH_2CH=CH$_2$), 1.09 (d, $^3J_{HH}$ = 6 Hz, 6H, CH_3 of ^{i}Pr).

Aromatic signals not assigned due to overlap with signals from Ru species present. ESI-MS, [M$^+$]: m/z calc'd for $C_{12}H_{16}O$, 176.1. Found: 176.1.

Characterization data for (E)-ArCH=CHCH$_3$ 4'. ^{1}H NMR (C$_6$D$_6$, 500.1 MHz): δ 6.17 (d of q, $^3J_{HH}$ = 16 Hz, $^3J_{HH}$ = 6 Hz, 1H, =C*H*CH$_3$), 4.24–4.13 (m, 1H, C*H* of ^{i}Pr, overlaps with **4**), 1.75 (dd, $^3J_{HH}$ = 7 Hz, $^4J_{HH}$ = 3 Hz, $^4J_{HH}$ = 3H, C=CHC*H$_3$*), 1.10 (d, $^3J_{HH}$ = 6 Hz, 6H, C*H$_3$* of ^{i}Pr). Aromatic signals not assigned due to overlap with signals from Ru species present. ESI-MS, [M$^+$]: m/z calc'd for $C_{12}H_{16}O$, 176.1. Found: 176.1.

ASSOCIATED CONTENT

Supporting Information. NMR spectra for isolated **Ru-1**, amine derivatives **1** and **1'**, in situ-generated **HIIb**, and NMR spectra and GC traces for base-induced decomposition of **HII**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

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(34) Precedent for a downfield shift in the [Ru]=C*H*Ar signal following adduct formation is found in the data reported for the PCy_3 adduct of **HII**, $RuCl_2(H_2IMes)(PCy_3)(=CHAr)$ (where Ar is the non-chelated aryl group o-^iPrO-C_6H_4). This signal appears at 19.88 ppm ($CDCl_3$). See: (a) Gessler, S.; Randl, S.; Blechert, S. *Tetrahedron Lett.* **2000**, *41*, 9973–9976. In comparison, a value of 16.56 ppm was reported for **HII** itself in $CDCl_3$ solvent. See: (b) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179.

(35) The identity of the benzylamine derivative is supported by GC-MS analysis of a reaction aliquot, and by comparison of the ^1H NMR spectrum with that of an authentic sample prepared by reductive amination of the parent aldehyde: see S.I.

(36) Reported pK_a values for the conjugate acids in acetonitrile: morpholine, **a**: 16.6; pyrrolidine **b**: 19.6; pyridine **c**: 12.6; DBU **d**: 24.1; triethylamine **e**: 18.5; n-butylamine **f**: 18.3; benzylamine **g**: 16.9. See: Cox, B. G., *Acids and Bases: Solvent Effects on Acid-Base Strength*. Oxford University Press: Croydon, 2013, p. 99–115.

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(38) The structure depicted for **Ru-2**, in which the chloride ligand has migrated to a site trans to the H_2IMes ligand, is proposed on the basis of the high symmetry evident by ^1H NMR analysis. Consistent with the presence of four equivalent butylamine ligands, one singlet is seen for the H_2IMes backbone protons, and for the mesityl C*H* protons, integrating 4:4:8 relative to the multiplet for the n-butylamine NC*H_2* protons.

(39) Nucleophilic attack of phosphines on Ru-benzylidene species has likewise been reported, although the occurrence is relatively rare, presumably owing to steric restrictions. Exceptions include Hofmann's $RuCl_2(^tBu_2PCH_2P^tBu_2)(=CHPh)$ system, in which the ring strain of the four-membered κ^2-PP chelate is relieved by attack at the benzylidene carbon. See: (a) Hansen, S. M.; Rominger, F.; Metz, M.; Hofmann, P. *Chem. Eur. J.* **1999**, *5*, 557–566. In a second example, reaction of **GI** with CO triggered migration of a PCy_3 ligand to the alkylidene carbon: the presence of the π-acceptor CO ligands renders the alkylidene carbon more electrophilic, while also reducing steric congestion at the metal. See: (b) Galan, B. R.; Pitak, M.; Keister, J. B.; Diver, S. T. *Organometallics* **2008**, *27*, 3630–3632.

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(44) Not seen was ArCH=CHPh, which would arise from a metallacyclobutane intermediate bearing the aryl and phenyl groups on adjacent carbons. This kinetically disfavoured "head to head" cycloaddition is further inhibited by competing decomposition.

(45) Isopropoxystyrene **2** is readily identified from the well-isolated signals for its geminal protons. Each gives rise to a characteristic doublet of doublets, one at 5.74 ppm ($^3J_{HH}$(trans) = 18 Hz, $^2J_{HH}$ = 2 Hz); the other at 5.21 ppm ($^3J_{HH}$(cis) = 11 Hz, $^2J_{HH}$ = 2 Hz).

(46) Such σ-alkyl species are highly reactive, and readily participate in E–H activation processes that liberate the alkyl ligand. See: Refs. 30 and 38b, and: (a) Leitao, E. M.; Dubberley, S. R.; Piers, W. E.; Wu, Q.; McDonald, R. *Chem. Eur. J.* **2008**, *14*, 11565–11572. (b) Leitao, E. M.; Piers, W. E.; Parvez, M. *Can. J. Chem.* **2013**, *91*, 935–942.

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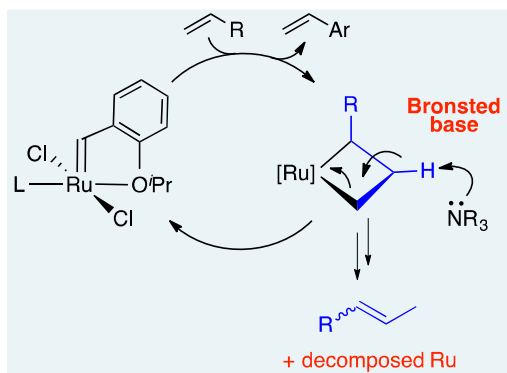
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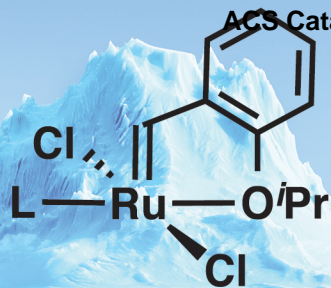
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TOC graphic:

metathesis

NR$_3$

Ru-NR$_3$ +

R