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Design and Application of *N,N′*-Diamidocarbenes: Expanding the Constraints of Stable Carbene Chemistry

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Design and Application of *N,N′*-Diamidocarbenes: Expanding the Constraints of Stable Carbene Chemistry

by

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Dedication

To my best friend and loving wife, Kate, for all her prayers, encouragement and support.

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As in most significant endeavors, I believe the success of the graduate school venture depends not only on the abilities, passion, and attitude of the person entering the commitment but on the people that surround and support that person during the journey. I have been blessed in that regard, and I thank God every day for the wonderful people that have propelled me along my way. Much of the work presented in this thesis and elsewhere from my time at the University of Texas would not have come to fruition without them. For that I am grateful to all who have played a part, seemingly large or small, in getting me to the point I am at today.

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Expanding the Constraints of Stable Carbene Chemistry: Design and Application of *N,N′*-Diamidocarbenes

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Strategic incorporation of carbonyl groups into an *N*-heterocyclic carbene (NHC) scaffold via rapid and high-yielding methodologies culminating in classical deprotonation methods or the novel reduction of geminal dichlorides afforded stable and relatively electrophilic diamidocarbenes (DACs). Similar to transient, electrophilic carbenes and unlike NHCs, DACs underwent a variety of transformations with a broad range of small molecules including the unprecedented reversible coupling of carbon monoxide, metal-free transfer hydrogenations, and insertion into pnictogen-H bonds. Additionally, formal [2+1] cycloadditions were observed between DACs and a variety of alkenes, aldehydes, alkynes, and nitriles including the first examples between an isolable carbene and alkynes or electron-rich alkenes. DACs also effected the only uncatalyzed intermolecular C–H insertions of a stable carbene with non-acidic substrates to date.

Beyond unprecedented reactivity scope, hydrolysis of the resultant diamidocyclopropenes or cyclopropanes afforded cyclopropenones or linear carboxylic acids. The latter constituted the formal, metal- and CO-free anti-Markovnikov hydrocarboxylation of an olefin and illustrated the ability of DACs to function as a reactive synthetic equivalent of carbon monoxide. Mechanistically, DACs were found to function primarily as nucleophiles in cycloadditions with alkynes, aldehydes, and various

styrene derivatives and as an electrophile in the activation of primary amines. Thus, DACs may best be considered as ambiphiles which alters the paradigm of stable carbenes functioning exclusively as nucleophilic species. The reversibility of numerous small molecule-DAC interactions under mild conditions also suggested the potential of these systems in catalytic applications wherein dynamic association and release assume critical roles. Regardless, the reactivity associated with transient, electrophilic carbenes was largely achieved within a stable carbene scaffold and is envisioned to aid and influence the design and application of stable carbenes.

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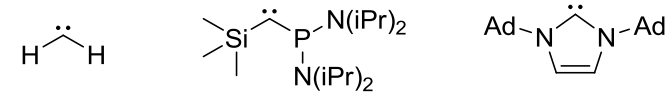
1.1 Introduction

The tetravalency of carbon constitutes a cornerstone of organic chemistry upon which is built the basis for understanding bonding and structure in systems ranging from the human body and carbon nanotubes to plastics and wood. While less prevalent, trivalent carbons (*i.e.*, carbocations, carbanions, and carbon-centered radicals) have also acquired long-standing recognition in mainstream organic chemistry either as isolable species or more often as reactive intermediates or transitions states in well-known transformations. In comparison, the prominence of divalent carbons have only arisen within the past 25 years following the isolation of free carbenes, a subclass of divalent carbons with two nonbonding electrons, by Bertrand[1] and Arduengo[2] even though the existence of divalent carbon was postulated two centuries ago before the tetravalency of carbon was established.



Methylene **1** **2**

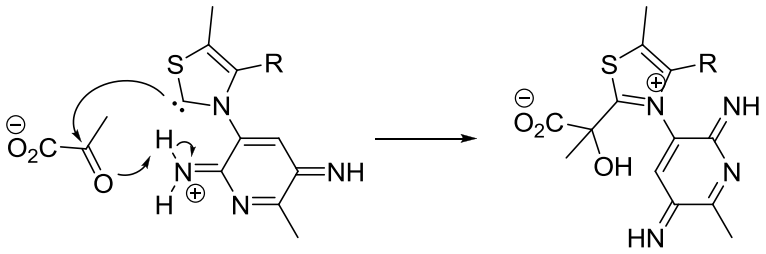
Figure 1.1: A prototypical, transient carbene, methylene, and the first isolable carbenes (**1**, **2**).[1,2]

1.2 Historical Perspective

Perhaps the earliest attempts to prepare carbenes were the failed dehydrations of methanol to methylene by Dumas in 1835[3] and later Regnault[4] followed by the successful but uncontrolled *in situ* generation of dichlorocarbene from chloroform under basic conditions in 1862.[5] Nearly a half century later, in combination with a report from

Curtius,[6] a series of studies by Staudinger demonstrated the decomposition of diazo compounds under photolytic or thermal conditions to controllably generate alkyl or α-carbonyl substituted transient carbenes.[7,8] The propensity of the resultant species to insert into unactivated C–H bonds also presaged the unique synthetic utility of these systems since exploited using metal-mediated processes to achieve high yields and selectivity.[9]

A shift in attention from carbon- to heteroatom-substituted carbenes began when Ugai revealed thiazolium salts under basic conditions as alternatives for cyanide in the benzoin condensation, although the intermediacy of a carbene was not postulated at the time.[10] Indeed, the now accepted mechanism involving an *in situ* generated carbene from azolium salts such as thiamine (vitamin B_1) was proposed by Breslow in 1958.[11] Subsequent mechanistic studies including the spectroscopic detection of a carbene[12] in pyruvate oxidase, a thiamine-based enzyme (Scheme 1.1),[13] have supported Breslow's mechanism and further emphasized the importance of free carbenes synthetically in the lab as well as within the human body.



Scheme 1.1: Carbene-based active mechanism of pyruvate oxidase.[13]

Shortly thereafter, Wanzlick reported the deprotonation of imidazolinium salts to afford enetetraamines through dimerization of the *in situ* generated free carbene.[14,15] To explain the similar reactivity of enetetramines with that of free carbenes, Wanzlick proposed the reversibility of the dimerization event to regenerate the free carbene, and the

existence of the so-called Wanzlick equilibrium (Figure 1.2)[16] became a topic of debate throughout the subsequent years. Data currently indicates dissociation of the enetetramine is acid catalyzed rather than a result of dynamic equilibrium except in select cases such as benzimidazolylidenes.[17-19] Regardless, despite the utility of carbenes as *in situ* generated organocatalysts and subsequent application as ligands for tungsten olefin metathesis catalysts (*i.e.*, Schrock-type catalysts[20,21]) during the mid-1970s on,[22-24] free carbenes remained largely viewed as highly reactive, transient species or as mere curiosities.

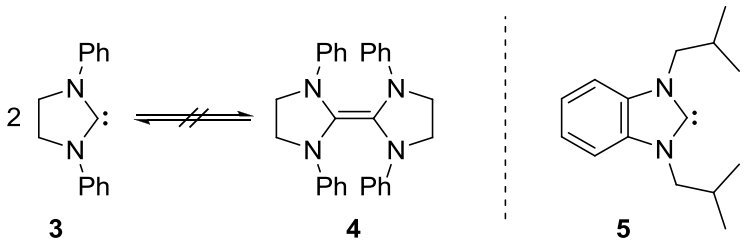


Figure 1.2: Proposed and since revised Wanzlick equilibrium for **3** and **4** and a benzimidazolylidene **5** for which the Wanzlick equilibrium has been spectroscopically observed.[16,17]

Such views were challenged in 1988 when Bertrand reported the synthesis of a distillable phosphinosilyl carbene.[1] However, likely due to debate over the phosphalkyne versus carbene nature of Bertrand's phosphinosilyl carbene and the lack of a solid state structure, the synthesis of a crystalline imidazolylidene by Arduengo in 1991[2] is often considered the tipping point in altering the view of carbenes from transient intermediates to potentially isolable species. Together, these two reports spawned an explosion in the design and application of stable (*i.e.*, isolable) carbenes that has focused on singlet carbenes.

1.3 Carbene Multiplicity and Stability

Determined by how the two nonbonding electrons are distributed across the two available molecular orbitals, all carbenes possess either a singlet or triplet ground state. Pairing of the electrons with opposite spins in the same orbital defines a singlet state while a triplet state arises when both electrons have the same spin and inhabit separate orbitals (Figure 1.3). The latter is thermodynamically favored by electron exchange energy as well as a lessening of coulombic repulsion, which when greater than the difference in energy between the two nonbonding orbitals results in a triplet ground state. If the difference in energy between the two orbitals surpasses the stabilization from dispersing the two electrons in separate orbitals, a singlet ground state with spin-paired electrons in a single orbital is favored. The difference in energy between the singlet and triplet ground states is defined as the singlet-triplet gap (S-T gap), and large S-T gaps are generally associated with higher stabilities and lower reactivities.

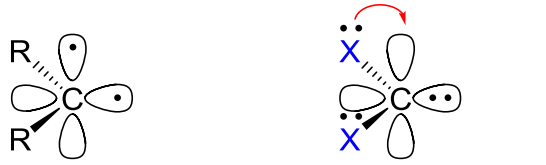


Figure 1.3: Generic representation of triplet and singlet carbene scaffolds.

Carbenes outside of methylene or diaryl derivatives almost exclusively possess singlet ground states due to a confluence of of π- and σ-effects.[25] In particular, mesomeric effects (*i.e.*, π-effects) typically dictate the ground state and comprise the greatest contributors to carbene stability. In essence, π-donating substituents (*e.g.*, PR_2, NR_2, OR) mix with the the p_π orbital of the carbene center and increase the S-T gap by raising the

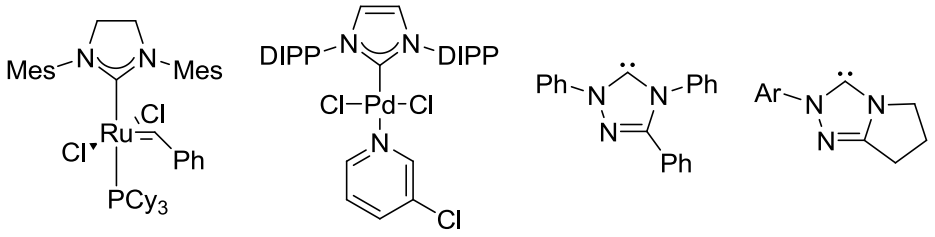
energy of the lowest unoccupied molecular orbital (LUMO). Thus, π-donating substituents lead to enhanced singlet and attenuated electrophilic character compared to triplet carbenes. Ylidic resonance structures arising from the donation of the heteroatom adjacent to the carbene center may also be used to explain the nucleophilicity of these carbene scaffolds. Besides mesomeric effects, substitution of the carbene center with atoms more electronegative than carbons (*i.e.*, σ-withdrawers) lowers the energy of the highest occupied molecular orbital (HOMO), σ, and increases the S-T gap.

In addition to thermodynamic stabilitzation, carbenes may be kinetically stabilized by sterics (usually arising from substituents on the atoms directly adjacent to the carbene center). Thus, the homocoupling of carbenes and other decomposition pathways, though thermodynamically favorable, may be inhibited kinetically and afford a persistant carbene. An example of the interplay between thermodynamic and kinetic stabilization are imidazolylidines and imidazolinylidenes which differ solely in the degree of saturation of the five-membered ring. The latter readily dimerizes unless protected by bulky *N*-substituents such as substituted aryl or bulky alkyl groups (*e.g.*, adamantyl or *tert*-butyl). In contrast, imidazolylidenes which possess nearly twice the S-T gap energy compared to their saturated analogues may be isolated even with small *N*-methyl substituents. Thus, through a combination of kinetic and thermodynamic parameters, a wide range of isolable cyclic and acyclic carbenes have been prepared with varying structural and electronic properties.[26]

1.4 Applications of Stable Carbenes

Despite the diversity of carbene scaffolds, no class has found greater application than *N*-heterocyclic carbenes (NHCs). Immense utility has been derived from the use of NHCs as metal ligands due to stronger σ-donicities than phosphine predecessors, a

readily amendable scaffold, and variable steric parameters. Often NHC-supported catalysts exhibit the highest activities and/or selectivities that is perhaps most visibly illustrated by the Grubbs-type olefin metathesis catalysts[27-30] but also in areas such as palladium coupling catalysts (*e.g.*, **6**,**7**; Figure 1.4).[31-35] Beyond metal catalysis, NHCs have also found exceptional utility as organocatalysts for carbon-carbon bond formation,[36-41] particularly with saturated or unsaturated carbonyl-containing substrates. These C-C couplings often may be carried out under mild conditions to high yield with excellent enantio- or diastereoselectivity. As such, much emphasis has focused on optimizing the properties of NHCs specifically for desired ligation and organocatalytic properties.



6 **7** **8** **9**

Figure 1.4: Selected examples of commercial transition metal catalysts (**6**,**7**) and organocatalysts (**8**,**9**) based on NHCs.

Beyond catalysis, NHCs and other carbenes have found a variety of uses in the stabilization of reactive intermediates or elemental allotropes. For example, Bertrand and others have shown the ability to stabilize white phosphorus, a highly pyrophoric starting material for almost all phosphine containing compounds, as carbene coordinated clusters ranging in size from P_1 to P_{12} (Figure 1.5).[42-45] Various phosphinyl radicals, cations, and radical cations, a boron-boron triple bond, digermanium(0), and a boryl anion have also been prepared and/or stabilized through the use of stable carbenes.[46-53] Additionally, the

stabilization of C(0), a so called carbone (*e.g.*, **10**), with benzimidazolylidenes or acyclic NHCs has been reported, although the more accurate structure may be more akin to the covalent, zwitterionic resonance structures (Figure 1.6).[54-57] Regardless, the stabilization afforded by carbenes to other reactive intermediates parallels results with transition metals, indicating that carbenes may find utility as mimics or alternatives for transition metals and highlights the shift in the perception of carbenes from transient curiosities to potentially stable species capable of stabilizing other reactive intermediates.

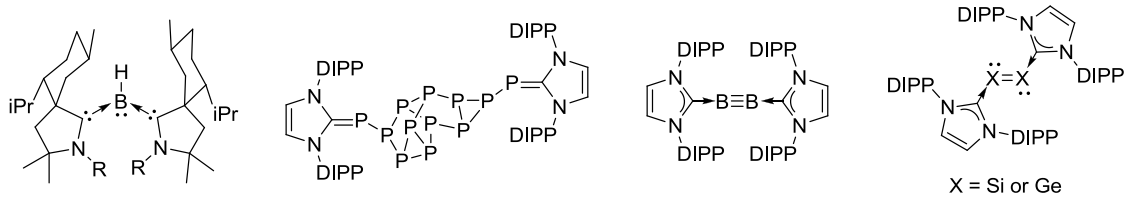


Figure 1.5: Selected examples of elemental allotropes and reactive intermediates stabilized by stable carbenes.

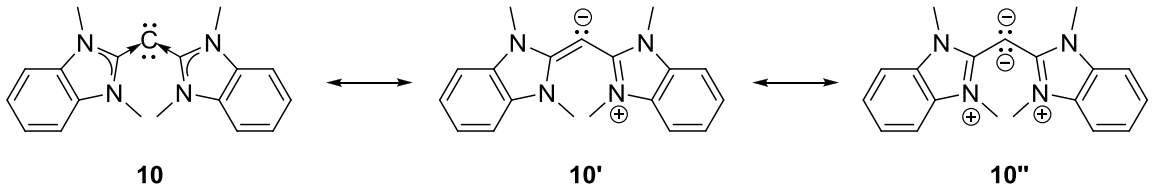
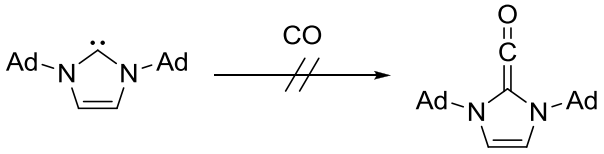


Figure 1.6: A so-called carbone, or C(0), stabilized by NHCs and the zwitterionic resonance structures.[54-57]

1.5 Transient Carbene Reactivity from Stable Carbenes

While carbenes have found great utility in catalysis and the stabilization of reactive intermediates, the high-lying HOMO/LUMO levels and large singlet-triplet gaps that benefit the use of NHCs in these areas may limit reactivity in archetypical carbene reactions such as C–H insertions, cyclopropanations and the activation of other abundant

but relatively inert substrates such as ammonia or carbon monoxide (Scheme 1.2). For example, exocyclic olefins or zwitterionic intermediates rather than cyclopropanes are obtained from NHCs and alkenes,[39,58] if any reaction is observed at all. NHCs also generally do not react with carbon monoxide (Scheme 1.2)[59,60] nor insert into nonacidic (pK_a > *ca.* 30) C–H bonds.[61-64]



Scheme 1.2: Purported coupling of an NHC and carbon monoxide subsequently refuted by Arduengo.[59,60]

Studies to explore and expand the chemistry of stable carbenes in areas traditionally associated with unstable, electrophilic carbenes (*e.g.*, methylene) have largely been pioneered by Bertrand[65-67] and more recently by others.[68-72] In particular, carbene centers substituted by atoms with attenuated electronegativities and π-donating properties compared to nitrogen (*e.g.*, phosphorus,[73-75] silicon,[1] carbon[76,77]) have resulted in a variety of isolable carbenes with reduced singlet-triplet gaps and increased reactivity compared to prototypical NHCs. A few of these systems such as the alkyl aminocarbenes (AACs) and phosphinosilyl carbenes (PSCs) participate in cyclopropanation chemistry, albeit on a scope confined to electron-deficient alkenes.[77,78] AACs have also been shown to activate ammonia and hydrogen gases through insertion across the carbene center (Figure 1.7).[79] However, other areas of reactivity such as uncatalyzed intermolecular C–H insertions and broadly applicable [2+1] cycloaddition chemistries have remained elusive and understudied compared to other areas like NHC-transition metal chemistry.

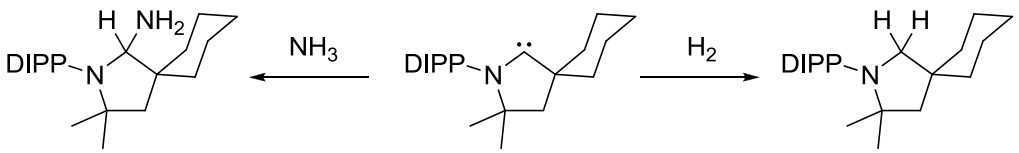


Figure 1.7: Activation of ammonia and hydrogen gas by a stable cyclic alkylamino carbene (CAAC).[79]

We envisioned that the activity exhibited by transient carbenes, which are often electrophilic, might be accessed through reducing the energy of the LUMO and by extension, decreasing the S-T gap. Therefore, we sought to modify NHC scaffolds by incorporating carbonyl groups adjacent to the nitrogens flanking the carbene center. The π-accepting character of the carbonyls were predicted to compete with the carbene center for the donation of the nitrogen lone pairs, thereby lowering the LUMO energy while potentially maintaining the stability enjoyed by many NHCs. Indeed, theoretical calculations supported the hypothesis, predicting a relatively low-lying LUMO and a reduction of the singlet-triplet gap by nearly half compared to the unsaturated imidazolylidene family.[80]

Synthetically, initial efforts targeted DAC **11** with sterically demanding 2,6-di-isopropylphenyl groups on the nitrogens to provide kinetic stabilization of the carbene center (Figure 1.8). Standard, acid-catalyzed condensation of 2,6-diisopropylaniline with triethylorthoformate afforded the corresponding formamidine which was subsequently silylated using n-butyl lithium and TMSCl. Treatment of the silyl-protected formamidine with dimethylmalonyl dichloride followed by treatment with trimethylsilyl trifluoromethanesulfonate readily effected cyclization to **12**. Subsequent deprotonation under strongly basic conditions (NaHMDS) afforded the free carbene *in situ* as evidenced by the downfield ^{13}C NMR shift (C_6D_6) at 278.4 ppm indicative of a carbene nucleus.[81]

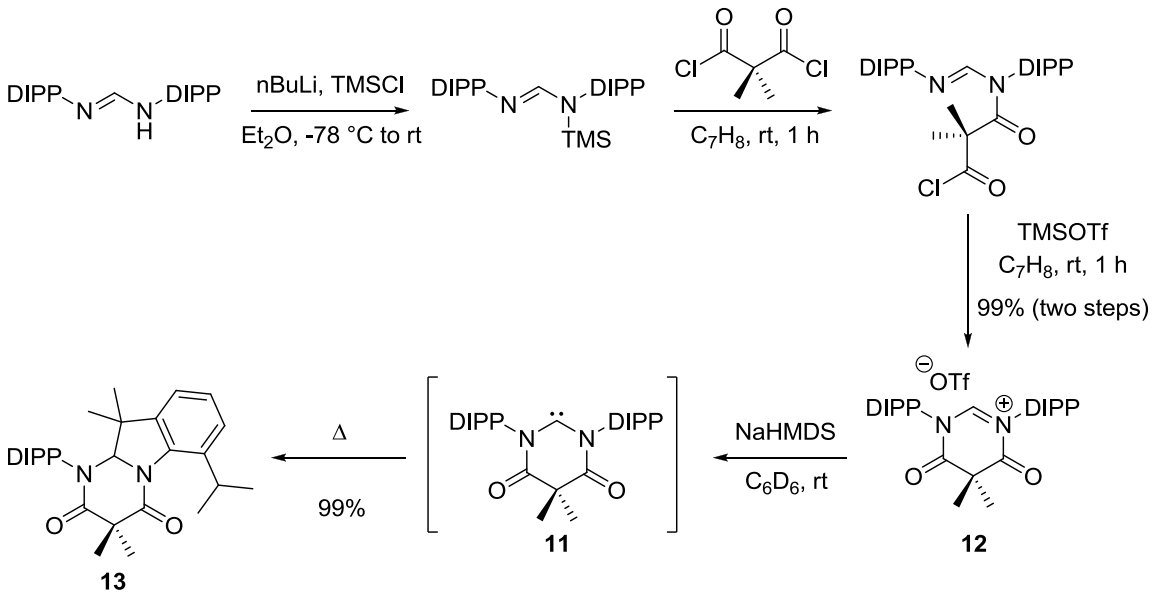


Figure 1.8: Synthesis of diamidocarbene **11** and decomposition to **13** through intramolecular C–H insertion.[81]

Unfortunately, concentration of DAC **11** and other efforts to isolate the free carbene were unsuccessful, instead leading to a variety of decomposition products.[81] Likewise, heating *in situ* generated **11** to 50 °C for 30 h resulted in quantitative decomposition to a single product **13** arising from intramolecular C–H insertion into the aryl isopropyl group. Despite the inability to isolate **11**, scope studies revealed the first, reversible coupling of carbon monoxide by a carbene as well as rare examples of forming ketenimines from a carbene and isonitriles using **11**. Analysis of metal complexes containing **11** by IR and NMR spectroscopies further supported the enhanced electrophilic character of DACs compared to NHCs.

The observation of C–H insertion was encouraging as the transformation resembled the reactivity of transient electrophilic carbenes; however, decomposition of **11** at elevated temperature or upon attempted isolation limited both the practicality and

reactivity scope of the scaffold. For instance, intramolecular C–H insertion was expected to outcompete entropically less-favored but synthetically more useful intermolecular C–H insertions. Isolable carbenes provide additional advantages over *in situ* generated derivates including ease of use, simplified reaction conditions, stricter control of stoichiometry, the potential for commercialization, and broader appeal within the scientific community, particularly in places where the capability for synthesizing the carbene may be lacking. Therefore, an isolable DAC was sought and along with the desire to expand the reactivity profiles of stable carbenes to include the synthetically attractive properties of transient electrophilic carbenes provided the initial impetus for much of the work presented in the subsequent chapters.

1.6 Conclusions and Outlook

From being viewed as chemical curiosities to stable species capable of stabilizing reactive intermediates, the scientific community's understanding and application of carbenes has experienced tremendous growth over the past quarter century. Stable carbenes now form the basis of many state-of-the-art transition metal catalysts as well as enantioselective organocatalysts and should continue to see widespread interest as conditions and structural properties are optimized and applications are broadened to less well-studied metals such as iron. Aided in part by an emphasis on more electrophilic carbenes such as DACs, stable carbene reactivity with small molecules has expanded and is expected to continue to grow to address future challenges including the activation of inert substrates such as methane or nitrogen gas as well as the preparation of an isolable triplet carbene.[82]

Perhaps the most challenging and potentially lucrative area of carbene chemistry lies in exploiting the similarities of carbenes to catalytically active transition metals (*i.e.*,

both possess full and empty orbitals and peripheral substituents/ligands) to realize organic alternatives to traditionally metal-catalyzed processes (*e.g.*, carbonylations, hydrogenation). Indeed, formal oxidative additions and reductive eliminations are already known for stable carbenes. As such, the viability of transition metal catalysis sans the metal may revolve around the ability to address the challenge of exchanging functionalities at the carbene center following initial activation but prior to release of the new product as well as the high bonds strengths of C-X bonds compared to M-X bonds. Regardless, the future of carbene chemistry appears bright with continued room for expansion and application.

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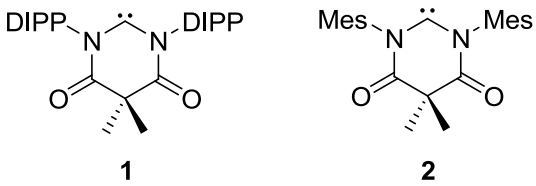
Chapter 2: Ammonia N–H Activation by an *N,N′*-Diamidocarbene*

2.1 INTRODUCTION

The activation of industrially-important small molecules, such as ammonia and dihydrogen, has garnered considerable attention over the past two decades.[1-4] Historically, transition metals have been employed for such purposes,[5-12] although main group species capable of facilitating these transformations have been reported more recently.[13-16] Of the two aforementioned small molecules, NH_3 activation remains relatively challenging due to the propensity to form stable Lewis acid–base adducts rather than undergo bond scission.[17-20] Recently, Bertrand and co-workers revealed the potential of alkyl amino carbenes to overcome many of these obstacles, resulting in the only hitherto examples of metal-free NH_3 activation.[21-23]



1 **2**

Figure 2.1: Examples of *N,N′*-diamidocarbenes (DACs). DIPP = 2,6-diisopropylphenyl. Mes = 2,4,6-trimethylphenyl.

Herein we demonstrate that readily-accessible *N,N′*–diamidocarbenes (DACs) split NH_3. These efforts are part of a burgeoning program aimed at expanding the reactivity exhibited by nucleophilic *N*-heterocyclic carbenes (NHCs)[24] to include reactions typically displayed by traditional, electrophilic carbenes (*e.g.*, methylidene). For example, we recently reported[25,26] that DAC **1** (Figure 2.1) exhibited substantial

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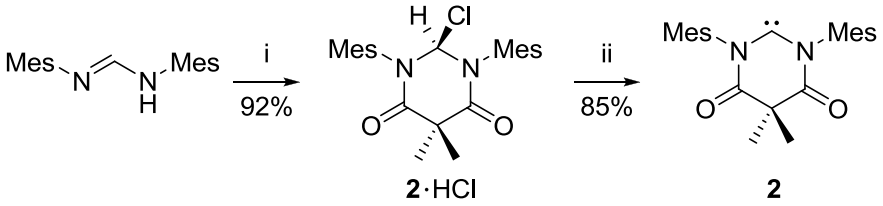
electrophilic character and could effect intramolecular C–H insertions into unactivated tertiary alkyl groups, reversibly affix carbon monoxide (CO), and quantitatively couple with organic isocyanides to afford diamidoketenimines.

2.2 Results and Discussion

To facilitate our studies into small molecule activation, we sought an isolable DAC. Despite our best efforts, **1** was found to undergo an intramolecular C–H insertion with a methine group of its diisopropylphenyl *N*-substituents[25] which complicated subsequent reactivity studies. We envisioned that a derivative featuring relatively less activated C–H bonds (*i.e.*, **2**) would inhibit intramolecular C–H insertion and enable access to a stable analogue.



Scheme 2.1: Synthesis of the stable diamidocarbene **2**. Conditions: *i*) dimethylmalonyl dichloride, NEt_3, CH_2Cl_2, 0 °C, 1 h.; *ii*) NaHMDS, C_6H_6, 25 °C, 30 min. Mes = 2,4,6-trimethylphenyl.

While we were working toward the preparation of **2**, Lavigne and co-workers reported[27] an elegant synthesis of this compound, but encountered difficulties with its isolation. They noted that **2** underwent rapid decomposition upon its generation *via* deprotonation of **2**·HCl in THF and must be trapped with S_8 or $(Rh(COD)Cl)_2$ (COD = 1,5-cyclooctadiene) at –40 °C. Based on our previous studies with **1**, which also proved to be problematic when generated in THF,[25] we reasoned that **2** may be accessed by performing the deprotonation reaction in a non-coordinating solvent.

To test this hypothesis, **2**·HCl was first prepared using a modified procedure reported[27] by Lavigne (Scheme 2.1). In addition to various spectroscopic techniques, the structure of **2**·HCl was elucidated by X-ray crystallography (see Figure 2.2). Close inspection of the solid state data revealed that the C1–Cl1 distance (1.888(2) Å) was relatively elongated compared to the average sp^3 C–Cl bond (ca. 1.76 Å),[28] suggesting that the Cl atom was weakly bound to the diamidomethine nucleus (see below for additional discussion).

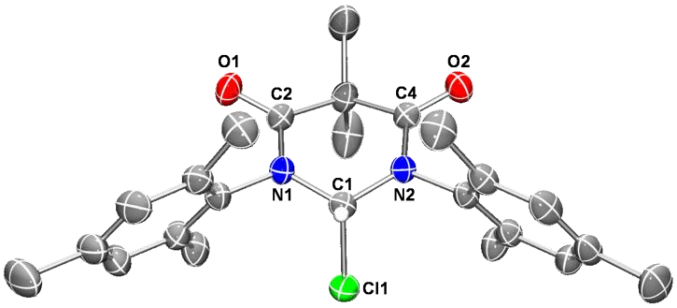


Figure 2.2: ORTEP diagram of **2**·HCl with thermal ellipsoids drawn at 50% probability and H-atoms except at C1 omitted for clarity.

Treatment of a suspension of **2**·HCl in benzene with sodium hexamethyldisilazide (NaHMDS) followed by solvent removal and washing with cold hexanes afforded the desired *N,N′*–diamidocarbene (**2**) in 85% isolated yield. A salient spectroscopic feature of **2** was a low-field ^{13}C resonance observed at δ = 277.7 ppm (C_6D_6). This signal was assigned to the carbene nucleus (C1) and determined to be consistent with the analogous signal exhibited by **1** (278.4 ppm, C_6D_6).[25] Moreover, FT-IR analysis revealed that the ν_{CO} displayed by **2** (1709 cm^{-1}; KBr) was at an energy intermediate of those exhibited by typical amides (ca. 1630–1695 cm^{-1}) and ketones (ca. 1710–1740 cm^{-1}). To gain additional insight into the structure of **2**, X-ray quality crystals were obtained by slow vapor diffusion of hexanes into a toluene solution saturated with this compound. As

shown in Figure 2.3, the $C_{carbene}$–N distances (avg. C1–N = 1.37 Å) were found to be significantly shorter than the N–C_{acyl} distances (avg. N–C_{acyl} = 1.41 Å). However, the C–O distances (avg. 1.21 Å) measured in the crystal structure of **2** were only slightly shorter than the analogous C–O distances found in the solid state structure of its amido precursor **2**·HCl (avg. 1.22 Å). Collectively, the X-ray crystallography results supported the IR spectroscopic data which characterized the NCO groups in **2** as hybrids of canonical amides and ketones.

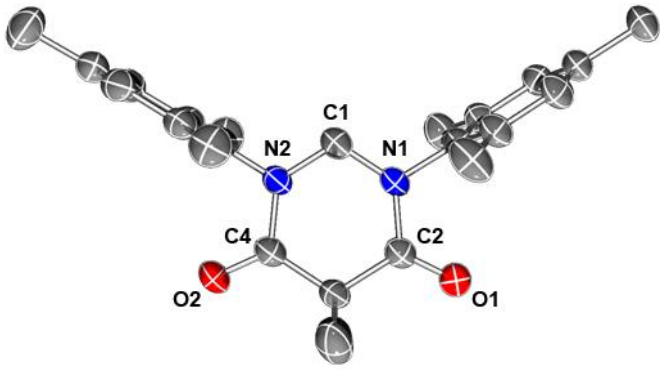
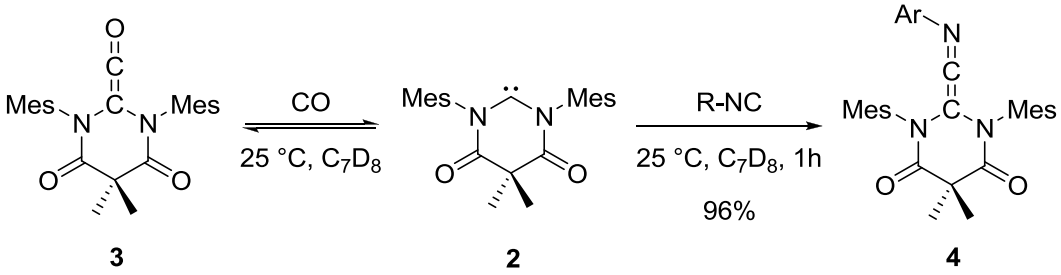


Figure 2.3: ORTEP diagram of **2** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

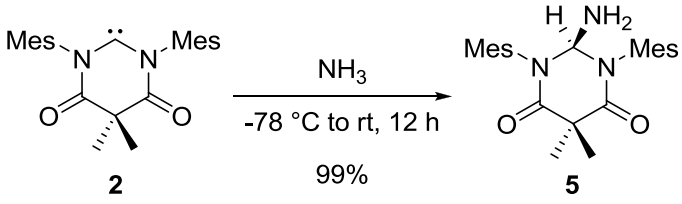
Upon the synthesis and characterization of **2**, its reactivity was explored. Similar to that observed with **1,** DAC **2** engaged in reactions typically exhibited by electrophilic carbenes (Scheme 2.2). For example, bubbling CO through a toluene solution of **2** resulted in the immediate formation of a purple color (λ_{max} = 543 nm) consistent with the formation of *N,N′*–diamidoketene **3**.[25] The observation of ^{13}C resonances at δ = 91.7 and 246.4 ppm (C_7D_8), corresponding to the carbenoid *C*CO and ketenoid C*C*O nuclei, respectively, and a ν_{CO} = 2091 cm^{-1} (C_7H_8) confirmed the formation of **3**. Notably, this carbonylation reaction was determined to be reversible with a K_{eq} = 4.78 M^{-1} in C_7D_8 at

20 °C (P_{CO} = 15 psi). In contrast, a thermally-robust compound (m.p. = 153–154 °C) was obtained in excellent yield when **2** was treated with 2,6-dimethylphenylisocyanide. This product displayed diagnostic[26] ^{13}C chemical shifts at δ = 106.3 and 202.7 ppm (C_6D_6) that were attributed to the *C*CN and C*C*N resonances of diamidoketenimine **4**, respectively, as well as a characteristic IR stretching mode at ν_{CCN} = 1978 cm^{-1} (KBr).



Scheme 2.2: Synthesis of diamidoketene **3** and diamidoketenimine **4**. Ar = 2,6-dimethylphenyl.

Next, our attention shifted toward exploring the ability of **2** to activate NH_3. Condensing NH_3 at –78 °C onto solid **2** followed by slowly warming to ambient temperature over 12 h led to the formation of the desired product (**5**) in nearly quantitative yield (Scheme 2.3). The ^{1}H NMR (C_6D_6) spectrum of **5** featured a diagnostic triplet at δ = 5.22 ppm (C*H*) and a broad doublet centered at 1.15 ppm (N*H*$_2$), results similar to those previously observed for the addition of NH_3 across a carbene nucleus.[21] Additionally, the IR spectrum (KBr) featured two peaks at ν = 3415 and 3339 cm^{-1}, which were consistent with N–H stretching modes of primary amines.



Scheme 2.3: Activation of ammonia by DAC **2**.

Single crystals suitable for X-ray diffraction analysis were obtained by cooling a hexanes:CH_2Cl_2 (2:1 v/v) solution saturated with **5** to –30 °C. As shown in Figure 2.4, the C1 atom of the respective structure exhibited a high degree of pyramidalization ($\sum_{(N-C-N)}$ = 339.4°) indicating that the carbene nucleus rehybridized upon reaction with NH_3. Additionally, the C1–N3 distance (1.406(3) Å) was in good agreement with the analogous distance (1.428(7) Å) observed in the solid state structure of an adduct formed between an alkyl amino carbene and NH_3.[21]

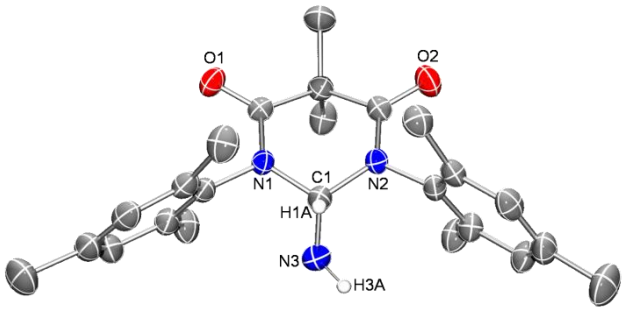
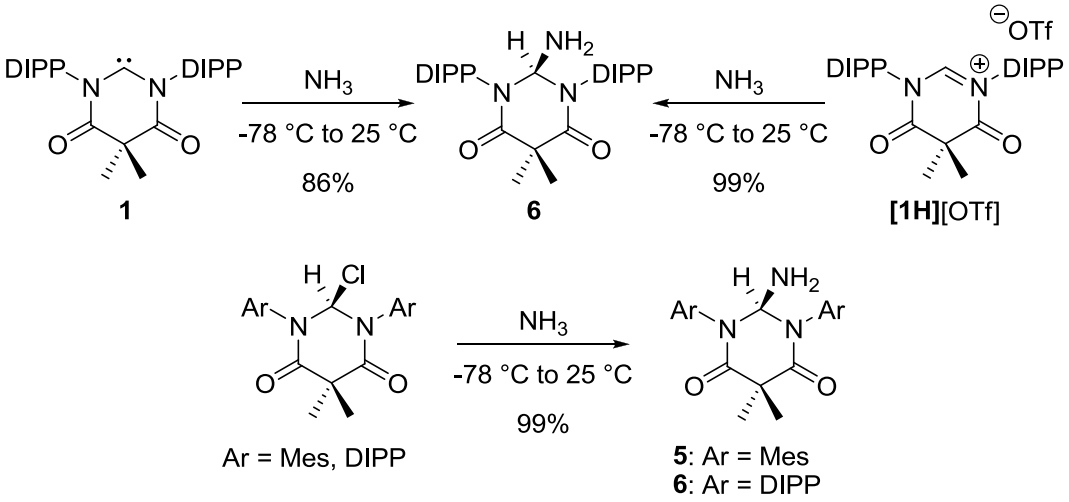


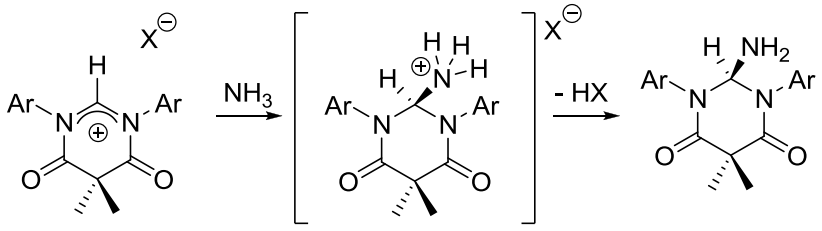
Figure 2.4: ORTEP diagram of **5** with thermal ellipsoids drawn at 50% probability and H-atoms except for H1A and H3A omitted for clarity.

To further explore the reactivities of DACs and their precursors, NH_3 was condensed into a toluene solution of **1** (generated in situ from **1**·HCl and NaHMDS) at –78 °C, which resulted in the formation of the expected product (**6**) in high yield (Scheme 2.4). Similarly, condensing NH_3 onto solid **2**·HCl, **1**·HCl or [**1**H][OTf] (OTf = triflate) followed by warming to ambient temperature also resulted in the formation of **5** and **6**, respectively, in excellent yields. The results of the reactions involving the HCl adducts or [**1**H][OTf] were in accord with previous observations[25,27] that [**1**H][OTf] and **2**·HCl readily react with alcohols and water to form the corresponding alkoxy or hydroxy adducts, respectively. As such, we suspect that NH_3 added directly to the C1 position of

[**1**H][OTf] (Scheme 2.5) or displaced the chloride atoms in the aforementioned HCl adducts via a nucleophilic type substitution reaction. The latter is supported by the relatively long C–Cl bond length observed in the solid state structure of **2**·HCl (Figure 2.2), an indicator of a weakened chloride bond.



Scheme 2.4: Synthesis of **5** and **6**.



Scheme 2.5: Proposed mechanism for the formation of NH_3 adducts **5** and **6** from their respective protonated precursors.

While tempting to suggest that the free DACs **1** and **2** reacted with NH_3 in a similar fashion as their protonated adducts (*i.e.*, via the formation of a Werner-type complex[17]), this requires the buildup of negative charge on the diamidocarbene nucleus.

Alternatively, the DACs may be activating the N–H bond of NH_3 in a concerted fashion and in a manner analogous to that proposed for the CAACs.[21] Regardless, **5** was observed to form instantaneously upon bubbling NH_3 through a C_6D_6 solution of **2**, even under dilute conditions ($[\mathbf{2}]_0 = 8.9 \times 10^{-2}$ M, 25 °C).

Unfortunately, no reaction was observed between **2** and H_2, even under forcing conditions (1000 psi H_2, 200 °C) in C_6H_6 or 1,4-dioxane. This lack of reactivity was surprising considering the similar bond-dissociation energies of NH_3 and H_2 (107 and 104 kcal/mol, respectively)[29,30] and given that Bertrand's alkyl amino carbenes, a class of carbenes which shares many similar reactivities as the DACs, were reported to activate both NH_3 and H_2.[21]

2.3 Conclusion

In conclusion, we report the synthesis and first solid state characterization of a DAC, and demonstrate the ability of this carbene to split ammonia. These results expand the few known organic[21] systems capable of activating this industrially important small molecule. An attractive feature of the substrates reported herein is that they can be obtained in high-yield over two steps starting from inexpensive, commercially-available materials and are readily-amenable to further modification. As a result, we believe that DACs offer promise in the development of new synthetic strategies for transforming NH_3 into structurally- and functionally-diverse nitrogen-containing compounds.

2.4 Experimental

General Considerations. All procedures were performed using standard Schlenck techniques under an atmosphere of nitrogen or in a nitrogen-filled glove box unless otherwise noted. *N,N′*–bis(2,4,6-trimethylphenyl)formamidine, 1,3-bis(2,6-di-*iso*-propylphenyl)-5,5-dimethyl-4,6-dioxopyrimidium triflate, 1,3-bis(2,6-di-*iso*-

propylphenyl)-4,6-diketo-5,5-dimethylpyrimidinyl-2-ylidene (**1**), and 2-chloro-1,3-dimesityl-5,5-dimethyl-4,6-diketopyrimidine (**2**·HCl) were synthesized using previously reported procedures.[25,27,31] Dimethylmalonyl dichloride and 2,4,6-trimethylaniline were obtained from TCI America and used as received. Triethylorthoformate was purchased from Alfa Aesar and used as received. Sodium bis(trimethylsilyl)amide (NaHMDS) and 2,6-di-*iso*-propylaniline were purchased from ACROS and were used as received. Benzene was dried over molecular sieves and distilled prior to use. Dichloromethane (CH_2Cl_2) and hexanes were dried and degassed by a Vacuum Atmospheres Company solvent purification system and stored over molecular sieves in a nitrogen-filled glove box. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrophotometer. UV–visible spectra were recorded using a Perkin Elmer Lambda 35 UV–vis spectrophotometer. High resolution mass spectra (HRMS) were obtained with a VG analytical ZAB2-E instrument (CI). NMR spectra were recorded on Varian UNITY+ 300, Varian Mercury 400, and Varian INOVA 500spectrometers. Chemical shifts (δ) are given in ppm and are referenced to the residual protio solvent (^{1}H: $CDCl_3$, 7.24 ppm; C_6D_6, 7.15 ppm; C_7H_8, 2.09 ppm; ^{13}C: $CDCl_3$, 77.0 ppm; C_6D_6, 128.0 ppm, C_7D_8, 128.3 ppm). Elemental analyses were performed at Midwest Microlab, LLC (Indianapolis, IN). Melting points were obtained using a Mel-Temp apparatus and are uncorrected.

Synthesis of 2-chloro-1,3-bis(2,6-di-*iso*-propylphenyl)-4,6-diketo-5,5-dimethylpyrimidine (1·HCl). Dimethylmalonyl dichloride (0.75 mL, 5.60 mmol, 1.05 eq) was added dropwise to a stirred solution of *N,N′*–di-*iso*-propylphenylformamidine (1.95 g, 5.35 mmol) and triethylamine (1.1 mL, 8.0 mmol, 1.5 eq) in CH_2Cl_2 (30 mL) at 0 °C. The solution was stirred at 0 °C for 1 h whereupon the volatiles were removed under reduced pressure. The resulting solid was taken up into a mixture of hexanes:CH_2Cl_2 (2:1 v:v) (24 mL) and passed through a plug of Celite. After removal of the residual solvent,

the residue was washed a mixture of hexanes:CH_2Cl_2 (2:1 v:v) (18 mL). Removal of the volatiles under reduced pressure afforded the desired product as a white solid (2.56 g, 96% yield). mp = 163–165 °C (dec.) ^{1}H NMR ($CDCl_3$, 300.15 MHz): 1.12 (d, J = 6.6 Hz, 12H), 1.32 (d, *J* = 6.6 Hz, 12H), 1.33 (s, 3H), 1.76 (s, 3H), 3.07 (sept., *J* = 6.9 Hz, 4H), 6.85 (s, 1H), 7.27 (s, 2H), 7.39 (d of d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): 8.56, 23.07, 24.00, 24.64, 29.20, 45.71, 47.85, 90.15, 124.63, 130.00, 132.11, 146.80, 171.71. IR (KBr): ν_{CO} = 1708, 1685 cm^{-1}. HRMS $[M+H]^+$ calcd. for $C_{30}H_{42}ClN_2O_2$: 497.2935; Found: 497.2942. Anal. Calcd. for $C_{30}H_{41}ClN_2O_2$: C, 72.48; H, 8.31; N, 5.64; Found: C, 72.49; H, 8.41; N, 5.41.

Synthesis of 2-chloro-1,3-dimesityl-4,6-diketo-5,5-dimethylpyrimidine (2·HCl). Dimethylmalonyl dichloride (0.75 mL, 5.60 mmol, 1.05 eq.) was added dropwise to a stirred solution of *N,N′*-dimesitylformamidine (1.5 g, 5.35 mmol) and triethylamine (1.1 mL, 8.0 mmol, 1.5 eq.) in CH_2Cl_2 (30 mL) at 0 °C. The solution was stirred at 0 °C for 1 h whereupon the residual solvent was removed under reduced pressure. The resulting solid was taken up into a mixture of hexanes:CH_2Cl_2 (2:1 v:v) (24 mL) and passed through a plug of Celite. The residue was washed with a mixture of hexanes:CH_2Cl_2 (2:1 v:v) (18 mL). Removal of the volatiles under reduced pressure afforded **2**·HCl as a white solid (2.04 g, 92% yield). Spectroscopic and melting point data were in accord with the reported literature values.[27]

Synthesis of *N,N′*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (2). A vial was charged with **2**·HCl (600 mg, 1.45 mmol), NaHMDS (267 mg, 1.46 mmol), benzene (25 mL), and a stir bar. The solution was stirred at ambient temperature for 30 min and then filtered through a PTFE filter. After removing the residual solvent under reduced pressure, the solid residue was washed with cold hexanes, decanted, and then dried under vacuum to afford the desired product as a white solid (462 mg, 85% yield).

mp = 166–168 °C (dec.) ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.48 (s, 6H, C(C*H*$_3$)$_2$), 2.11 (s, 18H, Ar-C*H*$_3$), 6.78 (s, 4H, Ar-*H*). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 18.24, 20.95, 24.49, 51.07, 129.60, 134.56, 137.69, 138.70, 170.19, 277.73. IR (KBr): ν_{CO} = 1709 cm^{-1}. HRMS: $[M+H]^+$ calcd. for $C_{24}H_{29}N_2O_2$: 377.2229; Found: 377.2228.

Synthesis of 2-oxomethylene-1,3-dimesityl-4,6-diketo-5,5-dimethylpyrimidine (3). An 8 mL vial was charged with C_7D_8 (1 mL) and **2** (39.2 mg, 0.104 mmol) and then transferred to a Wilmad QPV high pressure NMR tube. Three freeze-pump-thaw cycles were performed and the tube's headspace was filled with CO (g) (15 psi). Upon mixing, the solution turned purple in color, indicating the formation of **3** which was spectroscopically characterized but not isolated. The K_{eq} for the equilibrium for **2** + CO (15 psi) $\rightleftharpoons$ **3** was determined as previously described.[2] ^{1}H NMR (C_7D_8, 499.87 MHz): δ 1.70 (s, 6H, C(C*H*$_3$)$_2$), 1.88 (s, 6H, Ar-C*H*$_3$), 2.04 (s, 12H, Ar-C*H*$_3$), 6.38 (s, 4H, Ar-*H*). ^{13}C NMR (C_7D_8, 125.71 MHz): δ 18.37, 21.01, 21.97, 48.54, 91.70, 129.84, 131.816, 135.39, 137.09, 139.05, 167.98, 246.41. IR (C_7H_8, CaF_2): $\nu_{CC=O}$ = 2092 cm^{-1}; $\nu_{C=O}$ = 1681 cm^{-1}. UV–vis (C_7H_8): λ_{max} = 543 nm.

Synthesis of 2-((2,6-dimethylphenylimino)methylene)-1,3-dimesityl-4,6-diketo-5,5-dimethylpyrimidine (4). An 8 mL vial was charged with benzene (2 mL), 2,6-dimethylphenylisocyanide (26 mg, 0.198 mmol), **2** (74 mg, 0.198 mmol), and a stir bar. The resulting mixture was stirred at ambient temperature for 1 h. Removal of the residual solvent under reduced pressure afforded the desired product as a bright, orange solid (96 mg, 96% yield). mp = 153–154 °C. ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.63 (s, 6H, C(C*H*$_3$)$_2$), 1.84 (s, 6H, Ar-C*H*$_3$), 1.96 (s, 6H, Ar-C*H*$_3$), 2.21 (s, 12H, Ar-C*H*$_3$), 6.60 (s, 4H, Ar-*H*), 6.61-6.71 (m, 3H, Ar-*H*). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 17.91, 18.28, 20.79, 23.72, 47.96, 106.27, 126.80, 128.49, 129.73, 130.95, 132.90, 136.44, 138.56, 139.47, 167.84, 202.68. IR (KBr): $\nu_{C=N}$ = 1978 cm^{-1}; ν_{CO} = 1696, 1662 cm^{-1}. HRMS: $[M+H]^+$

calcd. for $C_{33}H_{38}N_3O_2$: 508.2957; Found: 508.2964. Anal. Calcd. for $C_{33}H_{37}N_3O_2$: C, 78.07; H, 7.35; N, 8.28; Found: C, 77.77; H, 7.19; N, 8.26.

Synthesis of 2-amino-1,3-dimesityl-4,6-diketo-5,5-dimethylpyrimidine (5). A 25 mL Schlenk flask was charged with **2** (53 mg, 0.14 mmol) and a stir bar, and then placed under an atmosphere of ammonia gas. The reaction vessel was then cooled to –78 °C. After approximately 3 mL of ammonia had condensed, the reaction mixture was slowly warmed to ambient temperature over 12 h. The residue, which was later determined to be the desired product, was isolated as a white solid (55 mg, 99% yield). Single crystals suitable for X-ray diffraction analysis were grown from a concentrated solution of hexanes:CH_2Cl_2 (2:1 v:v) at –30 °C. mp = 162–163 °C. ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.15 (d, J = 6.30 Hz, 2H, N*H*$_2$), 1.79 (s, 3H, CC*H*$_3$), 1.81 (s, 3H, CC*H*$_3$), 2.05 (s, 6H, Ar-C*H*$_3$), 2.10 (s, 6H, Ar-C*H*$_3$), 2.21 (s, 6H, Ar-C*H*$_3$), 5.22 (t, J = 6.60 Hz, 1H, C*H*NH$_2$), 6.70 (s, 2H, Ar-*H*), 6.73 (s, 2H, Ar-*H*). ^{13}C NMR (C_6D_6, 75.47 MHz): 18.46, 19.27, 20.86, 46.82, 79.11, 129.81, 129.92, 134.34, 135.36, 137.61, 137.99, 170.31. IR (KBr): ν_{NH} = 3415.7, 3339.4 cm^{-1}; ν_{CO} = 1672.4, 1645.6 cm^{-1}. HRMS: $[M+H]^+$ calcd. for $C_{24}H_{32}N_3O_2$: 394.2495; Found: 394.2495. Anal. Calcd. for $C_{24.5}H_{32}Cl_1N_3O_2$ ($C_{24}H_{31}N_3O_2 \cdot 0.5CH_2Cl_2$): C, 67.49; H, 7.40; N, 9.64; Found: C, 67.21; H, 7.36; N, 9.49.

Synthesis of 2-amino-1,3-bis(2,6-diisopropylphenyl)-4,6-diketo-5,5-dimethylpyrimidine (6). Compound **1** was prepared in situ from [**1**H][OTf] (100 mg, 0.164 mmol) and NaHMDS (30 mg, 0.164 mmol, 1 eq) in toluene (1 mL) using a previously reported procedure.[2] The resulting solution was then frozen in N_2 (liq.) and the reaction atmosphere was removed under vacuum. The reaction vessel was then placed under an atmosphere of ammonia gas. After approximately 3 mL of ammonia had condensed, the reaction mixture was slowly warmed to ambient temperature over 12 h. Recrystallization of the remaining residue from a mixture of CH_2Cl_2 and hexanes at –20

°C afforded the desired product as a white solid (65 mg, 83% yield). mp = 181–182 °C. ^{1}H NMR (C_6D_6, 300.14 MHz): δ 0.94 (d, *J* = 5.70 Hz, 2H, N*H*$_2$), 1.14 (s, 3H, CC*H*$_3$), 1.16 (s, 3H, CC*H*$_3$), 1.21 (s, 6H, Ar-C*H*$_3$), 1.23 (s, 6H, Ar-C*H*$_3$), 1.30 (s, 3H, Ar-C*H*$_3$), 1.33 (s, 3H, Ar-C*H*$_3$), 1.79 (s, 3H, Ar-C*H*$_3$), 1.83 (s, 3H, Ar-C*H*$_3$), 3.13 (sept., *J* = 6.90 Hz, 2H, C*H*(CH$_3$)$_2$), 3.26 (sept., *J* = 6.90 Hz, 2H, C*H*(CH$_3$)$_2$), 5.33 (t, *J* = 6.15 Hz, 1H, NC*H*N), 7.09 (d of t, *J* = 7.50 Hz, 4H, Ar-*H*), 7.15-7.23 (m, 2H, Ar-*H*). ^{13}C NMR (C_6D_6, 75.47 MHz): 23.24, 23.48, 23.58, 24.98, 25.18, 26.52, 29.44, 29.54, 46.61, 80.63, 124.17, 124.67, 129.37, 133.77, 146.12, 148.87, 171.58. IR (KBr): ν_{NH} = 3454, 3351 cm^{-1}; ν_{CO} = 1677, 1649 cm^{-1}. HRMS: $[M+H]^+$ calcd. for $C_{30}H_{44}N_3O_2$: 478.3434; Found: 478.3431. Anal. Calcd. for $C_{30}H_{43}N_3O_2$: C, 75.43; H, 9.07; N, 8.80; Found: C, 75.52; H, 9.06; N, 8.72.

2.5 ACKNOWLEDGEMENT

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Chapter 3: Diamidocarbenes as Versatile and Reversible [2+1] Cycloaddition Reagents*

3.1 INTRODUCTION

Highly strained rings, particularly cyclopropanes and epoxides, enjoy extraordinary utility in a broad range of synthetic[1–3] and biological[4,5] applications. Moreover, from a fundamental perspective, these compounds attract interest for their unique structural and bonding characteristics.[6,7] An efficient method for the synthesis of three-membered carbocycles and oxacycles involves metal-mediated delivery of a carbene to an olefin or aldehyde;[8,9] however, free carbenes have also been employed successfully.[10–12] Although most free carbenes used in [2+1] cycloadditions are generated *in situ*, the use of isolable derivatives as starting materials is particularly attractive as they offer avenues to streamline the synthetic procedure, aid in the discovery of novel transformations and provide opportunities to probe deeper into the mechanism and structure of reactive organic species.[13,14] Unfortunately, [2+1] cycloadditions that involve isolable carbenes remain extremely rare.

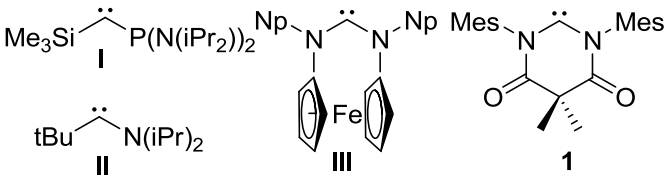

Figure 3.1: Structures of various isolable carbenes.[15,17,18,32] iPr = isopropyl, Np = neopentyl, Mes = 2,4,6-trimethylphenyl.

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The first example of an isolable free carbene capable of participating in cyclopropanation and epoxidation reactions was the phosphinosilylcarbene **I** (Figure 3.1),[15,16] which was reported by Bertrand and co-workers in 1989. Since then, the acyclic alkylamino **II** (in 2004) and diamino[3]ferrocenophane[17] (**III**) (in 2010) carbenes were found to display similar cyclopropanation reactivities.[18,19] The chemistry displayed by the latter was particularly surprising, as *N*-heterocyclic carbenes investigated previously[20–23] yielded exocyclic olefins rather than cyclopropane products.[24] Regardless, the cycloaddition chemistry displayed by **I–III** was restricted to electron-deficient olefins[16,18,19,25–27] and aldehydes,[16,28–30] and until now isolable carbenes have not been shown to engage in [2+1] cycloadditions with electron-rich olefins.[20]

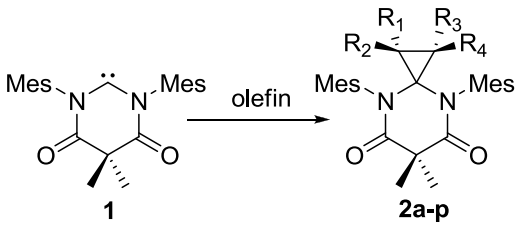
Given the unique reactivity profile of diamidocarbenes (DACs)[31-38] and their reduced singlet–triplet gap,[33] we reasoned that DACs would be excellent candidates for participating in [2+1] cycloadditions. Moreover, the carbene carbon in DACs is in the same oxidation state as the carbon atom in carbon monoxide and bears amides that should be susceptible to hydrolysis. As such, we predicted that DACs could also serve as a masked equivalent of CO (a molecule that does not readily undergo [2+1] cycloaddition chemistry) for use in accessing synthetically versatile cyclopropanone derivatives or other carbonyl-containing compounds. Indeed, as described below, we found that isolable DAC **1** not only effected a broad range of cyclopropanation and epoxidation reactions that involved electron-deficient as well as electron-rich olefins and aldehydes, but also that many of these reactions were thermally reversible. Additionally, we found that hydrolysis of a diamidocyclopropane derivative afforded the corresponding linear carboxylic acid via a metal- and carbon monoxide-free hydrocarboxylation, which presumably occurred through a cyclopropanone intermediate.[39,40] During the course of our

studies, we also discovered an unprecedented formal [4+1] cycloaddition between **1** and α,β-unsaturated ketones, which provided rapid access to a new class of dihydrofurans.

3.2 Results and Discussion

Given that known, isolable carbenes react with electron-deficient olefins,[16,18,19,25–27] our initial efforts focused on studying the cycloaddition chemistry of readily accessible **1** with methyl acrylate. Stirring equimolar quantities of **1** and methyl acrylate for two hours in benzene ($[\mathbf{1}]_0$ = 0.29 M) at ambient temperature, followed by the removal of the solvent and washing with cold hexanes, afforded a white solid in 98% yield (Table 3.1). ^{1}H NMR analysis of this material revealed diagnostic signals at δ = 0.96, 1.63 and 2.01 ppm (C_6D_6) consistent with the structure of cyclopropane **2a**. To explore the scope of this cyclopropanation chemistry, a variety of 1-substituted and 1,1-disubstituted olefins were treated with **1** (Table 3.1). In general, equimolar concentrations of **1** and an olefin were subjected to the reaction conditions and purification procedure described above. Using this method, the reaction of **1** with methyl methacrylate, acrylonitrile or methacrylonitrile afforded the expected cyclopropane products **2b**–**2d** in excellent yield (92–96%). Likewise, styrene and a variety of its *p*-substituted derivatives, including a relatively electron-rich derivative (*p*-methoxystyrene), were cyclopropanated readily by **1**, although a slightly elevated temperature (60 °C) was required to obtain a high yield of the corresponding products **2e**–**2i** (71–90%). Cyclopropane formation was determined unequivocally for **2e** by single-crystal X-ray diffraction analysis (Figure 3.2).

Next, we turned our attention toward evaluating the ability of **1** to cyclopropanate 1,2-disubstituted olefins. The reaction of equimolar quantities of diethyl maleate or diethyl fumarate with **1** was found to proceed at ambient temperature in C_6H_6 and exclusively afforded the same product (**2j**), as determined by ^{1}H NMR spectroscopy, and



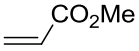
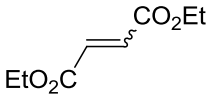
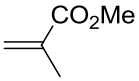
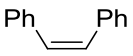
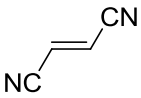
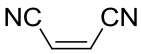
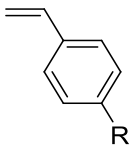
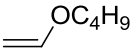
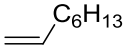
Product	Olefin	Isolated Yield (%)[b]	Product	Olefin	Isolated Yield (%)[b]
2a		98%	**2j**		93% (trans)
2b		92%	**2k**		39%[d] (trans)
2c		96%	**2l**		52% (trans)
2d		92%	**2m**		45% (cis)
2e: R = CF_3		71%[c]	**2n**		53%[d]
2f: R = Cl		82%[c]	**2o**		43%[e] (exo)
2g: R = F		74%[c]	**2p**		47%[d]
2h: R = H		90%[c]			
2i: R = OMe		76%[c]			

Table 3.1: Summary of Cyclopropanations of DAC **1** with Various Olefins. [a]In general, the cycloaddition reactions were performed using equimolar concentrations of **1** and the olefin indicated in C_6H_6 for 2 h at ambient temperature except where noted. [b] Isolated yield of the corresponding cyclopropane product. Where applicable, the stereochemistry of the cyclopropane product is indicated in parentheses. [c] The reaction was performed at 60 °C for 16 h. [d] The reaction was performed neat at 100 °C for 2 h. [e] The reaction was performed neat at 120 °C for 2 h.

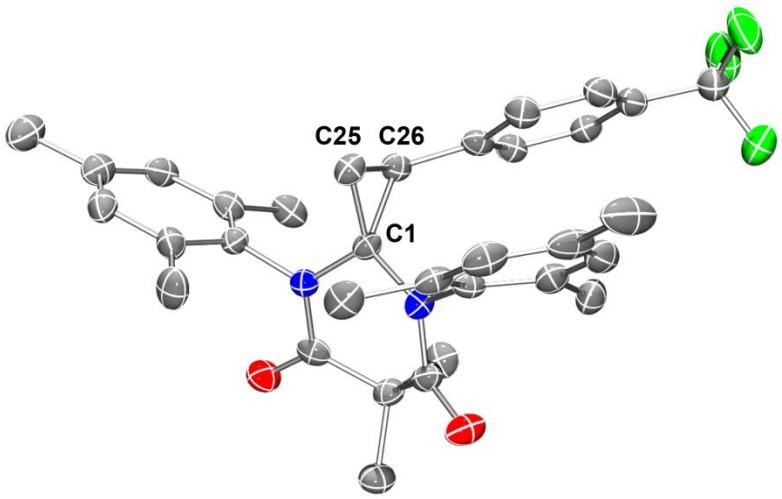
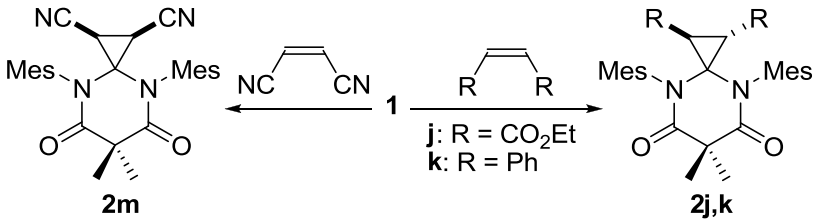


Figure 3.2: ORTEP diagram of **2e** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): C1-C25, 1.497(6); C1-C26, 1.551(6); C25-C26, 1.501(6); C25-C1-C26, 59.0(3); C25-C26-C1, 58.7(3); C1-C25-C26, 62.3(3).

in identical yield (93%, Figure 3.3, left). X-ray diffraction analysis of a single crystal obtained from the reaction of **1** and diethyl maleate revealed that **2j** was the *trans*-diastereomer. Although elevated temperatures (100–120 °C for two hours) were required, similar results were obtained when **1** was treated with *cis*- or *trans*-stilbene, which both formed *trans*-**2k** as the exclusive product, albeit in modest yield (up to 39%). In contrast, treatment of **1** with one equivalent of an 87:13 molar mixture of maleonitrile:fumaronitrile, prepared via the method of Linstead and Whalley,[41] at ambient temperature for one hour afforded an 87:13 ratio of the respective *cis*:*trans* products (**2m**:**2l**), as determined by NMR spectroscopy (C_6D_6). The structure of the *cis*-diastereomer was confirmed subsequently by single-crystal X-ray diffraction analysis (Figure 3.3, right). Whereas the retention of stereochemistry in the formation of **2m** was consistent with a concerted mechanism,[42–44] the rapid closure of a transient 1,3-dipole cannot be ruled out. In contrast, formation of the *trans*-diastereomeric cyclopropanes **2j**

and **2k** from their respective *cis*-olefins is in accord with a stepwise process that involves a 1,3-dipole intermediate capable of bond rotation prior to ring closure. Collectively, these results are similar to those observed with cycloheptatrienylidene, a carbene that must be generated in situ via photolysis or thermolysis of the sodium salt of tropone tosylhydrazone.[45,46]



Scheme 3.1: Treatment of **1** with maleonitrile afforded the cis-1,2-disubstituted cyclopropane **2m**; in constrast, the trans-1,2-disubstituted cyclopropanes **2j** and **2k** were obtained when **1** was treated with diethyl maleate or cis-stilbene, respectively.

Building on the aforementioned cyclopropanation of *p*-methoxystyrene, subsequent efforts were directed towards evaluating the ability of **1** to cyclopropanate electron-rich alkenes. Heating **1** ($[\mathbf{1}]_0$ = 0.4 M) in neat *n*-butyl vinyl ether (19 equiv.) to 100 °C for two hours followed by purification of the reaction mixture using silica-gel column chromatography afforded a white solid in 53% yield. The structure of this product was consistent with that of **2n**, as determined by a heteronuclear correlation NMR experiment, in which the ^{1}H NMR signals observed at δ = 3.49 (1H) and 0.84 ppm (2H) (C_6D_6) were correlated with the ^{13}C NMR signals found at 59.4 and 15.3 ppm, respectively. Similarly, cyclopropanes **2o** and **2p** were obtained in 43–47% yield by heating **1** for two hours in neat norbornene (120 °C) or 1-octene (100 °C), respectively. NMR spectroscopy and X-ray crystallography identified the structure of **2o** as the exo-isomer.

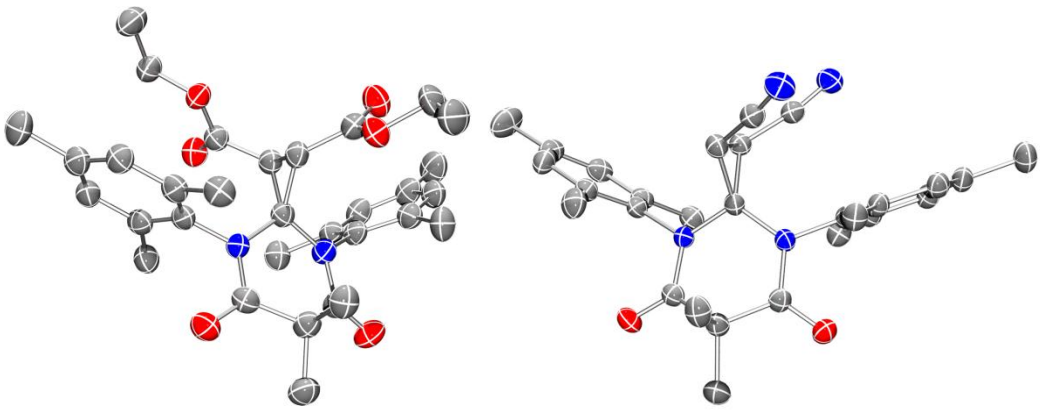
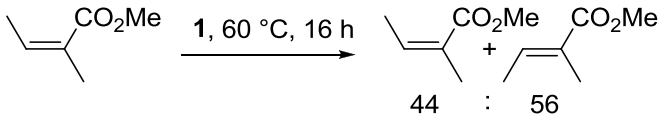


Figure 3.3: (left) ORTEP diagram of **2j** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. (right) ORTEP diagram of **2m** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

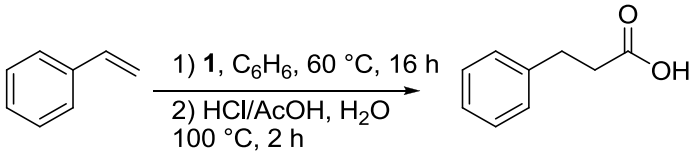
Having discovered that DAC **1** was capable of cyclopropanating electronically diverse alkenes, a number of trisubstituted olefins were examined next, primarily to clarify the role of sterics. The introduction of **1** to methyl-3-methyl-2-butenoate, a functionalized olefin that features a disubstituted β-carbon, resulted in no reaction, even at elevated temperatures (up to 100 °C). Hence, attack of the carbene lone pair at the β-position in substituted olefins may be pivotal in the cyclopropanation mechanism and inhibited by steric bulk. In light of this result, we reasoned that a 1,1,2-trisubstituted olefin, such as methyl angelate, should be more prone to cyclopropanation.

Although <20% of the cyclopropanated product formed when an equimolar mixture of methyl angelate and **1** were heated at 60 °C for 16 hours in C_6D_6, a 56:44 ratio of methyl tiglate:methyl angelate was observed by ^{1}H NMR spectroscopy (Scheme 3.2). As a control experiment, methyl angelate was heated to 100 °C for 24 hours (in the absence of **1**), which resulted in less than 2% isomerization. Collectively, these data are consistent with a reversible interaction between **1** and methyl angelate, which enables scrambling of the olefin's stereochemistry (see below for additional discussion).



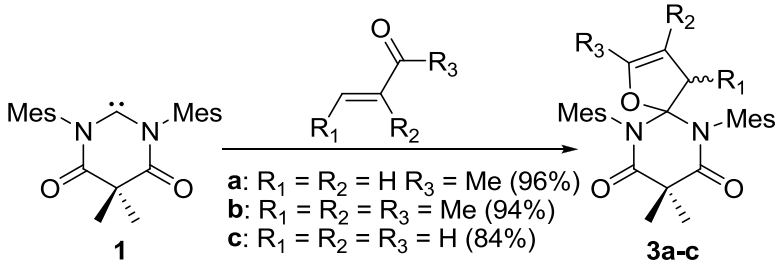
Scheme 3.2: Isomerization of methyl angelate in the presence of **1.**

Bearing in mind that the carbene center in **1** is in the same oxidation state as the carbon atom in carbon monoxide, we reasoned that the hydrolysis of the *N,N′*-diamidocyclopropanes described above would afford the corresponding cyclopropanones and/or their derivatives. To test this hypothesis, **2h** was treated with CH_3CO_2H/HCl. After two hours at 100 °C, hydrocinnamic acid was obtained in 56% isolated yield (unoptimized). Moreover, similar results were obtained when the two-step cyclopropanation/hydrolysis reaction was performed in a single reaction vessel (Scheme 3.3). Considering that *N,N′*-dimesityl-2,2-dimethylmalonamide and its partially hydrolysed derivative 3-(mesitylamino)-2,2-dimethyl-3-oxopropanoic acid were isolated as by-products from this reaction, we believe that the hydrolysis of **2h** affords a cyclopropanone intermediate that readily adds water and rearranges to give the corresponding propionic acid under aqueous conditions.[39] Regardless, the DAC effectively enabled the formal anti-Markovnikov hydrocarboxylation of an alkene to a linear carboxylic acid, an industrially useful process that typically requires transition metals and/or high pressures of carbon monoxide.[40]



Scheme 3.3: Treatment of styrene with **1** followed by hydrolysis of the cyclopropane product (*i.e.*, **2h**) under acidic conditions afforded hydrocinnamic acid in 56% isolated yield (unoptimized).

To further expand the utility of the cyclopropanation chemistry described above and considering the central role of cyclopropyl ketones in the synthesis of furans,[1] α,β-unsaturated ketones were also explored as potential cycloaddition partners for DAC **1**. Treatment of **1** with an equimolar quantity of methyl vinyl ketone in benzene at ambient temperature for two hours followed by removal of the solvent and washing of the residue with cold hexanes afforded a white solid in 96% yield. The lack of a ν_{CO} peak assignable to a ketone moiety in the infrared spectrum (KBr) and a signal indicative of a shielded olefinic proton (δ = 3.50 ppm; C_6D_6) in the ^{1}H NMR spectrum of the product were consistent with the formation of dihydrofuran **3a** (Scheme 3.4). The structural assignment of this compound was later confirmed by X-ray crystallography (Figure 3.4). Formally a [4+1] cycloaddition, the aforementioned transformation is unprecedented and may occur via the Michael addition of **1** into the α,β-unsaturated ketone followed by ring closure or via a 1,3-rearrangement of a [2+1] cycloadduct intermediate. Analogous results were obtained with 3-methyl-3-penten-2-one (which afforded a 93% yield of **3b**), although no reaction was observed with 4-methyl-3-penten-2-one, even at 100 °C, presumably due to steric inhibition.



Scheme 3.4: Formal [4+1] cycloaddition of **1** with α,β-unsaturated carbonyls.

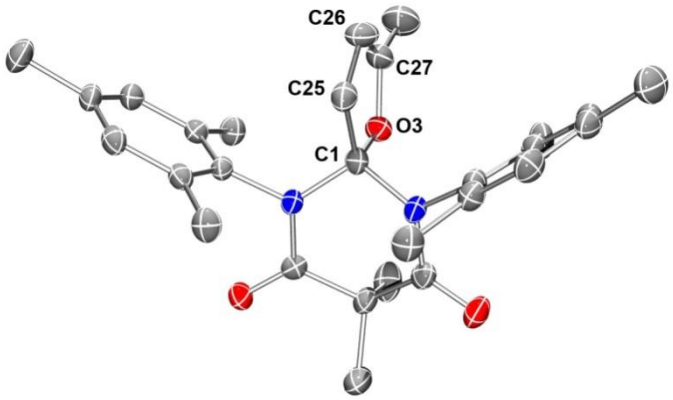
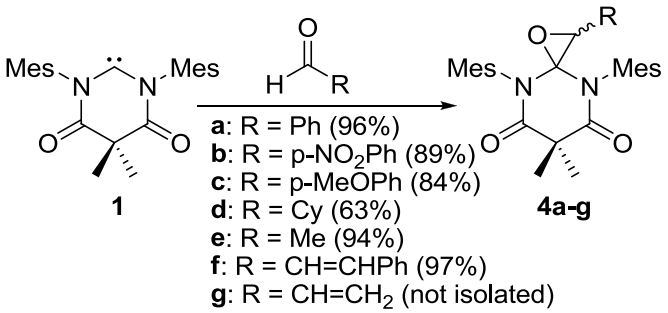


Figure 3.4: ORTEP diagram of **3a** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å): C1-C25, 1.543(3); C25-C26, 1.486(3); C26-C27, 1.307(3); C27-O3, 1.386(2); O3-C1, 1.460(2).

Subsequent attention shifted towards exploring the potential of **1** to react with aldehydes. As shown in Scheme 3.5, stirring benzaldehyde with an equimolar quantity of **1** in C_6H_6 at ambient temperature for two hours followed by washing the crude product with cold hexanes afforded **4a** in 96% yield. The structure of **4a** was supported by the disappearance of the ^{1}H NMR signal assigned to an aldehyde moiety (δ = 9.63 ppm) and the appearance of a new signal diagnostic of an epoxide at δ = 4.03 ppm (C_6D_6). Analogous results were obtained with electron-deficient and electron-rich derivatives of benzaldehyde (**4b** and **4c**, 84–89% yield); the structure of **4b** was confirmed by X-ray crystallography (Figure 3.5). Likewise, similar reactivity was observed with the aliphatic derivatives cyclohexanecarboxaldehyde and acetaldehyde, which afforded the epoxides **4d** and **4e** in 63% and 94% yield, respectively. Reflecting the chemoselectivity of DACs towards aldehydes versus olefins, exposure of **1** to cinnamaldehyde under similar conditions afforded the epoxide **4f** in 97% yield. Similarly, treatment of **1** with acrolein in benzene at ambient temperature for 16 hours yielded epoxide **4g** as the major product and furan **3c** as the minor product (5:1), as determined by ^{1}H NMR spectroscopy. However,

heating to 60 °C for 12 hours or stirring this mixture for two weeks at ambient temperature in solution afforded **3c** as the sole product, which was isolated subsequently in 84% yield (Scheme 3.4). Thus far, attempts to hydrolyse the diamidooxiranes have resulted in a range of products.



Scheme 3.5: Oxirane formation from **1** and various aldehydes.

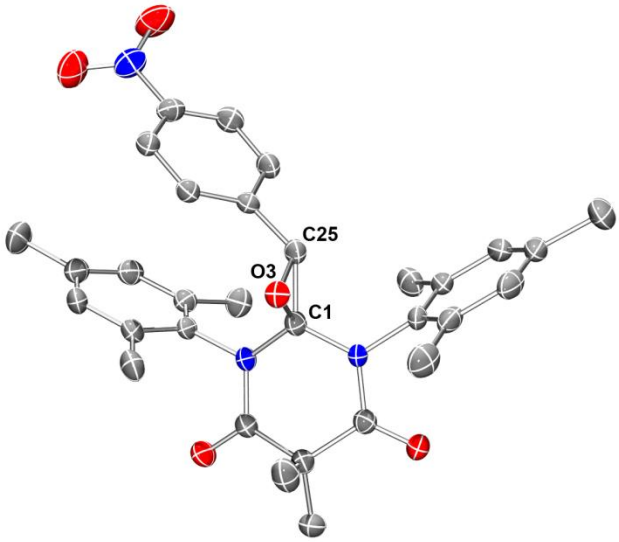


Figure 3.5: ORTEP diagram of **4b** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): C1-O3, 1.442(3); C1-C25, 1.481(3); O3-C25, 1.450(3); O3-C1-C25, 59.45(13); C1-O3-C25, 61.61(14); O3-C25-C1, 58.94(13).

Although the conversion of **4g** into **3c** requires cleavage of the epoxide C–C bond,[47] a retro epoxidation reaction followed by Michael addition would facilitate the formation of the observed product. To probe for such a retro [2+1] cycloaddition, a series of exchange reactions was performed. Heating a mixture of **4a** and diethyl fumarate (1.15 equiv.) to 80 °C in a sealed vial for 16 hours followed by NMR analysis revealed an 83:17 mixture of **2j**:**4a** (Figure 3.6). Similarly, heating a mixture of **2j** and benzaldehyde (1.15 equiv.) afforded the same ratio of the products after the same amount of time. Although a 5:95 ratio of **2j**:**4a** was observed after mixing diethyl fumarate, benzaldehyde and **1** (1.15:1.15:1) for 30 minutes at ambient temperature, an 80:20 ratio of **2j**:**4a** was obtained on heating this mixture to 80 °C for 16 hours.

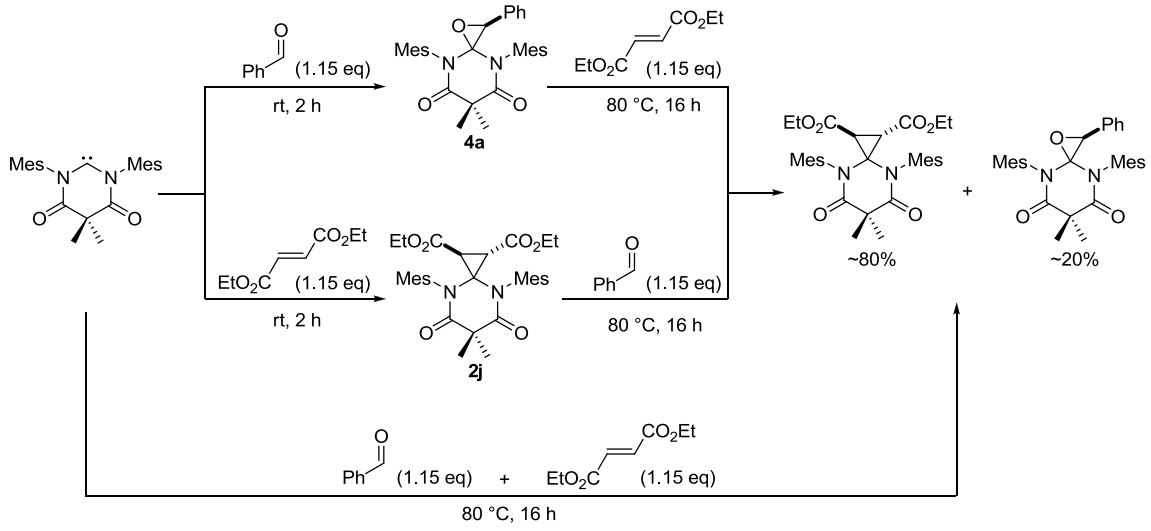


Figure 3.6: Treatment of (a) **1** with 1.15:1.15 benzaldehyde/diethyl fumarate, (b) **2j** with 1.15 eq benzaldehyde, or (c) **4a** with 1.15 eq diethyl fumarate afforded the same product mixture. Conditions: 80 °C, 16 h, C_6D_6.

Collectively, these results indicate that the cyclopropane and epoxide cycloadducts of **1** are capable of undergoing formal retro [2+1] cycloaddition reactions

under mild conditions. Additionally, heating **2j** to 100 °C in C_7D_8 resulted in the liberation of diethyl fumarate as determined by variable-temperature NMR spectroscopy, although the free carbene **1** was not observed because of a competitive intramolecular C–H insertion process that is facilitated at elevated temperatures.[31] To the best of our knowledge, these are the first examples of thermally reversible [2+1] cycloadditions that involve an isolable carbene.[48]

3.3 Conclusion

In summary, we report that DAC **1** is capable of participating in [2+1] cycloadditions with a wide range of olefins and aldehydes, including electron-rich derivatives. Structural and mechanistic studies support a stepwise addition process, although a *cis*-cyclopropane was observed when maleonitrile was used as the starting material, which suggests to us that some cycloadditions may be concerted. Whereas the ability of isolable carbenes to engage in [2+1] cycloaddition chemistry had been limited in scope (that is, restricted to electron-deficient olefins), the results reported herein effectively expand the utility of carbenes in the construction of three-membered carbocycles and oxacycles. Additionally, 1 was found to undergo an unprecedented, formal [4+1] cycloaddition with α,β-unsaturated ketones to afford dihydrofuran derivatives. In light of the broad scope of olefins and aldehydes, and recalling that the DAC was constructed from readily accessible and modular formamidine and malonyl precursors, we envision that many derivatives of these cycloaddition partners will be accessible using the methodology described above. Furthermore, hydrolysis of the diamidocarbene cyclopropane **2h** afforded hydrocinnamic acid, a linear carboxylic acid, via a formal metal- and carbon monoxide-free hydrocarboxylation of styrene.

Beyond their synthetic utility, DACs were also found to enable the first examples of reversible [2+1] cycloaddition reactions that proceed rapidly at relatively low temperatures, an advantage over many other dynamic covalent reactions. This surprising discovery is expected to initiate new fundamental studies and expand the applications of stable carbenes to include uses as protecting groups for olefins or aldehydes, or as latent sources of reactive intermediates. Akin to other reversible cycloadditions, such as the Diels–Alder reaction, reversible [2+1] cycloaddition processes also hold promise for use as the basis of structurally dynamic materials and reversible covalent inhibitors, and to facilitate applications that utilize dynamic combinatorial libraries (for example, sensor discovery and development).[49,50]

3.4 EXPERIMENTAL

General Considerations. All procedures were performed using standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen-filled glove box unless otherwise noted. *N,N′*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (**1**)[34] and maleonitrile[41] were synthesized according to literature procedures. 1-Octene which was distilled prior to use in order to remove trace amounts of 1-octanol. Norbornene was sublimed prior to use. All commercial liquid substrates were dried over molecular sieves prior to use. All commercial solid substrates were dried under reduced pressure for 24 hours prior to use. Benzene, dichloromethane (CH_2Cl_2), hexanes, and pentane were dried and degassed by a Vacuum Atmospheres Company solvent purification system (model number 103991-0319) and stored over molecular sieves in a nitrogen-filled glove box. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrophotometer. High resolution mass spectra (HRMS) were obtained with a VG analytical ZAB2-E instrument (CI or ESI). NMR spectra were recorded on Varian Unity+

300, Varian Mercury 400, Varian MR-400, or Varian Inova 500 spectrometers. Chemical shifts (δ) are given in ppm and are referenced to the residual solvent (^{1}H: $CDCl_3$, 7.24 ppm; C_6D_6, 7.15 ppm; ^{13}C: $CDCl_3$, 77.0 ppm; C_6D_6, 128.0 ppm) or an external standard (^{19}F: 0.00 ppm; $CFCl_3$). Elemental analyses were performed at Midwest Microlab, LLC (Indianapolis, IN). Melting points were obtained using a Mel-Temp apparatus and are uncorrected.

Synthesis of 2a. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, methyl acrylate (17.9 μL, 0.017 g, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 2 h, after which the volatiles were removed under reduced pressure. Washing of the residual solid with minimal cold hexanes followed by drying under reduced pressure afforded the desired product as a white solid (0.090 g, 0.194 mmol, 98% yield). mp = 152-153 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.96 (dd, *J* = 7.0 Hz), 1.63 (dd, *J* = 8.6 Hz, 1H), 1.85 (s, 3H), 1.93 (s, 3H), 2.01 (m overlapping a singlet, 1H), 2.04 (s, 3H), 2.05 (s, 3H), 2.08 (s, 3H), 2.09 (s, 3H), 2.12 (s, 3H), 2.25 (s, 3H), 3.14 (s, 3H), 6.63 (s, 2H), 6.69 (s, 1H), 6.70 (s, 1H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 13.18, 19.18, 19.57, 20.11, 20.73, 20.84, 21.84, 23.94, 25.05, 48.31, 51.68, 61.82, 129.274, 129.42, 129.92, 130.43, 132.21, 133.43, 136.61, 137.29, 137.83, 138.15, 138.84, 167.24, 171.30, 171.57. IR (KBr): ν_{CO} = 1662.1, 1694.9, 1747.8 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{28}H_{35}N_2O_4$: 463.2591; Found: 463.2594. Anal. calcd. for $C_{28}H_{34}N_2O_4$: C, 72.70; H, 7.41; N, 6.06; Found: C, 72.97; H, 7.34; N, 5.91.

Note: Although stable in the solid state over the course of months, **2a** was observed to isomerize to an exocyclic olefin at ambient temperature in solution over the course of weeks; similar results were observed for **2b-d**,**j**,**l**, and **m**. The respective ring-opening reaction is believed to proceed via a resonance-stabilized, zwitterionic

intermediate followed by a 1,2-hydride shift. A similar mechanism has been proposed for the reaction of triazolylidenes with diethyl fumarate/maleate.[24]

Synthesis of 2b. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, methyl methacrylate (21.2 μL, 0.020 g, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 2 h, after which the volatiles were removed under reduced pressure. Washing of the residual solid with minimal cold hexanes followed by drying under reduced pressure afforded the desired product as a white solid (0.087 g, 0.183 mmol, 92% yield). mp = 151-152 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.83 (s, 3H), 1.94 (s, 3H), 2.02 (s, 3H), 2.04 (s, 6H), 2.19 (s, 6H), 2.43 (s, 6H), 2.73 (s, 2H), 3.33 (s, 3H), 6.69 (s, 2H), 6.76 (s, 2H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 8.40, 18.90. 19.61, 20.82, 23.56, 26.99, 40.20, 48.01, 56.64, 76.69, 104.28, 129.01, 130.53, 134.78, 137.50, 137.90, 138.12, 151.79, 172.46. IR (KBr): ν_{CO} = 1669.1, 1701.3, cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{29}H_{37}N_2O_4$: 477.2748; Found: 477.2752. Anal. calcd. for $C_{29}H_{36}N_2O_4$: C, 73.08; H, 7.61; N, 5.88; Found: C, 73.35; H, 7.24; N, 5.94.

Synthesis of 2c. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, acrylonitrile (13 μL, 0.011 g, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 2 h, after which the volatiles were removed under reduced pressure. Washing of the residual solid with minimal cold hexanes followed by drying under reduced pressure afforded the desired product as a white solid (0.082 g, 0.191 mmol, 96% yield). mp = 208-210 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.75 (dd, J = 9.8 Hz, 1H), 1.13 (t, J = 8.0 Hz, 1H), 1.49 (dd, J = 9.8 Hz), 1.70 (s, 3H), 1.80 (s, 3H), 1.81 (s, 3H), 1.94 (s, 3H), 1.98 (s, 3H), 2.01 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 2.54 (s, 3H), 6.51 (s, 1H), 6.55 (s, 1H), 6.67 (s, 1H), 6.83 (s, 1H). ^{13}C NMR (C_6D_6, 75.47 MHz): 6.97, 14.58, 18.92, 19.28, 20.14,

20.69, 20.79, 21.26, 21.56, 24.51, 48.45, 61.50, 116.9, 129.27, 129.93, 130.62, 130.81, 131.25, 132.32, 136.47, 136.54, 137.73, 138.60, 139.94, 171.00, 171.39. IR (KBr): ν_{CO} = 1669.6, 1698.0 cm^{-1}; ν_{CN} = 2237.1 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{27}H_{32}N_3O_2$: 430.2489; Found: 430.2490. Anal. calcd. for $C_{27}H_{31}N_3O_2$: C, 75.49; H, 7.27; N, 9.78; Found: C, 75.66; H, 7.27; N, 9.40.

Synthesis of 2d. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, methacrylonitrile (16.7 μL, 0.013 g, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 2 h, after which the volatiles were removed under reduced pressure. Washing of the residual solid with minimal cold hexanes followed by drying under reduced pressure afforded the desired product as a white solid (0.082 g, 0.185 mmol, 92% yield). mp = 69-70 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.70 (d, *J* = 9.2 Hz, 1H), 0.99 (s, 3H), 1.76 (s, 3H), 1.77 (s, 3H). 1.79 (d, *J* = 8.8 Hz, 1H), 1.91 (s, 3H), 1.96 (s, 3H), 1.97 (s, 3H), 1.98 (s, 3H), 2.08 (s, 3H), 2.55 (s, 3H), 6.49 (s, 1H), 6.56 (s, 1H), 6.59 (s, 1H), 6.62 (s, 1H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 19.38, 19.64, 20.48, 20.56, 21.22, 21.86, 22.38, 22.47, 22.73, 23.58, 24.63, 51.88, 63.45, 120.53, 130.37, 130.47, 130.85, 131.08, 133.20, 135.00, 137.10, 137.30, 137.40, 137.63, 138.27, 139.10172.96, 176.15. IR (KBr): ν_{CO} = 1678.5, 1709.1 cm^{-1}, ν_{CN} = 2232.7 cm^{-1} . HRMS (ESI): $[M+H]^+$ calcd. for $C_{28}H_{34}N_3O_2$: 444.2646; Found: 444.2641. Anal. calcd. for $C_{28}H_{33}N_3O_2$: C, 75.81; H, 7.50; N, 9.47; Found: C, 76.00; H, 7.39; N, 9.13.

Synthesis of 2e. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, 4-(trifluoromethyl)styrene (29.4 μL, 0.034 g, 0.199 mmol, 1 eq) was added and the resultant mixture was heated to 60 °C for 16 h. After cooling the reaction mixture to room temperature, the volatiles were removed under reduced pressure. Washing the residue with minimal cold hexanes followed by drying

under reduced pressure afforded the desired product as a white solid (0.078 g, 0.142 mmol, 71% yield). mp = 197-199 °C (decomp.) ^{1}H NMR ($CDCl_3$, 300.14 MHz): δ 1.02 (s, 3H), 1.35 (dd, J = 9.8 Hz, 1H), 1.58 (s, 3H), 1.71 (dd, J = 8.9 Hz, 1H), 1.82 (s, 3H), 2.23 (s, 3H), 2.27 (s, 3H), 2.33 (s, 3H), 2.34 (s, 3H), 2.41 (s, 3H), 2.53 (t, J = 10.7 Hz), 6.42 (s, 1H), 6.87 (s, 1H), 6.95 (overlapping bs, 2H), 6.95(s, 1H), 6.97 (s, 1H), 7.32 (d, J = 8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 11.61, 16.89, 19.37, 19.57, 20.19, 20.74, 20.79, 20.85, 24.86, 26.01, 47.36, 61.76, 124.96 (q, J = 3.8 Hz), 128.94, 129.39, 129.44, 129.87, 130.19, 131.56, 133.07, 136.20, 136.38, 137.50, 137.91, 138.32, 138.56, 139.14, 171.20, 171.54. ^{19}F ($CDCl_3$, 282.41 (MHz): δ -62.89. IR (KBr): ν_{CO} = 1658.5, 1691.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{33}H_{36}F_3N_2O_2$: 549.2729. Found: 549.2724. Anal. calcd. for $C_{33}H_{35}F_3N_2O_2$: C, 72.24; H, 6.43; N, 5.11; Found: C, 72.05; H, 6.66; N, 5.31.

Synthesis of 2f. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, 4-chlorostyrene (23.9 μL, 0.028 g, 0.199 mmol, 1 eq) was added and the resultant mixture was heated to 60 °C for 16 h. After cooling the reaction mixture to room temperature, the volatiles were removed under reduced pressure. Washing the residue with minimal chilled benzene followed by drying under reduced pressure afforded the desired product as a white solid (0.084 g, 0.163 mmol, 82% yield). mp = 225-227 °C (decomp.) ^{1}H NMR ($CDCl_3$, 300.14 MHz): δ 1.08 (s, 3H), 1.27 (dd, J = 9.8 Hz, 1H), 1.56 (s, 3H), 1.60 (t, J = 8.4 Hz, 1H), 1.82 (s, 3H), 2.24 (s, 3H), 2.26 (s, 3H), 2.33 (s, 3H), 2.33 (s, 3H), 2.38 (s, 3H), 2.46 (t, J = 10.8 Hz, 1H), 6.49 (s, 3H), 6.67 (bs, 2H), 6.86 (s, 1H), 6.93 (s, 1H), 6.96 (s, 1H), 7.05 (d, J = 7.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 11.50, 16.90, 19.35, 19.60, 20.23, 20.58, 20.82, 24.94, 25.55, 47.33, 61.44, 128.21, 128.80, 129.50, 129.76, 130.14, 130.38 (m), 131.58, 132.13, 132.83, 133.22, 136.13, 136.38, 137.51, 138.13, 138.42, 139.28, 171.19, 171.54. IR (KBr): ν_{CO} = 1650.97, 1682.77 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{36}ClN_2O_2$:

515.2465. Found: 515.2454. Anal. calcd. for $C_{32}H_{35}ClN_2O_2$: C, 74.62; H, 6.85; N, 5.44; Found: C, 74.29; H, 6.78; N, 5.49.

Synthesis of 2g. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, 4-fluorostyrene (23.8 μL, 0.024 g, 0.199 mmol, 1 eq) was added and the reaction mixture was heated to 60 °C for 16 h. After cooling the reaction mixture to room temperature, the volatiles were removed under reduced pressure. Washing the residue with minimal chilled benzene followed by drying under reduced pressure afforded the desired product as a white solid (0.074 g, 0.148 mmol, 74% yield). mp = 223-225 °C (decomp.) ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.06 (s, 3H), 1.25 (dd, J = 9.8 Hz, 1H), 1.55 (s, 3H), 1.58 (m overlapping singlet, 1H), 1.83 (s, 3H), 2.23 (s, 3H), 2.26 (s, 3H), 2.33 (s, 6H), 2.38 (s, 3H), 2.47 (t, J = 10.7 Hz, 1H), 6.48 (s, 1H), 6.54-6.91 (5H), 6.92 (s, 1H), 6.95 (s, 1H). ^{13}C NMR (C_6D_6,): δ 11.59, 16.78, 19.36, 19.64, 20.28, 20.56, 20.83, 20.85, 25.02, 25.35, 47.34, 61.28, 114.94, 115.22, 128.78, 129.28 (d, ^{2}J = 2.7 Hz), 129.49, 129.76, 130.14, 131.65, 133.33, 136.18, 136.43, 137.56, 138.04, 138.41, 139.34, 171.21, 171.58. ^{19}F NMR ($CDCl_3$, 282.41 MHz): δ -115.69. IR (KBr): ν_{CO} = 1655.95, 1691.50 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{36}FN_2O_2$: 499.2761. Found: 499.2757. Anal. calcd. for $C_{32}H_{35}FN_2O_2$: C, 77.08; H, 7.07; N, 5.62; Found: C, 76.85; H, 7.05; N, 5.57.

Synthesis of 2h. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, styrene (22.8 μL, 0.021 g, 0.199 mmol, 1 eq) was added and the reaction heated to 60 °C for 16 h. After cooling the reaction mixture to room temperature, the volatiles were removed under reduced pressure. Washing the residue with minimal cold hexanes followed by drying under reduced pressure afforded the desired product as a white solid (0.086 g, 0.179 mmol, 90% yield). mp = 210-212 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.98 (dd, *J* = 7.6 Hz. 1H),

1.19 (s, 3H), 1.43 (dd, *J* = 8.8 Hz, 1H), 1.87 (s, 3H), 1.92 (s, 3H), 2.06 (s, 3H), 2.09 (s, 6H), 2.22 (s, 3H), 2.23 (s, 3H), 2.30 (s, 3H), 2.42 (t, *J* = 10.8 Hz, 1H), 6.37 (s, 1H), 6.67 (s, 3H), 6.71 (s, 1H), 6.88-6.99 (m, 3H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 11.34, 17.09, 19.63, 19.80, 20.47, 20.81, 21.46, 25.27, 26.37, 47.93, 61.76, 127.06, 128.76, 129.65, 129.72, 130.36, 132.80, 134.31, 134.56, 136.87, 137.15, 137.48, 137.88, 138.23, 140.46, 170.98, 171.44. IR (KBr): ν_{CO} = 1657.9, 1693.3 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{32}H_{37}N_2O_2$: 481.2850; Found: 481.2852. Anal. calcd. for $C_{32}H_{37}N_2O_2$: C, 79.96; H, 7.55; N, 5.83; Found: C, 79.98; H, 7.60; N, 5.68.

Synthesis of 2i. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, 4-methoxystyrene (26.8 μL, 0.027 g, 0.199 mmol, 1 eq) was added and the resultant mixture was heated to 60 °C for 16 h. After cooling the mixture to room temperature, the volatiles were removed under reduced pressure. Washing the residue with minimal chilled benzene followed by drying under reduced pressure afforded the desired product as a white solid (0.077 g, 0.151 mmol, 76% yield). mp = 187-189 °C (decomp.) ^{1}H NMR ($CDCl_3$, 300.14 MHz): δ 1.20 (dd, J = 9.9 Hz, 1H), 1.52-1.58 (m, overlapping singlet, 1H), 1.55 (s, 3H), 1.85 (s, 3H), 2.23 (s, 3H), 2.26 (s, 3H), 2.33 (s, 3H), 2.34 (s, 3H), 2.39 (s, 3H), 2.47 (dd, J = 10.8 Hz, 1H), 6.48 (s, 1H), 6.51-6.80 (4H), 6.85 (s, 1H), 6.92 (s, 1H), 6.95 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 11.37, 16.68, 19.35, 19.66, 20.32, 20.49, 20.81, 24.95, 25.33, 47.32, 55.31, 61.19, 113.63, 125.33, 128.60, 129.47, 129.65, 130.08, 131.74, 133.46, 136.04, 136.47, 137.51, 137.72, 138.24, 139.54, 158.80, 171.23, 171.61. IR (KBr): ν_{CO} = 1658.88, 1690.95 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{33}H_{39}N_2O_3$: 511.2961. Found: 511.2951. Anal. calcd. for CHNO: C, 77.61; H, 7.50; N, 5.49; Found: C, 77.39; H, 7.08; N, 5.14.

Synthesis of 2j. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, diethyl fumarate (32.6 μL, 0.034 g, 0.199

mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 2 h, after which the volatiles were removed under reduced pressure. Washing of the residual solid with minimal cold hexanes followed by drying under reduced pressure afforded the desired product as a white solid (0.102 g, 0.186 mmol, 93% yield). mp = 158-159 °C (decomp.) ^{1}H NMR (C_6D_6, 300.14 MHz): δ 0.69 (t, *J* = 7.05 Hz, 6H), 1.94 (s, 6H), 2.01 (s, 6H), 2.20 (s, 6H), 2.49 (s, 6H), 3.10 (s, 2H), 3.40 (m, 2H), 3.59 (m, 2H), 6.64 (s, 2H), 6.70 (s, 2H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 13.46, 19.66, 19.97, 20.57, 22.76, 29.73, 48.35, 61.70, 66.74, 129.53, 129.96, 132.98, 137.64, 138.44, 139.26, 165.14, 171.52. IR (KBr): ν_{CO} = 1666.0, 1697.1, 1715.4, 1745.1 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{32}H_{41}N_2O_6$: 549.2959; Found: 549.2958. Anal. calcd. for $C_{32}H_{40}N_2O_6$: C, 70.05; H, 7.35; N, 5.11; Found: C, 69.71; H, 7.32; N, 4.95.

Synthesis of 2k. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), cis-stilbene (0.5 mL, 2.8 mmol, 14.1 eq), and a stir bar. The resultant reaction mixture was then heated to 100 °C in an oil bath for 2 h. Afterward, the reaction mixture was cooled to room temperature and the product purified by silica gel column chromatography using 3:1 v/v hexanes/ethyl acetate as the eluent. Removal of the volatiles followed by drying under reduced pressure afforded the desired product as a white solid (0.042 g, 0.075 mmol, 38% yield). mp = 115-117 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.31 (s, 6H), 1.63 (s, 6H), 2.06 (s, 6H), 2.43 (s, 6H), 3.17 (s, 2H), 6.17 (s, 2H), 6.68-6.86 (overlapping singlets, 4H), 6.94 (t, J = 7.6 Hz, 4H), 7.01 (t, J = 7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.04, 19.92, 20.75, 22.97, 29.15, 47.06, 68.28, 126.60, 127.98, 129.05, 129.46, 132.85, 133.33, 135.54, 138.13, 138.43, 171.86. IR (KBr): ν_{CO} = 1658.1, 1691.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{38}H_{41}N_2O_2$: 557.3168. Found: 557.3165. Anal. calcd. for $C_{38}H_{40}N_2O_2$: C,81.98 ; H, 7.24; N, 5.03; Found: C, 82.04; H, 7.29; N, 5.02.

Synthesis of 2l. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), fumaronitrile (0.020 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. The resultant reaction mixture was stirred at ambient temperature for 2 h during which time a precipitate formed. The volatiles were removed under reduced pressure and the crude product washed with minimal cold toluene. The residue was dried under reduced pressure to afford the desired product as a white solid (0.047 g, 0.104 mmol, 52% yield). mp = 131-132 °C (decomp.) ^{1}H NMR (C_6D_6, 399.67 MHz): δ 1.58 (s, 6H), 1.84 (s, 6H), 1.99 (s, 6H), 2.26 (overlapping singlets, 8H), 6.53 (s, 2H), 6.73 (overlapping sing lets, 2H). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 13.92, 19.37, 20.43, 20.79, 22.72, 48.37, 64.08, 112.38, 130.37, 130.78, 130.85, 136.10, 139.88, 140.28, 170.80. IR (KBr): ν_{CN} = 2247.3 cm^{-1}; ν_{CO} = 1682.8 1714.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{28}H_{30}N_4O_2$: 454.2369. Found: 454.2365. Anal. calcd. for $C_{28}H_{29}N_4O_2$: C, 73.98; H, 6.65; N, 12.33; Found: C, 73.68; H, 6.58; N, 12.04.

Synthesis of 2m. A 25 mL Schlenk flask was charged with **1** (0.100 g, 0.266 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this flask, maleonitrile (0.020 g, 0.199 mmol, 1 eq) was added and the resultant reaction mixture stirred at ambient temperature for 2 h. The volatiles were then removed under reduced pressure and the crude product recrystallized from toluene. Drying under reduced pressure afforded the desired product as a white solid (0.054 g, 0.12 mmol, 45% yield). mp = 130-132 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.61 (s, 6H), 1.70 (s, 2H), 1.76 (s, 6H), 1.97 (s, 3H), 2.07 (s, 3H), 2.37 (s, 6H), 6.46 (s, 2H), 6.81 (s, 2H). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 13.35, 19.19, 20.63, 20.87, 20.94, 22.69, 48.42, 63.34, 111.56, 130.12, 130.22, 130.94, 131.34, 137.20, 138.98, 139.38, 140.38, 170.75, 170.95. IR (KBr): ν_{CN} = 2240.9 cm^{-1}; ν_{CO} = 1680.1, 1711.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{28}H_{30}N_4O_2$: 454.2369. Found: 454.2364.

Anal. calcd. for $C_{28}H_{29}N_4O_2$: C, 73.98; H, 6.65; N, 12.33; Found: C, 74.05; H, 6.56; N, 12.35.

Note: Although a 75% conversion of **1** to **2m** was observed by ^{1}H NMR spectroscopy, the isolation of the desired product in pure form was challenged by its high sensitivity toward water.

Synthesis of 2n. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), n-butyl vinyl ether (0.5 mL, 0.385 g, 3.84 mmol, 19.3 eq), and a stir bar. Afterward, the resultant reaction mixture was then heated to 100 °C in an oil bath for 2 h. The reaction mixture was then cooled to room temperature and the volatiles removed under reduced pressure. The residue was purified by silica gel column chromatography using 3:1 v/v hexanes/ethyl acetate as the eluent. Removal of the volatiles under reduced pressure afforded the desired product as a white solid (0.050 g, 0.104 mmol, 53% yield). mp = 162-163 °C. ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.72 (t, J = 7.4 Hz, 3H), 0.84 (m, 2H), 0.93-1.06 (m, 2H), 1.09-1.28 (m, 2H), 1.91 (s, 3H), 1.98 (s, 3H), 2.04 (s, 3H), 2.08 (s, 3H), 2.11 (s, 3H), 2.18 (s, 3H), 2.21 (s, 3H), 2.42 (s, 3H), 2.68 (m, 1H), 2.78 (m, 1H), 3.49 (t, J = 6.6 Hz), 6.65 (s, 1H), 6.67 (s, 1H), 6.68 (s, 1H), 6.77 (s, 1H). ^{13}C NMR (C_6D_6, 125.71 MHz): δ 13.87, 15.33, 19.41, 19.64, 20.18, 20.24, 20.53, 20.72, 20.77, 21.87, 23.88, 31.36, 49.19, 59.37, 59.74, 70.18, 128.85, 129.79, 130.10, 130.13, 133.74, 134.69, 136.50, 137.03, 137.80, 138.01, 139.98, 171.47, 172.45. IR (KBr): ν_{CO} = 1663.4, 1693.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{30}H_{41}N_2O_3$: 477.3117. Found: 477.3121. Anal. calcd. for $C_{30}H_{40}N_2O_3$: C, 75.59; H, 8.46; N, 5.88; Found: C, 75.57; H, 8.46; N, 5.89.

Synthesis of 2o. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), norbornene (0.120 g, 1.27 mmol, 6.4 eq), and a stir bar. The vial was heated to 120 °C in an oil bath for 2 h. Upon cooling to room temperature, the volatiles were removed under reduced pressure and the crude residue purified by silica gel column chromatography

using 3:1 v/v hexanes/ethyl acetate as the eluent. Removal of volatiles under reduced pressure afforded the desired product as a white solid (0.040 g, 0.085 mmol, 43% yield). mp = 204-206 °C (decomp.) ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 0.41 (d, J = 11.2 Hz, 1H), 0.76 (d, J = 11.2 Hz, 1H), 1.23 (d, J = 8.4 Hz, 2H), 1.42 (d, J = 8.4 Hz, 2H), 1.71 (s, 6H), 1.75 (s, 2H), 2.07 (s, 6H), 2.09 (s, 6H), 2.20 (overlapping singlets, 5H), 2.26 (s, 3H), 6.78 (s, 2H), 6.87 (s, 2H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 19.63, 20.63, 20.68, 20.79, 22.23, 29.40, 30.71, 36.89, 50.96, 62.06, 130.02, 134.47, 135.23, 136.20, 137.83, 174.20, 175.92. IR (KBr): ν_{CO} = 1669.4, 1700.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{38}N_2O_2$: 471.3012; Found: 471.3008. Anal. calcd. for $C_{28}H_{34}N_2O_3$: C, 79.11; H, 8.14; N, 5.95; Found: C, 79.03; H, 8.07; N, 6.03.

Synthesis of 2p. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), 1-octene (0.5 mL, 0.7 g, 6.23 mmol, 16 eq), and a stir bar. The resultant reaction mixture was heated to 100 °C for 2 h in an oil bath. The reaction mixture was then cooled to ambient temperature and purified by silica gel column chromatography using 3:1 v/v hexanes/ethyl acetate as the eluent. Removal of the volatiles under reduced pressure afforded the desired product as a white solid (0.046 g, 0.094 mmol, 47% yield). mp = 134-136 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 0.59 (dd, J = 7.6 Hz, 1H), 0.80 (t, J = 7.2 Hz, 3H), 0.98 (dd, J = 9.2 Hz, 1H), 1.02-1.26 (m, 10H), 1.59 (overlapping peaks, 4H), 1.79 (s, 3H), 2.13 (s, 3H), 2.17 (s, 3H), 2.24 (s, 3H), 2.25 (s, 6H), 2.28 (s, 3H), 6.85-6.87 (overlapping singlets, 3H), 6.90 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 14.01, 14.58, 19.49, 19.63, 19.76, 20.50, 20.78, 20.84, 20.89, 22.46, 22.98, 23.91, 27.62, 28.69, 29.55, 31.42, 47.67, 60.14, 129.33, 129.64, 129.67, 129.93, 132.14, 134.01, 136.29, 136.65, 137.39, 137.46, 137.60, 137.96, 171.87, 171.94. IR (KBr): ν_{CO} = 1654.0, 1691.8 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{45}N_2O_2$: 489.3481. Found: 489.3481. Anal. calcd. for $C_{32}H_{45}N_2O_2$: C, 78.65; H, 9.07; N, 5.73; Found: C, 78.38; H, 8.92; N, 5.68.

Synthesis of 3a. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, methyl vinyl ketone (16.6 μL, 0.014 g, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 2 h after which the volatiles were removed under reduced pressure. Washing of the residual solid with minimal cold hexanes and drying under reduced pressure afforded the desired product as a white solid (0.086 g, 0.193 mmol, 96% yield). mp = 181-182 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 1.44 (d, *J* = 1.2 Hz, 3H), 1.94 (s, 3H), 2.04 (s, 3H), 2.05 (s, 6H), 2.16 (s, 6H), 2.34 (s, 6H), 2.66 (t, *J* = 2.0 Hz, 2H), 3.50 (q, J = 1.2 Hz, 1H), 6.68 (s, 2H), 6.75 (s, 2H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 13.72, 18.71, 19.51, 20.83, 23.56, 27.07, 36.84, 47.88, 93.87, 107.58, 129.05, 130.49, 134.82, 137.63, 137.85, 138.07, 151.52, 172.31. IR (KBr): ν_{CO} = 1666.4, 1700.9 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{28}H_{35}N_2O_3$: 447.2642; Found: 447.2644. Anal. calcd. for $C_{28}H_{34}N_2O_3$: C, 75.31; H, 7.67; N, 6.27; Found: C, 75.42; H, 7.65; N, 6.40.

Synthesis of 3b. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this vial, 3-methyl-3-penten-2-one (22.3 μL, 0.020 g, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 2 h after which the volatiles were removed under reduced pressure. Washing of the residual solid with minimal cold hexanes followed by drying under reduced pressure afforded the desired product as a white solid (0.088 g, 0.185 mmol, 93% yield). mp = 183-184 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.38 (d, *J* = 7.6 Hz, 3H), 0.77 (s, 3H), 1.42 (m, 3H), 1.97 (s, 3H), 2.05 (s, 3H), 2.07 (s, 3H), 2.26 (s, 3H), 2.27-2.28 (9H), 3.34 (m, 1H), 6.66 (s, 1H), 6.70 (s, 1H), 6.72 (s, 1H), 6.74 (s, 1H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 8.75, 11.43, 14.26, 18.96, 19.46, 19.74, 19.97, 20.80, 25.48, 26.84, 47.77, 48.39, 106.88, 107.12, 128.85, 129.03, 130.20, 130.30, 135.78, 136.64, 137.522, 137.54, 137.69, 137.96, 138.26, 138.88, 142.81, 173.50, 174.43. IR (KBr): ν_{CO} = 1663.6, 1699.8 cm^{-1}.

HRMS (ESI): $[M+H]^+$ calcd. for $C_{30}H_{39}N_2O_3$: 475.2955; Found: 475.2958. Anal. calcd. for $C_{30}H_{38}N_2O_3$: C, 75.92; H, 8.07; N, 5.90; Found: C, 76.30; H, 8.09; N, 5.90.

Synthesis of 3c. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), C_6D_6 (0.75 mL), and a stir bar. To this flask, acrolein (8.2 μL, 0.008 g, 1 eq) was added and the resultant solution stirred at ambient temperature for 16 h to afford a 5 : 1 ratio of **4g** : **3c**. This solution was then stirred at ambient temperature for 2 weeks after which removal of the volatiles, washing with cold hexanes, and drying under reduced pressure afforded **3c** as a white solid (0.072 g, 0.169 mmol, 84% yield). mp = 183-185 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.92 (s, 3H), 2.01 (s, 3H), 2.05 (s, 6H), 2.13 (s, 6H), 2.32 (s, 6H), 2.61 (t, J = 2.5 Hz, 2H), 3.77 (q, J = 2.5 Hz, 1H), 3.66 (q, J = 2.5 Hz, 1H), 6.67 (s, 2H), 6.75 (s, 2H). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 18.82, 19.35, 20.83, 23.41, 27.00, 35.45, 47.84, 98.85, 107.78, 129.05, 130.74, 134.83, 137.51, 137.92, 138.17, 142.74, 172.24. IR (KBr): ν_{CO} = 1667.6, 1700.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{27}H_{33}N_2O_3$: 433.2491. Found: 433.2489. Anal. calcd. for $C_{27}H_{33}N_2O_3$: C, 74.97; H, 7.46; N, 6.48; Found: C, 74.86; H, 7.43; N, 6.34.

Spectroscopic data for 4g. mp = 87-90 °C (decomp). ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.85 (s, 3H), 1.87 (s, 3H), 2.03 (s, 3H), 2.05 (s, 3H), 2.10 (s, 3H), 2.19 (s, 3H), 2.35 (s, 3H), 2.37 (s, 3H), 3.35 (d, J = 7.8 Hz, 1H), 4.22 (m, 1H), 4.36 (d, J = 10.5 Hz, 1H), 4.58 (d, J = 16.8 Hz, 1H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 18.82, 18.84, 18.87, 18.95, 20.86, 20.89, 21.47, 27.17, 48.22, 65.59, 82.97, 120.22, 129.19, 129.38, 129.38, 130.00, 130.12, 130.45, 132.73, 133.54, 136.67, 137.67, 138.30, 138.51, 138.79, 172.10, 172.62. IR (KBr): ν_{CO} = 1675.1, 1713.7 cm^{-1}.

Synthesis of 4a. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this flask, benzaldehyde (20.3 μL, 0.021 g, 0.199 mmol, 1 eq) was added and the resultant solution was stirred at ambient

temperature for 2 h during which time the solution became cloudy. Removal of volatiles under reduced pressure and washing with minimal cold hexanes followed by drying under reduced pressure afforded the desired product as a white solid (0.092 g, 0.191 mmol, 96% yield). mp = 165-166 °C (decomp.) ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.85 (s, 6H), 1.86 (s, 3H), 1.91 (s, 3H), 2.05 (s, 3H), 2.33 (s, 3H), 2.36 (s, 3H), 2.43 (s, 3H), 4.03 (s, 1H), 5.89 (s, 1), 6.46 (s, 1H), 6.52-6.61 (m, 4H), 6.67-6.71 (m, 2H), 6.75 (s, 1H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 18.82, 18.90, 18.97, 19.00, 20.61, 20.89, 22.17, 26.81, 47.97, 64.83, 83.33, 124.92, 126.15, 127.29, 128.53, 128.84, 129.52, 130.44, 131.45, 131.81, 132.89, 136.40, 136.59, 137.46, 138.05, 138.37, 138.52, 172.03, 172.40. IR (KBr): ν_{CO} = 1677.5, 1708.5 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{35}N_2O_3$: 483.2642. Found: 483.2648. Anal. calcd. for $C_{31}H_{34}N_2O_3$: C, 77.15; H, 7.10; N, 5.80; Found: C, 77.03; H, 7.25; N, 5.80.

Synthesis of 4b. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), 4-nitrobenzaldehyde (0.030 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. The resultant solution was then stirred at ambient temperature for 2 h. Removal of the volatiles under reduced pressure and washing with a 3:1 v/v mixture of toluene/pentane followed by drying under reduced pressure afforded the desired product as an off-white solid (0.094 g, 0.178 mmol, 89% yeild). mp = 115-117 °C (decomp.) ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.67 (s, 3H), 1.75 (s, 3H), 1.79 (s, 3H), 1.84 (s, 3H), 2.07 (s, 3H), 2.20 (s, 3H), 2.25 (s, 3H), 2.38 (s, 3H), 3.82 (s, 1H), 5.62 (s, 1H), 6.26-6.31 (broad doublet overlapping a singlet, 3H), 6.73 (s, 1H), 6.78 (s, 1H), 7.38 (bd, J = 8.4 Hz, 2H). ^{13}C NMR (C_6D_6, 75.47 MHz): 18.62, 18.71, 18.78, 20.35, 20.88, 21.82, 27.07, 47.93, 64.02, 83.61, 122.19, 125.33, 128.70, 129.62, 129.65, 130.58, 131.54, 132.63, 136.35, 136.39, 137.40, 137.94, 138.36, 138.95, 139.43. IR (KBr): ν_{NO2} = 1340.9, 1521.6 cm^{-1}; ν_{CO} = 1682.5, 1715.5 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd for $C_{31}H_{34}N_3O_5$: 528.2498;

Found: 528.2496. Anal. calcd. for $C_{31}H_{33}N_3O_5$: C, 70.57; H, 6.30; N, 7.96; Found: C, 70.43; H, 6.29; N, 7.91.

Synthesis of 4c. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this flask, 4-methoxybenzaldehyde (24.2 μL, 0.27 g, 0.199 mmol, 1 eq) was added and the resultant solution was stirred at ambient temperature for 2 h. Removal of the volatiles under reduced pressure, washing with minimal cold hexanes and drying under reduced pressure afforded the desired product as a white solid (0.086 g, 0.168 mmol, 84% yield). mp = 123-125 °C (decomp.) ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.85 (s, 3H), 1.88 (s, 6H), 1.93 (s, 3H), 2.05 (s, 3H), 2.34 (s, 3H), 2.39 (s, 3H), 2.44 (s, 3H), 3.19 (s, 3H), 4.05 (s, 1H), 5.98 (s, 1H), 6.21 (d, J = 8.7 Hz), 6.45-6.48 (doublet overlapping singlet, 3H), 6.70 (s, 1H), 6.76 (s, 1H). ^{13}C NMR (C_6D_6, 75.47 MHz): 18.87, 18.93, 19.01, 19.09, 20.62, 20.89, 22.10, 26.87, 48.02, 54.66, 64.82, 82.96, 112.98, 123.49, 126.06, 128.87, 129.51, 129.57, 130.45, 131.84, 132.96, 136.40, 136.54, 137.38, 137.86, 138.36, 138.47, 158.93, 172.08, 172.50. IR (KBr): ν_{CO} = 1679.2, 1711.8 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd for $C_{32}H_{37}N_2O_4$: 513.2748; Found: 513.2750. Anal. calcd. for $C_{32}H_{36}N_2O_4$: C, 74.97; H, 7.08; N, 5.46; Found: C, 75.08; H, 7.20; N, 5.54.

Synthesis of 4d. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this flask, cyclohexanecarboxaldehyde (24.1 μL, 0.022 g, 0.199 mmol, 1 eq) was added and the resultant solution stirred at ambient temperature for 2 h. Removal of the volatiles under reduced pressure followed by recrystallization of the residue from hexanes afforded the desired product as a white solid (0.061 g, 0.125 mmol, 63% yield). mp = 134-136 °C (decomp.) ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ .-0.01 (bq, J = 10.4 Hz, 1H), 0.39-0.70 (m, 4H), 0.85 (m, 1H), 1.10 (bd, J = 10 Hz, 1H), 1.38 (d, J = 10.8 Hz, 3H), 1.45 (m, 1H), 1.58 (s, 3H), 1.91 (s, 3H), 2.22-

2.28 (18H), 2.39 (d, J = 10.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.47MHz): δ 18.61, 18.62, 18.83, 19.11, 20.67, 20.91, 20.96, 24.78, 25.71, 26.72, 29.08, 29.78, 34.83, 48.01, 69.38, 82.51, 129.17, 129.23, 129.47, 130.08, 132.10, 132.48, 135.76, 136.31, 137.42, 138.01, 138.42, 138.81, 172.66, 173.41. IR (KBr): ν_{CO} = 1678.4, 1713.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{41}N_2O_3$: 489.3118; Found: 489.3117. Anal. calcd. for $C_{31}H_{40}N_2O_3$: C, 76.19; H, 8.25; N, 5.73; Found: C, 76.21; H, 8.12; N, 5.40.

Synthesis of 4e. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this flask, acetaldehyde (33.4 μL, 0.026 g, 0.598 mmol, 3 eq) was added and the resultant solution stirred at ambient temperature for 24 h during which time a white precipitate formed. Removal of volatiles under reduced pressure and washing the residue with chilled benzene afforded the desired product as a white solid (0.079 g, 0.188 mmol, 94% yield). mp = 167-168 °C (decomp.) ^{1}H NMR ($CDCl_3$, 300.14 MHz): δ 0.46 (d, J = 6.0 Hz, 3H), 1.58 (s, 3H), 1.91 (s, 3H), 2.22-2.26 (overlapping singlets, 18H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 13.32, 18.49, 18.59, 18.80, 18.98, 20.62, 20.93, 20.99, 26.97, 47.95, 60.93, 80.99129.23, 129.33, 130.02, 130.10, 131.89, 132.12, 1356.00, 136.37, 137.59, 137.70, 138.49, 138.87, 172.69, 173.30. IR (KBr): ν_{CO} = 1673.2, 1709.6 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{26}H_{33}N_2O_3$: 421.2491. Found: 421.2488. Anal. calcd. for CHNO: C, 74.26; H, 7.67; N, 6.66; Found: C, 73.87; H, 7.37; N, 6.17.

Synthesis of 4f. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (0.75 mL), and a stir bar. To this flask, cinnamaldehyde (25 μL, 0.026 g, 0.199 mmol, 1 eq) was added and the resultant solution was stirred at ambient temperature for 2 h. Removal of volatiles under reduced pressure, washing with minimal cold hexanes, and drying under reduced pressure afforded the desired product as a white solid (0.098 g, 0.193 mmol, 97% yield). mp = 77-78 °C (decomp.) ^{1}H NMR (C_6D_6,

400.27 MHz): δ 1.87 (s, 3H), 1.91 (s, 3H), 2.03 (s, 3H), 2.05 (s, 3H), 2.09 (s, 3H), 2.25 (s, 3H), 2.41 (s, 3H), 2.43 (s, 3H), 3.57 (dd, *J* = 8.8 Hz, 1H), 4.51 (dd, *J* = 12.0 Hz, 1H), 5.95 (d, *J* = 16.4 Hz, 1H), 6.45 (s, 1H), 6.60 (m, 2H), 6.70 (s, 1H), 6.77 (s, 1H), 6.78 (s, 1H), 6.93-6.98 (m, 3H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 18.82, 18.93, 18.95, 20.80, 20.91, 21.37, 27.33, 48.29, 65.90, 83.01, 121.53, 127.06, 128.42, 129.49, 129.81, 130.16, 130.53, 132.88, 133.36, 135.59, 135.82, 136.83, 137.31, 138.36, 138.44, 138.60, 138.81, 172.17, 172.64. IR (KBr): ν_{CO} = 1677.0, 1711.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{33}H_{37}N_2O_3$: 509.2799; Found: 509.2804. Anal. calcd. for $C_{33}H_{36}N_2O_3$: C, 77.92; H, 7.13; N, 5.51; Found: C, 78.13; H, 7.08; N, 5.46.

Isomerization of Methyl Angelate. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), C_6D_6 (0.7 mL), and a stir bar. To this vial, methyl angelate (24 μL, 0.023g, 0.200 mmol, 1 eq) was added. The resultant reaction vessel was then sealed and heated to 60 °C for 16 h in an oil bath. The ratio of methyl angelate : methyl tiglate was determined by comparing the ratio of the integrals of the signal assigned to the methyl group in methyl angelate observed at δ = 3.36 ppm with the signal assigned to the methyl group in methyl tiglate at δ = 3.42 ppm. The signal assignments were verified via comparison with authentic samples. As a control experiment, an 8 mL vial was charged with C_6D_6 (0.7 mL), methyl angelate (24 μL, 0.023g, 0.200 mmol, 1 eq), and a stir bar. The reaction vessel was then sealed and heated to 100 °C for 24 h in an oil bath. The ratio of methyl angelate : methyl tiglate was determined as described above.

Exchange Studies. The ratio of **2j**:**4a** was measured by comparing the ratio of the integrals of the signals associated with the epoxide group found in **4a** (δ = 4.02 ppm; singlet; 1H) with the integral of the methylene found in **2j** (δ 3.42; multiplet; 2H). Note that the latter integral was divided by two to account for the two sets of hydrogen atoms.

Conversion of 2j to 4a. An 8 mL vial was charged with **1** (0.050 g, 0.133 mmol), C_6D_6 (0.75 mL), and a stir bar. To this vial, diethyl fumarate (25 μL, 0.152 mmol, 1.15 eq) was added, and the resultant solution stirred at ambient temperature for 30 min. Benzaldehyde (15.5 μL, 0.016 g, 0.152 mmol, 1.15 eq) was added and the ratio of the products were immediately determined by ^{1}H NMR spectroscopy as described above. The solution was subsequently heated in the NMR tube for 16 h at 80 °C in an oil bath after which time the product mixture was measured by ^{1}H NMR spectroscopy.

Conversion of 4a to 2j. An 8 mL vial was charged with **1** (0.050 g, 0.133 mmol), C_6D_6 (0.75 mL), and a stir bar. To this vial, benzaldehdye (15.5 μL, 0.152 mmol, 1.15 eq) was added, and the resultant solution stirred at ambient temperature for 30 min. Diethyl fumarate (25 μL, 0.152 mmol, 1.15 eq) was added and the ratio of products was immediately determined by ^{1}H NMR spectroscopy as described above. The solution was heated in the NMR tube for 16 h at 80 °C in an oil bath after which the product mixture was measured by ^{1}H NMR spectroscopy.

1 + diethyl maleate + benzaldehyde. A stock solution of 1:1 benzaldehyde/diethyl maleate in C_6D_6 was prepared by adding diethyl maleate (100 mL, 0.61 mmol) and benzaldehdye (62 mL, 0.608 mmol) to C_6D_6 (1.0 mL). Separately, an 8 mL vial was charged with **1** (0.050 g, 0.133 mmol), C_6D_6 (0.5 mL), and a stir bar. To this stirring suspension was added all at once 0.25 mL of the freshly prepared stock solution of benzaldehyde/diethyl fumarate (0.152 mmol, 1.15 eq), and the resultant solution stirred at ambient temperature for 30 min. The product mixture was then determined by ^{1}H NMR spectroscopy as described above. The solution was then heated in the NMR tube for 16 h at 80 °C in an oil bath whereupon the product mixture was re-measured by ^{1}H NMR spectroscopy.

Hydrolysis of 2h. A 30 mL vial was charged with **2h** (0.500 g, 1.04 mmol) and a stir bar. To this was added glacial acetic acid (3.3 mL) followed by concentrated hydrochloric acid (3.3 mL) at 0 °C. The vial was then sealed and heated to 100 °C for 16 h during which time the solid dissolved. The reaction was cooled to room temperature, made basic with 3M NaOH, and extracted with diethyl ether (100 mL) three times. The aqueous layer was acidified with 10% HCl and extracted with diethyl ether (100 mL) three times. This organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The residue was recrystallized from 1:3 $CHCl_3$/hexanes at –20 °C. The crystalline solid was washed with pentane to afford 3-(mesitylamino)-2,2-dimethyl-3-oxopropanoic acid as a white solid (0.049 g, 0.197 mmol, 19% yield). Concentration of the filtrate and recrystallization from pentane afforded hydrocinnamic acid as a white solid (0.087 g, 0.579 mmol, 56% yield). Similar results were obtained when the reaction was performed for 2 h under otherwise identical conditions.

Characterization data for 3-(mesitylamino)-2,2-dimethyl-3-oxopropanoic acid: mp = 146-147 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 1.67 (s, 6H), 2.10 (s, 6H), 2.24 (s, 3H), 6.85 (s, 2H), 7.66 (s, 1H), 9.40 (bs, 1H). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 16.96, 21.91, 25.19, 50.06, 129.99, 131.06, 135.96, 138.46, 173.69, 178.29. IR (KBr): ν_{COOH} = 3291.3; ν_{CO} = 1653.0, 1718.5 cm^{-1}. HRMS (CI): $[M\text{-}H^-]^+$ calcd. for $C_{14}H_{18}NO_3$: 248.1287; Found: 248.1286.

Spectral data for hydrocinnamic acid (in agreement with literature values):[51] ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 2.67 (t, J = 7.8Hz, 2H), 2.95 (t, J = 7.8 Hz, 2H), 7.18-7.22 (m, 3H), 7.25-7.31 (m, 2H). ^{13}C NMR ($CDCl_3$, 399.68 MHz): δ 31.57, 36.46, 127.37, 129.25, 129.55, 141.13, 179.37. HRMS (CI): $[M\text{-}H^-]^+$ calcd. for $C_9H_9O_2$: 149.0603; Found: 149.0603.

Kinetics and Hammett Plots. To gain mechanistic insight into the cyclopropanation reactions, the cycloaddition between **1** and each of the aforementioned styrene derivatives (10 eq) was monitored over time by ^{1}H NMR spectroscopy (15 °C, C_7D_8). A strong, positive correlation between the pseudo-first order rate constants was measured for each reaction and the respective Hammett σ substituent constants (ρ = 1.64; see Figures A3-A8) revealed a significant buildup of negative charge at the benzylic carbon of the styrene derivative. In these experiments, a 0.133 M stock solution of **1** was first prepared by dissolving **1** (0.210 g, 0.558 mmol) in C_7D_8 (4.2 mL). An NMR tube equipped with a screw-cap septum was then charged inside a glove box with the stock solution of **1** (0.6 mL, 0.08 mmol) and a sufficient quantity of C_7D_8 such that the final volume reached 0.8 mL upon the addition of 10 eq of the styrene derivative analyzed. The resultant sample was then equilibrated in the NMR probe at 15 °C. Upon equilibration, the sample was ejected from the instrument and 0.8 mmol (10 eq) of the appropriate styrene derivative added via syringe. The NMR tube was then vigorously shaken to ensure mixing, and the sample was reinserted into the NMR probe. After shimming, 4 scan spectra were run every 30 seconds for 1 h. The conversion to the cyclopropanated product (**2e-i**, Figure S1) was measured by comparing the ratio of the ^{1}H NMR integrals assigned to the methyl protons of **1** at δ = 1.48 ppm (s, 6H) with the corresponding product methyl protons at ca. 1.02-1.19 ppm (s, 3H). Note, to account for the differing number of hydrogen atoms in each compound, the latter integral was doubled prior to computing the integral ratio. Additionally, pseudo-first order rate constants were determined for these reactions by plotting the ln [**1**] versus time (Figures S2-S6). A linear fit of all data points, except in the case of **2e** wherein only the data for <97.5% conversion was utilized, provided the observed rate for each reaction as determined by the negative slope. Subsequently, these observed rates were utilized to

construct a Hammett plot by plotting the log of the relative rate for a given styrene derivative and **1** compared to the reaction of **1** with styrene (i.e., log (K/K_H)) versus its Hammett σ value (see Table A4 and Figure A9). A linear fit of these data was used to calculate the Hammett σ value from the slope of the fitted line.

3.5 ACKNOWLEDGEMENTS

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Chapter 4: Alkyne and Reversible Nitrile Activation: *N,N′*-Diamidocarbene-Facilitated Synthesis of Cyclopropenes, Cyclopropenones, and Azirines*

4.1 INTRODUCTION

As members of the smallest unsaturated carbo- and heterocycles, cyclopropenes and azirines have attracted considerable interest for their unique structural characteristics.[1] Indeed, the high degree of ring strain possessed by these species has enabled them to serve many roles in the synthesis of substituted alkynes, allenes, heterocycles, and other important substrates.[2-6] Cyclopropenes are typically prepared via the metal-mediated addition of electrophilic carbenes to alkynes or the 1,2-elimination of halocyclopropanes.[1,3,4,7,8] In contrast, azirines are often synthesized *in situ* using the Neber rearrangement of activated oximes or via the pyrolysis/photolysis of vinyl azides.[2,9-11] A practical and atom economical alternative to the aforementioned methods is the [2+1] cycloaddition of isolable carbenes with alkynes or nitriles. Unfortunately, such synthetic approaches are relatively unexplored, largely due to a lack of suitable carbenes. For example, Arduengo has shown that exposure of *N,N'*-dimesityl-4,5-dihydroimidazol-2-ylidene (SIMes), a well-known, stable, and basic[12] *N*-heterocyclic carbene (NHC),[13] to acetylene (see Figure 4.1, top) or acetonitrile resulted in formal C–H insertion rather than cycloaddition.[14] Indeed, Bertrand's phosphinosilyl carbene[15,16] is the only stable carbene known to undergo chelotropic reactions with compounds possessing triple bonds and may be limited to phosphaalkynes (R-C$\equiv$P) and aryl nitriles (Ar-C$\equiv$N).[17-21]

Herein, we disclose that the *N,N′*-diamidocarbene (DAC)[22-31] **1** is the first isolable carbene to undergo formal [2+1] cycloadditions with alkynes as well as alkyl and aryl

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nitriles. DACs are an emerging class of stable carbenes that display many reactivities often expected from *in situ* generated electrophilic carbenes, such as methylene.[22-31] Simply exposing **1**, which can be isolated in one step from the condensation product of *N,N′*-dimesitylformamidine and dimethylmalonyl dichloride,[25] to various alkynes was found to afford the corresponding diamidocyclopropenes in high yields. These products were successfully hydrolyzed to afford cyclopropenones or α,β-unsaturated acids.[32] Additionally, treatment of **1** with aryl or alkyl nitriles resulted in the first examples of forming 2*H*-azirines in a reversible fashion.[33] In all cases, the cycloaddition reactions were found to proceed rapidly to high conversions under mild conditions.

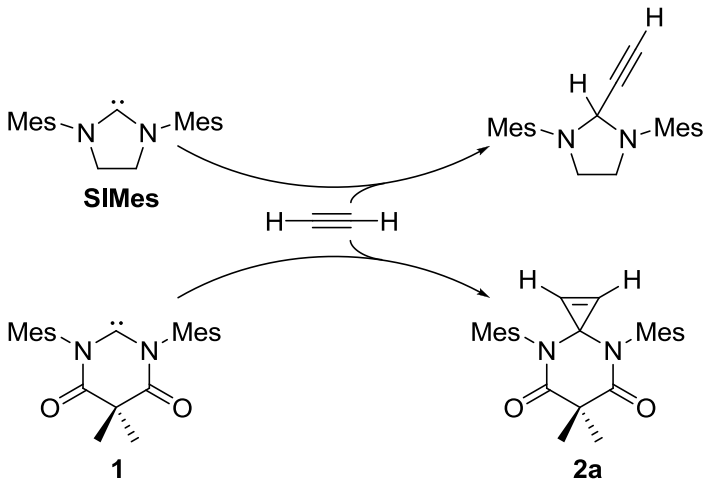


Figure 4.1: (top) Exposure of SIMes to acetylene afforded the formal C–H insertion product shown.[7] Conditions: 1.1 equiv. acetylene, THF, -196 to 23 °C, 16 h (93% yield).[7] (bottom) Exposure of DAC **1** to acetylene afforded the cyclopropene **2a**. Conditions: 1 atm acetylene, C_6H_6, 23 °C, 8 h (81% yield). Mes = 2,4,6-trimethylphenyl.

4.2 Results and Discussion

Our initial experiments explored the reaction of **1** with acetylene. Stirring a solution of **1** in C_6H_6 ($[\mathbf{1}]_o$ = 0.13 M) under 1 atm of acetylene for 8 h at ambient

temperature resulted in the formation of a cloudy solution that, upon concentration and washing with diethyl ether, afforded a white solid in 81% yield.[34] The isolated product was identified as the cyclopropene **2a** (Figure 4.1, bottom), in part based on the appearance of signals associated with a strained olefin observed at δ 7.23 ppm (2H) and 117.9 ppm ($CDCl_3$) in the compound's ^{1}H NMR and ^{13}C NMR spectra, respectively. As shown in Figure 4.2, the structure of **2a**, which constitutes a rare[35] example of a diamidocyclopropene, was unambiguously elucidated by single crystal X-ray diffraction analysis.

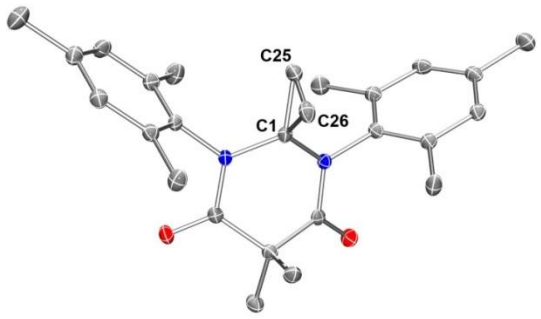
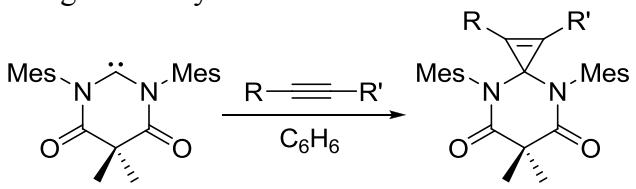


Figure 4.2: ORTEP diagram of **2a** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): C1-C25, 1.464(2); C1-C26, 1.471(2); C25-C26, 1.285(2); C25-C1-C26, 51.90(10); C26-C25-C1, 64.32(11); C25-C26-C1, 63.78(11).

As summarized in Table 4.1, DAC **1** was found to undergo [2+1] cycloadditions with a variety of terminal, internal, aryl, alkyl, and silyl functionalized alkynes to give the respective cyclopropenes in good to excellent isolated yields (68-97%). In general, the terminal alkynes were reacted at equimolar concentration with **1** ($[\mathbf{1}]_0$ = 0.20 M) in C_6H_6 for 16 h at 23 °C, whereas the internal alkynes were stirred at 60 °C using two equiv. of alkyne under otherwise identical conditions. With the exception of **2h**, all of the cyclopropenes synthesized were found to be high melting point solids (mp > 140 °C) and

stable to the ambient atmosphere. Regardless, in all cases, no competitive alkyne C–H insertion processes were observed, and the cyclopropenes formed constituted the first examples of their kind arising from alkynes and an isolable carbene.



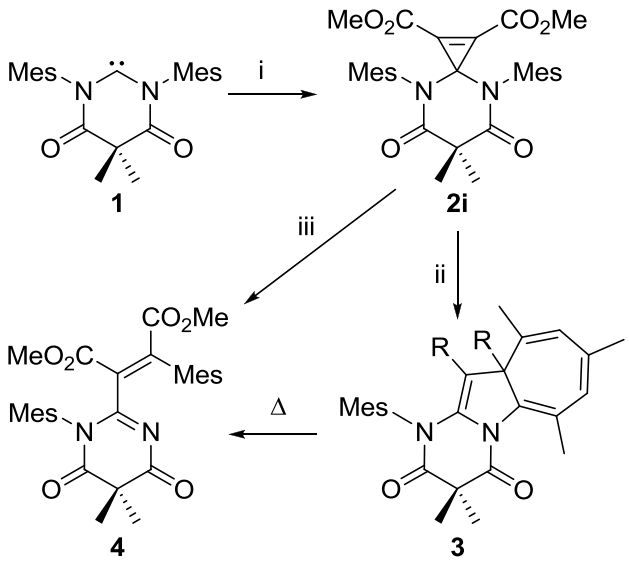
1 **2a-h**

Product	Alkyne	Isolated Yield[b]
2a	H—≡—H	81%[c]
2b	H—≡—4-^{t}BuPh	74%
2c	H—≡—Cy	68%[d]
2d	H—≡—Bu	93%[d]
2e	—≡—Pr	89%[e]
2f	Ph—≡—Et	97%
2g	Ph—≡—Ph	92%[e]
2h	—≡—TMS	93%[e]

Table 4.1: Summary of the [2+1] Cycloadditions of the DAC **1** with Various Alkynes.[a] Unless otherwise noted, all reactions were performed in C_6H_6 at 23 °C for 16 h using equimolar concentrations of **1** ($[\mathbf{1}]_o$ = 0.2 M) and the alkyne shown. [b] Isolated yield of the corresponding cyclopropene product. Conditions: [c] 1 atm acetylene, $[\mathbf{1}]_o$ = 0.13 M, 8 h. [d] 60 °C. [e] $[alkyne]_o$ = 0.4 M, 60 °C. ^{t}Bu = tert-butyl. Ph = phenyl. Cy = cyclohexyl. Bu = butyl. Pr = propyl. Et = ethyl.

While the aforementioned reactions afforded stable cyclopropenes as the sole products, the outcome of the reaction of **1** with an electron deficient alkyne, dimethyl acetylenedicarboxylate (DMAD), was found to be time dependent (Scheme 4.1). Stirring

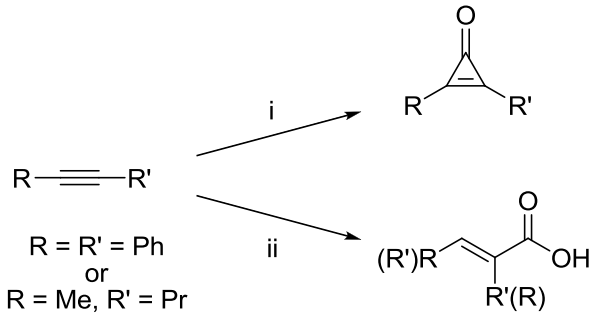
1 with a stoichiometric quantity of DMAD in C_6D_6 at 23 °C for 5 min afforded the cyclopropene product **2i** (97% isolated yield) as evidenced, in part, by a diagnostic signal observed at δ 125.8 ppm in the ^{13}C NMR spectrum acquired for this compound. However, when the same reaction was allowed to proceed for more than 30 min at 23 °C, a second product which exhibited upfield ^{1}H and ^{13}C NMR shifts (^{1}H: δ 5.98 and 6.14 ppm; ^{13}C: δ 119.58 and 121.05 ppm) gradually formed. The new spectroscopic signals were consistent with a loss of aromaticity and the formation of the fused cycloheptatriene **3**. The structural assignment was subsequently confirmed by single crystal X-ray diffraction analysis following isolation of the product (41% yield; Figure A21). Additionally, heating either **2i** or **3** at 60 °C for 12 h resulted in the formation of a third product that displayed downfield ^{1}H NMR shifts (δ 6.54 (2H) and 6.62 (2H)) as well as a lack of olefinic ^{13}C NMR signals. In agreement with these data, single crystal X-ray diffraction analysis (see Figure A22) of the isolated solid (80% yield based on **1**) revealed this compound to be the conjugated alkylideneamide **4**. We believe the overall transformation of **2i** to **4** was driven by the ring-opening rearrangement of the cyclopropene to a norcaradiene derivative that underwent electrocyclic ring expansion to its respective cycloheptatriene (**3**),[36] and ultimately rearrangement to its more stable isomer **4**. Regardless, the overall transformation represents a novel, metal-free C-C bond forming reaction that involved the migration of a sterically-hindered aryl group.



Scheme 4.1: The reaction of **1** with dimethyl acetylenedicarboxylate (DMAD) initially formed cyclopropene **2i**, followed by ring expansion to **3** and subsequent isomerization to the alkylideneamide **4**. Conditions: i) DMAD (1 equiv.), C_6H_6, 23 °C, 5 min, 97% yield; ii) C_6H_6, 23 °C, 40 h, 41% yield from **1**; R = CO_2Me; iii) C_6H_6, 60 °C, 12 h, 80% yield from **1**.

Considering that the carbene center in **1** is in the same oxidation state as the carbon atom in carbon monoxide, a gas reluctant to undergo [2+1] cycloaddition reactions,[16] we reasoned that hydrolysis of the aforementioned *N,N*-diamidocyclopropenes would provide a new synthetic route[32,39] to cyclopropenones, substrates desired for their utility in preparing heterocycles, cyclopropenyliums, and other unsaturated carbonyl species.[39,40] To test this hypothesis, **2g** was heated to 80 °C in a 1:1 v/v mixture of glacial acetic acid and concentrated HCl for 2 h. Following purification over silica gel, 2,3-diphenylcyclo-propenone was isolated in 66% yield (Scheme 4.2, Route i). Although no ring-opened products were observed under these conditions, heating **2g** at 100 °C for 48 h in the same acid mixture followed by extraction afforded *trans*-α-phenylcinnamic acid, albeit in modest yield (32%, Scheme 4.2, Route ii). Similarly, hydrolysis of **2e** afforded either 2-methyl-3-propylcyclopropenone (70%) or a

mixture of the isomeric ring-opened carboxylic acids, *trans*-2-methylhex-2-enoic acid and *trans*-2-ethylidenepentanoic acid (53:47, respectively; 43% overall yield), depending on the reaction conditions employed. Considering the relatively few methods[39b,c] to prepare dialkylcyclopropenones in an efficient manner, especially compared to their diaryl analogues, the synthesis of 2-methyl-3-propylcyclopropenone in a single vessel and good yield is particularly noteworthy and underscores the ability of DACs to serve as an equivalent to CO in useful cycloaddition reactions.

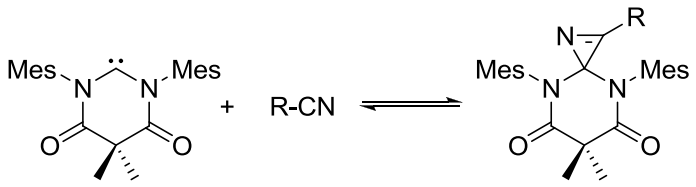


Scheme 4.2: Treatment of various alkynes with **1** followed by hydrolysis of the resultant cyclopropene (e.g., **2e** and **2g**) under acidic conditions enabled selective access of the corresponding cyclopropenone or α,β-unsaturated acid(s) depending on the reaction temperature and time. Conditions: i) **1**, C_6H_6, 60 °C, 16 h then 50:50 v/v HCl/AcOH, 80 °C, 2 h (66-70% yield); ii) **1**, C_6H_6, 60 °C, 16 h then 50:50 v/v HCl/AcOH, 100 °C, 48 h (32-43% yield).

Having successfully demonstrated that DAC **1** is a suitable [2+1] cycloaddition partner for alkynes, subsequent attention shifted toward studying the reaction of **1** with nitriles, another class of substates that contain triple bonds.[41] The addition of excess benzonitrile (2 equiv.) to **1** in C_6D_6 ($[\mathbf{1}]_o$ = 0.09 M) at 23 °C for 2 h afforded a product that displayed NMR signals consistent with the formation of 2*H*-azirine **5a**. For example, ^{13}C NMR analysis of the abovementioned reaction mixture revealed a signal at δ 167.6 ppm (C_6D_6) that was diagnostic[17-21,42] of a 1:1 cycloadduct of the nitrile and the DAC as

opposed to an ylide.[43] To our surprise, attempts to isolate the azirine product by removing the residual solvent under vacuum followed by washing with pentane returned the starting material, **1**. Similar results were obtained with other functionalized derivatives of benzonitrile as well as acetonitrile. Collectively, these observations suggested to us that the interaction between the DAC and the aforementioned nitriles was reversible (see below). Nevertheless, the formation of a 2*H*-azirine product was later unequivocally determined by single crystal X-ray diffraction analysis of **5c** (see Figure 4.3).

The equilibrium constants (K_{eq}s) for the reversible reactions observed between **1** and various nitriles were measured in C_7D_8 by variable temperature (VT) NMR spectroscopy and used to construct van't Hoff plots (see Figures A10-A13). Linear fits of these data enabled the determination of the respective ΔH and ΔS parameters for each reaction investigated. As summarized in Table 4.2, these studies revealed that the [2+1] cycloaddition of **1** was more favored for electron-deficient nitriles, as evidenced by the larger K_{eq} and more negative ΔH values measured. Treatment of **1** with acetonitrile was also found to afford the corresponding azirine **5d** (diagnostic ^{13}C NMR signal in C_6D_6: δ 169.9 ppm) in a reversible manner (K_{eq} = 4 M^{-1} at 30 °C).[44,45] Although the K_{eq} for the reaction with the alkyl nitrile was lower than those measured for the aryl analogues, this result represents the first example of an isolable carbene undergoing a [2+1] cycloaddition with an alkyl nitrile as opposed to affording the formal C–H insertion product that is typically observed.[14,46]



1 **5a-d**

Product	R	ΔH (kJ·mol^{-1})	ΔS (J·mol^{-1}·K^{-1})	K_{eq}, 30 °C (M^{-1})
5a	Ph	-47.4	-129	26
5b	p-NO_2Ph	-50.0	-129	72
5c	p-MeOPh	-38.6	-101	23
5d[b]	CH_3	-36.8	-110	4

Table 4.2: Thermodynamic Data for the Reversible [2+1] Cycloadditions of 1 with Various Nitriles. [a] Unless otherwise noted, conditions: 1 equiv. RCN, C_7D_8. [b] Conditions: 10 equiv. CH_3CN, C_7D_8.

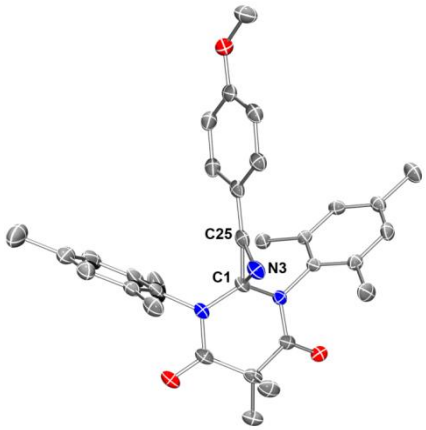


Figure 4.3: ORTEP diagram of **5c** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): C1-C25, 1.436(2); C1-N3, 1.5184(18); N3-C25, 1.2753(19); N3-C25-C1, 67.81(10); C25-N3-C1, 61.15(10); C25-C1-N3, 51.05(9).

4.3 Conclusion

In sum, we report a series of [2+1] cycloaddition reactions that combine a stable, isolable diamidocarbene (DAC) with various alkynes and nitriles to afford cyclopropenes

and 2*H*-azirines, respectively. In all cases, the reactions proceeded under mild conditions (23–60 °C) and reached high conversions. The azirination reactions were found to be reversible at ambient temperature, which is more typical of given transition metals and a first for an organic compound,[47] and may complement known[48-50] methods for activating nitriles. Aside from being among the first examples of their kind, the aforementioned diamidocyclopropenes were hydrolyzed to selectively afford either the corresponding cyclopropenones or ring-opened acids, depending on the conditions employed. Additionally, exposure of the DAC to electron-deficient substrates facilitated the discovery of new C-C bond forming reactions. Collectively, these transformations underscore the ability of DACs to function as useful synthetic reagents in applications that extend beyond facilitating the formation of three-membered rings. We expect these results to broaden the utility of isolable carbenes in synthesis, structural analysis and dynamic covalent chemistry.[51,52]

4.4 EXPERIMENTAL

General Considerations. All procedures were performed using standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen-filled glove box unless otherwise noted. *N*,*N*´-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (**1**) was synthesized according to literature procedures.[25] Dimethyl acetylenedicarboxylate was distilled prior to use. All commercial liquid substrates were dried over molecular sieves prior to use. All commercial solid substrates were dried under reduced pressure for 24 h prior to use. Benzene, toluene, pentane, and diethyl ether were dried and degassed using a Vacuum Atmospheres Company solvent purification system (model number 103991-0319) and stored over molecular sieves in a nitrogen-filled glove box. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrophotometer. High

resolution mass spectra (HRMS) were obtained with a VG analytical ZAB2-E instrument (CI or ESI). NMR spectra were recorded on Varian Unity+ 300, Varian Mercury 400, Varian MR-400, or Varian Inova 500 spectrometers. Chemical shifts (δ) are given in ppm and are referenced to the residual solvent (^{1}H: $CDCl_3$, 7.24 ppm; C_6D_6, 7.15 ppm; C_7D_8, 7.09 ppm; ^{13}C: $CDCl_3$, 77.0 ppm; C_6D_6, 128.0 ppm). Elemental analyses were performed at Midwest Microlab, LLC (Indianapolis, IN). Melting points were obtained using a Stanford Research Systems automated melting point system and are uncorrected.

Synthesis of 2a. A 100 mL Schlenk flask was charged with **1** (1.0 g, 2.66 mmol, 1 eq), benzene (20 mL), and a stir bar, and then capped with a rubber septum. A needle, attached to a balloon of acetylene, was inserted through the septum into the reaction flask. The septum was then punctured with another needle to relieve pressure, enabling bubbling of acetylene through the reaction mixture. After approximately one minute of bubbling, the needles were removed from the reaction flask, and the mixture was stirred at 23 °C. A white solid was observed to precipitate from the reaction mixture over time. After 8 h, the volatiles were removed under reduced pressure and the residue was repeatedly washed with dry diethyl ether. Removal of the residual solvent under reduced pressure afforded **2a** as a white solid (0.87 g, 2.16 mmol, 81% yield). mp = 166-168 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.72 (s, 6H, C(C*H*$_3$)$_2$), 2.13 (s, 12H, Ar-C*H*$_3$), 2.23 (s, 6H, Ar-C*H*$_3$), 6.84 (s, 4H, Ar-*H*), 7.23 (s, 2H, *H*C=C*H*). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 19.76, 21.87, 23.78, 48.57, 57.60, 117.93, 130.27, 132.68, 137.25, 139.00, 172.76. IR (KBr): ν = 3135.9, 2978.0, 29.19.4, 2861.3, 1695.4, 1654.0, 1620.0, 1462.7, 1407.4, 1223.1, 1039.0, 861.4 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{26}H_{31}N_2O_2$: 403.2386; Found: 403.2385. Anal. calcd. for $C_{26}H_{30}N_2O_2$: C,77.58 ; H, 7.51; N, 6.96; Found: C, 77.46; H, 7.56; N, 7.02.

Synthesis of 2b. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (1 mL), and a stir bar. The vial was then charged with 4-tert-butylphenylacetylene (0.032 g, 35.9 μL, 0.199 mmol, 1 eq) and the resultant mixture stirred at 23 °C. After 16 h, the volatiles were removed under reduced pressure and the residue was purified by silica gel column chromatography using 2:1 hexanes/ethyl acetate as the eluent (R_f = 0.28). Removal of the residual solvent under reduced pressure afforded **2b** as a white solid (0.079 g, 0.148 mmol, 74% yield). mp = 144-145 °C. ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.04 (s, 9H, C(C*H*$_3$)$_3$), 1.94 (s, 6H, Ar-C*H*$_3$), 2.00 (s, 3H, C(C*H*$_3$)), 2.16 (bs, 9H, Ar-C*H*$_3$/C(C*H*$_3$)), 2.18 (s, 6H, Ar-C*H*$_3$), 6.47 (s, 2H, Ar-*H*), 6.65 (s, 1H, *H*C=C), 6.66 (s, 2H, Ar-*H*), 6.96-7.02 (m, 4H, Ar-*H*). ^{13}C NMR (C_6D_6,100.50 MHz): δ 19.22, 19.46, 20.75, 23.14, 24.18, 30.97, 34.65, 48.02, 61.39, 109.21, 123.97, 125.48, 127.33, 128.94, 129.30, 129.63, 133.63, 136.81, 137.37, 137.69, 153.33, 171.81. IR (KBr): ν = 3087.7, 2966.5, 2928.2, 2868.2, 1680.8, 1649.9, 1461.8, 1405.7, 1354.8, 1216.0, 844.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{36}H_{43}N_2O_2$: 535.3325; Found: 535.3312. Anal. calcd. for $C_{36}H_{42}N_2O_2$: C, 80.86; H, 7.92; N, 5.24; Found: C, 80.57; H, 7.69; N, 4.90.

Synthesis of 2c. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (1 mL), and a stir bar. To this vial, cyclohexylacetylene (0.022 g, 26 μL, 0.199 mmol, 1 eq), was added and the resultant mixture was stirred at 60 °C. After 16 h, the reaction mixture was cooled to ambient temperature and the volatiles were removed under reduced pressure. Recrystallization of the residue from toluene at -20 °C followed by washing with cold pentane afforded **2c** as a white solid (0.067 g, 0.138 mmol, 68% yield). mp = 185-187 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 0.19-0.28 (m, 2H, cy-*H*), 0.43-0.47 (m, 2H, cy-*H*), 0.75-0.90 (m, 3H, cy-*H*), 1.08-1.12 (m, 3H, cy-*H*), 1.74 (m overlapping singlet, 4H, cy-*H* and C(C*H*$_3$)), 1.90 (s, 6H, Ar-C*H*$_3$), 2.03 (s, 3H, C(C*H*$_3$)), 2.04 (s, 6H, Ar-C*H*$_3$), 2.35 (s, 6H, Ar-C*H*$_3$), 6.64 (s, 2H, Ar-*H*), 6.70 (s, 2H, Ar-

H), 6.83 (s, 1H, *H*C=C). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 19.12, 19.32, 20.79, 21.63, 24.34, 24.78, 25.86, 30.36, 33.70, 48.37, 59.95, 109.90, 129.26, 129.33, 131.14, 134.05, 137.11, 137.59, 137.67, 171.90. IR (KBr): ν = 3124.0, 3088.5, 2978.5, 2927.9, 2854.4, 1678.6, 1647.0, 1413.1, 1356.4, 1221.9, 1173.8, 1042.5, 851.8, 797.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{41}N_2O_2$: 485.3168; Found: 485.3164. Anal. calcd. for $C_{32}H_{40}N_2O_2$: C, 79.30; H, 8.32; N, 5.78; Found: C, 79.44; H, 8.18; N, 5.52.

Synthesis of 2d. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (1 mL), and a stir bar. To this vial, 1-hexyne (0.016 g, 23 μL, 0.199 mmol, 1 eq) was added and the resultant mixture heated to 60 °C. After 16 h, the reaction was cooled to ambient temperature, and the volatiles were removed under reduced pressure. Washing the residue with a minimum amount of cold diethyl ether followed by drying under reduced pressure afforded **2d** as a white solid (0.085 g, 0.185 mmol, 93% yield). mp = 158-160 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.41 (t, J = 6.8 Hz, 3H, CH_2CH_3), 0.50-0.59 (m, 4H, $CH_2CH_2CH_3$), 1.46 (t, J = 6.4 Hz, 2H, C=CCH_2CH_2), 1.76 (s, 3H, Ar-CH_3), 1.92 (s, 6H, Ar-CH_3), 1.99 (s, 3H, Ar-CH_3), 2.04 (s, 6H, Ar-CH_3), 2.31 (s, 6H, Ar-CH_3), 6.64 (s, 2H, Ar-*H*), 6.67 (s, 2H, Ar-*H*), 6.82 (s, 1H, *H*C=C). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 13.42, 19.02, 19.10, 20.81, 21.39, 21.83, 23.49, 24.51, 28.39, 48.24, 59.20, 109.34, 128.35, 129.29, 129.35, 133.62, 137.03, 137.07, 137.60, 171.80. IR (KBr): ν = 3083.7, 2964.9, 2929.6, 2861.1, 1682.9, 1646.0, 1465.2, 1409.9, 1359.5, 1217.4, 1174.7, 1042.6, 849.0, 830.1, 801.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{30}H_{39}N_2O_2$: 459.3012; Found: 459.3017. Anal. calcd. for $C_{30}H_{38}N_2O_2$: C, 78.56; H,8.35 ; N, 6.11; Found: C, 78.76; H, 8.19; N, 5.85.

Synthesis of 2e. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (1 mL), and a stir bar. To this vial, 2-hexyne (0.033 g, 44.8 μL, 0.398 mmol, 2 eq) was added and the resultant mixture heated to 60 °C. After 16 h, the reaction was

cooled to ambient temperature and the volatiles removed under reduced pressure. Washing the residue with a minimum amount of cold diethyl ether followed by drying under reduced pressure afforded **2e** as a white solid (0.081 g, 0.177 mmol, 89% yield). mp = 146-147 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 0.28 (t, J = 7.6 Hz, 3H, CH_2CH_3), 0.79 (sextet, J = 7.2 Hz, 2H, $CH_2CH_2CH_3$), 1.44 (t, J = 1.4 Hz, 3H, $CH_3C{=}CCH_2$), 1.68 (m, 2H, $CH_3C{=}CCH_2CH_2$), 1.91 (s, 3H, $C(CH_3)$), 1.97 (s, 3H, $C(CH_3)$), 2.03 (s, 6H, Ar-CH_3), 2.11 (s, 6H, Ar-CH_3), 2.21 (s, 6H, Ar-CH_3), 6.64 (overlapping singlets, 4H, Ar-*H*). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 9.87, 13.19, 18.98, 19.24, 20.34, 20.80, 23.12, 24.36, 26.72, 48.20, 61.74, 118.17, 122.31, 129.23, 129.26, 134.02, 137.17, 137.20, 137.25, 172.00. IR (KBr): ν = 2992.9, 2978.9, 2952.6, 2924.6, 2872.0, 1837.1, 1685.7, 1648.0, 1607.7, 1461.2, 1410.7, 1216.1, 1172.7, 861.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{30}H_{39}N_2O_2$: 459.3012; Found: 459.3009. Anal. calcd. for $C_{30}H_{38}N_2O_2$: C, 78.56; H, 8.35; N, 6.11; Found: C, 78.66; H, 8.19 ; N, 5.98.

Synthesis of 2f. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (1 mL), and a stir bar. To this vial, 1-phenyl-1-butyne (0.052 g, 56.6 μL, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at 23 °C. After 16 h, the volatiles were removed under reduced pressure. Washing the residue with a minimum amount of cold diethyl ether followed by drying under reduced pressure afforded **2f** as a white solid (0.098 g, 0.192 mmol, 97% yield). mp = 169-171 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 0.36 (t, J = 7.40 Hz, 3H, CH_2CH_3), 1.76 (q, J = 7.40 Hz, 2H, CH_2CH_3), 1.95 (s, 6H, Ar-CH_3), 1.99 (s, 6H, Ar-CH_3), 2.11 (s, 3H, $C(CH_3)$), 2.12 (s, 3H, $C(CH_3)$), 2.36 (s, 6H, Ar-CH_3), 6.48 (s, 2H, Ar-*H*), 6.68 (s, 2H, Ar-*H*), 6.95-6.98 (m, 3H, Ar-*H*), 7.24-7.27 (m, 2H, Ar-*H*). ^{13}C NMR (C_6D_6, 100.49 MHz): δ 11.63, 18.50, 19.33, 19.50, 20.74, 23.07, 25.03, 47.82, 62.75, 121.80, 123.97, 128.75, 129.11, 129.26, 129.44, 129.74, 134.28, 136.99, 137.24, 138.33, 172.19. IR (KBr): ν = 3046.3, 2977.6, 2858.1, 1679.7,

1643.6, 1408.3, 1353.5, 1215.0, 1173.8, 774.5, 732.4, 695.5 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{34}H_{39}N_2O_2$: 507.3012; Found: 507.3009. Anal. calcd. for $C_{34}H_{38}N_2O_2$: C, 80.60; H, 7.56; N, 5.53; Found: C, 80.69; H, 7.59; N, 5.55.

Synthesis of 2g. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), diphenylacetylene (0.071 g, 0.398 mmol, 2 eq), benzene (1 mL), and a stir bar. The resultant mixture was then stirred at 60 °C for 16 h. Upon cooling to ambient temperature, the volatiles were removed under reduced pressure. Washing the residue with pentane followed by drying under reduced pressure afforded **2g** as a white solid (0.102 g, 0.184 mmol, 92% yield). mp = 184-186 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.97 (s, 6H, C(C*H*$_3$)$_2$), 2.13 (s, 12H, Ar-C*H*$_3$), 2.16 (s, 6H, Ar-C*H*$_3$), 6.53 (s, 4H, Ar-*H*), 6.89-6.97 (bm, 10H, Ar-*H*). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 19.68, 20.71, 24.26, 47.92, 64.44, 122.93, 128.49, 128.97, 129.47, 129.57, 134.46, 137.45, 138.04, 172.41. IR (KBr): ν = 3059.9, 2984.6, 2923.5, 2859.0, 1801.2, 1685.0, 1648.5, 1607.6, 1458.4, 1401.7, 1212.9, 1171.2, 778.8, 761.1, 692.6, 611.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{38}H_{39}N_2O_2$: 555.3012; Found: 555.3006. Anal. calcd. for $C_{38}H_{38}N_2O_2$: C, 82.28; H, 6.90; N, 5.05; Found: C, 82.09; H, 7.07; N, 4.92.

Synthesis of 2h. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (1 mL), and a stir bar. To this vial, 1-(trimethylsilyl)-1-propyne (0.076 g, 56.4 μL, 0.398 mmol, 2 eq) was added and the resultant mixture heated to 60 °C. After 16 h, the reaction was then cooled to ambient temperature, and the volatiles were removed under reduced pressure. Washing the residue with a minimum amount of cold diethyl ether followed by drying under reduced pressure afforded **2h** as a white solid (0.090 g, 0.184 mmol, 93% yield). mp = 166-167 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ -0.29 (s, 9H, Si(C*H*$_3$)$_3$), 1.54 (s, 3H, C=CC*H*$_3$), 1.92 (s, 3H, (C(C*H*$_3$)), 2.00 (s, 3H, C(C*H*$_3$)), 2.04 (s, 6H, Ar-C*H*$_3$), 2.08 (s, 6H, Ar-C*H*$_3$), 2.22 (s, 6H, Ar-C*H*$_3$), 6.64 (s,

4H, Ar-*H*). ^{13}C NMR (C_6D_6, 100.50 MHz): δ -1.11, 11.52, 19.09, 19.98, 20.79, 23.25, 23.36, 48.34, 62.33, 123.41, 129.19, 129.24, 133.88, 137.06, 137.38, 137.57, 140.70, 172.00. IR (KBr): ν = 2995.8, 2981.1, 2962.4, 1922.6, 2861.5, 1750.8, 1683.1, 1648.1, 1607.1, 1461.9, 1404.5, 1353.9, 1251.8, 1215.2, 1031.9, 846.0, 774.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{30}H_{41}N_2O_2Si$: 489.2937; Found: 489.2931. Anal. calcd. for $C_{30}H_{40}N_2O_2Si$: C, 73.73; H, 8.25; N, 5.73; Found: C, 73.61; H, 8.12; N, 5.43.

Synthesis of 2i. A 25 mL Schlenk flask was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (5 mL), and a stir bar. To this flask, dimethyl acetylenedicarboxylate (0.028 g, 24.5 μL, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at 23 °C. After 5 min, the volatiles were removed under reduced pressure. Washing the residue with minimal pentane followed by drying under reduced pressure afforded **2i** as a white solid (0.100 g, 0.193 mmol, 97% yield). mp = 97-99 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 1.96 (s, 6H, C(C*H*$_3$)$_2$), 2.06 (s, 6H, Ar-C*H*$_3$), 2.34 (s, 12H, Ar-C*H*$_3$), 2.98 (s, 6H, OC*H*$_3$), 6.65 (s, 4H, Ar-*H*). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 18.84, 20.78, 23.24, 46.67, 52.43, 63.83, 125.78, 129.60, 132.17, 138.06, 138.35, 156.88, 171.59. IR (KBr): ν = 2954.6, 2926.0, 1813.2, 1723.0, 1696.5, 1665.3, 1406.4, 1247.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{30}H_{35}N_2O_6$: 519.2495; Found: 519.2491. Anal. calcd. for $C_{30}H_{34}N_2O_6$: C, 69.48; H, 6.61; N, 5.40; Found: C, 69.63; H, 6.60; N, 5.34.

Synthesis of 3. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (1 mL), and a stir bar. To this vial, dimethyl acetylenedicarboxylate (0.028 g, 24.5 μL, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at 23 °C. After 48 h, the volatiles were removed under reduced pressure and the residue was purified by silica gel column chromatography using 1:1 hexanes/ethyl acetate as the eluent (R_f = 0.73). Removal of the volatiles under reduced pressure afforded **3** as a white solid (0.042 g, 0.081 mmol, 41% yield). mp = 156-158 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ

1.42 (s, 3H, C=CCH_3), 1.63 (s, 3H, C=CCH_3), 1.89 (overlapping singlets, 6H, C(CH_3)$_2$), 2.00 (s, 3H, C=CCH_3), 2.13 (s, 3H, Ar-CH_3), 2.23 (s, 3H, Ar-CH_3), 2.32 (s, 3H, Ar-CH_3), 2.85 (3H, OCH_3), 3.29 (s, 3H, OCH_3), 5.98 (s, 1H, C=C*H*), 6.14 (s, 1H, C=C*H*), 6.57 (s, 1H, Ar-*H*), 6.67 (s, 1H, Ar-*H*). ^{13}C NMR (C_6D_6, 74.47 MHz): δ 17.55, 18.53, 20.81, 21.30, 21.80, 22.15, 24.47, 25.28, 48.81, 51.21, 51.97, 62.22, 101.42, 119.58, 121.05, 127.12, 129.03, 129.17, 130.13, 132.74, 135.26, 138.07, 138.12, 143.28, 163.33, 167.52, 170.10, 170.62. IR (KBr): ν = 2981.2, 1937.6, 1737.9, 1720.1, 1698.3, 1664.6, 1640.0, 1447.3, 1387.8, 1351.3, 1233.8, 1150.7, 1018.7, 850.9, 840.6 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{30}H_{35}N_2O_6$:519.2495; Found: 519.2496. Anal. calcd. for $C_{30}H_{34}N_2O_6$: C, 69.48; H, 6.61; N, 5.40; Found: C, 69.48; H, 6.58; N, 5.38.

Synthesis of 4. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol, 1 eq), benzene (1 mL), and a stir bar. To this vial, dimethyl acetylenedicarboxylate (0.028 g, 24.5 μL, 0.199 mmol, 1 eq) was added and the resultant mixture heated to 60 °C. After 12 h, the reaction mixture was cooled to ambient temperature and the volatiles were removed under reduced pressure. The residue was purified by silica gel column chromatography using 1:1 hexanes/ethyl acetate as the eluent (R_f = 0.68). Removal of the volatiles under reduced pressure afforded **4** as a white solid (0.083 g, 0.160 mmol, 80% yield). mp = 189-190 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.46 (s, 6H, Ar-CH_3), 1.71 (s, 6H, Ar-CH_3), 1.99 (s, 3H, C(CH_3)), 2.01, (s, 3H, C(CH_3)), 2.32 (s, 6H, Ar-CH_3), 3.17 (s, 3H, OCH_3), 3.20 (s, 3H, OCH_3), 6.54 (s, 2H, Ar-*H*), 6.62 (s, 2H, Ar-*H*). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 17.79, 20.85, 20.89, 21.25, 22.01, 51.36, 52.16, 52.26, 128.68, 128.95, 129.89, 130.66, 130.75, 137.95, 138.14, 138.95, 139.61, 159.42, 164.56, 167.01, 174.71, 182.58. IR (KBr): ν = 2992.9, 2948.3, 2925.3, 1732.5, 1708.9, 1576.7, 1436.8, 1251.9, 1232.6 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{30}H_{35}N_2O_6$:519.2495;

Found: 514.2495. Anal. calcd. for $C_{30}H_{34}N_2O_6$: C, 69.48; H, 6.61; N, 5.40; Found: C, 69.46; H, 6.59; N, 5.37.

***In situ* generation of 5a-c.** An 8 mL vial was charged with **1** (0.025 g, 0.066 mmol, 1 eq), C_6D_6 (0.8 mL), and a stir bar. To this vial, aryl nitrile (2 eq), was added and then stirred at 23 °C for 2 h prior to spectroscopic analysis.

Spectroscopic data for 5a. ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.80 (s, 6H, Ar-CH_3), 2.03 (s, 3H, C(CH_3)), 2.15 (s, 3H, C(CH_3)), 2.25 (s, 6H, Ar-CH_3), 2.40 (s, 6H, Ar-CH_3), 6.46 (s 2H, Ar-*H*), 6.52 (s, 2H, Ar-*H*), 6.57-6.67 (m, 3H, Ar-*H*), 6.93-6.99 (m, 2H, Ar-*H*). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 19.09, 19.30, 20.65, 21.11, 25.68, 49.54, 123.83, 127.11, 128.51, 129.34, 129.85, 132.16, 132.67, 136.64, 137.79, 138.50, 167.62, 172.17. IR (CH_2Cl_2): ν = 3061.6, 3029.5, 2979.8, 2923.6, 2860.0, 2229.9, 1740.2, 1712.3, 1699.9, 1666.0, 1608.8, 1490.7, 1447.9, 1411.3, 1384.6, 1329.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{34}N_3O_2$: 480.2651; Found: 480.2650.

Spectroscopic data for 5b. ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.83 (s, 6H, Ar-CH_3), 1.97 (s, 3H, C(CH_3)), 2.10 (s, 3H, C(CH_3)), 2.18 (s, 6H, Ar-CH_3), 2.32 (s, 6H, Ar-CH_3), 6.48 (s, 2H, Ar-*H*), 6.52 (s, 2H, Ar-*H*), 6.66-6.69 (overlapping m, 2H), 7.29-7.32 (m, 2H). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 18.95, 19.19, 20.66, 20.94, 25.65, 49.61, 69.65, 127.54, 128.81, 129.44, 129.95, 132.14, 136.63, 137.92, 139.05, 149.81, 161.74, 171.98. IR (CH_2Cl_2): ν = 3110.4, 3062.0, 298.9, 2926.2, 2867.7, 2236.7, 1701.9, 1671.9, 1605.2, 1532.5, 1402.2, 1346.5 cm^{-1}. HRMS (CI): $[M]^+$ calcd. for $C_{31}H_{32}N_4O_4$: 524.2424; Found: 524.2419.

Spectroscopic data for 5c. ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.80 (s, 6H, Ar-CH_3), 2.00 (s, 3H, C(CH_3)), 2.16 (s, 3H, C(CH_3)), 2.27 (s, 6H, Ar-CH_3), 2.48 (s, 6H, Ar-CH_3), 2.84 (s, 3H, Ar-CH_3), 6.21 (d, J = 8.8 Hz, 2H, Ar-*H*), 6.48 (s, 2H, Ar-*H*), 6.59 (s, 2H, Ar-*H*), 7.05 (overlapping d, 2H, Ar-*H*). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 19.17,

19.36, 20.70, 21.16, 25.70, 49.50, 54.58, 68.95, 114.31, 115.77, 119.19, 129.33, 129.86, 132.69, 136.57, 137.85, 138.43, 163.35, 165.87, 172.30. IR (CH_2Cl_2): ν = 3060.3, 3013.0, 2971.6, 2938.8, 2842.6, 2226.0, 1712.3, 1698.5, 1663.8, 1606.7, 1509.5, 1407.7, 1303.6, 1172.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{36}N_3O_3$: 510.2757; Found: 510.2745.

***In situ* generation of 5d.** An 8 mL vial was charged with **1** (0.015 g, 0.04 mmol, 1 eq), C_6D_6 (0.8 mL), and a stir bar. To this vial, acetonitrile (0.012 g, 15 μL, 0.288 mmol, 7.2 eq) was added and then stirred at 23 °C for 2 h prior to spectroscopic analysis.

Spectroscopic data for 5d. ^1H NMR (C_6D_6, 400.27 MHz): δ 0.95 (s, 3H, N=CCH_3), 1.85 (s, 3H, C(CH_3)), 1.97 (s, 3H, C(CH_3)), 2.03 (s, 6H, Ar-CH_3), 2.13 (s, 6H, Ar-CH_3), 2.19 (s, 6H, Ar-CH_3), 6.60 (s, 2H, Ar-*H*), 6.66 (s, 2H, Ar-*H*). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 11.36, 18.71, 19.09, 20.80, 20.86, 25.99, 49.21, 65.11, 129.27, 129.96, 132.12, 136.35, 138.25, 138.52, 169.93, 171.92. IR (CH_2Cl_2): ν = 3164.7, 3058.8, 2998.5, 2939.9, 2924.5, 2290.9, 2253.9, 1740.6, 1712.3, 1698.4, 1663.5, 1608.6, 1461.7, 1442.7, 1410.8, 1373.0, 1328.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{26}H_{32}N_3O_2$: 418.2495; Found: 418.2491.

Synthesis of 6. An 8 mL vial was charged with **1** (0.500 g, 1.33 mmol, 1 eq), tetracyanoethylene (0.170 g, 0.199 mmol, 1 eq), $CHCl_3$ (6 mL), and a stir bar. The resultant mixture was stirred at 23 °C. After 1 h, the volatiles were removed under reduced pressure which afforded a dark red residue. The residue was dissolved in CH_2Cl_2 and filtered through a six inch silica gel plug with copious amounts of CH_2Cl_2. The residual solvent volatiles were then removed under reduced pressure, and the residue was washed with toluene until it became colorless. Drying under reduced pressure afforded **6** as an off-white solid (0.107 g, 0.0.212 mmol, 16% yield). mp = 169-170 °C. ^1H NMR ($CDCl_3$, 400.27 MHz): δ 1.73 (s, 6H, C(CH_3)$_2$), 1.81 (s, 3H, C(CH_3)), 1.87 (d, J = 1.2 Hz, 6H, HC=CCH_3), 2.06 (s, 6H, Ar-CH_3), 2.32 (s, 3H, Ar-CH_3), 5.78 (d, J = 1.2 Hz, C=C*H*),

6.97 (s, 2H, Ar-*H*). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 16.88, 17.53, 21.16, 24.32, 24.97, 41.43, 45.19, 48.57, 73.41, 83.91, 111.33, 114.51, 125.71, 128.79, 129.89, 134.13, 140.27, 145.74, 157.19, 167.60, 167.77, 170.62. IR (KBr): ν = 2955.6, 2921.5, 2215.8, 1744.4, 1711.6, 1541.7, 1447.0, 1390.7, 1354.2, 1249.6, 1104.8, 975.7, 855.2 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{30}H_{29}N_6O_2$: 505.2347; Found: 505.2346.

Hydrolysis of 2g to 2,3-diphenylcyclopropenone. An 8 mL vial was charged with **1** (0.500 g, 1.33 mmol, 1 eq), diphenylacetylene (0.473 g, 2.66 mmol, 2 eq), benzene (6 mL), and a stir bar. After the resultant mixture was stirred at 60 °C for 16 h, the volatiles were removed under reduced pressure. Glacial acetic acid (3 mL) and concentrated hydrochloric acid (3 mL) were added to the reaction flask and the mixture was heated at 80 °C. After 2 h, the reaction mixture was cooled to ambient temperature, and the volatiles were removed under reduced pressure. The residue was purified via silica gel column chromatography using 1:1 hexanes/ethyl acetate (R_f = 0.34) followed by 100% ethyl acetate (R_f = 0.68) as the eluent. Removal of the volatiles under reduced pressure afforded 2,3-diphenylcycloprop-2-enone as a white solid (178 mg, 0.863 mmol, 66% yield). In agreement with literature values[40a]: mp = 114-116 °C. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 7.53-7.61 (m, 6H, Ar-*H*), 7.96-7.98 (m, 4H, Ar-*H*). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 123.95, 129.31, 131.42, 132.65, 148.28, 155.74. IR (KBr): ν = 2923.3, 1839.1, 1618.8, 1440.8, 1338.4, 782.3, 759.1, 684.0, 511.8, 471.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{15}H_{11}O$: 207.0810; Found: 207.0813.

Hydrolysis of 2g to trans-α-phenylcinnamic acid. An 8 mL vial was charged with **2g** (0.200 g, 0.361 mmol), glacial acetic acid (1.5 mL), concentrated hydrochloric acid (1.5 mL), and a stir bar. After stirring the resultant mixture at 100 °C for 48 h, the reaction mixture was cooled to ambient temperature and the volatiles were removed under reduced pressure. The residue was dissolved in diethyl ether (20 mL) and extracted

with an aqueous solution saturated with $NaHCO_3$ (3 × 20 mL). The aqueous layer was acidified with 10 mol % HCl, and extracted with diethyl ether (3 × 50 mL). The organic layer from the acidic extract was then dried over Na_2SO_4 and filtered. The volatiles from the filtrate were removed under reduced pressure. Washing of the residue with a minimal quantity of pentane followed by drying under reduced pressure afforded trans-α-phenylcinnamic acid as a white solid (26 mg, 0.116 mmol, 32% yield). In agreement with literature values[53]: mp = 173-174 °C. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 7.04-7.06 (m, 2H, Ar-*H*), 7.13-7.17 (m, 2H, Ar-*H*), 7.20-7.24 (m, 3H, Ar-*H*), 7.32-7.39 (m, 3H, Ar-*H*), 7.94 (s, 1H, C=C*H*), 11.6 (bs, 1H, CO_2*H*). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 128.06, 128.26, 128.72, 129.49, 129.74, 130.84, 131.52, 134.25, 135.25, 142.46, 172.67. IR (KBr): ν = 3053.9, 3023.9, 2954.9, 2841.0, 2799.0, 2631.9, 1678.3, 1429.2, 1273.9, 707.4, 690.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{15}H_{12}O_2$: 224.0837. Found: 224.0837.

Hydrolysis of 2e to 2-methyl-3-propylcycloprop-2-enone. An 8 mL vial was charged with **1** (0.500 g, 1.33 mmol, 1 eq), benzene (6 mL), and a stir bar. To this vial, 2-hexyne (0.218 g, 299 μL, 2.66 mmol, 2 eq) was added and the resultant mixture was stirred at 60 °C. After 16 h, the volatiles were removed under reduced pressure. Glacial acetic acid (3 mL) and concentrated hydrochloric acid (3 mL) were added and the resultant mixture heated to 80 °C for 2 h. Upon cooling to ambient temperature, the volatiles were removed under reduced pressure. The residue was triturated with pentane and filtered. The filtrate was concentrated under reduced pressure. Vacuum distillation (20 mtorr) with heating (90 °C) of the crude residue afforded 2-methyl-3-propylcycloprop-2-enone as a clear liquid (103 mg, 0.935 mmol, 70% yield). In agreement with literature values[54]: ^{1}H NMR: ($CDCl_3$, 399.68 MHz): δ 0.92 (t, J = 7.6 Hz, 3H, C*H*$_3$CH$_2$), 1.62 (sextet, J = 7.2 Hz, 2H, CH$_2$C*H*$_2$CH$_3$), 2.15 (t, J = 0.8 Hz, 3H, C=CC*H*$_3$), 2.47 (dt, J = 4.0 Hz, 2H, C=CCH$_2$CH$_2$). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ

11.02, 13.56, 19.31, 27.91, 156.81, 159.67, 161.17. IR (CH_2Cl_2): 3054.1, 2966.6, 2936.4, 2876.0, 1846.4, 1633.4 cm^{-1}. HRMS (CI):$[M+H]^+$ calcd. for $C_7H_{11}O$: 111.0810. Found: 111.0811.

Hydrolysis of 2e to trans-2-methylhex-2-enoic acid and trans-2-ethylidenepentanoic acid. An 8 mL vial was charged with **2e** (0.150 g, 0.327 mmol, 1 eq), glacial acetic acid (1 mL), concentrated hydrochloric acid (1 mL), and a stir bar. The resultant mixture was then stirred at 100 °C for 48 h. Upon cooling to ambient temperature, the solution was basified with 1 M NaOH and extracted with diethyl ether (3 × 20 mL). The aqueous layer was acidified with 10% HCl and extracted with diethyl ether (3 × 50 mL). The organic layer from the acidic extract was dried over Na_2SO_4, filtered, and the volatiles removed under reduced pressure. The resultant residue was triturated with pentane and filtered. Removal of the volatiles from the filtrate under reduced pressure afforded a mixture of trans-2-methylhex-2-enoic acid and trans-2-ethylidenepentanoic acid (53:47) as a viscous clear liquid (18 mg, 0.140 mmol, 43% yield). In agreement with literature values[55,56]: ^{1}H NMR: ($CDCl_3$, 399.68 MHz): δ 0.90 (t, J = 7.4 Hz, 3H, CH_2CH_3), 0.92 (t, J = 7.4 Hz, 3H, $CH_2CH_2CH_3$), 1.44 (overlapping multiplets, 4H, $CH_2CH_2CH_3$), 1.82 (overlapping m, 6H, $C=CCH_3$), 2.16 (q, J = 7.4 Hz, 2H, $C=CHCH_2CH_2$), 2.26 (t, J = 7.8 Hz, 2H, $C=CCH_2CH_2$), 6.90 (dt, J = 4.5 Hz, 1H, C=CH), 7.00 (q, J = 7.2 Hz, 1H, C=CH). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 11.96, 13.84, 13.88, 14.52, 21.70, 22.12, 27.96, 30.87, 127.06, 132.59, 140.31, 145.31, 173.31, 173.59. IR (CH_2Cl_2): 3505.9, 2962.1, 2932.7, 2872.9, 1715.8, 1685.2, 1641.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_7H_{13}O_2$: 129.0916. Found: 129.0917.

4.5 Acknowledgements

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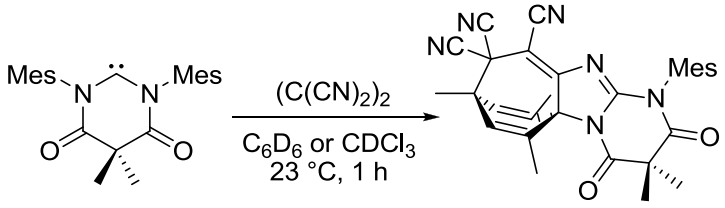

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Chapter 5: *N,N′*-Diamidocarbenes Facilitate Selective C–H Insertions and Transfer Hydrogenations*

5.1 INTRODUCTION

Over the past several decades, C–H activation has emerged as an attractive method for transforming abundant starting materials into valuable products.[1-4] With the potential to streamline synthetic strategies, increase atom economy, and minimize waste, methods for the selective activation of ubiquitous C–H bonds are of intense interest.[5-9] Carbenes are well-positioned for such purposes as C–H activation has been a hallmark reaction of such species since an early report by Curtius in 1885,[10] though most carbenes capable of these transformations are typically generated *in situ* and utilize directing transition metals.[11-16] Isolable carbenes, in comparison, offer the potential for streamlined syntheses of new classes of highly functionalized substrates without byproduct formation. While stable phosphinosilyl,[17] arylamino,[18,19] aminophosphino,[20,21] and diaminocarbenes[22,23] (Figure 5.1) have been shown to undergo intramolecular C–H insertions, the more versatile intermolecular analogues have remained elusive. Indeed, the only examples of intermolecular C–H insertions involving isolable carbenes to date have either been metal-catalyzed[24] or utilized substrates containing relatively acidic C–H bonds ($pK_a \leq 25$).[25-27]

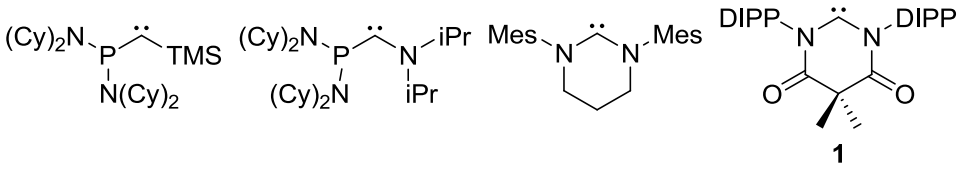

Figure 5.1: Selected examples of carbenes reported to undergo intramolecular C–H insertion.

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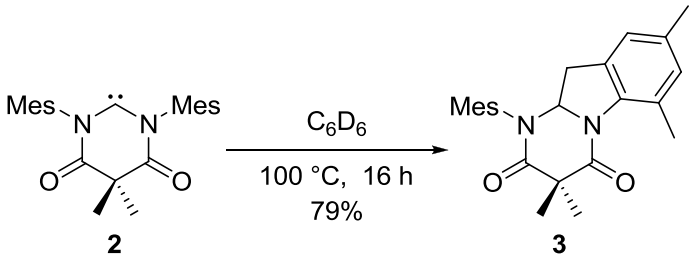
In 2009, we reported that the diamidocarbene (DAC)[28] **1** (Figure 5.1), underwent intramolecular C–H insertion into its *N*-2,6-diisopropylphenyl (DIPP) substituent to form a fused [5,6]-bicycle.[29] However, replacement of the DIPP groups with mesityls (*i.e.*, **2**) enabled the isolation of the corresponding free carbene[30] and facilitated its study.[31,32] During the course of these investigations, side reactions were discovered at elevated temperatures which we surmised were due to competitive C–H activation processes and warranted further investigation. Herein we report intramolecular as well as the first intermolecular C–H insertions involving an isolable carbene that are neither catalyzed by residual base nor exclusive to acidic substrates. Surprisingly, a DAC was also found to facilitate metal- and additive-free transfer hydrogenations via C–H activation pathways.



Scheme 5.1: Intramolecular C–H insertion of DAC **2**.

5.2 Results and Discussion

Our studies began by probing the propensity of **2** to insert into its *N*-mesityl group (Scheme 5.1). After heating the DAC in C_6H_6 to 100 °C for 16 h ($[\mathbf{2}]_0$ = 0.04 M), the product formed was purified by silica gel column chromatography and characterized. The NMR spectra ($CDCl_3$) recorded for the compound were consistent with the structure of **3**: a ^{13}C NMR signal was observed at 72.5 ppm and assigned to an *N,N′*-diamidomethine nucleus (*c.f.*, **2** exhibits a signal at 277.7 ppm). Additionally, ^{1}H NMR signals were observed at 5.87 (attributed to the methine) and 3.00 and 2.63 ppm for which the latter two signals were assigned to the diastereotopic methylene protons. Unambiguous

structural elucidation was subsequently obtained via single crystal X-ray diffraction (XRD) analysis (see Figure 5.2).

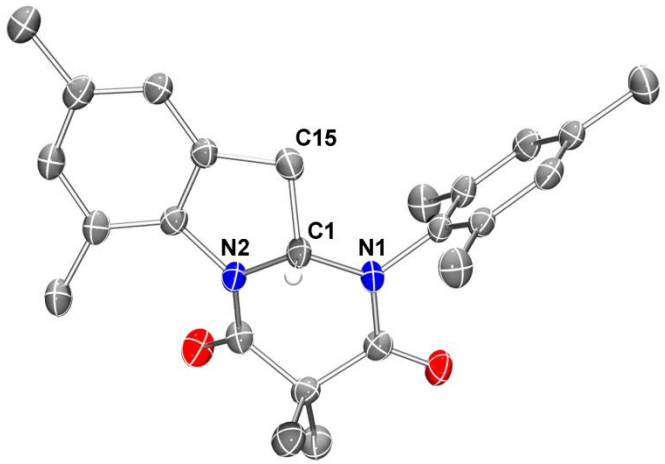


Figure 5.2: ORTEP diagram of **3** with thermal ellipsoids drawn at the 50% probability. H-atoms except at the carbenoid carbon are omitted for clarity. Select bond lengths (Å) and angles (°): C1–N1, 1.470(3); C1–N2, 1.478(4); C1–C15, 1.528(4); N1–C1–N2, 110.4(2); N1–C1–C15, 113.1(2); N2–C1–C15, 103.7(2).

As previously noted, DAC **1** was observed to readily undergo intramolecular C–H insertion at 50 °C.[29] The increased temperature required for **2**, which features *N*-mesityl (vs. *N*-diisopropylphenyl in **1**), to react in a similar manner suggested to us that the DACs favored more substituted and/or electron-rich C–H bonds. To test this hypothesis, a series of differentially substituted *N,N′*-diamidocarbenes (**4a-c**) were synthesized and studied. Acid-catalyzed condensation of the respective anilines with triethyl orthoformate followed by condensation with dimethylmalonyl dichloride in the presence of triethylamine afforded the requisite carbene precursors **4a-c**·HCl in 42-66% yield over the two steps. Although the free carbenes **4a-c** were successfully formed *in situ* via deprotonation with sodium hexamethyldisilazide (NaHMDS), as shown by the ^{13}C NMR signals observed in the 276.3-277.8 ppm (C_6D_6) range in the recorded spectra, the

compounds could not be isolated due to an unidentified side reaction that occurred upon concentration. Regardless, as summarized in Figure 5.3, heating **4a-c** to 80 °C for 16 h in C_6D_6 induced intramolecular C–H insertion to **5a-c** as evidenced by the formation of methine groups via ^{1}H NMR spectroscopy. Integration of the diagnostic NMR signals revealed the relative chemoselectivity of the DAC in intramolecular C–H insertions: *i*Pr > Et >> Me.

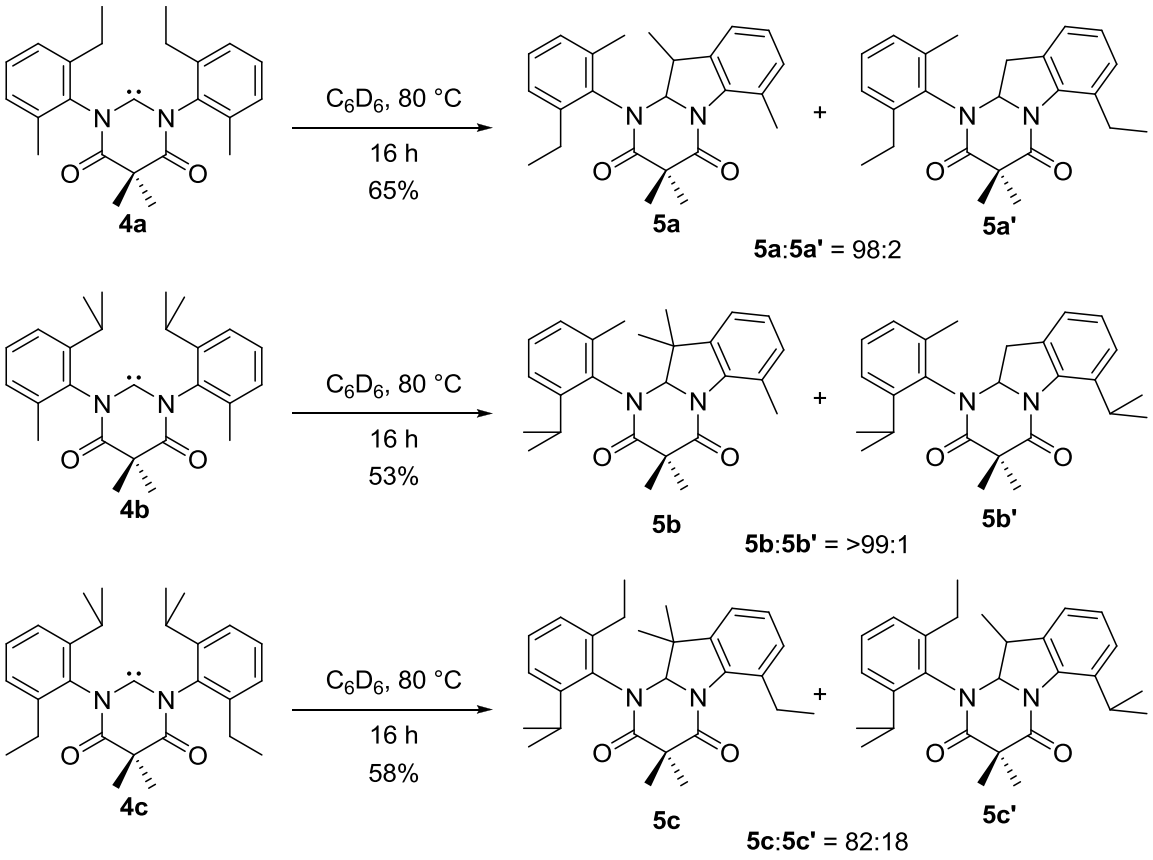


Figure 5.3: Chemoselective intramolecular C–H insertion of **4a-c**.

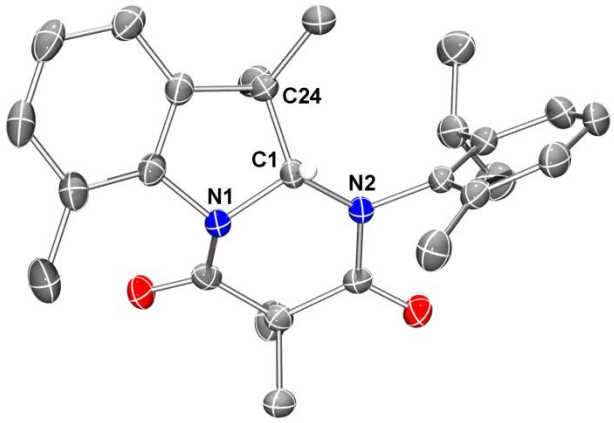


Figure 5.4: ORTEP diagram of **5c** with thermal ellipsoids drawn at the 50% probability. H-atoms except at the carbenoid carbon are omitted for clarity. Select bond lengths (Å) and angles (°): C1–N1, 1.480(2); C1–N2, 1.462(2); C1–C24, 1.554(3); N1–C1–N2, 112.74(15); N1–C1–C24, 103.62(15); N2–C1–C24, 119.70(17).

Considering the aforementioned chemoselectivity was similar to that displayed by *in situ* generated electrophilic carbenes,[11-16] we hypothesized that **2** should insert in an intermolecular fashion into substrates that featured substituents which stabilized a radical or cationic species more readily than an aryl methyl. To explore, a preliminary reaction was conducted in which **2** was heated to 100 °C for 16 h in neat 4-(methylthio)toluene. Analysis of the crude product mixture by ^{1}H NMR spectroscopy ($CDCl_3$) revealed signals consistent with **3** as well as a new triplet at 5.90 ppm, which was assigned to the carbenoid proton expected from an intermolecular C–H insertion product. Indeed, **6a** was subsequently isolated by column chromatography (37% yield) and characterized using XRD analysis (Figure 5.5) as well as other techniques.

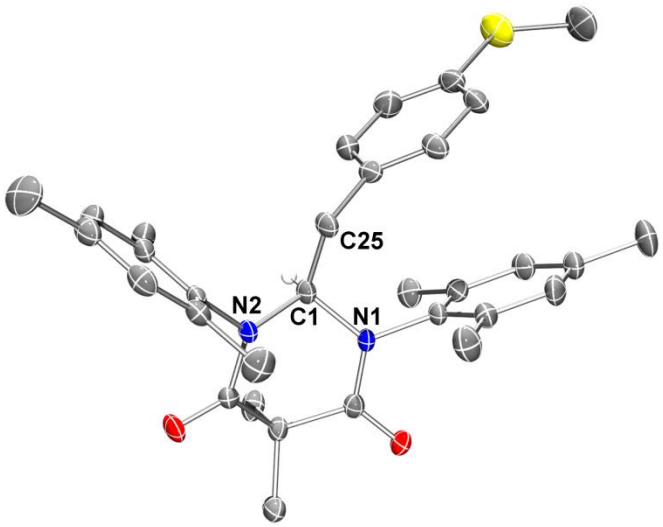


Figure 5.5: ORTEP diagram of **6a** with thermal ellipsoids drawn at the 50% probability. H-atoms except at the carbenoid carbon are omitted for clarity. Select bond lengths (Å) and angles (°): C1–N1, 1.482(3); C1–N2, 1.481(3); C1–C25, 1.530(3); N1–C1–N2, 108.48(17); N1–C1–C25, 112.84(18); N2–C1–C25, 110.53(18). ∑ N-C-N, N-C1-C25 = 331.85°.

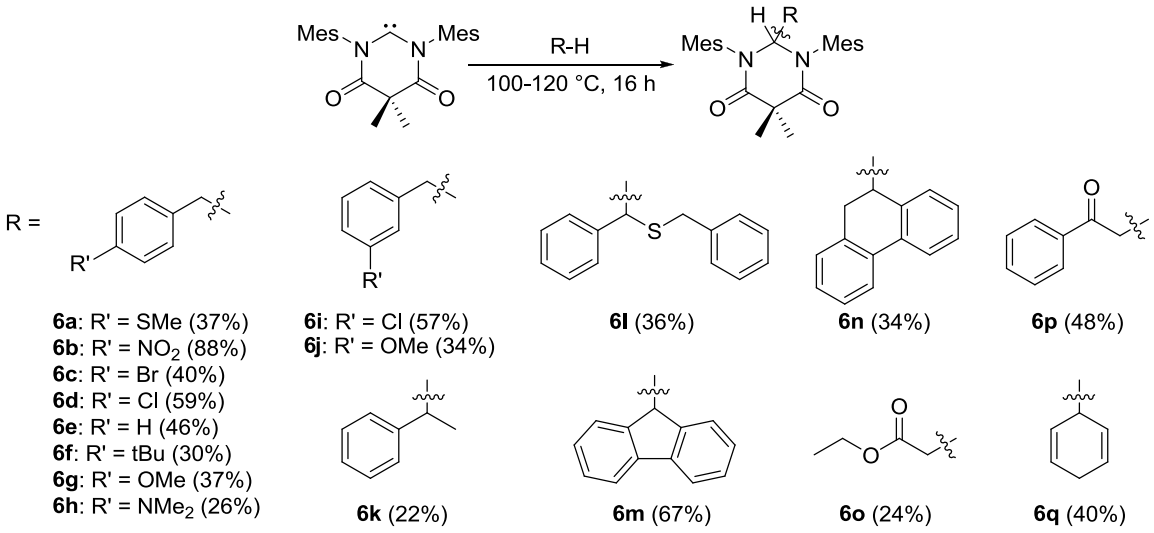


Figure 5.6: C–H insertion of **2** into various organic substrates.

As summarized in Figure 5.6, intermolecular C–H insertions with **2** were found to be general for a variety of electron-rich as well as electron-deficient *p*- or *m*-substituted tolyl derivatives (**6a-6j**, 26-88%). Additionally, insertions into secondary aryl C–H bonds were also successful (**6k-n**), although attempts to extend the chemistry to include tertiary analogues (*e.g.,* triphenylmethane) afforded only **3**, presumably due to steric inhibition. Under similar conditions, **2** also inserted alpha to the carbonyl groups of acetophenone and ethyl acetate (**6o**,**p**) as well as into the allylic C–H bond of 1,4-cyclohexadiene.[33]

Close inspection of the aforementioned data revealed that higher yields were obtained when relatively electron-deficient substrates were used, a result that seemed to contrast with the intramolecular C–H insertion studies described above which indicated that the DAC reacted more readily with relatively electron-rich substituents. To probe the intermolecular C–H insertion mechanism, a series of competition reactions were performed by heating a mixture of **2**, toluene (10 equiv.) and a *p*-substituted toluene derivative (10 equiv.) in C_6D_6 at 80 °C for 16 h. Subsequent analysis of the crude mixture by ^{1}H NMR spectroscopy determined the molar ratio of the para-substituted product (**6a-d, f-h**) versus **6e** (defined as P_R/P_H, where R is the para-substituent). As shown in Figure 5.7, the relationship between log (P_R/P_H) versus the Hammett parameter σ^- was linear with a positive slope of 1.3 reflecting the build-up of negative charge at the benzylic carbon (see Figures A25-A27 for additional plots). Thus, the intermolecular C–H insertion was consistent with a concerted, asynchronous process wherein the DAC functioned as a nucleophile and polarized the C–H bond prior to insertion.

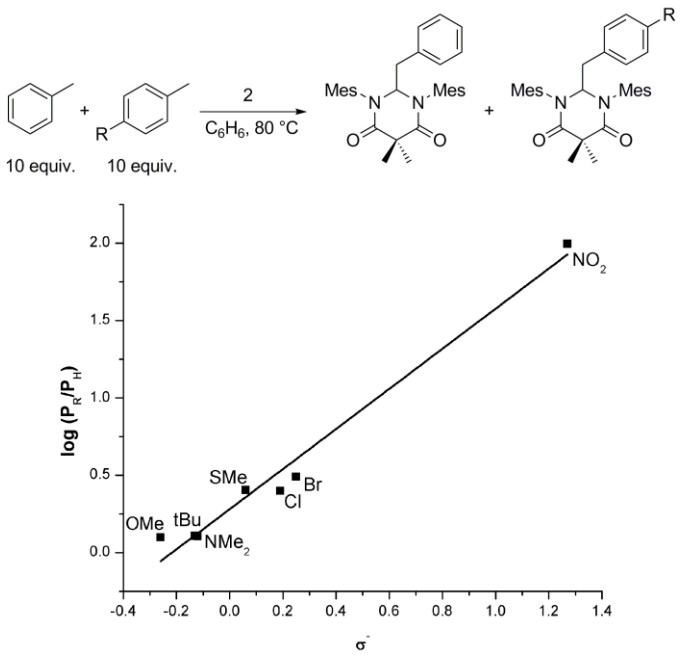


Figure 5.7: Plot of the logarithm of the product ratios (P_R/P_H) versus σ^- for the competitive reaction of **2** with toluene and the indicated p-substituted toluene derivative (10 equiv. each). The data points shown are the numerical average of three separate experiments.

In addition to the C–H insertion product **6q**, a highly symmetrical secondary product was isolated from the reaction between 1,4-cyclohexadiene and **2** via column chromatography. Based on a singlet observed at 4.76 ppm (2H, $CDCl_3$) in the ^{1}H NMR spectrum and the presence of a new ^{13}C NMR signal attributed to a methylene group at 61.1 ppm (confirmed via DEPT), the product was assigned as the formally hydrogenated DAC, **7** (29%; Figure 5.8). The aforementioned reaction was subsequently repeated using trimethoxybenzene as an internal standard, which revealed the generation of a 51:49:49 mixture of **6q**:**7**:benzene. Moreover, a similar study using 9,10-dihydrophenanthrene resulted in a 63:24:24 mixture of **6n**:**7**:phenanthrene. Collectively, the data suggested to us that the DAC successfully facilitated the dehydrogenation of several organic substrates

to their respective aromatic products via a novel, metal-free transfer hydrogenation mechanism.[34]

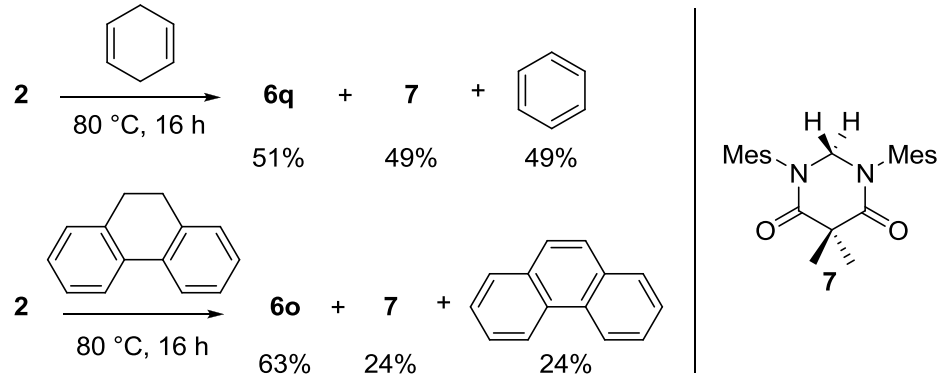


Figure 5.8: Transfer hydrogenation of **2** with 1,4-cyclohexadiene (top) or 9,10-dihydrophenanthrene (bottom). The percent conversions were calculated by ^{1}H NMR spectroscopy against a trimethoxybenzene internal standard.

5.3 CONCLUSIONS

In sum, a series of competitive studies revealed that DACs prefer to intramolecularly insert into more substituted C–H bonds, whereas analogous intermolecular reactions favored relatively electron-deficient substrates. The latter result was consistent with the polarization of the C–H bond by a nucleophilic carbene while the former may reflect a pathway involving an electrophilic carbene or a steric effect wherein the reactive C–H group is oriented in closer proximity to the carbene center by the bulkier substituent. Regardless, the results constitute rare examples of an isolable carbene facilitating intramolecular C–H insertions and the first metal- and additive-free intermolecular C–H insertions not exclusive to highly acidic substrates. More broadly, the results underscore the potential of isolable carbenes to selectively functionalize a variety of C–H bonds, akin to their transient counterparts but without the need for *in situ* generation or directing metal groups. Moreover, hydrolysis or reduction of the inserted products may lead to streamlined syntheses of aldehydes and other functionalized

derivatives.[31,32] Finally, **2** was found to facilitate metal-free dehydrogenations of hydrocarbons. To the best of our knowledge this is the first example of a carbene effecting transfer hydrogenation with an organic substrate and may aid in the development of metal-free hydrogenations[35,36] using carbene-based organocatalysts.

5.4 EXPERIMENTAL

General Considerations. All procedures were performed using standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen-filled glove box unless otherwise noted. *N,N′*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (**2**) was prepared according to literature procedure.[29] All liquid substrates were dried over molecular sieves for 24 h prior to mixing with **2**. All commercial solid substrates were dried under reduced pressure for 24 h. Benzene, toluene, dichloromethane and hexanes were dried and degassed using a Vacuum Atmospheres Company solvent purification system. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer. High resolution mass spectra (HRMS) were obtained with a Waters Micromass Autospec-Ultima (CI) or Agilent 6530 QTOF (ESI) mass spectrometer. NMR spectra were recorded on a Varian Unity+ 300, Varian Mercury 400, Varian Directdrive 400, Agilent MR400, Varian Inova 500 or Varian Directdrive 600 spectrometer. Chemical shifts (δ) are reported in ppm relative to the residual benzene (^{1}H: 7.15 ppm, ^{13}C: 128.0 ppm) or chloroform (^{1}H: 7.24 ppm, ^{13}C: 77.0 ppm) as reference. Elemental analyses were performed at Midwest Microlab, LLC (Indianapolis, IN) or with a ThermoScientific Flash 2000 Organic Elemental Analyzer. Melting points were obtained using a Stanford Research Systems MPA100 OptiMelt automated melting point apparatus (ramp rate: 1 °C·min^{-1}) and are uncorrected.

Synthesis of 3. An 8 mL vial was charged with **2** (0.075 g, 0.199 mmol), benzene (5 mL) and a stir bar. After mixing, the resultant solution was heated at 100 °C for 16 h, cooled to ambient temperature and the volatiles removed under reduced pressure. Purification of the resultant residue by silica gel column chromatography (eluent = 2:1 v/v hexanes/ethyl acetate) afforded the desired compound as a white solid (0.059 g, 0.157 mmol, 79% yield). m.p. 212-213 °C. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.55 (s, 3H), 1.63 (s, 3H), 2.13 (s, 3H), 2.21 (s, 3H), 2.25 (s, 3H), 2.29 (s, 3H), 2.31 (s, 3H), 2.63 (dd, J = 11 Hz, 1H), 3.00 (dd, J = 12.6 Hz, 1H), 5.87 (dd, J = 8.6 Hz, 1H), 6.72 (s, 1H), 6.89 (s, 1H), 6.92 (s, 1H), 6.95 (s, 1H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.16, 18.55, 20.58, 20.61, 20.92, 20.96, 24.51, 37.01, 47.29, 72.52, 122.48, 128.31, 129.78, 129.94, 130.13, 131.37, 133.33, 134.53, 135.79, 136.63, 137.02, 138.32, 168.33, 171.11. IR (KBr): ν = 2970.0, 2921.7, 2857.2, 1685.2, 1661.8, 1482.0, 1426.4, 1364.3, 1239.8, 1105.2, 861.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{24}H_{29}N_2O_2$: 377.2229. Found: 377.2220. Anal. calcd. for $C_{24}H_{38}N_2O_2$: C, 76.56; H, 7.50; N, 7.44; Found: C, 76.54; H, 7.52; N, 7.46.

Synthesis of *N,N′*-bis(2-ethyl-6-methylphenyl)formamidine. Under ambient conditions, a 50 mL round bottom flask equipped with a short-path distillation head was charged with 2-ethyl-6-methylaniline (2.7 g, 20 mmol, 2 equiv.), triethyl orthoformate (1.48 g, 10 mmol, 1 equiv.), two drops of formic acid and a stir bar. The resultant mixture was heated at 115 °C for 2 h followed by heating at 150 °C for 16 h. Upon cooling to ambient temperature, the crude solid was ground using a glass rod. Trituration with pentane followed by collection on a medium porosity frit, washing with pentane until colorless and drying under reduced pressure afforded the desired compound as a white solid (2.24 g, 8.0 mmol, 80% yield). m.p. 130-131 °C. NMR analysis revealed a mixture of rotational isomers that coalesced at elevated temperature. ^{1}H NMR (C_6D_6, 399.68 MHz): δ (major isomer) 1.14 (t, J = 7.2 Hz, 6H), 2.17 (s, 6H), 2.60 (q, J = 7.2 Hz, 4H),

6.80 (s, 1H), 6.85-7.02 (m, 6H), 9.45 (bs, 1H). (DMSO-d_6, 130 °C, 499.87 MHz): δ 1.16 (t, J = 7.6 Hz, 6H), 2.24 (s, 6H), 2.62 (q, J = 7.6 Hz, 4H), 6.94 (t, J = 7.4 Hz, 2H), 7.01-7.03 (overlapping m, 4H), 7.36 (s, 1H), 7.69 (bs, 1H). ^{13}C NMR (DMSO-d_6, 130 °C, 125.70 MHz): δ 13.68, 17.41, 23.39, 123.19, 125.17, 126.92, 131.20, 137.37, 142.16, 148.92. IR (KBr): ν = 3138.3, 3039.5, 2960.6, 2865.4, 1669.9, 1589.1, 1458.4, 1293.6, 1239.9, 1189.9, 1099.0, 783.0, 768.7, 752.5 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{19}H_{25}N_2$: 281.2018. Found: 281.2006. Anal. calcd. for $C_{19}H_{24}N_2$: C, 81.38; H, 8.63; N, 9.99; Found: C, 81.24; H, 8.67; N, 10.00.

Synthesis of *N,N′*-bis(2-isopropyl-6-methylphenyl)formamidine. Under ambient conditions, a 50 mL round bottom flask equipped with a short-path distillation head was charged with 2-isopropyl-6-methylaniline (3.0 g, 20 mmol, 2 equiv.), triethyl orthoformate (1.48 g, 10 mmol, 1 equiv.), two drops of formic acid and a stir bar. The resultant mixture was heated at 115 °C for 2 h followed by heating at 150 °C for 16 h. Upon cooling to ambient temperature, the crude solid was ground using a glass rod. Trituration with pentane followed by collection on a medium porosity frit, washing with pentane until colorless and drying under reduced pressure afforded the desired compound as a white solid (1.81 g, 5.9 mmol, 59% yield). m.p. 128-129 °C. NMR analysis revealed a mixture of rotational isomers that coalesced at elevated temperature. ^{1}H NMR (C_6D_6, 399.68 MHz): δ (major isomer) 1.11 (d, J = 6.8 Hz, 12H), 2.19 (s, 6H), 3.37 (septet, J = 6.8 Hz, 2H), 6.77 (s, 1H), 6.92-7.12 (m, 6H). (DMSO-d_6, 130 °C, 499.87 MHz): δ 1.17 (d, J = 6.8 Hz, 12H), 2.24 (s, 6H), 3.30 (septet, J = 6.8 Hz, 2H), 6.94-7.02 (m, 4H), 7.09 (dd, J = 7.1 Hz, 2H), 7.34 (s, 1H), 7.71 (bs, 1H). ^{13}C NMR (DMSO-d_6, 130 °C, 125.70 MHz): δ 17.75, 22.74, 26.85, 122.30, 123.59, 126.85, 131.32, 141.64, 142.35, 149.37. IR (KBr): ν = 3162.0, 2964.9, 1646.2, 1587.5, 1542.9, 1461.5, 1369.6, 1194.2, 1144.8, 1098.7, 778.0, 758.1, 449.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{21}H_{29}N_2$: 309.2331.

Found: 309.2331. Anal. calcd. for $C_{21}H_{28}N_2$: C, 81.77; H, 9.15; N, 9.08; Found: C, 81.60; H, 9.09; N, 8.94.

Synthesis of *N,N′*-bis(2-ethyl-6-isopropylphenyl)formamidine. Under ambient conditions, a 25 mL round bottom flask equipped with a short-path distillation head was charged with 2-ethyl-6-isopropylaniline (0.75 g, 4.6 mmol, 2 equiv.), triethyl orthoformate (0.34 g, 2.3 mmol, 1 equiv.), one drop of formic acid and a stir bar. The resultant mixture was heated at 100 °C for 1 h followed by heating at 140 °C for 16 h. Upon cooling to ambient temperature, the crude solid was ground using a glass rod. Trituration with pentane followed by collection on a medium porosity frit, washing with pentane until colorless and drying under reduced pressure afforded the desired compound as a white solid (0.363 g, 1.27 mmol, 47% yield). m.p. 152-153 °C. NMR analysis revealed a mixture of rotational isomers that coalesced at elevated temperature. ^{1}H NMR (C_6D_6, 399.68 MHz): δ (major isomer) 1.08 (bd, J = 6.8 Hz, 12H), 1.18 (t, J = 7.6 Hz, 6H), 2.63 (q, J = 7.6 Hz), 3.37 (septet, J = 6.8 Hz, 2H), 6.90 (s, 1H), 6.95-6.97 (m, 2H), 7.00-7.04 (m, 4H), 10.28 (bs, 1H). (DMSO-d_6, 130 °C, 499.87 MHz): δ 1.15-1.18 (overlapping m, 18H), 2.64 (q, J = 7.6 Hz, 4H), 3.31 (septet, J = 6.8 Hz, 2H), 7.02-7.05 (overlapping m, 4H), 7.09 (m, 2H), 7.31 (s, 1H), 7.75 (s, 1H). ^{13}C NMR (DMSO-d_6, 130 °C, 125.70 MHz): δ 13.69, 22.67, 23.50, 26.68, 122.10, 123.70, 124.85, 137.45, 140.97, 142.30, 149.24. IR (KBr): ν = 3060.7, 2962.8, 2867.7, 1672.2, 1592.0, 1453.3, 1326.9, 1290.2, 1186.5, 948.3, 865.9, 757.6, 708.5 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{23}H_{33}N_2$: 337.26383. Found: 337.26380. Anal. calcd. for $C_{23}H_{32}N_2$: C, 82.09; H, 9.58; N, 8.32; Found: C, 81.97; H, 9.37; N, 8.38.

Synthesis of 2-chloro-1,3-bis(2-ethyl-6-methylphenyl)-5,5-dimethyldihydropyrimidine-4,6(1H,5H)-dione, 4a·HCl. A 25 mL Schlenk flask was charged with N,N’-bis(2-ethyl-6-methylphenyl)formamidine (1.0 g, 3.57 mmol),

dichloromethane (15 mL), triethylamine (0.541 g, 5.35 mmol, 1.5 equiv.), and a stir bar. The resultant mixture was cooled to 0 °C whereupon dimethylmalonyl dichloride (0.633 g, 3.74 mmol, 1.05 equiv.) was added dropwise. The ice bath was removed and the reaction allowed to warm to room temperature with stirring for 2 h. After removing the volatiles under reduced pressure, the crude residue was extracted with 25 mL of toluene and filtered through a medium porosity frit into a 50 mL Schlenk flask. Concentration under reduced pressure afforded the desired product as a white solid (1.21 g, 2.93 mmol, 82% yield). m.p. 170-172 °C (decomp.) NMR analysis revealed a mixture of rotational isomers. ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.19-1.24 (overlapping t, 6H), 1.75-1.84 (s, 6H), 2.35-2.36 (overlapping s, 6H), 2.65 (m, 4H), 6.87-6.89 (s, 1H), 7.13-7.16 (m, 2H), 7.19-7.22 (m, 2H), 7.25-7.30 (m, 2H). ^{13}C NMR (C_6D_6, 100.60 MHz): δ 14.37, 14.49, 19.23, 19.57, 22.95, 23.68, 24.42, 24.57, 24.66, 48.17, 48.20, 90.14, 90.27, 127.17, 127.22, 129.27, 129.37, 129.39, 134.12, 134.15, 136.28, 136.83, 141.67, 142.14. IR (KBr): ν = 2977.2, 2934.3, 2873.9, 1712.1, 1688.6, 1589.9, 1460.0, 1402.5, 1260.1, 1183.4, 1129.5, 1050.5, 795.0, 645.6, 542.8, 439.5 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{24}H_{30}N_2O_2{}^{35}Cl$: 413.1996. Found: 413.1988. Anal. calcd. for $C_{24}H_{29}N_2O_2$: C, 69.80; H, 7.08; N, 6.78; Found: C, 69.68; H, 7.32; N, 7.08.

Synthesis of 2-chloro-1,3-bis(2-isopropyl-6-methylphenyl)-5,5-dimethyldihydropyrimidine-4,6(1H,5H)-dione, 4b·HCl. A 50 mL Schlenk flask was charged with N,N'-bis(2-isopropyl-6-methylphenyl)formamidine (1.0 g, 3.24 mmol), dichloromethane (25 mL), triethylamine (0.49 g, 4.86 mmol, 1.5 equiv.), and a stir bar. The resultant mixture was cooled to 0 °C whereupon dimethylmalonyl dichloride (0.575 g, 3.40 mmol, 1.05 equiv.) was added dropwise. The ice bath was removed and the reaction allowed to warm to room temperature with stirring for 2 h. After removing the volatiles under reduced pressure, the crude residue was extracted with 40 mL of toluene

and filtered through a medium porosity frit into a 100 mL Schlenk flask. Concentration under reduced pressure afforded the desired product as a white solid (1.11 g, 2.51 mmol, 78% yield). m.p. 165-167 °C (decomp.) NMR analysis revealed a mixture of rotational isomers. ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.10-1.13 (overlapping d, 6H), 1.29-1.34 (overlapping d, 6H), 1.74-1.82 (singlets, 6H), 2.34-2.35 overlapping s, 6H), 3.10 (septet, J = 6.7 Hz, 2H), 6.79-6.86 (s, 1H), 7.12-7.15 (m, 2H), 7.24-7.33 m, 4H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 19.10, 19.59, 22.87, 23.13, 23.70, 24.45, 24.68, 24.87, 28.69, 29.05, 48.08, 48.17, 89.89, 90.11, 124.85, 129.15, 129.64, 129.65, 133.26, 133.41, 135.98, 136.23, 147.11, 147.31171.11, 171.21. IR (KBr): ν = 2962.5, 2929.5, 2867.5, 1707.9, 1678.7, 1591.8, 1463.5, 1398.8, 1260.2, 1186.7, 1126.5, 1043.2, 785.6, 653.5, 541.9, 448.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{26}H_{34}N_2O_2{}^{35}Cl$: 441.2309. Found: 441.2308. Anal. calcd. for $C_{26}H_{33}N_2O_2Cl$: C, 70.81; H, 7.54; N, 6.35; Found: C, 70.43; H, 7.34; N, 6.07.

Synthesis of 2-chloro-1,3-bis(2-ethyl-6-isopropylphenyl)-5,5-dimethyldihydropyrimidine-4,6(1H,5H)-dione, 4c·HCl. A 25 mL, Schlenk flask was charged with N,N'-bis(2-ethyl-6-isopropylphenyl)formamidine (0.200 g, 0.59 mmol), dichloromethane (5 mL), triethylamine (0.090 g, 0.89 mmol, 1.5 equiv.), and a stir bar. The resultant mixture was cooled to 0 °C whereupon dimethylmalonyl dichloride (0.105 g, 0.62 mmol, 1.05 equiv.) was added dropwise. The ice bath was removed and the reaction allowed to warm to room temperature with stirring for 1 h. After removing the volatiles under reduced pressure, the crude residue was extracted with 18 mL of a 2:1 v/v mixture of hexanes/dichloromethane and filtered through a 0.2 μm PTFE filter into a 50 mL Schlenk flask. Concentration under reduced pressure afforded the desired product as a white solid (0.249 g, 0.53 mmol, 89% yield). m.p. 157-160 °C (decomp). NMR analysis revealed a mixture of rotational isomers. ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.07-1.23

(overlapping s and d, 18H), 1.54 (overlapping s, 6H), 2.57 (overlapping q, 4H), 3.06 (septet, J = 7.4 Hz, 2H), 7.04 (m, 2H), 7.14-7.17 (m overlapping solvent, 3H), 7.20-7.25 (m, 2H). ^{13}C NMR (C_6D_6, 100.60 MHz): δ 14.49, 14.63, 22.78, 23.08, 24.71, 25.09, 25.35, 23.95, 25.43, 29.21, 29.47, 48.61, 91.38, 91.76, 124.99, 125.22, 127.19, 127.25, 128.53, 129.92, 133.65, 141.67, 142.43, 147.39, 148.22, 171.66, 171.71. IR (KBr): ν = 2965.6, 2933.9, 2871.2, 1705.3, 1679.4, 1634.8, 1589.4, 1456.3, 1397.6, 1357.4, 1224.2, 1188.6, 1130.0, 1052.6, 803.4, 651.6 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{28}H_{38}N_2O_2Cl$: 469.2622. Found: 469.2621. Anal. calcd. for $C_{28}H_{37}N_2O_2Cl$: C, 71.70; H, 7.95; N, 5.97; Found: C, 71.32; H, 7.86; N, 5.82.

***In situ* generation of 4a.** An 8 mL vial was charged with **4b**·HCl (0.025 g, 0.061 mmol), NaHMDS (0.012 g, 0.064 mmol, 1.05 equiv.), C_6D_6 (0.7 mL), and a stir bar. The resultant mixture was stirred at ambient temperature for 1 h and subsequently filtered through a 0.2 μm PTFE filter prior to analysis. Attempts to concentrate to dryness resulted in decomposition to unidentified products. NMR analysis revealed a mixture of two rotational isomers. ^{1}H NMR (C_6D_6, 400.27 MHz): δ 1.06 (triplets, 6H), 1.09 (singlets, 6H), 2.09 (two s, 6H), 2.54 (m, 4H), 6.98 (bd, 2H), 7.04 (m, 2H), 7.12 (m, 2H). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 13.38, 13.43, 17.33, 17.52, 23.02, 23.54, 23.75, 23.81, 23.99, 50.07, 126.08, 127.24, 127.76, 133.95, 134.03, 139.44, 139.52, 169.35, 276.10, 276.33. IR (C_6H_6, CaF_2): ν = 2954.2, 1744.2, 1715.4, 1476.5, 1382.5, 1372.6, 1324.2, 1250.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{24}H_{29}N_2O_2$: 377.2229. Found: 377.2225.

***In situ* generation of 4b.** An 8 mL vial was charged with **4b**·HCl (0.025 g, 0.057 mmol), NaHMDS (0.011 g, 0.060 mmol, 1.05 equiv.), C_6D_6 (0.7 mL), and a stir bar. The resultant mixture was stirred at ambient temperature for 1 h and subsequently filtered through a 0.2 μm PTFE filter prior to analysis. Attempts to concentrate to dryness resulted in decomposition to unidentified products. NMR analysis revealed a mixture of

two rotational isomers. ^{1}H NMR (C_6D_6, 100.50 MHz): δ 1.09-1.18 (m, 12H), 1.43, 1.47, 1.49 (three s, 6H), 2.06 (s, 3H), 2.11 (s, 3H), 3.0-3.07 (m, 2H), 6.93-6.95 (m, 2H), 7.10-7.13 (m, 4H). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 17.49, 17.77, 22.50, 22.55, 22.62, 22.71, 23.15, 23.54, 24.00, 27.79, 49.98, 50.07, 123.36, 127.51, 127.75, 133.78, 133.86, 138.61, 138.62, 144.20, 144.23, 169.43, 169.46, 276.62, 276.89. IR (C_6H_6, CaF_2): ν = 2960.9, 1744.5, 1715.2, 1382.3, 1323.0, 1250.4 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{24}H_{33}N_2O_2$: 405.2542. Found: 405.2534.

***In situ* generation of 4c.** An 8 mL vial was charged with **4c**·HCl (0.025 g, 0.053 mmol), NaHMDS (0.010 g, 0.056 mmol, 1.05 equiv.), C_6D_6 (0.7 mL), and a stir bar. The resultant mixture was stirred at ambient temperature for 1 h and subsequently filtered through a 0.2 μm PTFE filter prior to analysis. Attempts to concentrate to dryness resulted in decomposition to unidentified products. NMR analysis revealed a mixture of two rotational isomers. ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.07-1.23 (overlapping m, 18H), 1.54 (overlapping s, 6H), 2.53-2.61 (overlapping m, 4H), 3.06, (septet, J = 7.1 Hz, 2H), 7.04 (broad dd, 2H), 7.15-7.17 (m overlapping solvent, 2H), 7.23 (t, J = 7.5 Hz, 2H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 14.37, 14.43, 23.69, 23.80, 24.56, 24.65, 24.87, 24.92, 24.98, 28.85, 28.92, 50.94, 51.01, 124.28, 124.30, 128.54, 128.95, 138.96, 140.34, 140.38, 145.27, 145.332, 170.87, 277.75, 277.82. IR (C_6H_6, CaF_2): ν = 2963.0, 1742.4, 1714.7, 1474.5, 1382.5, 1369.6, 1323.4, 1250.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{28}H_{37}N_2O_2$: 433.2855. Found: 433.2840.

Synthesis of 5a/5a'. A 30 mL vial was charged with **4a**·HCl (0.200 g, 0.484 mmol), NaHMDS (0.093 g, 0.509 mmol, 1.05 equiv.), benzene (25 mL), and a stir bar. The resultant mixture was stirred at ambient temperature for 30 minutes and filtered through a 0.2 μm PTFE filter into a 30 mL vial. The solution was heated at 80 °C for 16 h followed by removal of the volatiles under reduced pressure. Purification of the crude

residue by silica gel column chromatography using 3:1 v/v hexanes/ethyl acetate as the eluent afforded the desired product as a white solid (0.118 mg, 0.313 mmol, 65% yield). The 98:2 ratio of **5a:5a'** was calculated by conducting the reaction in C_6D_6 and comparing the integrals of the ^{1}H NMR signals at 5.03 (d) and 5.05 (d) for **5a** with the signals at 5.32 (d of d) and 5.39 (d of d) for **5a'**. m.p. 67-75 °C (decomp.) NMR analysis revealed two isomers each for **5a** and **5a'** which were determined by ^{1}H NOESY NMR spectroscopy for **5a** to be rotational isomers arising from orientation of the *N*-2-ethyl-6-methylphenyl ethyl group either inside or outside of the concave face of **5a**. ^{1}H NMR ($CDCl_3$, 599.75 MHz): δ 0.68 (overlapping d, 3H), 1.14-1.25 (two t, J = 7.5 Hz, 3H), 1.56 (s, 3H), 1.65 and 1.66 (two s, 3H), 2.18 and 2.27 (two s, 3H), 2.33 (s, 3H), 2.49-2.61 (m, 2H), 3.35 (m, 1H), 5.49 (overlapping d, 1H), 6.88 (d, J = 7.20 Hz, 1H), 7.05-7.22 (m, 3H), 7.26-7.29 (m, 2H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 14.15, 14.29, 16.48, 16.64, 18.37, 18.81, 20.39, 20.47, 20.71, 20.80, 24.09, 24.13, 24.27, 24.41, 42.93, 42.98, 47.19, 47.33, 78.71, 79.51, 120.39, 125.95, 126.01, 126.83, 126.95, 128.29, 128.43, 128.82, 128.93, 128.95, 128.98, 130.87, 130.93, 134.96, 135.09, 135.37, 135.49, 135.60, 137.07, 138.25, 138.27, 141.49, 142.74, 168.38, 168.43, 171.33, 171.71. IR (KBr): ν = 2970.2, 2932.6, 2874.8, 1692.6, 1664.0, 1465.8, 1414.6, 1227.1, 1046.5, 781.6 cm^{-1}. HRMS (CI): $[M]^+$ calcd. for $C_{24}H_{28}N_2O_2$: 376.2151. Found: 376.2148. Anal. calcd. for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44; Found: C, 76.29; H, 7.49; N, 7.24.

Synthesis of 5b/5b'. A 30 mL vial was charged with **4b**·HCl (0.200 g, 0.454 mmol), NaHMDS (0.087 g, 0.476 mmol, 1.05 equiv.), benzene (25 mL), and a stir bar. The resultant mixture was stirred at ambient temperature for 30 minutes and filtered through a 0.2 μm PTFE filter into a 30 mL vial. The solution was heated at 80 °C for 16 h followed by removal of the volatiles under reduced pressure. Purification of the crude residue by silica gel column chromatography using 3:1 v/v hexanes/ethyl acetate as the

eluent afforded the desired product as a white solid (0.097 mg, 0.240 mmol, 53% yield). Conducting the reaction in C_6D_6 and analysis of the crude reaction by ^1H NMR spectroscopy revealed no discernable doublet of doublets indicative of the formation of **5b'**. m.p. 205-210 °C (decomp.) NMR analysis revealed two isomers of **5b** which were determined by ^1H NOESY NMR spectroscopy to be rotational isomers arising from orientation of the *N*-2-isopropyl-6-methylphenyl isopropyl group inside or outside of the concave face of **5b**. ^1H NMR ($CDCl_3$, 599.75 MHz): δ 0.86 (s, 3H), 1.15-1.20 (d overlapping s, 6H), 1.33 (d, J = 6.6 Hz, 3H), 1.64 (s, 3H), 1.70 (s, 3H), 2.22 (s, 3H), 2.35 (s, 3H), 3.21 (septet, J = 6.9 Hz, 1H), 5.02 (s, 1H), 6.91-6.93 (m, 1H), 7.08-7.15 (m, 3H), 7.23-7.29 (m, 2H) and 0.84 (s, 3H), 1.07 (d, J = 6.8 Hz, 3H), 1.14 (s, 3H), 1.25 (d, J = 6.8 Hz, 3H), 1.62 (s, 3H), 1.69 (s, 3H), 2.36 (s, 6H), 2.86 (septet, J = 6.8 Hz, 1H), 4.96 (s, 1H), 6.91-6.94 (m, 1H), 7.10-7.16 (m, 3H), 7.18-7.21 (m, 1H), 7.24-7.28 m, 1H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.49, 19.05, 21.03, 21.67, 22.89, 24.39, 25.49, 27.03, 28.68, 45.67, 46.82, 83.34, 118.91, 124.71, 127.07, 128.67, 129.52, 129.79, 130.82, 133.62, 136.57, 137.56, 142.58, 147.66, 172.87, 173.43 and 19.15, 19.75, 21.61, 21.80, 22.97, 23.74, 25.45, 27.65, 28.64, 45.76, 46.95, 84.93, 118.86, 125.11, 127.01, 128.67, 128.69, 129.84, 130.77, 136.46, 136.90, 137.63, 142.46, 145.25. IR (KBr): ν = 2973.4, 2931.3, 2869.7, 1691.4, 1661.8, 1460.9, 1404.2, 1199.5, 1103.0, 791.2 cm^{-1}. HRMS (CI): $[M]^+$ calcd. for $C_{26}H_{32}N_2O_2$: 404.2464. Found: 404.2468. Anal. calcd. for $C_{26}H_{32}N_2O_2$: C, 77.19; H, 7.97; N, 6.92; Found: C, 77.06; H, 7.89; N, 6.61.

Synthesis of 5c/5c'. A 30 mL vial was charged with **4c**·HCl (0.100 g, 0.213 mmol), NaHMDS (0.041 g, 0.224 mmol, 1.05 equiv.), benzene (10 mL) and a stir bar. The resultant mixture was stirred at ambient temperature for 1 h and filtered through a 0.2 μm PTFE filter into a 30 mL vial. The solution was heated at 80 °C for 16 h followed by removal of the volatiles under reduced pressure. Purification of the crude residue by silica

gel column chromatography using 4:1 v/v hexanes/ethyl acetate as the eluent afforded the desired product as a tacky, colorless solid (0.053 g, 0.123 mmol, 58% yield). The 82:18 ratio of **5c:5c'** was calculated by conducting the reaction in C_6D_6 and comparing the integrals of the ^{1}H NMR signals at 5.01 (s) and 5.07 (s) for **5c** with the signals at 5.22-5.25 (overlapping d) for **5c'**. m.p. 48-52 °C (decomp.) NMR analysis revealed two isomers each for **5c**:**5c'** which were attributed to rotational isomers arising from orientation of the *N*-2-ethyl-6-isopropylphenyl substituent isopropyl group inside or outside of the concave face of **5c**/**5c'**. The NMR signals for the major isomers of **5c** are given. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 0.87 (s, 3H), 1.16-1.28 (m, 12H), 1.35 (d, J = 6.8 Hz, 3H), 1.64 (s, 3H), 1.70 (s, 3H), 2.50 (m, 2H), 2.76 (m, 2H), 3.21 (septet, J = 6.8 Hz, 1H), 4.97 (s, 1H), 6.93 (m, 1H), 7.15-7.19 (m, 3H), 7.22-7.24 (m, 1H), 7.30-7.34 (m, 1H) and 0.84 (s, 3H), 1.08-1.45 (m, 15H), 1.63 (s, 3H), 1.69 (s, 3H), 2.44-2.61 (m, 2H), 2.67-2.88 (m, 2H), 3.15-3.28 (m, 1H), 4.90 (s, 1H), 6.91-6.95 (m, 1H), 7.15-7.26 (4H), 7.31-7.34 (m, 1H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 13.36, 14.94, 20.93, 21.76, 22.90, 24.08, 24.41, 25.51, 25.61, 27.17, 28.79, 45.65, 46.66, 84.56, 119.04, 124.47, 127.38, 127.52, 127.76, 128.86, 136.28, 136.65, 136.95, 139.69, 142.80, 147.51, 173.21, 173.46 and 13.40, 14.34, 21.38, 21.83, 23.93, 24.82.25.36, 25.67, 27.50, 28.68, 45.70, 46.67, 85.16, 119.00, 125.00, 126.26, 127.33, 127.88, 128.81,136.16, 136.62, 136.95, 142.44, 142.65, 144.89, 172.90, 173.02. IR (KBr): ν = 2967.6, 2933.5, 2871.4, 1694.7, 1667.5, 1458.2, 1400.5, 1364.0, 1267.5, 1196.7, 1101.7, 1049.1, 802.7, 770.6, 759.8 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{28}H_{37}N_2O_2$: 433.2855. Found: 433.2840. Anal. calcd. for $C_{28}H_{36}N_2O_2$: C, 77.74; H, 8.39; N, 6.48; Found: C, 78.00; H, 8.51; N, 6.16.

General procedure for the intermolecular C–H insertion reactions involving 2. An 8 mL vial was charged with **2** (0.075 g, 0.199 mmol), 0.75 mL of the specified substrate (or 0.5 g for solid substrates) and a stir bar. The vial was sealed and heated to

100 °C for 16 h unless otherwise specified. The crude reaction mixture was purified via silica gel column chromatography (eluent = 2:1 v/v hexanes/ethyl acetate unless otherwise specified).

Synthesis of 6a. Substrate: p-methylthioanisole. Following the general procedure, **6a** was obtained as a white solid (0.038 g, 0.074 mmol, 37% yield). m.p. 266-267 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.61 (s, 3H), 1.62 (s, 3H), 1.99 (s, 6H), 2.23 (s, 6H), 2.30 (s, 6H), 2.35 (s, 3H), 2.76 (d, J = 5.2 Hz, 2H), 5.90 (t, J = 5.2 Hz, 1H), 6.13 (d, J = 8.4 Hz, 2H), 6.68 (s, 2H), 6.79 (d, J = 8 Hz, 2H), 6.92 (s, 2H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 16.32, 18.55, 19.04, 20.88, 22.02, 22.96, 36.61, 46.77, 72.15, 126.38, 128.27, 129.48, 129.78, 132.98, 134.06, 135.35, 135.96, 136.85, 138.22, 171.52. IR (KBr): ν = 2996.5, 2972.9, 2918.7, 1693.7, 1662.9, 1607.9, 1483.7, 1428.9, 1404.1, 1355.6, 1249.2, 1217.0, 1158.4, 1099.9, 849.9, 800.4, 522.8 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{38}N_2O_2S$: 515.2732. Found: 515.2729. Anal. calcd. for $C_{32}H_{38}N_2O_2S$: C, 74.67; H, 7.44; N, 5.44; Found: C, 74.76; H, 7.46; N, 5.36.

Synthesis of 6b. Substrate: 4-nitrotoluene. Following the general procedure, **6b** was obtained as an off white solid (0.090 g, 0.175 mmol, 88% yield). Eluent = 1:1 v/v hexanes/ethyl acetate. m.p. 241-242 °C (decomp.). ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 1.63 (s, 6H), 2.02 (s, 6H), 2.22 (s, 6H), 2.31 (s, 6H), 2.92 (d, J = 5.6 Hz, 2H), 5.93 (t, J = 5.6 Hz, 1H), 6.39 (d, J = 8.6 Hz, 2H), 6.66 (s, 2H), 6.93 (s, 2H), 7.75 (d, J = 8.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.53, 18.98, 20.82, 22.16, 23.33, 37.56, 46.69, 71.97, 122.70, 128.37, 129.71, 129.83, 133.84, 135.10, 136.93, 138.75, 143.35, 145.95, 171.21. IR (KBr): ν = 2973.8, 2924.5, 1688.5, 16.56.3, 1606.4, 1520.2, 1409.6, 1345.2, 1209.8, 1105.0, 852.4, 734.5, 511.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{36}N_3O_4$: 514.2706. Found: 514.2701. Anal. calcd. for $C_{31}H_{35}N_3O_4$: C, 72.49; H, 6.87; N, 8.18; Found: C, 72.21; H, 6.87; N, 8.02.

Synthesis of 6c. Substrate: 4-bromotoluene. Following the general procedure, **6c** was obtained as a white solid (0.058 g, 0.106 mmol, 40% yield). m.p. 221-222 °C (decomp). ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 1.62 (overlapping s, 6H), .99 (s, 6H), 2.23 (s, 6H), 2.29 (s, 6H), 2.75 (d, J = 5.4 Hz, 2H), 5.87 (t, J = 5.4 Hz, 1H), 6.07 (d, J = 8.4 Hz, 2H), 6.70 (s, 2H), 6.92 (s, 2H), 7.00 (d, J = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.52, 18.99, 20.85, 22.03, 23.08, 36.70, 46.71, 72.04, 119.81, 129.41, 129.53, 129.81, 130.66, 133.93, 134.89, 135.23, 136.82, 138.39, 171.38. IR (KBr): ν = 2975.0, 2947.5, 2924.3, 1687.9, 1657.3, 1607.9, 1489.8, 1459.6, 1406.1, 1376.1, 1358.6, 1213.1, 1009.9, 800.4, 511.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{36}N_2O_2{}^{79}Br$: 547.1960. Found: 547.1953. Anal. calcd. for $C_{31}H_{36}N_2O_2Br$: C, 68.00; H, 6.44; N, 5.12; Found: C, 67.75; H, 6.43; N, 5.09.

Synthesis of 6d. Substrate: 4-chlorotoluene. Following the general procedure, **6d** was obtained as a white solid (0.059 g, 0.117 mmol, 59% yield). m.p. 220-221 °C (decomp). ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.61 (s, 3H), 1.62 (s, 3H), 1.99 (s, 6H), 2.24 (s, 6H), 2.30 (s, 6H), 2.77 (d, J = 5.6 Hz, 2H), 5.88 (t, J = 5.6 Hz, 1H), 6.13 (d, J = 8.4 Hz, 2H), 6.70 (s, 2H), 6.85 (d, J = 8.4 Hz), 6.92 (s, 2H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 18.50, 18.99, 20.84, 22.03, 23.03, 36.60, 46.71, 127.71, 129.07, 129.52, 129.80, 131.84, 133.95, 134.40, 135.26, 136.84, 138.38, 171.41. IR (KBr): ν = 2976.0, 2948.0, 2924.8, 2860.1, 1687.9, 1656.8, 1607.1, 1493.5, 1460.1, 1407.9, 1374.6, 1358.4, 1251.4, 1211.0, 1098.5, 1013.3, 843.1, 803.9, 779.1, 511.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{36}N_2O_2Cl$: 503.2465. Found: 503.2460. Anal. calcd. for $C_{31}H_{35}N_2O_2Cl$: C, 74.01; H, 7.01; N, 5.57; Found: C, 74.28; H, 6.96; N, 5.60.

Synthesis of 6e. Substrate: toluene. Following the general procedure, **6e** was obtained as a white solid (0.043 g, 0.092 mmol, 46% yield). m.p. 183-185 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.61 (s, 3H), 1.63 (s, 3H), 1.97 (s, 6H), 2.22 (s, 6H),

2.31 (s, 6H), 2.79 (d, J = 5.6 Hz, 2H), 5.97 (t, J = 5.6 Hz, 1H), 6.23 (d, J = 7.6 Hz, 2H), 6.65 (s, 2H), 6.86-6.98 (m, 5H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.50, 19.05, 20.85, 21.99, 22.80, 37.00, 46.82, 72.16, 125.95, 127.70, 127.83, 129.43, 129.75, 134.07, 135.42, 135.87, 136.83, 138.17, 171.59. IR (KBr): ν = 2967.2, 2920.4, 1695.2, 1660.8, 1607.0, 1483.2, 1462.2, 1408.2, 1358.5, 1219.0, 1159.5, 849.8, 713.6, 693.3, 511.0 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{37}N_2O_2$: 469.2855. Found: 469.2852. Anal. calcd. for $C_{31}H_{36}N_2O_2$: C, 79.45; H, 7.74; N, 5.98; Found: C, 79.33; H, 7.74; N, 6.05.

Synthesis of 6f. Substrate: 4-tert-butyltoluene. Following the general procedure, **6f** was obtained as a white solid (0.042 g, 0.080 mmol, 30% yield). m.p. = 92-94 °C (decomp). ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.19 (s, 9H), 1.61 (s, 3H), 1.63 (s, 3H), 1.98 (s, 6H), 2.20 (s, 6H), 2.30 (s, 6H), 2.76 (d, J = 5.2 Hz, 2H), 5.97 (t, J = 5.2 Hz, 1H), 6.21 (d, J = 8.4 Hz, 2H), 6.60 (s, 2H), 6.89 (d overlapping s, 4H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.55, 19.03, 20.85, 21.98, 22.96, 31.23, 34.14, 36.57, 46.79, 72.01, 124.46, 127.17, 129.35, 129.63, 132.61, 134.09, 135.24, 136.72, 137.99, 148.95, 171.57. IR (KBr): ν = 2962.8, 2868.3, 1694.0, 1663.5, 1608.9, 1461.9, 1406.6, 1356.2, 1217.19, 1163.5, 1107.0, 1033.2, 852.3, 558.0, 510.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{35}H_{45}N_2O_2$: 525.3481. Found: 525.3478. Anal. calcd. for $C_{35}H_{44}N_2O_2$: C, 80.11; H, 8.45; N, 5.34; Found: C, 79.83; H, 8.42; N, 5.40.

Synthesis of 6g. Substrate: p-methylanisole. Following the general procedure, **6g** was obtained as a white solid (0.037 g, 0.074 mmol, 37% yield). m.p. 212-213 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.60 (s, 3H), 1.62 (s, 3H), 1.97 (s, 6H), 2.23 (s, 6H), 2.31 (s, 6H), 2.73 (d, J = 5.6 Hz, 2H), 3.67 (s, 3H), 5.90 (t, J = 5.6 Hz, 1H), 6.10 (m, 2H), 6.42 (m, 2H), 6.69 (s, 2H), 6.92 (s, 2H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.51, 19.04, 20.87, 21.95, 22.78, 36.06, 36.06, 46.79, 55.20, 72.30, 113.12, 128.11, 128.93, 129.41, 129.75, 134.11, 135.43, 136.83, 138.10, 157.80, 171.61. IR (KBr): ν =

2974.9, 2951.8, 2922.5, 1693.4, 1663.3, 1609.7, 1513.4, 1405.8, 1355.2, 1247.8, 1216.6, 1025.4, 853.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{37}N_2O_3$: 499.2961. Found: 499.2962. Anal. calcd. for $C_{32}H_{36}N_2O_3$: C, 77.08; H, 7.68; N, 5.62; Found: C, 76.89; H, 7.64; N, 5.53.

Synthesis of 6h. Substrate: *N,N*-dimethyl-p-toluidine. Following the general procedure, **6h** was obtained as a white solid (0.026 g, 0.051 mmol, 26% yield). m.p. 159-161 °C (decomp.) ^1H NMR ($CDCl_3$, 399.68 MHz): δ 1.60 (s, 3H), 1.62 (s, 3H), 1.97 (s, 6H), 2.23 (s, 6H), 2.30 (s, 6H), 2.69 (d, J = 5.2 Hz, 2H), 2.79 (s, 6H), 5.89 (t, J = 5.2 Hz, 1H), 6.05 (d, J = 8.6 Hz, 2H), 6.27 (d, J = 8.6 Hz, 2H), 6.68 (s, 2H), 6.91 (s, 2H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 18.55, 19.08, 20.89, 21.94, 22.77, 35.85, 40.79, 46.82, 72.37, 112.32, 124.14, 128.57, 129.35, 129.74, 134.22, 135.50, 136.83, 137.91, 149.09, 171.69. IR (KBr): ν = 2975.7, 2918.1, 2869.6, 1692.0, 1661.9, 1608.1, 1521.1, 1461.3, 1408.5, 1355.3, 1264.5, 1208.4, 1165.1, 1103.6, 866.8, 803.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{33}H_{42}N_3O_2$: 512.3277. Found: 512.3281. Anal. calcd. for $C_{33}H_{41}N_3O_2$: C, 77.46; H, 8.08; N, 8.21; Found: C, 77.40; H, 8.10; N, 8.12.

Synthesis of 6i. Substrate: 3-chlorotoluene. Following the general procedure, **6i** was afforded as a white solid (0.057 g, 0.113 mmol, 57% yield). m.p. = 184-186 °C (decomp.) ^1H NMR ($CDCl_3$, 399.68 MHz): δ 1.60 (s, 3H), 1.63 (s, 3H), 1.98 (s, 6H), 2.25 (s, 6H), 2.31 (s, 6H), 2.75 (d, J = 5.2 Hz, 2H), 5.88 (s, 1H), 5.92 (t, J = 5.2 Hz, 1H), 6.35 (d, J = 7.6 Hz), 6.69 (s, 2H), 6.88-6.96 (m, 4H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 18.48, 19.01, 20.94, 22.07, 22.82, 36.89, 46.81, 71.95, 125.58, 126.17, 128.58, 128.82, 129.60, 129.82, 133.86, 135.41, 136.84, 137.83, 138.58, 171.52. IR (KBr): ν = 2969.4, 2920.3, 1695.7, 1661.9, 1602.0, 1408.4, 1358.8, 1218.0, 1157.8, 773.2, 690.9, 510.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{35}N_2O_2{}^{35}Cl$: 503.2465. Found: 503.2458. Anal. calcd. for $C_{31}H_{35}N_2O_2Cl$: C, 74.01; H, 7.01; N, 5.57; Found: C, 73.82; H, 7.17; N, 5.68.

Synthesis of 6j. Substrate: m-methylanisole. Following the general procedure, **6j** was obtained as a white solid (0.034 g, 0.068 mmol, 34% yield). m.p. = 192-193 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.60 (s, 3H), 1.63 (s, 3H), 1.99 (s, 6H), 2.22 (s, 6H), 2.31 (s, 6H), 2.76 (d, J = 5.2 Hz, 2H), 3.57 (s, 3H), 5.60 (t, J = 2.0 Hz, 1H), 5.98 (t, ^{3}H, 5.2 Hz, 1H), 6.01 (d, J = 8.0 Hz, 1H), 6.51 (dd, J = 5.0 Hz, 1H), 6.66 (s, 2H), 6.86 (t, J = 8.0 Hz, 1H), 6.93 (s, 2H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.55, 19.07, 20.85, 22.01, 22.81, 37.10, 46.84, 54.74, 72.10, 111.51, 113.73, 119.82, 128.66, 129.44, 129.72, 134.06, 135.53, 136.87, 137.42, 138.21, 158.97, 171.59. IR (KBr): ν = 2978.2, 2918.8, 2837.4, 1692.2, 1661.6, 1601.9, 1461.9, 1407.6, 1355.7, 1269.4, 1212.3, 1163.8, 1036.7, 853.7, 783.2, 692.4, 510.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{39}N_2O_3$: 499.2961. Found: 499.2965. Anal. calcd. for $C_{32}H_{38}N_2O_3$: C, 77.08; H, 7.68; N, 5.62; Found: C, 76.82; H, 7.85; N, 5.55.

Synthesis of 6k. Substrate: ethylbenzene. Following the general procedure, **6k** was obtained as a white solid (0.021 g, 0.044 mmol, 22% yield). m.p. 183-185 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.40 (d, J = 7.2 Hz, 3H), 1.59 (s, 3H), 1.73 (s, 3H), 1.79 (s, 3H), 2.10 (s, 3H), 2.27 (overlapping singlets, 6H), 2.30 (s, 3H), 2.33 (s, 3H), 3.20 (q, J = 7.2 Hz, 1H), 5.70 (s, 1H), 6.14 (s, 1H), 6.25 (d, J = 6.8 Hz, 2H), 6.81-6.85 (m, 3H), 6.87-6.92 (m, 1H), 6.95 (s, 1H), 7.03 (s, 1H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 11.59, 18.58, 18.81, 19.64, 20.06, 20.51, 20.92, 23.39, 27.16, 40.54, 45.39, 78.40, 125.45, 126.32, 127.41, 129.40, 129.75, 129.99, 130.19, 133.16, 133.98, 133.99, 134.53, 136.24, 137.18, 138.06, 138.10, 140.00, 170.92, 171.20. IR (KBr): ν = 2977.5, 2923.0, 2870.8, 1683.4, 1654.4, 1608.1, 1423.9, 1218.0, 1168.3, 851.5, 699.5 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{32}H_{39}N_2O_2$: 483.3012. Found: 483.3016. Anal. calcd. for $C_{32}H_{38}N_2O_2$: C, 79.63; H, 7.94; N, 5.80; Found: C, 79.38; H, 7.96; N, 5.92.

Synthesis of 6l. Substrate: dibenzyl sulfide. Following the general procedure, **6l** was obtained as a white solid (0.042 g, 0.071 mmol, 36% yield). m.p. 183-185 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.56 (s, 3H), 1.58 (s, 3H), 1.75 (s, 3H), 1.91 (s, 3H), 2.12 (s, 3H), 2.33 (s, 6H), 2.38 (s, 3H), 2.40 (s, 3H), 3.29 (m, 2H), 4.19 (s, 1H), 5.79 (s, 1H), 6.16 (s, 1H), 6.50 (d, J = 7.6 Hz, 2H), 6.83-6.94 (m, 4H), 7.01-7.04 (m, 3H), 7.20-7.23 (m, 3H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.10, 18.80, 19.70, 20.53, 20.85, 20.96, 22.64, 27.73, 37.14, 45.70, 53.71, 78.65, 126.09, 127.24, 127.71, 128.52, 128.89, 129.41, 129.72, 130.04, 132.93, 133.15, 133.76, 134.12, 136.43, 136.52, 137.23, 138.00, 138.08, 139.13, 170.61, 170.66. IR (KBr): ν = 2919.2, 1685.4, 1657.0, 1604.1, 1423.1, 1348.9, 1209.2, 1106.7, 1029.7, 849.1, 711.1, 693.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{38}H_{43}N_2O_2S$: 591.3045. Found: 591.3045. Anal. calcd. for $C_{38}H_{42}N_2O_2S$: C, 77.25; H, 7.17; N, 4.74; Found: C, 77.19; H, 7.27; N, 4.67.

Synthesis of 6m. Substrate: fluorene. Following the general procedure with the exception that the reaction was conducted at 120 °C for 2 h, **6m** was obtained as a white solid (0.096 g, 0.177 mmol, 67% yield). m.p. 253-255 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 0.85 (s, 3H), 1.67 (s, 3H), 1.85 (s, 3H), 1.87 (s, 3H), 2.16 (s, 3H), 2.28 (s, 3H), 2.46 (s, 3H), 2.48 (s, 3H), 4.18 (s, 1H), 6.10 (s, 1H), 6.13 (s, 2H), 6.83 (d, J = 7.2 Hz, 1H), 6.91-6.93 (overlapping s and m, 2H), 7.03 (t, J = 7.4 Hz, 1H), 7.09 (s, 1H), 7.27 (d, 7.2 Hz, 1H), 7.35 (dt, J = 7.4 Hz, 1.2 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 7.61 (d, J = 8 Hz, 1H), 7.96 (d, J = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 16.39, 18.57, 19.92, 20.29, 20.82, 25.73, 26.47, 45.16, 50.37, 74.88, 119.35, 120.73, 121.14, 126.09, 126.30, 126.66, 126.81, 128.38, 128.55, 128.80, 130.38, 130.68, 131.47, 133.10, 134.30, 134.79, 136.93, 137.25, 138.45, 138.70, 139.67, 141.14, 142.59, 143.42, 169.80, 171.71. IR (KBr): ν = 2985.6, 2939.7, 2915.0, 2870.9, 1677.5, 1652.3, 1609.5, 1449.0, 1421.2, 1353.6, 1216.1, 848.2, 750.2, 644.1, 635.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for

$C_{37}H_{39}N_2O_2$: 543.3012. Found: 543.3007. Anal. calcd. for $C_{37}H_{38}N_2O_2$: C, 81.88; H, 7.06; N, 5.16; Found: C, 81.56; H, 7.19; N, 5.42.

Synthesis of 6n. Substrate: 9,10-dihydrophenanthrene. Following the general procedure, **6n** was obtained as a white solid (0.051 g, 0.092 mmol, 34% yield). m.p. 212-213 °C. ^{1}H NMR (DMSO-d_6, 100 °C, 599.76 MHz): δ 1.56 (s, 3H), 1.76 (s, 3H), 1.81 (s, 3H), 1.97 (s, 3H), 2.13 (s, 3H), 2.15 (s, 3H), 2.19 (s, 3H), 2.29 (s, 3H), 2.78-2.93 (overlapping m, 3H), 3.38 (dt, J = 2.2, 8.5 Hz, 1H), 5.92 (d, J = 2.3 Hz, 1H), 6.40 (s, 1H), 6.75 (s, 2H), 6.90-6.94 (overlapping m, 3H), 7.03 (d, J = 7.4 Hz, 1H), 7.12-7.23 (overlapping m, 3H), 7.51 (d, J = 7.2 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H). ^{13}C NMR (DMSO-d_6, 150.82 MHz, 100 °C): δ 18.18, 18.44, 18.52, 18.99, 19.48, 19.52, 24.47, 24.95, 28.75, 44.67, 74.91, 122.84, 123.06, 125.97, 126.18, 126.29, 126.38, 126.94, 127.49, 128.53, 128.68, 128.98, 129.25, 132.11, 132.96, 133.09, 133.12, 133.66, 133.77, 134.07, 134.45, 136.38, 136.43, 137.01, 137.14170.06, 170.31. IR (KBr): ν = 2995.2, 2962.6, 2918.5, 1685.2, 1656.0, 1483.8, 1413.0, 1350.1, 1210.8, 758.6, 748.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{38}H_{41}N_2O_2$: 557.3168. Found: 557.3165. Anal. calcd. for $C_{38}H_{41}N_2O_2$: C, 81.98; H, 7.24; N, 5.03; Found: C, 82.01; H, 7.41; N, 5.25.

Synthesis of 6o. Substrate: ethyl acetate. Following the general procedure, **6o** was obtained as a white solid (0.022 g, 0.047 mmol, 24% yield). m.p. 193-194 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 0.90 (t, J = 7.0 Hz, 3H), 1.61 (s, 3H), 1.65 (s, 3H), 2.22 (s, 12H), 2.24 (s, 6H), 2.42 (d, J = 6.0 Hz, 2H), 3.48 (q, J = 7.0 Hz, 2H), 6.11 (t, J = 5.6 Hz, 1H), 6.87 (s, 2H), 6.91 (s, 2H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 13.52, 18.49, 18.76, 20.89, 22.19, 23.31, 36.80, 46.73, 60.92, 67.97, 129.58, 129.91, 133.14, 135.92, 137.11, 138.39, 168.31, 171.17. IR (KBr): ν = 2983.9, 2928.6, 1731.1, 1697.0, 1659.8, 1608.3, 1465.0, 1411.1, 1359.8, 1306.1, 1244.8, 1178.2, 1024.2, 864.2, 511.9 cm^{-1}. HRMS (CI):

$[M+H]^+$ calcd. for $C_{28}H_{37}N_2O_4$: 465.2753. Found: 465.2743. Anal. calcd. for $C_{28}H_{36}N_2O_4$: C, 72.39; H, 7.81; N, 6.03; Found: C, 72.56; H, 7.73; N, 6.27.

Synthesis of 6p. Substrate: acetophenone. Following the general procedure, **6p** was obtained as a white solid (0.047 g, 0.095 mmol, 48% yield). m.p. 88-90 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.60 (s, 3H), 1.70 (s, 3H), 2.01 (s, 6H), 2.18 (s, 6H), 2.27 (s, 6H), 2.90 (d, J = 5.2 Hz, 2H), 6.57 (t, J = 5.2 Hz, 1H), 6.67 (s, 2H), 6.69 (s, 2H), 7.16-7.23 (m, 4H), 7.39 (tt, J = 4.2 Hz). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 18.41, 18.85, 20.70, 22.09, 22.31, 38.32, 47.10, 68.19, 127.38, 127.69, 129.38, 130.05, 132.94, 133.83, 135.03, 136.05, 136.61, 138.36, 171.53, 192.99. IR (KBr): ν = 2982.1, 2918.9, 1695.2, 1662.0, 1608.1, 1448.1, 1409.2, 1377.8, 1357.0, 1298.0, 1249.5, 1213.4, 857.8, 766.0, 689.1, 604.9 cm^{-1}. HRMS (CI): $[M]^+$ calcd. for $C_{32}H_{36}N_2O_3$: 496.2726. Found: 496.2727. Anal. calcd. for $C_{32}H_{36}N_2O_3$: C, 77.39; H, 7.31; N, 5.64; Found: C, 77.67; H, 7.33; N, 5.63.

Synthesis of 6q. Substrate: 1,4-cyclohexadiene. Following the general procedure, **6q** was obtained as a white solid (0.049 g, 0.107 mmol, 40% yield). m.p. 187-189 °C. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.61 (s, 3H), 1.75 (s, 3H), 2.17 (s, 6H), 2.33-2.42 (m, 14H), 3.09 (m, 1H), 5.32-5.35 (m, 3H), 5.38-5.42 (m, 2H), 6.82 (s, 2H), 6.84 (s, 2H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 19.27, 19.79, 20.78, 23.86, 26.33, 26.48, 38.89, 45.49, 75.82, 123.35, 125.92, 129.61, 129.70, 134.08, 137.70, 138.42, 171.08. IR (KBr): ν = 3029.5, 3018.7, 2973.5, 2949.0, 2920.6, 2878.9, 1678.7, 1650.2, 1607.8, 1420.4, 1411.1, 1362.1, 1296.0, 1217.4, 1108.0, 938.8, 858.4, 672.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{30}H_{37}N_2O_2$: 457.2855. Found: 457.2854. Anal. calcd. for $C_{30}H_{36}N_2O_2$: C, 78.91; H, 7.95; N, 6.13; Found: C, 78.77; H, 7.91; N, 6.11. The reaction of **2** with 1,4-cyclohexadiene also afforded **7**, which was isolated from the silica gel column as a white solid (0.029 g, 0.077 mmol, 29% yield). m.p. 230-231 °C. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.63 (s,

6H), 2.21 (s, 12H), 2.44 (s, 6H), 4.76 (s, 2H), 6.90 (s, 4H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 17.97, 20.89, 22.47, 47.14, 61.05, 129.71, 134.12, 135.15, 138.34, 170.49. IR (KBr): ν = 2979.1, 2917.6, 2817.9, 1696.9, 1665.6, 1607.9, 1494.9, 1435.5, 1414.2, 1356.1, 1435.5, 1414.2, 1258.0, 1228.2, 1210.4, 1100.8, 862.6, 857.1 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{24}H_{31}N_2O_2$: 379.2386. Found: 379.2385. Anal. calcd. for $C_{24}H_{30}N_2O_2$: C, 76.16; H, 7.99; N, 7.40; Found: C, 7.43; H, 76.26; N, 8.05.

Competition Studies. An 8 mL vial was charged with **2** (0.025 g, 0.066 mmol), 0.1 mL C_6D_6, toluene (70 μL, 0.66 mmol, 10 equiv.), a p-substituted toluene derivative (10 equiv.), and a stir bar. After stirring the resultant mixture at 100 °C for 16 h, the reaction vessel was cooled to room temperature and the crude reaction mixture was analyzed by ^1H NMR spectroscopy. The C–H insertion product ratio (P_R/P_H, where R is the para-substituent) was calculated by comparing the ratio of the integrals associated with **6a-d,f-h** to **6e**. The experiment was repeated a total of three times for each para-substituted toluene. A Hammett plot was constructed by plotting the logarithm of the average P_R/P_H values versus the corresponding substituent parameter, σ^-. Hammett plots utilizing σ^+ or σ_{para} were also constructed. When 4-nitrotoluene was used, the formation **6e** was not observed and a selectivity of 99:1 was used.

5.5 Acknowledgements

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33) Intramolecular DAC C–H insertions have been previously demonstrated to be independent of exogenous base (see ref. 29). Likewise, conducting C–H insertion reactions in the presence of 0.2 equiv. of **2**·HCl yielded similar results to those obtained with free **2**, consistent with the reactions not being catalyzed by potential trace NaHMDS impurities.

34) Heating **6q** at 100 °C in C_7D_8 for 24 h afforded no change by ^{1}H NMR; however, treatment of **6q** with an equivalent of **2** or NaHMDS afforded **7** and benzene, indicating that the transfer hydrogenation mechanism may proceed in a stepwise fashion.

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Chapter 6: Elucidation of Carbene Ambiphilicity Leading to the Discovery of Reversible Ammonia Activation*

6.1 INTRODUCTION

While the activation of ammonia has garnered immense interest from both fundamental and practical perspectives, the process remains a challenging endeavor due to the high N–H bond strength (104 kcal/mol) and the propensity of ammonia to form Werner-type complexes with electrophilic reagents, particularly transition metals.[1-7] As first demonstrated by Bertrand with the alkylaminocarbenes[8,9] (AACs; e.g., **1**) in 2007[10] as well as more recently by our group with the diamidocarbenes[11-14] (DACs; e.g., **2**)[15] and Siemeling with the ferrocenophane **3**,[16] isolable carbenes[17] have emerged as attractive, metal-free alternatives for activating ammonia and other small molecules. Bertrand proposed that the high nucleophilicity intrinsic to the AACs facilitates N–H insertion processes and prevents the formation of Lewis acid-base adducts.[10,18d] However, high nucleophilicity may not be the only criterion for N–H activation as conventional *N*-heterocyclic carbenes (NHCs), which are also strongly nucleophilic,[18] have traditionally been considered to be inert toward ammonia and have even been generated in liquid NH_3.[18d,19,20] Regardless, little is known about the scope[21,22] of stable carbene N–H insertion chemistry or its mechanism,[10] which encumbers optimization and utilization efforts.

We envisioned that the DACs, which feature relatively low HOMO and LUMO levels,[18] may function as electrophiles or ambiphiles in N–H activation processes and

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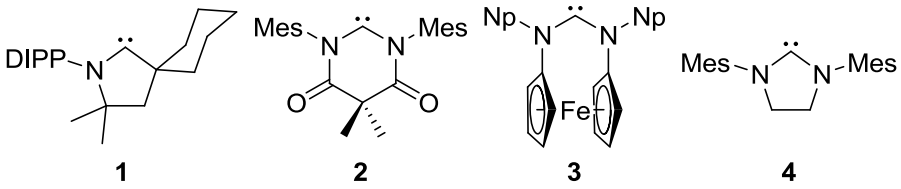
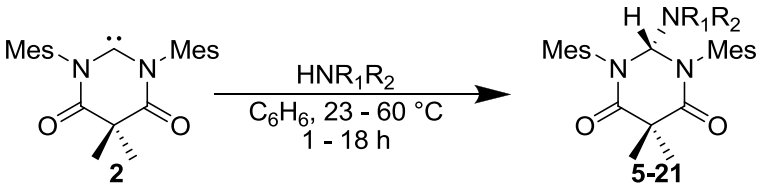


Figure 6.1: Structures of various carbenes. DIPP = 2,6-di-isopropylphenyl. Mes = 2,4,6-trimethylphenyl. Np = neopentyl.

offer new organocatalyzed synthetic strategies,[23-29] small molecule activation pathways,[18d] and other transformations. While Moss established the ambiphilicity[30] of transient chloroalkoxycarbenes more than three decades ago through elegant olefin cyclopropanation studies,[31-33] isolable carbenes have not hitherto displayed analogous reactivities within a given transformation.[34] Herein, we show that an isolable DAC is capable of undergoing N–H insertion processes via nucleophilic as well as electrophilic pathways. Moreover, through a comprehensive comparison to a prototypical NHC, we disclose the first example of an organic compound activating ammonia in a reversible manner.

6.2 Results and Discussion

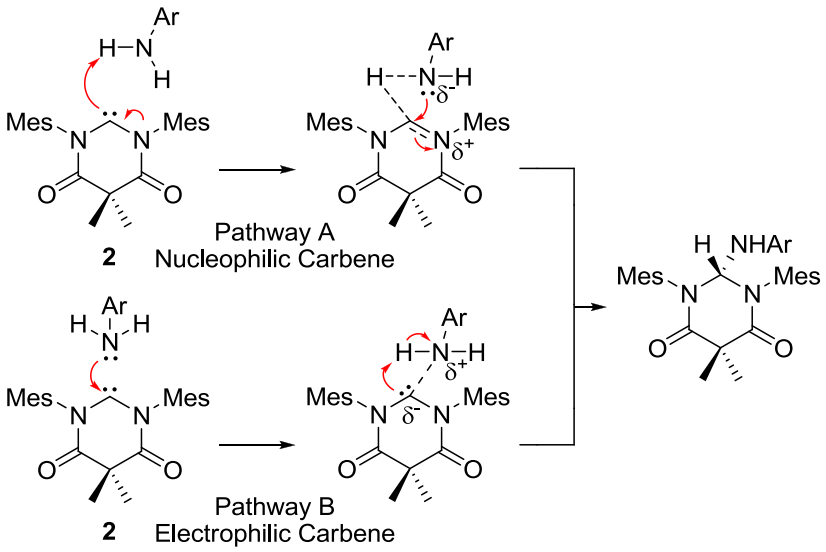


5: R^1 = H, R^2 = nBu, 86%	**14**: R^1 = H, R^2 = 4-BrPh, 95%
6: R^1 = H, R^2 = Ph, 73%	**15**: R^1 = H, R^2 = 4-CF_3Ph, 88%
7: R^1 = H, R^2 = 4-Me_2NPh, 89%	**16**: R^1 = R^2 = Et, 69%
8: R^1 = H, R^2 = 4-MeOPh, 88%	**17**: R^1 = R^2 = nBu, 72%
9: R^1 = H, R^2 = 4-MePh, 97%	**18**: R^1 = Me, R^2 = Ph, 55%
10: R^1 = H, R^2 = 4-tBuPh, 97%	**19**: R^1 = R^2 = 4-MeOPh, 88%
11: R^1 = H, R^2 = 4-FPh, 90%	**20**: R^1 = R^2 = Ph, 59%
12: R^1 = H, R^2 = 4-MeSPh, 90%	**21**: R^1 = R^2 = 4-BrPh, 87%
13: R^1 = H, R^2 = 4-ClPh, 97%	

Scheme 6.1: Summary of N-H Activation Reactions Using **2**.

Our efforts began by exploring the ability of a DAC to react with a broad range of amines. As summarized in Scheme 6.1, the N–H insertion products derived from **2** and a variety of alkyl (**5**, **16**, **17**) as well as electron rich and deficient aryl amines (**6-15**, **18-21**) were obtained under mild conditions in good to excellent yield (55-98%). Mechanistically, the N–H insertion processes may reside between two distinct, asynchronous pathways as depicted in Scheme 6.2. Polarization of an amino N–H bond followed by the formation of a C–N bond (Pathway A) would be expected if **2** functioned as the nucleophile. Alternatively, the amine could attack electrophilic **2** to form an aza-ylide-type intermediate followed by proton transfer (Pathway B). To differentiate, we evaluated the kinetics of the aforementioned N–H insertion reactions using ^{1}H NMR spectroscopy. Unfortunately, due to the rapid rate of N–H insertion, attempts to determine the rate constants (k) for the formation of **5-15** under pseudo first-order conditions via variable temperature (VT) ^{1}H NMR spectroscopy were unsuccessful. For example, treating a C_7D_8 solution of **2** ($[\mathbf{2}]_0 = 66$ mM) with 10 equiv. of aniline was found to quantitatively form **5** within 120 sec at –80 °C. However, the rate of DAC insertion into secondary amines was relatively slow and enabled the calculation of the corresponding rate constants for the formation of **16-21** in C_6D_6 at 30 °C (Table 6.1).

Inspection of the kinetic data revealed that the rate constants measured for reactions involving electron-deficient diarylamines were higher than those measured for analogous reactions involving electron-rich analogues and were consistent with **2** functioning as a nucleophile. Moreover, a small kinetic isotope effect (KIE) of 1.5 was measured for reactions that utilized diphenylamine or its d_1-analogue as substrates, consistent with an early transition state wherein the carbene polarized the N–H (D) bond prior to C–N bond scission.[35] Surprisingly, however, *N*-methyl aniline was found to be less reactive toward **2** than more basic dibutyl- or diethylamine which suggested to us an



Scheme 6.2: Mechanistic Pathways Leading to N-H Activation.

inflection point in the insertion mechanism. Thus, a series of competition studies were performed wherein a C_6D_6 solution of **2** was added dropwise to a vigorously stirred mixture of aniline and a para-substituted aniline derivative (5 equiv. of each aniline) in C_6D_6 at 23 °C. The proton signals corresponding to the resultant products **6** and **7-15** were then integrated and used to calculate the molar ratio of the para-substituted product versus **6** (defined as P_R/P_H, where R is the corresponding para-substituent). As shown in Figure 6.2 (left), an inverse relationship between the $\log(P_R/P_H)$ values and the corresponding Hammett substituent parameters, σ_{para},[36,37] was observed which indicated that the DAC **2** served as the electrophile in the aforementioned aniline N–H insertion processes (*c.f.*, Pathway B).

For comparison, the analogous diaminocarbene **4** was treated with various aniline derivatives in C_6D_6 under similar conditions to those described above. A broad range of substrates were observed to undergo activation (see Scheme 6.3), although the products were found to ring-open (**32-41**) upon prolonged standing or in the presence of excess

base. Thus, to elucidate the N–H activation mechanism involving **4**, a series of competition experiments involving aniline and its derivatives with isolated **4** (devoid of the residual base used for its synthesis) were conducted in an analogous manner to those described above for the DAC. For these studies, the P_R/P_H ratios were calculated <15 min after the addition of **4** to a C_6D_6 solution of the amines as the N–H insertion process was found to be reversible over the course of hours via ^{1}H NMR scrambling experiments.[38,39] As shown in Figure 6.2 (right), the relationship between $\log(P_R/P_H)$ versus σ^- was linear and positive,[40] consistent with the NHC functioning as a nucleophile (*c.f.*, Pathway A).

Product	R^1	R^2	k ($M^{-1}\cdot min^{-1}$)
16	Et	Et	0.036
17	Bu	Bu	0.009
18	Me	Ph	0.0009
19	4-OMe-Ph	4-OMePh	0.62
20	Ph	Ph	0.82
21	4-Br-Ph	4-Br-Ph	$\geq$ 3.5[b]

Table 6.1: Observed second-order rate constants (k). [a]Conditions: [**2**]$_o$ = 0.066 M, [amine]$_o$ = 0.66 M, 30 °C, C_6D_6, 1 h. [b] Rate constant calculated based on $\geq$ 99% conversion in 2 min.

To corroborate this conclusion and preclude the influence of amine exchange or other side reactions, the rate constants for the reaction between the NHC **4** and various aniline derivatives were determined at –25 °C in C_7D_8 using VT NMR spectroscopy. In general, the NHC was treated with excess amine ($\geq$ 10 equiv) and the corresponding reaction was monitored over time, with the exception of 4-trifluoromethylaniline which was found to proceed too rapidly under these conditions. Consistent with the

aforementioned competition studies, the measured rate constants were found to increase in accordance with the electron-withdrawing nature of the para-substituent. Indeed, a plot of the logarithm of the ratio of the observed rate constants (k_R/k_H), where R is the corresponding para-substituent, against σ^- resulted in a linear, positive relationship (Figure 6.3). Collectively, these results are consistent with a mechanism analogous to Pathway A shown in Scheme 6.2, wherein the NHC functioned as the nucleophile during the N–H activation process.

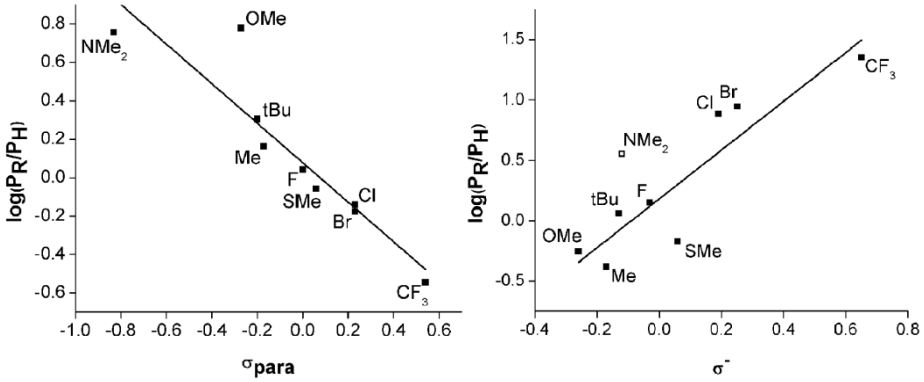
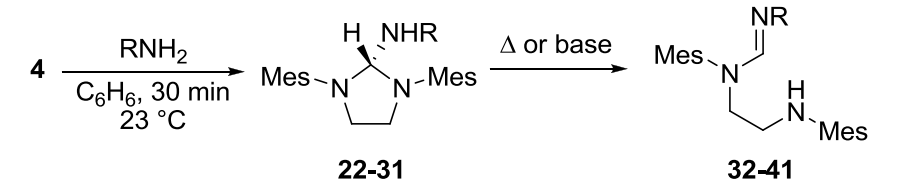


Figure 6.2: Plots of the logarithm of the product ratios (P_R/P_H) versus (left) σ_{para} for the reaction of DAC **2** or (right) σ^- for the reaction of NHC **4** with a mixture of aniline and the indicated para-substituted derivative (5 equiv. each).[20] Conditions: C_6D_6, 23 °C. The data points are the numerical average of three separate experiments.



22-31 **32-41**

R = X

22: X = H, 92%	**32**: X = H, 93%
23: X = NMe_2, 82%	**33**: X = NMe_2, 83%
24: X = OMe, 86%	**34**: X = OMe, 81%
25: X = tBu, 74%	**35**: X = tBu, 76%
26: X = Me, 79%	**36**: X = Me, 75%
27: X = SMe, 88%	**37**: X = SMe, 84%
28: X = F, 88%	**38**: X = F, 79%
29: X = Cl, 84%	**39**: X = Cl, 79%
30: X = Br, 80%	**40**: X = Br, 85%
31: X = CF_3, 81%	**41**: X = CF_3, 78%

Scheme 6.3: Summary of N-H Activation Reactions Using **4**.

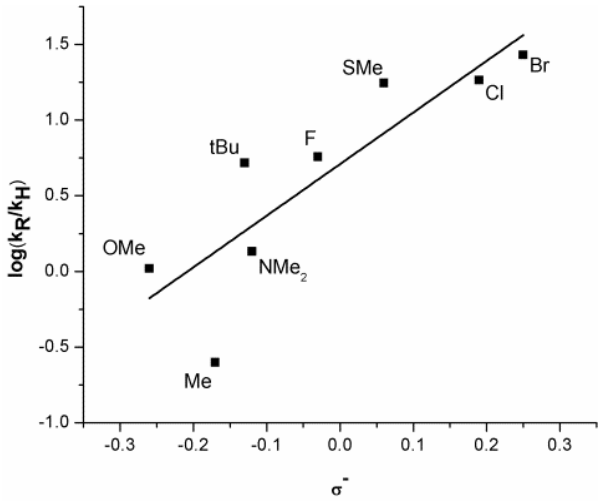
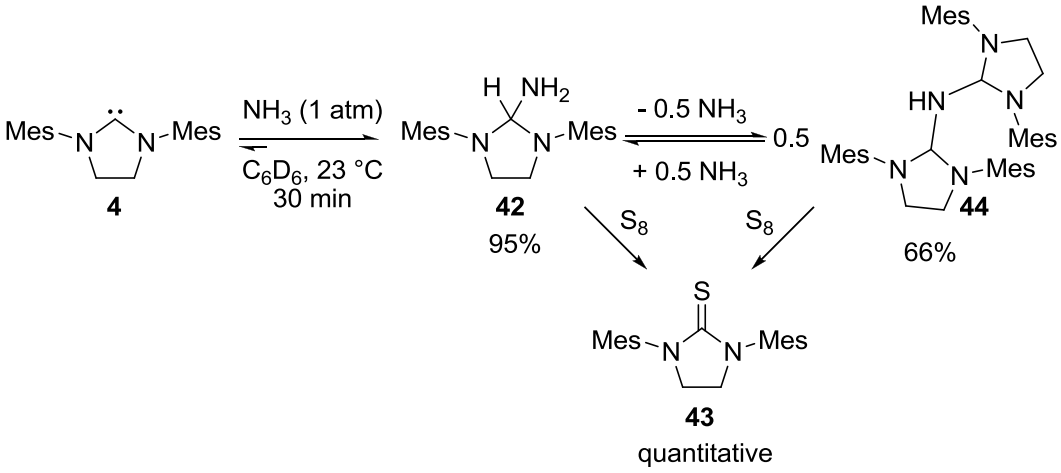


Figure 6.3: Plot of the logarithm of the rate constant ratio (k_R/k_H) versus σ^- for the reaction of **4** with aniline and a variety of para-substituted anilines. Conditions: C_7D_8, –25 °C.

While more basic amines should disfavor a nucleophilic carbene insertion mechanism, Merten reported in 1972 that the electron-rich olefin 1,1',3,3'-tetraphenyl-2,2'-bisimidazolinylidene (*i.e.*, an NHC dimer) inserted into cyclohexylamine.[41,42] This suggested to us that **4** may also react with relatively basic amines including ammonia

(pK_a = 41).[43] To test, a solution of the NHC in C_6D_6 ([**4**]$_0$ = 0.2 M) was transferred to a medium pressure NMR tube equipped with a PTFE screw cap. Upon cooling to -78 °C, the atmosphere was removed under reduced pressure and replaced with ammonia upon warming to 23 °C. Complete consumption of **4** was observed within 30 min at 23 °C and was accompanied with the appearance of new ^{1}H NMR signals recorded at 1.15 (d, 2H) and 5.44 ppm (t, 1H), consistent with the formation of the N–H inserted product **42**, as well as a minor product with a doublet at 5.22 ppm. Moreover, the addition of excess sulfur to the crude reaction mixture cleanly and quantitatively afforded the thiourea **43**.[44] These results led us to conclude that the ammonia activation process was reversible and that the secondary product formed was the doubly inserted ammonia adduct **44** (Scheme 6.4).



Scheme 6.4: Reversible Ammonia Activation.

To verify the reversibility of the aforementioned reaction, **42** was isolated in 95% yield by mixing **4** (0.4 mmol) in hexanes (5 mL) under an atmosphere of ammonia at 0 °C for 1 h followed by rapid removal of the solvent. Subsequent stirring of **42** in C_6H_6 under nitrogen for 48 h followed by the removal of the residual solvent and washing the

residue with pentane afforded **44** in 66% isolated yield as indicated by the observation of the aforementioned doublet as well as a triplet at 2.13 ppm in the corresponding ^{1}H NMR spectrum. Subsequent addition of ammonia to **44** afforded a mixture containing **42** and **44** which, in combination with the formation of thiourea **43** upon stirring either **42** or **44** (or a mixture thereof) with elemental sulfur, corroborated the reversibility of the N–H insertion processes. In parallel with the aforementioned experiments, a C_6D_6 solution of **42** was frozen at –30 °C before adding a suspension of sulfur in C_6D_6 and sealing the NMR tube. Upon warming to room temperature, the ^{1}H NMR spectrum of the product mixture revealed the formation of **43** as well as a broad triplet at -0.17 ppm characteristic of ammonia. Moreover, stirring **42** in benzene for 2 h, followed by gas chromatography and high resolution mass spectroscopic analysis of the reaction mixture confirmed the presence of ammonia (Figure A52).[45] While it is tempting to suggest that **4** activated ammonia through a nucleophilic carbene pathway and that the reversibility is due to the relatively high LUMO of the NHC, a change in mechanism wherein **4** functioned as an electrophile cannot be excluded.[46] Regardless, the result adds to the paucity of carbenes reported to activate ammonia and is the first example to do so in a reversible manner.

6.3 Conclusion

In summary, a DAC was found to function as a nucleophile in the activation of diaryl N–H bonds and as an electrophile when treated with anilines, which together comprised the first example of an isolable carbene functioning as an ambiphile within a given class of transformation. While nearly all current applications of isolable carbenes originate from their nucleophilic properties, the results herein validate the ability of isolable carbenes to react as electrophiles. Such electrophilic characteristics are expected to inspire new applications of stable carbenes wherein the carbene serves primarily as an

electrophile. Moreover, the ambiphilic N–H activation processes described above underscore the potential to control product selectivity and scope through the modification of the carbene's electronic properties.

In addition to activating aniline N–H bonds via a nucleophilic mechanism, an NHC was found to reversibly activate ammonia under mild conditions. Dynamic N–H insertion is an important step toward understanding the role and mechanism of carbenes in transformations such as amidations[47-50] and incorporating ammonia and other amines into organocatalytic processes (e.g., metal-free aminations or hydroaminations)[49] wherein the transfer or release of the activated/functionalized substrate is essential for catalytic turnover. Exploiting the reversibility of the N–H insertion process may also find utility in sensing or the latent release of amines, particularly gaseous ammonia, from a solid precursor.

6.4 EXPERIMENTAL

General Considerations. All procedures were performed using standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen-filled glove box unless otherwise noted. *N*,*N'*-dimesityl-4,5-dihydroimidazol-2-ylidene[51] and *N*,*N'*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (**2**)[15] were prepared according to literature procedures. All liquid substrates were dried over molecular sieves for 24 h or distilled (4-fluoroaniline and *N*,*N*-dimethyl-*p*-phenylene-diamine). All commercial solid substrates were dried under reduced pressure for 24 h. *p*-Toluidine was recrystallized from pentane. Benzene, hexanes, and pentane were dried and degassed using a Vacuum Atmospheres Company solvent purification system. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer. High resolution mass spectra (HRMS) were obtained with a Waters Micromass Autospec-Ultima (CI) or Agilent 6530 QTOF (ESI)

mass spectrometer. NMR spectra were recorded on a Varian Unity+ 300, Varian Mercury 400, Varian Directdrive 400, or Agilent MR400 spectrometer. Chemical shifts (δ) are reported in ppm relative to the residual benzene (^{1}H: 7.15 ppm, ^{13}C: 128.0 ppm) or chloroform (^{1}H: 7.24 ppm, ^{13}C: 78.0 ppm) as reference. Elemental analyses were performed at Midwest Microlab, LLC (Indianapolis, IN) or with a ThermoScientific Flash 2000 Organic Elemental Analyzer. Melting points were obtained using a Stanford Research Systems MPA100 OptiMelt automated melting point apparatus (ramp rate: 1 °C·min^{-1}) and are uncorrected.

Synthesis of 5. An 8 mL vial was charged with **2** (0.100 g, 0.266 mmol), benzene (2 mL) and a stir bar. To this vial, n-butylamine (26.3 μL, 0.266 mmol, 1 equiv.) was added and the resultant mixture stirred at ambient temperature for 30 min. Concentration of the crude reaction mixture under reduced pressure followed by a series of pentane washes and drying under reduced pressure afforded the desired compound as a colorless solid (0.103 g, 0.229 mmol, 86% yield). m.p. 147-149 °C. ^{1}H NMR ($CDCl_3$): δ 6.90 (s, 4H), 5.47 (d, *J* = 9.2 Hz, 1H), 2.25 (s, 6H), 2.24 (s, 6H), 2.23 (s, 6H), 1.84 (bq, *J* = 5.6 Hz, 2H), 1.70 (s, 3H), 1.58 (s, 3H), 1.38 (m, 1H), 0.71 (m, 4H), 0.50 (bt, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 170.5, 137.8, 137.2, 134.3, 133.6, 129.6, 129.5, 84.5, 47.4, 46.0, 32.4, 26.3, 22.3, 20.9, 19.3, 19.0, 18.4, 13.4. IR (KBr): ν = 3394.2, 2968.7, 2926.4, 2868.1, 1672.6, 1641.4, 1610.0, 1484.8, 1459.5, 1438.0, 1353.2, 1219.0, 1165.7, 850.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{28}H_{40}N_3O_2$: 450.3121; Found: 450.3117. Anal. calcd. for $C_{28}H_{39}N_3O_2$: C, 74.80; H, 8.74; N, 9.35; Found: C, 74.95; H, 8.76; N, 9.29.

Synthesis of DAC-Aniline Adducts: General Procedure. An 8 mL vial was charged with **2** (0.100 g, 0.266 mmol), benzene (2 mL) and a stir bar. To this vial, the corresponding aniline (0.266 mmol, 1 equiv.) was added and the mixture stirred at ambient temperature for 1 h. Concentration of the crude reaction mixture under reduced

pressure followed by a series of pentane washes and drying under reduced pressure afforded the desired compound as a colorless solid.

Synthesis of 6. Substrate: aniline. Yield: 0.091 g, 0.194 mmol, 73%. m.p. 216 °C. ^{1}H NMR ($CDCl_3$): δ 6.86 (s, 2H), 6.84 (s, 2H), 6.82 (t, *J* = 7.2 Hz, 2H), 6.59 (t, *J* = 7 Hz, 1H), 6.16 (d, *J* = 10 Hz, 1H), 5.85 (d, *J* = 8 Hz, 2H), 3.98 (d, *J* = 10 Hz, 1H), 2.28 (s, 12H), 2.21 (s, 6H), 1.82 (s, 3H), 1.68 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.8, 144.3, 138.4, 136.9, 134.5, 133.1, 130.04, 129.96, 129.0, 114.1, 81.5, 46.3, 26.9, 22.8, 21.1, 19.3, 18.6. IR (KBr): ν = 2978, 2932, 1873, 1685, 1657, 1609, 1496, 1478, 1436, 1402, 1275, 1236, 1225, 1208, 1884, 1165, 1154, 1105, 1066, 1030 cm^{-1}. HRMS (ESI) for $C_{30}H_{36}N_3O_2$: $[M+H]^+$: calcd. 470.2802, Found: 470.2803. Anal. calcd. for $C_{30}H_{35}N_3O_2$: C, 76.73; H, 7.51; N, 8.95; Found: C, 76.81; H, 7.76; N, 9.21.

Synthesis of 7. Substrate: *N*,*N*-dimethyl-*p*-phenylenediamine. Yield: 0.121 g, 0.236 mmol, 89%. m.p. 186-189 °C. ^{1}H NMR (C_6D_6): δ 6.73 (s, 2H), 6.65 (s, 2H), 6.15 (d, *J* = 8 Hz, 2H), 6.13 (d, *J* = 10 Hz, 1H), 5.81 (d, *J* = 10 Hz, 2H), 3.63 (d, *J* =10 Hz, 1H), 2.32 (s, 6H), 2.25 (s, 6H), 2.19 (s, 6H), 2.01 (s, 6H), 1.87 (d, *J* = 5 Hz, 6H); ^{13}C NMR (C_6D_6): δ 170.7, 146.4, 138.1, 135.6, 134.8, 130.4, 130.3, 117.5, 114.5, 84.5, 47.0, 41.1, 27.4, 23.4, 21.3, 20.0, 19.0. IR (KBr): *v* = 3403, 2942, 2901, 1679, 1647, 1509, 1444, 1372, 1249, 1212, 1191, 1062, 1028, 849, 789, 752, cm^{-1}. HRMS (ESI) for $C_{32}H_{40}N_4O_2$: $[M+H]^+$: calcd. 513.32240, Found: 513.32334. Anal. calcd. for $C_{32}H_{40}N_4O_2$: C, 74.97; H, 7.86; N, 10.93; Found: C, 74.84; H, 7.76; N, 10.96.

Synthesis of 8. Substrate: *p*-anisidine. Yield: 0.123 g, 0.223 mmol, 88%. m.p. 125-126 °C. ^{1}H NMR (C_6D_6): δ 7.27 (s, 1H), 6.77 (d, *J* = 4 Hz, 2H), 6.28 (t, *J* = 10 Hz, 2H), 5.94 (d, *J* = 10 Hz, 1H), 5.61 (d, *J* = 10.0 Hz, 2H), 3.61 (d, *J* =10 Hz, 1H), 3.50 (s, 3H), 2.20 (s, 6H), 2.13 (s, 12H), 1.68 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (C_6D_6): δ 170.3, 154.3, 137.9, 137.6, 135.1, 130.0, 129.9, 116.4, 114.5, 86.6, 54.6, 27.1, 23.0, 20.8, 19.4,

18.5. IR (KBr): ν = 3401, 2957, 2924, 2854, 1681, 1646, 1513, 1488, 1461, 1435, 1407, 1377, 1242, 1217, 1194, 1126, 1082, 1047, 855, 817, 790 cm^{-1}. HRMS (ESI) for $C_{31}H_{37}N_3O_3$: $[M+H]^+$: calcd. 500.29077, Found: 500.29045. Anal. calcd. for $C_{31}H_{37}N_3O_3$: C, 74.52; H, 7.46; N, 8.41; Found: C, 74.59; H, 7.72; N, 8.69.

Synthesis of 9. Substrate: *p*-toluidine. Yield: 0.126 g, 0.259 mmol, 97%. m.p. 173-176 °C. ^{1}H NMR (C_6D_6): δ 7.28 (s, 1H), 6.77 (s, 4H), 6.53 (t, J = 10 Hz, 2H), 6.00 (d, J = 8 Hz, 1H), 5.61 (d, J = 10.0 Hz, 2H), 3.80 (d, J =10 Hz, 1H), 2.20 (d, J = 6 Hz, 12H), 2.12 (s, 6H), 1.98 (s, 3H), 1.71 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (C_6D_6): δ 170.3, 142.5, 137.5, 134.1, 130.0, 129.7, 129.2, 114.0, 82.4, 46.6, 27.3, 22.9, 20.8, 20.2, 19.4, 18.5. IR (KBr): ν = 3400, 2925, 2857, 1685, 1648, 1611, 1523, 1431, 1374, 1246, 1215, 1197, 1133, 1086, 1031, 858, 814, 791, 776, 739, 723 cm^{-1}. HRMS (ESI) for $C_{31}H_{37}N_3O_2$: $[M+H]^+$: calcd. 484.29585, Found: 484.29551. Anal. calcd. for $C_{31}H_{37}N_3O_2$: C, 76.98; H, 7.71; N, 8.69; Found: C, 77.16; H, 8.02; N, 8.41.

Synthesis of 10. Substrate: 4-tert-butylaniline. Yield: 0.135 g, 0.257 mmol, 97%. 180-181 °C (decomp.) ^{1}H NMR ($CDCl_3$): δ 6.77-6.79 (s overlapping m, 6H), 6.15 (d, J = 10.8 Hz, 1H), 5.77 (m, 2H), 3.75 (d, J = 10.8 Hz, 1H), 2.24 (s, 6H), 2.23 (s, 6H), 2.17 (s, 6H), 1.76 (s, 3H), 1.64 (s, 3H), 1.10 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 170.5, 142.8, 141.5, 138.0, 136.7, 134.2, 133.0, 129.7, 129.6, 125.3, 114.0, 81.6, 46.1, 33.8, 31.3, 26.5, 22.6, 20.8, 19.1, 18.4. IR (KBr): ν = 3400.8, 2961.2, 2866.4, 1685.5, 1649.4, 1611.3, 1518.5, 1430.8, 1407.5, 1248.1, 1218.3, 1193.6, 1082.4, 828.5, 772.8, 684.0, 489.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{34}H_{44}N_3O_2$: 526.3434; Found: 526.3431. Anal. calcd. for $C_{34}H_{43}N_3O_2$: C, 77.68; H, 8.24; N, 7.99; Found: C, 77.78; H, 8.26; N, 7.98.

Synthesis of 11. Substrate: 4-fluoroaniline. Yield: 0.117 g, 0.240 mmol, 90%. m.p. 179-182 °C. ^{1}H NMR (C_6D_6): δ 6.64 (s, 2H), 6.60 (s, 2H), 6.29 (t, J = 10 Hz, 1H), 6.03 (d, J = 10 Hz, 1H), 5.55 (m, 2H), 3.70 (d, J =10 Hz, 1H), 2.21 (s, 6H), 2.12 (s, 6H),

1.97 (s, 6H), 1.83 (d, J = 4 Hz, 6H); ^{13}C NMR (C_6D_6): δ 170.6, 138.4, 137.8, 135.3, 134.4, 130.4, 130.3, 116.1, 116.0, 115.9, 115.8, 83.2, 47.0, 27.5, 23.4, 21.1, 19.7, 18.8. IR (KBr): ν = 3401, 2963, 2861, 1683, 1651, 1616, 1520, 1491, 1436, 1412, 1379, 1250, 1201, 1171, 1049, 863, 820, 794, 728 cm^{-1}. HRMS (ESI) for $C_{30}H_{34}N_3O_2F$: $[M+H]^+$: calcd. 488.27078, Found: 488.27078. Anal. calcd. for $C_{30}H_{34}N_3O_2F$: C, 73.90; H, 7.03; N, 8.62; Found: C, 73.54; H, 6.99; N, 8.43.

Synthesis of 12. Substrate: 4-(methylthio)aniline. Yield: 0.122 g, 0.239 mmol, 90%. 165-166 °C (decomp.) ^{1}H NMR ($CDCl_3$): δ 6.83 (s, 2H), 6.82 (s, 2H), 6.75 (m, 2H), 6.03 (d, J = 10.2 Hz, 1H), 5.74 (m, 2H), 3.93 (d, J = 10.2 Hz, 1H), 2.27 (s, 3H), 2.24 (s, 6H), 2.23 (s, 6H), 2.19 (s, 6H), 1.77 (s, 3H), 1.63 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.5, 142.4, 138.2, 136.7, 134.3, 132.8, 129.9, 129.8, 129.3, 127.9, 114.6, 81.5, 46.1, 26.9, 22.5, 20.9, 19.0, 18.4, 17.6. IR (KBr): ν = 3391.7, 2974.3, 2918.6, 2860.5, 1686.4, 1648.2, 1600.1, 1507.8, 1428.2, 1354.8, 1286.9, 1242.4, 1220.0, 1195.8, 1079.4, 772.7, 510.8 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{38}N_3O_2S$: 516.2685; Found: 516.2686. Anal. calcd. for $C_{31}H_{37}N_3O_2S$: C, 72.20; H, 7.23; N, 8.15; Found: C, 72.23; H, 7.33; N, 8.07.

Synthesis of 13. Substrate: 4-chloroaniline. Yield: 0.130 g, 0.258 mmol, 97%. m.p. 213-217 °C. ^{1}H NMR (C_6D_6): δ 6.64 (d, J = 12 Hz, 4H), 6.55 (d, J = 9 Hz, 2H), 5.79 (d, J = 10 Hz, 1H), 5.52 (d, J = 10 Hz, 2H), 3.81 (d, J =8 Hz, 1H), 2.04 (s, 6H), 2.01 (s, 12H), 1.56 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (C_6D_6): δ 170.2, 143.3, 137.3, 133.8, 130.0, 129.9, 129.0, 114.9, 81.9, 46.6, 27.3, 22.9, 20.7, 19.3, 18.4. IR (KBr): ν = 3401, 2968, 2920, 2859, 1682, 1647, 1602, 1503, 1485, 1436, 1437, 1404, 1353, 1245, 1219, 1196, 1168, 1079, 1031, 854, 815, 776, 735, 724 cm^{-1}. HRMS (ESI) for $C_{30}H_{34}N_3O_2Cl$: $[M+H]^+$: calcd. 504.24123, Found: 504.24508. Anal. calcd. for $C_{30}H_{34}N_3O_2Cl$: C, 71.48; H, 6.80; N, 8.34; Found: C, 71.24; H, 6.79; N, 7.98.

Synthesis of 14. Substrate: 4-bromoaniline. Yield: 0.138 g, 0.251 mmol, 95%. m.p. 223-225 °C. ^{1}H NMR (C_6D_6): δ 6.79 (d, *J* = 10 Hz, 2H), 6.66 (d, *J* = 12 Hz, 2H), 5.80 (d, *J* = 10 Hz, 1H), 5.49 (d, *J* = 10 Hz, 2H), 3.83 (d, *J* =10 Hz, 1H), 2.07 (s, 6H), 2.04 (s, 6H), 2.01 (s, 6H), 1.59 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (C_6D_6): δ 170.2, 143.7, 137.2, 133.8, 131.9, 130.0, 129.9, 115.2, 81.6, 46.6, 27.4, 27.4, 22.9, 20.7, 19.3, 18.4. IR (KBr): *v* = 3404, 2949, 2918, 2872, 1684, 1648, 1597, 1487, 1434, 1402, 1244, 1218, 1196, 1107, 1072, 1032, 854, 814, 774, 723 cm^{-1}. HRMS (ESI) for $C_{30}H_{34}N_3O_2Br$: $[M+H]^+$: calcd. 550.18915, Found: 550.18832. Anal. calcd. for $C_{30}H_{34}N_3O_2Br$: C, 65.69; H, 6.25; N, 7.66; Found: C, 65.89; H, 6.13; N, 7.59.

Synthesis of 15. Substrate: 4-(trifluoromethyl)aniline. Yield: 0.126 g, 0.234 mmol, 88%. m.p. 202-205 °C (decomp.) ^{1}H NMR (C_6D_6): 6.81 (d, *J* = 9 Hz, 2H), 6.60 (s, 2H), 6.55 (s, 2H), 6.12 (d, *J* = 10 Hz, 1H), 5.62 (d, *J* = 10 Hz, 2H), 4.10 (d, *J* =10 Hz, 1H), 2.16 (s, 6H), 2.14 (s, 6H), 1.92 (s, 6H), 1.86 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (C_6D_6): δ 170.5, 138.7, 137.6, 135.1, 134.0 130.5, 130.3, 112.9, 81.0, 47.0, 28.1, 23.3, 21.1, 19.7, 18.8. IR (KBr): *v* = 3405, 2960, 2925, 2851, 1687, 1648, 1599, 1432, 1398, 1239, 1221, 1199, 1100, 1063, 1028, 861, 767, 719 cm^{-1}. HRMS (ESI) for $C_{31}H_{34}N_3O_2F_3$: $[M+H]^+$: calcd. 538.26759, Found: 538.26681. Anal. calcd. for $C_{31}H_{34}N_3O_2F_3$: C, 69.26; H, 6.37; N, 7.82; Found: C, 69.13; H, 6.52; N, 7.97.

Synthesis of 16. An 8 mL vial was charged with **2** (0.100 g, 0.266 mmol), benzene (2 mL) and a stir bar. To this vial, diethylamine (24.2 μL, 0.266 mmol, 1 equiv.) was added and the resultant mixture was heated at 60 °C for 3 h. Concentration of the crude reaction mixture under reduced pressure followed by a series of pentane washes afforded the desired compound as a colorless solid (0.082 g, 0.174 mmol, 69% yield). m.p. 139-140 °C. ^{1}H NMR ($CDCl_3$): δ 6.89 (s, 2H), 6.85 (s, 2H), 6.34 (s, 1H), 2.47 (bm, 2H), 2.31 (bm, 2H), 2.24 (s, 6H), 2.23 (s, 6H), 2.21 (s, 6H), 1.64 (s, 3H), 1.58 (s, 3H),

0.31 (t, J = 7.1 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 171.8, 137.2, 137.1, 134.4, 134.2, 129.5, 129.4, 87.8, 46.0, 45.9, 38.6, 24.7, 23.1, 20.8, 19.2, 18.8, 13.8, 12.7. IR (KBr): ν = 2982, 2923, 2867, 1684, 1653, 1607, 1483, 1456, 1391, 1368, 1354, 1249, 1213, 1186, 1138, 1105, 1071, 1013 cm^{-1}. HRMS (ESI): $[M+Na]^+$ calcd. for $C_{28}H_{39}N_3O_2Na$: 472.2934; Found: 472.2936. Anal. calcd. for $C_{28}H_{39}N_3O_2$: C, 74.80; H, 8.74; N, 9.35; Found: C, 74.65; H, 8.65; N, 9.33.

Synthesis of 17. An 8 mL vial was charged with **2** (0.100 g, 0.266 mmol), benzene (2 mL) and a stir bar. To this vial, dibutylamine (220 μL, 1.06 mmol, 5 equiv.) was added and the resultant mixture was heated at 60 °C for 18 h. Concentration of the crude reaction mixture under reduced pressure followed by a series of pentane washes afforded the desired compound as a colorless solid (0.097 g, 0.192 mmol, 72% yield). m.p. 132-134 °C. ^{1}H NMR ($CDCl_3$): δ 6.89 (s, 2H), 6.85 (s, 2H), 2.36 (m, 2H), 2.25 (s, 6H), 2.22 (s, 6H), 2.21 (s, 6H), 2.16 (m, 2H), 1.65 (s, 3H), 1.58 (s, 3H), 1.01 (m, 2H), 0.70-0.80 (overlapping m, 5H), 0.45-0.64 (overlapping m, 7H). ^{13}C NMR ($CDCl_3$): δ 171.8, 137.2, 134.5, 134.2, 129.5, 129.4, 87.6, 52.4, 45.8, 30.5, 29.7, 24.9, 23.1, 20.8, 20.7, 20.0, 19.2, 19.0, 14.0, 13.8. IR (KBr): ν = 2956, 2926, 2871, 1692, 1654, 1607, 1486, 1456, 1394, 1377, 1367, 1356, 1281, 1209, 1196, 1187, 1138, 1116, 1067, 1034, 1012 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{32}H_{48}N_3O_2$: 506.3747; Found: 506.3747. Anal. calcd. for $C_{32}H_{47}N_3O_2$: C, 76.00; H, 9.37; N, 8.31; Found: C, 76.07; H, 9.23; N, 8.20.

Synthesis of 18. An 8 mL vial was charged with **2** (0.250 g, 0.664 mmol), benzene (5 mL) and a stir bar. To this vial, N-methylaniline (144 μL, 1.33 mmol, 2 equiv.) was added and the resultant mixture was stirred at 60 °C for 16 h. After removing the residual solvent under reduced pressure, the crude residue was purified by silica gel column chromatography using 2:1 v/v hexanes/ethyl acetate as the eluent to afford the

desired compound as a white solid (0.176 g, 0.364 mmol, 55% yield). m.p. 159-160 °C. ^{1}H NMR ($CDCl_3$): δ 6.79-6.84 (m overlapping s, 4H), 6.71 (s, 2H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.40 (s, 1H), 5.87 (d, *J* = 7.8 Hz, 2H), 2.84 (s, 3H), 2.22 (s, 6H), 2.17 (s, 12 H), 1.86 (s, 3H), 1.66 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 171.3, 147.7, 137.6, 137.0, 133.6, 133.2, 130.0, 129.7, 128.4, 120.5, 116.1, 85.8, 45.3, 32.5, 27.5, 24.4, 20.7, 19.4, 19.0. IR (KBr): ν = 2988.3, 2926.3, 2868.2, 1683.5, 1653.3, 1599.2, 1438.5, 1392.6, 1362.7, 1302.9, 1209.6, 1166.9, 1088.0, 949.8, 857.6, 754.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{38}N_3O_2$: 484.2964; Found: 484.2959. Anal. calcd. for $C_{31}H_{37}N_3O_2$: C, 76.98; H, 7.71; N, 8.69; Found: C, 77.23; H, 7.76; N, 8.59.

Synthesis of 19. An 8 mL vial was charged with **2** (0.100 g, 0.266 mmol), benzene (2 mL) and a stir bar. To this vial, 4,4'-dimethoxydiphenylamine (0.061 g, 0.266 mmol, 1 equiv.) was added and the resultant mixture was stirred at ambient temperature for 1 h. Concentration of the crude reaction mixture under reduced pressure followed by a series of pentane washes afforded the desired compound as an off white solid (0.142 g, 0.234 mmol, 88% yield). m.p. 202-204 °C (decomp.) ^{1}H NMR ($CDCl_3$): δ 6.82 (s, 2H), 6.81 (s, 2H), 6.58-6.65 (overlapping bs, 4H), 6.34 (bs, 2H), 6.22 (s, 1H), 5.46 (bs, 2H), 3.65-3.71 (overlapping bs, 6H), 2.24 (s, 6H), 2.14 (s, 6H), 1.92 (s, 3H), 1.74 (overlapping s, 9H). ^{13}C NMR ($CDCl_3$): δ 171.4, 157.4 (b), 153.2 (b), 139.6, 138.7 (b), 137.8, 133.9, 133.8, 130.3, 129.7, 129.3 (b), 118.2 (b), 114.0 (b), 113.5 (b), 87.1, 55.5 (b), 55.2 (b), 45.3, 28.6, 23.6, 20.7, 19.6, 19.0. IR (KBr): ν = 3005.9, 2953.5, 2932.9, 1679.6, 1649.9, 1608.9, 1509.1, 1423.3, 1404.0, 1240.4, 1186.6, 1168.2, 1068.8, 1032.1, 821.8, 751.6, 601.6 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{38}H_{44}N_3O_4$: 606.3332; Found: 606.3333. Anal. calcd. for $C_{38}H_{43}N_3O_4$: C, 75.34; H, 7.15; N, 6.94; Found: C, 75.49; H, 7.31; N, 7.30.

Synthesis of 20. An 8 mL vial was charged with **2** (0.100 g, 0.266 mmol), benzene (2 mL), and a stir bar. To this vial, diphenylamine (0.046 g, 0.266 mmol, 1 equiv.) was added and the resultant mixture was stirred at ambient temperature for 1 h. Concentration of the crude reaction mixture under reduced pressure followed by a series of pentane washes afforded the desired compound as a colorless solid (0.085 g, 0.156 mmol, 59% yield). m.p. 212-213 °C. ^{1}H NMR ($CDCl_3$): δ 7.09 (bm, 2H), 6.78-6.97 (m, 10H), 6.70 (bm, 2H), 6.30 (s, 1H), 5.63 (bm, 2H), 2.23 (s, 6H), 2.14 (s, 6H), 1.94 (s, 3H), 1.76 (s, 3H), 1.73 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 171.4, 145.4, 144.4, 139.6, 137.9, 133.8, 133.6, 130.4, 129.7, 129.0, 128.1, 127.7, 126.2, 119.9, 117.7, 87.0, 45.4, 28.7, 23.5, 20.7, 19.5, 19.0. IR (KBr): ν = 2978, 2933, 1685, 1654, 1608, 1497, 1437, 1400, 1376, 1364, 1275, 1236, 1225, 1208, 1184, 1165, 1154, 1105, 1066, 1030 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{36}H_{40}N_3O_2$: 546.31150; Found: 546.31122. Anal. calcd. for $C_{36}H_{39}N_3O_2$: C, 79.23; H, 7.20; N, 7.70; Found: C, 78.99; H, 7.22; N, 7.56.

Synthesis of 21. An 8 mL vial was charged with **2** (0.100 g, 0.266 mmol), benzene (2 mL) and a stir bar. To this vial, bis(4-bromophenyl)aniline (0.087 g, 0.266 mmol, 1 equiv.) was added and the resultant mixture stirred at ambient temperature for 1 h. Concentration of the crude reaction mixture under reduced pressure followed by a series of pentane washes afforded the desired compound as a white solid (0.162 g, 0.230 mmol, 87% yield). m.p. 215-216 °C (decomp.) ^{1}H NMR ($CDCl_3$): δ 7.21 (bm, 2H), 6.98 (bm, 2H), 6.83 (s, 2H), 6.81 (s, 2H), 6.55 (bs, 2H), 6.18 (s, 1H), 5.39 (bm, 2H), 2.24 (s, 6H), 2.13 (s, 6H), 1.90 (s, 3H), 1.74 (s, 3H), 1.73 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 171.2, 143.9 (b), 143.2 (b), 139.4, 138.3, 133.9, 133.4, 132.5 (b), 131.1 (b), 130.5, 129.9, 129.7 (b), 120.5 (b), 119.1 (b), 112.6 (b), 86.8, 45.4, 28.5, 23.6, 20.7, 19.7, 19.0. IR (KBr): ν = 2974.5, 2933.8, 2873.1, 1686.7, 1658.3, 1607.7, 1590.6, 1494.4, 1403.6, 1283.9, 1208.9, 1187.0, 1058.2, 1011.5, 854.0, 808.1, 767.3, 524.5 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for

$C_{36}H_{38}Br_2N_3O_2$: 704.13194; Found: 704.13083. Anal. calcd. for $C_{36}H_{37}Br_2N_3O_2$: C, 61.46; H, 5.30; N, 5.97; Found: C, 61.14; H, 5.33; N, 5.62.

Synthesis of NHC 4 / Aniline Adducts: General Procedure. A 20 mL vial was charged with 1,3-dimesityl-4,5-dihydroimidazolium bromide (0.100 g, 0.258 mmol), sodium hexamethyldisilazane (0.050 g, 0.271 mmol, 1.05 equiv.), benzene (10 mL) and a stir bar. The resultant solution was then stirred at ambient temperature for 1 h. After adding the aniline derivative (0.258 mmol, 1 equiv.) dissolved in 5 mL benzene, the mixture was stirred at ambient temperature for 30 min and then filtered to remove inorganic salts. Concentration of the crude reaction mixture under reduced pressure followed by a series of pentane washes afforded the desired compound as a colorless solid.

Synthesis of 22. Substrate: aniline. Yield: 0.095 g, 0.237 mmol, 92%. m.p. 187-191 °C. ^{1}H NMR ($CDCl_3$): δ 6.79 (s, 4H), 6.30 (t, J = 8 Hz, 2H), 6.20 (d, J = 8 Hz, 2H), 6.05 (d, J = 8 Hz, 1H), 3.68 (d, J = 10 Hz, 1H), 3.59 (d, J = 6 Hz, 1H), 3.21 (d, J = 6 Hz, 2H), 2.32 (s, 12H), 1.99 (s, 6H). ^{13}C NMR (C_6D_6): δ 164.1, 153.5, 152.4, 145.1, 137.7, 137.1, 130.7, 130.2, 129.7, 129.4, 123.5, 122.1, 118.7, 115.4, 50.4, 48.4, 21.21, 21.1, 19.46, 19.3, 18.7, 18.5. IR (KBr): v = 3017, 2920, 2835, 1614, 1584, 1479, 1481, 1369, 1311, 1227, 1123, 847, 815, 770 cm^{-1}. HRMS (ESI) for $C_{27}H_{33}N_3$: $[M+H]^+$: calcd. 400.2753, Found: 400.2744. Anal. calcd. for $C_{27}H_{33}N_3$: C, 81.16; H, 8.32; N, 10.52, Found: C, 81.32; H, 8.49; N, 10.24.

Synthesis of 23. Substrate: N,N-dimethyl-*p*-phenylenediamine. Yield: 0.094 g, 0.212 mmol, 82%. m.p. 162-165 °C (decomp.) ^{1}H NMR (C_6D_6): 6.79 (s, 4H), 6.30 (d, J = 8 Hz, 2H), 6.20 (d, J = 8 Hz, 2H), 6.04 (d, J = 10 Hz, 1H), 3.68 (d, J =10 Hz, 1H), 3.58 (q, J = 6 Hz, 2H), 3.21 (q, J = 6 Hz, 2H), 2.29 (s, 6H), 2.27 (s, 6H), 2.16 (s, 6H), 2.11 (s, 6H). ^{13}C NMR (C_6D_6): δ 152.3, 148.2, 145.4, 142.9, 140.7, 137.3 (b), 130.3, 130.1, 129.2,

122.4, 114.8, 50.3, 48.7, 41.5, 21.2, 21.1, 19.6, 19.3, 18.8. IR (KBr): ν = 2969, 2829, 1623, 1472, 1422, 1301, 1248, 1152, 1095, 929, 875, 791 cm^{-1}. HRMS (ESI) for $C_{29}H_{38}N_4$: $[M+H]^+$: calcd. 443.3175, Found: 443.3169. Anal. calcd. for $C_{29}H_{38}N_4$: calcd. C, 78.69; H, 8.65; N, 12.66, Found: C, 78.90; H, 8.79; N, 12,49.

Synthesis of 24. Substrate: *p*-anisidine. Yield: 0.095 g, 0.222 mmol, 86%. m.p. 147-149 °C. ^{1}H NMR (C_6D_6): 6.68 (d, J = 4 Hz, 4H), 6.40 (d, J = 10 Hz, 2H), 6.13 (d, J = 10 Hz, 2H), 6.03 (d, J = 10 Hz, 1H), 3.70 (d, J =7 Hz, 1H), 3.56 (q, J = 6 Hz, 2H), 3.20 (q, J = 6 Hz, 2H), 3.11 (s, 3H), 2.42 (s, 12H), 2.10 (s, 6H). ^{13}C NMR (C_6D_6): δ 153.9, 149.9, 142.7, 142.2, 137.5, 134.6, 134.2, 134.1, 127.3, 127.1, 119.6, 112,1, 52.4, 47.3, 45.6, 18.2, 18.1, 16.6, 15.7. IR (KBr): ν = 3402, 2957, 2925, 2854, 1679, 1646, 1512, 1488, 1435, 1407, 1377, 1352, 1194, 1124, 1047, 855, 816, 790, 775 cm^{-1}. HRMS (ESI) for $C_{28}H_{35}N_3O$: $[M+H]^+$: calcd. 430.2858, Found: 430.2859. Anal. calcd. for $C_{28}H_{35}N_3O$: C, 78.28; H, 8.21; N, 9.78, Found: C, 78.43; H, 8.45; N, 9.46.

Synthesis of 25. Substrate: 4-tert-butylaniline. Yield: 0.087 g, 0.190 mmol, 74%. m.p. 204-209 °C. ^{1}H NMR (C_6D_6): δ 6.85 (d, J =10 Hz, 2H), 6.76 (s, 4H), 6.22 (d, J =10 Hz, 2H), 6.13 (d, J = 8 Hz, 1H), 3.95 (d, J = 8 Hz, 1H), 3.57 (q, J = 6 Hz, 2H), 3.21 (q, J = 6 Hz, 2H), 2.44 (s, 12H), 2.09 (s, 6H), 1.03 (s, 9H). ^{13}C NMR (C_6D_6): δ 144.5, 140.1, 139.2, 139.1, 135.9, 135.1, 129.7, 129.0, 125.7, 125.5, 114.5, 114.0, 87.5, 50.4, 48.9, 33.4, 33.3, 31.4, 31.1, 20.6, 20.5, 19.3, 17.9. IR (KBr): ν = 3339, 3236, 2956, 1618, 1592, 1516, 1453, 1462, 1391, 1330, 1292, 1252, 1180, 1051, 932, 837, 812 cm^{-1}. HRMS (ESI) for $C_{31}H_{41}N_3$: $[M+H]^+$: calcd. 456.3379, Found: 456.3376. Anal. calcd. for $C_{31}H_{41}N_3$: C, 81.71; H, 9.07; N, 9.22, Found: C, 81.92; H, 9.21; N, 9.08.

Synthesis of 26. Substrate: *p*-toluidine. Yield: 0.084 g, 0.204 mmol, 79%. m.p. 173-179 °C. ^{1}H NMR (C_6D_6): δ 6.89 (d, J = 8 Hz, 2H), 6.76 (s, 4H), 6.58 (d, J = 8 Hz, 2H), 6.13 (d, J = 8 Hz, 1H), 3.87 (d, J =10 Hz, 1H), 3.55 (d, J = 6 Hz, 2H), 3.20 (d, J = 6

Hz, 2H), 2.42 (s, 12H), 2.09 (s, 6H), 1.87 (s, 3H). ^{13}C NMR (C_6D_6): δ.145.3, 143.8, 139.0, 137.4, 135.4, 130.7, 130.3, 130.0, 129.7, 115.8, 115.6, 86.4, 48.5, 28.3, 21.2, 21.0, 20.8, 20.7, 20.5, 18.9, 18.6. IR (KBr): v = 2924, 2857, 1624, 1603, 1509, 1467, 1452, 1331, 1203, 853, 813, 740 cm^{-1}. HRMS (ESI) for $C_{28}H_{35}N_3$: $[M+H]^+$: calcd. 414.2909, Found: 414.2912. Anal. calcd. for $C_{28}H_{35}N_3$: C, 81.31; H, 8.53; N, 10.16, Found: C, 81.49; H, 8.68; N, 9.95.

Synthesis of 27. Substrate: 4-(methylthio)aniline. Yield: 0.101 g, 0.227 mmol, 88%. m.p. 155-158 °C. ^{1}H NMR (C_6D_6): δ 6.88 (d, J = 8 Hz, 2H), 6.75 (s, 4H), 6.09 (d, J = 8 Hz, 3H), 3.95 (d, J = 8 Hz, 1H), 3.53 (q, J = 4 Hz, 2H), 3.18 (q, J = 4 Hz, 2H), 2.40 (s, 12H), 2.08 (s, 6H), 1.89 (s, 3H). ^{13}C NMR (C_6D_6): δ 146.2, 139.6, 136.1, 132.1, 131.5, 130.4, 126.1, 116.0, 115.3, 87.6, 49.6, 21.24, 21.23, 20.0, 19.2, 18.8. IR (KBr): v = 3401, 2981, 2917, 2855, 1598, 1570, 1496, 1470, 1371, 1350, 1305, 1283, 1253, 1226, 1178, 1148, 1055, 1025, 852, 813 cm^{-1}. HRMS (ESI) for $C_{28}H_{35}N_3S$: $[M+H]^+$: calcd. 446.2631, Found: 446.2627. Anal. calcd. for $C_{28}H_{35}N_3S$: C, 75.46; H, 7.92; N, 9.43, Found: C, 75.31; H, 8.14; N, 9.33.

Synthesis of 28. Substrate: 4-fluoroaniline. Yield: 0.095 g, 0.227 mmol, 88%. m.p. 144-147 °C. ^{1}H NMR (C_6D_6): 6.75 (s, 4H), 6.43 (t, J = 7 Hz, 2H), 6.00 (d, J = 8 Hz, 1H), 5.99 (d, J = 8 Hz, 2H), 3.76 (d, J =10 Hz, 1H), 3.52 (q, J =10 Hz, 2H), 3.17 (q, J =10 Hz, 2H), 2.38 (s, 12H), 2.09 (s, 6H). ^{13}C NMR (C_6D_6): δ 163.7, 153.1, 148.1, 144.6, 139.9, 137.5, 136.7, 130.5, 129.9, 129.8, 129.7, 128.9, 128.8, 128.2, 122.5, 122.4, 115.9, 115.7, 49.9, 47.9, 47.6, 47.4, 20.8, 20.7, 19.0, 18.9, 18.3, 18.1. IR (KBr): v = 2976, 2962, 2881, 1642, 1581, 1514, 1461, 1379, 1336, 1293, 1202, 957, 884, 835, 809, 736 cm^{-1}. HRMS (ESI) for $C_{27}H_{32}N_3F$: $[M+H]^+$: calcd. 418.2659, Found: 418.2660. Anal. calcd. for $C_{27}H_{32}N_3F$: C, 77.66; H, 7.72; N, 10.06, Found: C, 77.29; H, 7.43; N, 9.92.

Synthesis of 29. Substrate: 4-chloroaniline. Yield: 0.094 g, 0.217 mmol, 84%. m.p. 158-163 °C. ^{1}H NMR (C_6D_6): 6.74 (s, 4H), 6.68 (d, J = 7 Hz, 2H), 6.00 (d, J = 8 Hz, 1H), 5.92 (d, J = 8 Hz, 2H), 3.86 (d, J =10 Hz, 1H), 3.49 (q, J =10 Hz, 2H), 3.15 (q, J =10 Hz, 2H), 2.35 (s, 12H), 2.08 (s, 6H). ^{13}C NMR (C_6D_6): δ 163.7, 153.2, 150.5, 145.6, 144.5, 144.3, 139.7, 137.9, 137.6, 136.7, 136.6, 130.5, 129.7, 129.3, 129.2, 129.0, 128.8, 122.8, 116.0, 50.0, 47.8, 47.6, 47.4, 20.8, 20.7, 19.0, 18.9, 18.3, 18.1. IR (KBr): v = 2981, 2971, 2916, 1601, 1581, 1472, 1448, 1367, 1299, 1203, 1016, 958, 889, 831, 711 cm^{-1}. HRMS (ESI) for $C_{27}H_{32}N_3Cl$: $[M+H]^+$: calcd. 434.2363, Found: 434.2361. Anal. calcd. for $C_{27}H_{32}N_3Cl$: C, 74.72; H, 7.43; N, 9.68, Found: C, 74.54; H, 7.79; N, 9.87.

Synthesis of 30. Substrate: 4-bromoaniline. Yield: 0.099 g, 0.206 mmol, 80%. m.p. 180-182 °C. ^{1}H NMR (C_6D_6) 6.81 (d, J = 7 Hz, 2H), 6.73 (s, 4H), 6.00 (d, J = 8 Hz, 1H), 5.86 (d, J = 8 Hz, 2H), 3.87 (d, J =10 Hz, 1H), 3.49 (q, J =10 Hz, 2H), 3.14 (q, J =10 Hz, 2H), 2.35 (s, 12H), 2.08 (s, 6H). ^{13}C NMR (C_6D_6): δ 164.1, 153.6, 144.9, 144.7, 140.1, 137.1, 137.0, 132.7, 132.5, 130.3, 130.2, 130.1, 130.0, 129.4, 129.2, 128,7, 123.7, 116.9, 50.4, 49.6, 48.2, 48.0, 47.8, 21.2, 21.1, 21.0, 19.4, 19.3, 18.7, 18.5. IR (KBr): v = 2981, 2919, 1678, 1630, 1566, 1472, 1452, 1338, 1203, 1005, 881, 853, 831, 707 cm^{-1}. HRMS (ESI) for $C_{27}H_{32}N_3Br$: $[M+H]^+$: calcd. 478.1858, Found: 478.1857. Anal. calcd. for $C_{27}H_{32}N_3Br$: C, 67.78; H, 6.74; N, 8.78, Found: C, 67.64; H, 6.89; N, 8.91.

Synthesis of 31. Substrate: 4-(trifluoromethyl)aniline. Yield: 0.098 g, 0.209 mmol, 81%. m.p. 176-180 °C ^{1}H NMR (C_6D_6): 6.93 (d, J = 8 Hz, 2H), 6.72 (s, 4H), 6.07 (d, J = 8 Hz, 1H), 5.95 (d, J = 8 Hz, 2H), 4.14 (d, J =10 Hz, 1H), 3.47 (q, J =10 Hz, 2H), 3.13 (q, J =10 Hz, 2H), 2.34 (s, 12H), 2.06 (s, 6H). ^{13}C NMR (C_6D_6): δ 164.1, 149.9, 139.2, 137.1, 136.4, 130.5, 130.3, 130.1, 126.7, 114.4, 86.4, 49.7, 21.2, 19.9, 19.3, 18.5. IR (KBr): v = 3400, 2979, 2862, 1613, 1564, 1512, 1467, 1365, 1342, 1293, 1283, 1253, 1229, 1158, 1112, 1055, 930, 853, 771 cm^{-1}. HRMS (ESI) for $C_{28}H_{32}N_3F_3$: $[M+H]^+$: calcd.

468.2627, Found: 468.2631. Anal. calcd. for $C_{28}H_{32}N_3F_3$: C, 71.93; H, 6.90; N, 8.99, Found: C, 72.01; H, 7.06; N, 9.14.

Synthesis of Ring-Opened NHC 4 / Aniline Adducts: General Procedure. A 20 mL vial was charged with 1,3-dimesityl-4,5-dihydroimidazolium bromide (0.100 g, 0.258 mmol), sodium hexamethyldisilazane (0.071 g, 0.387 mmol, 1.50 equiv.) benzene (10 mL) and a stir bar. The resultant solution was stirred at ambient temperature for 1 h. After adding an aniline (0.258 mmol, 1 equiv.) dissolved in 5 mL benzene and stirring at ambient temperature for 1 h, the mixture was filtered to remove inorganic salts. Concentration of the crude reaction mixture under reduced pressure followed by a series of pentane washes afforded the desired compound as a colorless solid.

Synthesis of 32. Substrate: aniline. Yield: 0.096 g, 0.240 mmol, 93%. m.p. 165-168 °C (decomp.) ^{1}H NMR (C_6D_6): δ 7.43 (s, 1H), 7.21 (t, *J* = 7 Hz, 2H), 7.10 (d, *J* = 7 Hz, 2H), 7.00 (d, *J* = 7 Hz, 1H), 6.77 (s, 2H), 6.67 (s, 2H), 3.95 (t, *J* = 7 Hz, 1H), 3.85 (t, *J* = 7 Hz, 2H), 3.24 (q, *J* = 7 Hz, 2H), 2.25 (s, 6H), 2.17 (s, 3H), 2.07 (s, 3H), 2.05 (s, 6H). ^{13}C NMR (C_6D_6): δ 153.51, 152.4, 145.4, 140.3, 137.7, 136.1, 130.7, 130.3, 130.1, 129.7, 129.3, 123.5, 122.1, 50.3, 48.4, 21.2, 21.1, 19.5, 18.7. IR (KBr): *v* = 2919, 2858, 1628, 1588, 1486, 1450, 1339, 1306, 1203, 1108, 853, 813, 764 cm^{-1}. HRMS (ESI) for $C_{27}H_{33}N_3$: $[M+H]^+$: calcd. 400.2750, Found: 400.2749. Anal. calcd. for $C_{27}H_{33}N_3$: C, 81.16; H, 8.32; N, 10.52, Found: C, 81.23; H, 8.41; N, 10.45.

Synthesis of 33. Substrate: N,N-dimethyl-p-phenylenediamine. Yield: 0.095 g, 0.214 mmol, 83%. m.p. 240-246 °C (decomp.) ^{1}H NMR (C_6D_6): δ 7.56 (s, 1H), 6.80 (s, 4H), 6.65 (m, 4H), 4.11 (t, *J* = 7 Hz, 1H), 3.87 (t, *J* = 7 Hz, 2H), 3.24(q, *J* = 7 Hz, 2H), 2.53 (s, 6H), 2.18 (s, 12H), 2.06 (s, 6H). NMR (C_6D_6): δ 152.3, 148.2, 136.7, 130.3, 130.1, 129.9, 122.4, 114.8, 51.08, 48.8, 41.5, 21.4, 21.2, 21.1, 19.6, 18.8, 18.5. IR (KBr): *v* = 2972, 2924, 2832, 1619, 1488, 1453, 1330, 1251, 1162, 1107, 932, 881, 812 cm^{-1}.

HRMS (ESI) for $C_{29}H_{38}N_4$: $[M+H]^+$: calcd. 443.3178, Found: 443.3171. Anal. calcd. for $C_{29}H_{38}N_4$: C, 78.69; H, 8.65; N, 12.66, Found: C, 78.81; H, 8.87; N, 12,52.

Synthesis of 34. Substrate: *p*-anisidine. Yield: 0.090 g, 0.209 mmol, 81%. m.p. 199-206 °C (decomp.) ^{1}H NMR (C_6D_6) δ 7.48 (s, 1H), 7.05 (d, J = 9 Hz, 2H), 6.83 (d, J = 9 Hz, 2H), 6.79 (s, 2H), 6.69 (s, 2H), 4.04 (t, J = 6 Hz, 1H), 3.88 (t, J = 6 Hz, 2H), 3.37 (s, 3H), 3.26 (q, J = 6 Hz, 2H), 2.27 (s, 6H), 2.24 (s, 6H), 2.18 (s, 6H). ^{13}C NMR (C_6D_6): δ 156.9, 152.9, 146.7, 145.2, 140.5, 137.6, 137.2, 137.0, 136.7, 130.3, 130.1, 129.9, 129.2, 122.6, 115.1, 55.4, 51.1, 50.3, 48.6, 21.4, 21.2, 21.1, 19.6, 18.8, 18.5. IR (KBr): v = 2924, 2858, 1629, 1601, 1509, 1487, 1452, 1331, 1203, 1114, 853, 813, 740 cm^{-1}. HRMS (ESI) for $C_{28}H_{35}N_3O$: $[M+H]^+$: calcd. 430.2863, Found: 430.2867. Anal. calcd. for $C_{28}H_{35}N_3O$: C, 78.28; H, 8.21; N, 9.78, Found: C, 78.54; H, 8.51; N, 9.62.

Synthesis of 35. Substrate: 4-tert-butylaniline. Yield: 0.089 g, 0.215 mmol, 76%. m.p. 178-183 °C (decomp.) ^{1}H NMR (C_6D_6): δ 7.52 (s, 1H), 7.28 (d, J = 10 Hz, 2H), 7.11 (d, J = 10 Hz, 2H), 6.78 (s, 2H), 6.68 (s, 2H), 4.01 (t, J = 8 Hz, 1H), 3.88 (t, J = 6 Hz, 2H), 3.26 (q, J = 6 Hz, 2H), 2.27 (s, 6H), 2.17 (s, 3H), 2.12 (s, 3H), 2.08 (s, 6H), 1.28 (s, 9H). ^{13}C NMR (C_6D_6): δ 153.4, 149.9, 146.0, 145.2, 140.4, 137.7, 137.2, 136.6, 130.7, 130.3, 130.2, 130.1, 129.3, 126.5, 121.6, 51.1, 50.3, 48.5, 34.6, 32.7, 32.1, 21.4, 21.2, 21.1, 19.6, 18.7, 18.3. IR (KBr): v = 2956, 2858, 1624, 1602, 1509, 1471, 1456, 1340, 1208, 855, 814, 742 cm^{-1}. HRMS (ESI) for $C_{31}H_{41}N_3$: $[M+H]^+$: calcd. 456.3379, Found: 456.3380. Anal. calcd. for $C_{31}H_{41}N_3$: C, 81.71; H, 9.07; N, 9.22, Found: C, 81.52; H, 8.81; N, 9.43.

Synthesis of 36. Substrate: *p*-toluidine. 0.080 g, 0.193 mmol, 75%. m.p. 144-151 °C. ^{1}H NMR (C_6D_6): δ 7.50 (s, 1H), 7.06 (m, 4H), 6.78 (s, 2H), 6.67 (s, 2H), 4.02 (t, J = 7 Hz, 1H), 3.87 (t, J = 7 Hz, 2H), 3.25 (q, J = 7 Hz, 2H), 2.26 (s, 6H), 2.19 (s, 6H), 2.17 (s, 3H), 2.07 (s, 3H), 2.06 (s, 6H). ^{13}C NMR (C_6D_6): δ 153.2, 149.9, 145.2, 140.4, 137.6,

137.5, 137.2, 136.6, 132.5, 130.3, 130.2, 130.1, 129.3, 121.9, 50.3, 48.5, 21.3, 21.2, 21.1, 19.5, 18.7, 18.4. IR (KBr): ν = 2918, 2854, 1630, 1599, 1507, 1484, 1449, 1228, 1199, 849, 807, 732 cm^{-1}. HRMS (ESI) for $C_{28}H_{35}N_3$: $[M+H]^+$: calcd. 414.2714, Found: 414.2910. Anal. calcd. for $C_{28}H_{35}N_3$: C, 81.31; H, 8.53; N, 10.16, Found: C, 81.19; H, 8.39; N, 10.24.

Synthesis of 37. Substrate: 4-(methylthio)aniline. Yield: 0.097 g, 0.218 mmol, 84%. m.p. 159-164 °C (decomp.) ^1H NMR (C_6D_6): δ 7.42 (s, 1H), 7.23 (d, J = 8 Hz, 2H), 6.98 (d, J = 8 Hz, 2H), 6.78 (s, 2H), 6.68 (s, 2H), 3.92 (t, J = 8 Hz, 1H), 3.84 (t, J = 6 Hz, 2H), 3.23 (q, J = 7 Hz, 2H), 2.25 (s, 6H), 2.17 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.05 (s, 6H). ^{13}C NMR (C_6D_6): δ 153.4, 150.2, 145.1, 140.3, 137.8, 137.1, 132.6, 130.8, 130.3, 130.2, 129.8, 129.3, 122.6, 50.3, 48.4, 21.2, 21.1, 19.5, 18.7, 17.5. IR (KBr): ν = 2919, 2858, 1625, 1585, 1486, 1451, 1330, 1307, 1204, 1107, 882, 853, 812, 751 cm^{-1}. HRMS (ESI) for $C_{28}H_{35}N_3S$: $[M+H]^+$: calcd. 446.2630, Found: 446.2629. Anal. calcd. for $C_{28}H_{35}N_3S$: C, 75.46; H, 7.92; N, 9.43, Found: C, 75.26; H, 8.19; N, 9.27.

Synthesis of 38. Substrate: 4-fluoroaniline. Yield: 0.085 g, 0.204 mmol, 79%. m.p. 190-193 °C (decomp.) ^1H NMR (C_6D_6): δ 7.29 (s, 1H), 6.83 (m, 4H), 6.78 (s, 2H), 6.69 (s 2H), 3.87 (t, J = 8 Hz, 1H), 3.81 (t, J = 6 Hz, 2H), 3.22 (q, J = 6 Hz, 2H), 2.23 (s, 6H), 2.17 (s, 3H), 2.08 (s, 3H), 2.04 (s, 6H). ^{13}C NMR (C_6D_6): δ 161.4, 159.0, 153.5, 148.5, 145.0, 140.2, 137.9, 137.1, 136.5, 130.8, 130.3, 130.2, 129.3, 122.9, 122.8, 116.3, 116.1, 50.3, 48.3, 21.2, 21.1, 19.5, 18.7. IR (KBr): ν = 2981, 2971, 2918, 1628, 1596, 1504, 1487, 1452, 1382, 1341, 1300, 1199, 954, 881, 854, 834, 742 cm^{-1}. HRMS (ESI) for $C_{27}H_{32}N_3F$: $[M+H]^+$: calcd. 418.2660, Found: 418.2658. Anal. calcd. for $C_{27}H_{32}N_3F$: C, 77.66; H, 7.72; N, 10.06, Found: C, 77.38; H, 7.59; N, 10.17.

Synthesis of 39. Substrate: 4-chloroaniline. Yield: 0.088 g, 0.203 mmol, 79%. m.p. 171-175 °C (decomp.) ^1H NMR (C_6D_6): δ 7.29 (s, 1H), 7.18 (s, 2H), 6.84 (s, 2H),

6.80 (s, 2H), 6.70 (s, 2H), 3.82 (t, J = 5 Hz, 2H), 3.22 (q, J = 5 Hz, 2H), 3.04 (s, 1H), 2.24 (s, 6H), 2.12 (s, 6H), 2.04 (s, 6H). ^{13}C NMR (C_6D_6): δ 156.7, 150.8, 145.0, 140.1, 138.0, 137.9, 137.7, 137.0, 136.5, 130.9, 130.3, 130.2, 130.1, 129.7, 129.3, 123.2, 51.0, 50.3, 48.2, 21.4, 21.2, 21.1, 19.4, 18.7, 18.3. IR (KBr): v = 2982, 2970, 2919, 1678, 1625, 1585, 1486, 1452, 1381, 1314, 1203, 1009, 952, 853, 829, 764 cm^{-1}. HRMS (ESI) for $C_{27}H_{32}N_3Cl$: $[M+H]^+$: calcd. 434.2364, Found: 434.2362. Anal. calcd. for $C_{27}H_{32}N_3Cl$: C, 74.72; H, 7.43; N, 9.68, Found: C, 74.86; H, 7.61; N, 9.72.

Synthesis of 40. Substrate: 4-bromoaniline. Yield: 0.105 g, 0.219 mmol, 85%. m.p. 189-191°C (decomp.) ^{1}H NMR (C_6D_6): δ 7.29 (d, J = 9 Hz, 2H), 7.26 (s, 1H), 6.78 (s, 2H), 6.74 (d, J = 9 Hz, 2H), 6.67 (s, 2H), 3.80 (t, J = 5 Hz, 1H), 3.79 (t, J = 8 Hz, 2H), 3.19 (q, J = 7 Hz, 2H), 2.21 (s, 6H), 2.17 (s, 3H), 2.07 (s, 3H), 2.01 (s, 6H). ^{13}C NMR (C_6D_6): δ 153.6, 151.3, 144.94, 140.1, 138.0, 137.7, 137.0, 136.5, 132.7, 130.9, 130.2, 129.3, 123.7, 116.34, 51.04, 50.32, 48.2, 21.4, 21.2, 21.1, 19.4, 18.7, 18.3. IR (KBr): v = 2979, 2921, 1681, 1625, 1579, 1486, 1449, 1378, 1342, 1198, 880, 849, 826, 813, 740 cm^{-1}. HRMS (ESI) for $C_{27}H_{32}N_3Br$: $[M+H]^+$: calcd. 478.1861, Found: 478.1859. Anal. calcd. for $C_{27}H_{32}N_3Br$: C, 67.78; H, 6.74; N, 8.78, Found: C, 67.56; H, 6.54; N, 8.69.

Synthesis of 41. Substrate: 4-(trifluoromethyl)aniline. Yield: 0.094 g, 0.201 mmol, 78%. m.p. 218-222 °C (decomp.) ^{1}H NMR (C_6D_6): δ 7.26 (s, 1H), 6.73 (s, 4H), 6.09 (d, J = 8 Hz, 2H), 5.96 (d, J = 8 Hz, 2H), 3.80 (t, J = 8 Hz, 1H), 3.48 (t, J = 6 Hz, 2H), 3.15 (q, J = 6 Hz, 2H), 2.35 (s, 12H), 2.07 (s, 6H). ^{13}C NMR (C_6D_6): δ 154.2, 149.9, 139.2, 136.9, 136.4, 130.5, 130.3, 130.2, 126.8, 126.7, 122.0, 113.2, 86.4, 49.7, 21.2, 19.9, 19.4, 18.6. IR (KBr): v =2981, 2971, 2919, 1679, 1631, 1613, 1593, 1529, 1486, 1461, 1380, 1323, 1284, 1252, 1158, 1113, 1012, 935, 853, 824 cm^{-1}. HRMS (ESI) for $C_{28}H_{32}N_3F_3$: $[M+H]^+$: calcd. 468.2624, Found: 468.2621. Anal. calcd. for $C_{28}H_{32}N_3F_3$: C, 71.93; H, 6.90; N, 8.99, Found: C, 71.67; H, 7.15; N, 9.26.

Synthesis of 42. A 25 mL Schlenk flask was charged with **4** (0.125 g, 0.41 mmol) and hexanes (5 mL). The heterogeneous mixture was cooled to –78 °C and placed under reduced pressure (100 mtorr). Upon warming to 0 °C, the atmosphere was replaced with ammonia from a balloon. Stirring for 1 h followed by removal of the solvent under reduced pressure at 0 °C afforded the desired compound as a white solid (0.127 g, 0.39 mmol, 95% yield). m.p. 128-130 °C (decomp.) ^{1}H NMR (C_6D_6): δ 6.84 (s, 4H), 5.44 (t, *J* = 7.2 Hz, 1H), 3.50 (m, 2H), 3.21 (m, 2H), 2.34 (s, 12H), 2.17 (s, 6H), 1.14 (d, *J* = 7.0 Hz, 2H). ^{13}C NMR (C_6D_6): δ 139.9, 135.2, 130.0, 129.9, 84.5, 48.7, 20.9, 19.7. IR (KBr): ν = 3386.0, 3304.1, 2912.8, 2848.7, 1481.9, 1354.5, 1251.1, 1132.6, 1030.0, 987.9, 850.0, 572.4 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{21}H_{30}N_3$: 324.2440; Found: 324.2437. Anal. calcd. for $C_{21}H_{29}N_2$: C, 77.97; H, 9.04; N, 12.99; Found: C, 77.68; H, 9.27; N, 12.60.

Synthesis of 44. An 8 mL vial was charged with **4** (0.250 g, 0.82 mmol), hexanes (10 mL), and a stir bar. The heterogeneous mixture was cooled to –78 °C and placed under reduced pressure (75 mtorr). Upon warming to 0 °C, the atmosphere was replaced with ammonia from a balloon. After stirring the mixture for 1 h, volatiles were removed under reduced pressure and redissolved in benzene (10 mL). The reaction was stirred under nitrogen at 23 °C for 48 h and the volatiles removed under reduced pressure. Washing with minimal pentane and drying under reduced pressure afforded the desired compound as a white solid (0.169 g, 0.268 mmol, 66% yield). m.p. 112-114 °C (decomp.) ^{1}H NMR (C_6D_6): δ 6.83 (s, 4H), 6.79 (s, 4H), 5.22 (d, *J* = 5.9 Hz, 2H), 3.32 (m, 4H), 2.82 (m, 4H), 2.27 (s, 12H), 2.13 (t, *J* = 6.2 Hz, 1H), 2.09 (s, 12H), 1.99 (s, 12H). ^{13}C NMR (C_6D_6): δ 140.6, 139.1, 137.6, 134.6, 130.0, 83.7, 49.6, 21.0, 19.5, 19.4. IR (KBr): ν = 3266.1, 2951.4, 2912.0, 2848.9, 1481.9, 1435.1, 1230.2, 1033.8, 847.9, 571.6

cm^{-1}. HRMS (CI): $[M\text{-}H^-]^+$ calcd. for $C_{42}H_{54}N_5$: 628.4379; Found: 628.4387. Anal. calcd. for $C_{42}H_{55}N_5$: C, 80.08; H, 8.80; N, 11.12; Found: C, 79.95; H, 8.78; N, 10.93.

Aniline Competition Studies. For **2**: A 0.106 M stock solution of **2** in C_6D_6 was prepared by dissolving **2** (0.600 g, 1.6 mmol) in C_6D_6 (15 mL). Separately, a 20 mL vial was charged with aniline (0.099 g, 96.8 μL, 1.06 mmol), a para-substituted aniline (1.06 mmol, 1 equiv.), and C_6D_6 (2 mL) to afford an amine stock solution ($[amine]_0$ = 0.53 M). An 8 mL vial was charged with 0.5 mL of the amine stock solution (0.27 mmol of amine, 5 equiv.) and a stir bar. To this vigorously stirred solution was added dropwise 0.5 mL of the 0.106 M stock solution of **2** (0.053 mmol, 1 equiv.) Afterward, the solution was transferred to an NMR tube and a ^1H NMR spectrum taken. Complete consumption of **2** was observed. The N-H insertion product ratio (P_R/P_H, where R is the para-substituent) was calculated by comparing the ratio of the integrals associated with **7-15** to **6**. The experiment was repeated a total of three times for each amino substrate studied. A Hammett plot was constructed by plotting the logarithm of the average P_R/P_H values versus the corresponding substituent parameter, σ_{para} (Figure A28). Hammett plots utilizing σ^+ or σ^- were also constructed (Figure A29, A30). A similar study using **2** and five equiv. each of bis(4-methoxyphenyl)aniline and diphenylamine afforded a 42:58 mixture of **19**/**20**. The result was in good agreement with the ratio of **19**/**20** predicted from the ratio of the respective rate constants (i.e., $k_{HN(MeOPh)2}$:k_{HNPh2} = 0.62 $M^{-1}\cdot min^{-1}$:0.82 $M^{-1}\cdot min^{-1}$ = 43:57). An analogous experiment with bis(4-bromophenyl)aniline and diphenylamine exclusively afforded **21**.

For **4**: A 0.131 M stock solution of **4** in C_6D_6 was prepared by dissolving **4** (0.440 g, 1.44 mmol) in C_6D_6 (11 mL). Separately, a 20 mL vial was charged with aniline (0.122 g, 119 μL, 1.31 mmol), a para-substituted aniline (1.31 mmol, 1 equiv.), and C_6D_6 (2 mL) to afford an amine stock solution ($[amine]_0$ = 0.65 M). An 8 mL vial was charged with

0.5 mL of the amine stock solution (0.326 mmol of amine, 5 equiv.) and a stir bar. To this vigorously stirred solution, 0.5 mL of the 0.131 M stock solution of **4** was added dropwise. Following addition, the solution was transferred to an NMR tube and a ^{1}H NMR spectrum taken 15 min after initial addition of **4** due to slow reversibility of the N-H insertion process. Complete consumption of **4** was observed. With the *N,N*-dimethyl-*p*-phenylenediamine/aniline solution, only the ring-opened products **32** and **33** were observed, and the product ratio (P_{NMe2}/P_H) was calculated by comparing the ratio of the integral associated with **33** at 7.60 ppm to the integral associated with **32** at 7.43 ppm. The reversibility of the N-H insertion combined with the irreversibility of the ring-opening suggested to us that the P_{NMe2}/P_H ratio may have been influenced by thermodynamic rather than kinetic factors, and was thus excluded from the fit line (data point shaded in grey) although linear fits that included the P_{NMe2}/P_H data point were also performed. The N-H insertion product ratio (P_R/P_H) for the other anilines was calculated by comparing the ratio of the integrals associated with **24-31** to **22**. The experiment was repeated a total of three times for each para-substituted aniline. A Hammett plot was constructed by plotting the logarithm of the average P_R/P_H values versus the corresponding substituent parameter, σ^- (Figure A32). Hammett plots utilizing σ_{para} or σ^+ were also constructed (Figure A31, A33).

Kinetic Studies. For liquid amines and **2**: A 0.089 M stock solution of **2** was prepared by dissolving **2** (0.100 g, 0.266 mmol) in C_6D_6 (3 mL). An NMR tube equipped with a screw-cap septum was then charged inside of a glove box with the stock solution of **2** (0.6 mL, 0.053 mmol) and a sufficient quantity of C_6D_6 such that the total volume equaled 0.8 mL upon the addition of 10 equiv. of the amine analyzed. The sample was then equilibrated in an NMR probe at 30 °C. Upon equilibration, the sample was ejected from the instrument and 0.53 mmol (10 equiv.) of an amine was added via syringe. The

NMR tube was then vigorously shaken to ensure proper mixing, and the sample reinserted into the NMR probe. After shimming, spectra (four scans each) were acquired every 30 sec for 1 h.

For solid amines and **2**: A 0.177 M stock solution of **2** was prepared by dissolving **2** (0.100 g, 0.266 mmol) in C_6D_6 (1.5 mL). A 0.106 M stock solution of the amine was prepared by dissolving the amine (1.06 mmol) in C_6D_6 (1 mL). An NMR tube equipped with a screw-cap septum was then charged inside of a glove box with the stock solution of **2** (0.3 mL, 0.053 mmol). The sample was then equilibrated in an NMR probe at 30 °C. Upon equilibration, the sample was ejected from the instrument and 0.5 mL of the amine stock solution (0.53 mmol, 10 equiv.) was added via syringe. The NMR tube was then vigorously shaken to ensure proper mixing, and the sample reinserted into the NMR probe. After shimming, spectra (four scans each) were acquired every 30 sec for 1 h.

Conversions of the aforementioned starting materials to the corresponding N-H inserted products were measured by comparing the ratio of the ^{1}H NMR integrals assigned to the alkyl backbone protons of **2** (δ = 1.48 ppm; s, 6H) with the corresponding protons attributed to the respective product (**16**: 1.87 ppm, 3H; **17**: 1.88 ppm, s, 3H; **18**: 1.91 ppm; 6H; **19**: 1.93 ppm, s, 3H; **20**: 1.92 ppm, s, 3H). To account for the differing number of hydrogen atoms in each compound, the integrals for **16**, **17**, **19**, and **20** were doubled prior to calculating the integral ratio. Pseudo-first order rate constants were determined for these reactions by plotting the ln [**2**] versus time (Figures A34-A38). Linear fits of all data points collected for conversions < 99% were used to calculate the rate constants from the absolute value of the corresponding slopes divided by the initial concentration of the amine.

Synthesis of diphenylamine-d_1. A 30 mL vial was charged with diphenylamine (2.0 g, 11.8 mmol, 1.05 equiv.), sodium hexamethyldisilazide (2.06 g, 11.2 mmol), and

toluene (20 mL) under an atmosphere of nitrogen. The resultant mixture was stirred at ambient temperature for 3 h. The solid precipitate was collected over a medium porosity fritted funnel and washed with toluene (3 × 5 mL) and pentane (3 × 5 mL). The solid was transferred to a 50 mL Schlenk flask and suspended in 15 mL toluene. The mixture was cooled to 0 °C and 5 mL of D_2O was added dropwise. The mixture was stirred at 0 °C for 1 h during which time the solution cleared. The organic layer was separated and dried over sodium sulfate. Filtration and removal of the volatiles under reduced pressure afforded diphenylamine-*d*$_1$ (1.4 g, 8.2 mmol, 74%) with 92% D incorporation at the nitrogen as determined by ^{1}H NMR spectroscopy.

An identical kinetic rate study to that with diphenylamine and **2** described above was performed with diphenylamine-*d*$_1$ and **2** (Figure A39). A kinetic isotope effect (KIE) was calculated by dividing the rate constant for the reaction of diphenylamine and **2** by the rate constant for the reaction of diphenylamine-*d*$_1$ and **2** (k_H/k_D) which afforded a KIE value of 1.5. A competition experiment with diphenylamine (5 equiv.), diphenylamine-*d*$_1$ (5 equiv.), and **2** identical to those described above afforded a 62:38 ratio of H/D containing **20** from which a KIE value of 1.3 was calculated, showing good agreement with the rate measurements.

For liquid anilines and **4**: An NMR tube equipped with a screw-cap septum was charged inside of a glove box with 0.7 mL of a stock solution containing **4** (40 mM) and trimethoxybenzene (10.6 mM) in C_7D_8. To this sample was added a sufficient quantity of C_7D_8 such that the total sample volume equaled 0.8 mL after the subsequent addition of the excess amine (≥ 10 equiv.) The sample was then equilibrated in an NMR probe at –25 °C. Upon equilibration, the sample was ejected from the instrument, and the neat amine was added via syringe. The NMR tube was then vigorously shaken to ensure proper mixing, and the sample reinserted into the NMR probe. After shimming, spectra

(four scans each) were acquired every 30 sec for 1 h. For 4-(trifluoromethyl)aniline, the NMR tube was charged with 0.35 mL of the stock solution and 0.35 mL of C_7D_8 rather than 0.7 mL of the stock solution in order to reduce the rate of the reaction, however complete consumption of **4** was still observed by the time the first ^{1}H NMR spectrum was acquired (t = 2 min).

For solid anilines and **4**: An NMR tube equipped with a screw-cap septum was charged inside of a glove box with 0.7 mL of a stock solution containing **4** (40 mM) and trimethoxybenzene (10.6 mM) in C_7D_8. The sample was then equilibrated in an NMR probe at –25 °C. Upon equilibration, the sample was ejected from the instrument, and the excess amine (≥ 10 equiv.) dissolved in 0.1 mL C_7D_8 was added via syringe. The NMR tube was then vigorously shaken to ensure proper mixing, and the sample reinserted into the NMR probe. After shimming, spectra (four scans each) were acquired every 30 sec for 1 h. For 4-bromoaniline and 4-chloroaniline, the NMR tube was charged with 0.35 mL of the stock solution and 0.35 mL of C_7D_8 rather than 0.7 mL of the stock solution in order to reduce the rate of the reaction. For *p*-anisidine, 0.35 mL of stock solution, 0.25 mL C_7D_8, and 0.2 mL of the *p*-anisidine in C_7D_8 was utilized due to the low solubility of the *p*-anisidine under the conditions used for these experiments.

Pseudo-first order rate constants were determined for these reactions by plotting the ln [**4**] versus time (Figures A40-A48). The second-order rate constants were calculated by dividing the absolute value of the corresponding slopes by the initial concentration of aniline or its derivative.

6.5 Acknowledgements

Portions of this chapter were reproduced with permission from Moerdyk, J. P.; Blake, G. A.; Chase, D. T.; Bielawski, C. W. *J. Am. Chem. Soc.* **2013**, *135*, 18798.

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35) Adding **2** to a stirred mixture of 5 equiv. of diphenylamine and 5 equiv. of diphenylamine-d_1 afforded a 62:38 mixture of H:D products containing **20** and a measured KIE value of 1.3.

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37) As the negative slope reflected the build-up of positive charge at the amine nitrogen that could not be resonance delocalized, the σ_{para} value (which also

provided the best linear fit) was utilized rather than σ^- or σ^+ values although a negative slope was observed in all cases.

38) For example, the addition of 5 equiv. of 4-chloroaniline to **4** in C_6D_6 at 23 °C resulted in the quantitative formation of **29**; subsequent addition of aniline (5 equiv.) resulted in a 9:1 mixture of **29**/**22** after 1 h at 23 °C. Similar studies with **2** showed no detectable scrambling, even after several days.

39) Even in the absence of exogenous base, treating a *N,N*-dimethyl-*p*-phenylenediamine/aniline mixture to **4** irreversibly afforded the ring-opened products **32** and **33** rather than **22** and **23**. The reversibility of the N–H insertion combined with the irreversibility of the ring-opening indicated that the P_{NMe2}/P_H ratio may have been influenced by thermodynamic rather than kinetic factors, and therefore these data were excluded from the fit. However, including the P_{NMe2}/P_H data still afforded a linear fit with a positive slope of similar magnitude.

40) As the positive slope reflected the build-up of negative charge that could be resonance stabilized through delocalizing the amine lone pair into the aromatic ring, the σ^- value (which also provided the best linear fit)was utilized rather than σ_{para} or σ^+ values although a positive slope was observed in all cases.

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Chapter 7: Exploring the Chemistry of *N,N′*-Diamidocarbenes with Organophosphorus Compounds*

7.1 INTRODUCTION

The rapidly evolving view of stable carbenes[1] as functional mimics for transition metals has coincided with the rise of carbene−phosphorus chemistry. For example, recent studies have realized the stabilization of white phosphorus,[2-5] phosphanyl cations,[6] and phosphorus centered-radicals[7] using carbenes – chemistry that has historically required the use of transition metals (e.g., vanadium, tungsten, niobium, etc.) Additionally, analysis of the ^{13}C NMR chemical shifts displayed by carbene-derived phosphinidenes has been introduced as a new method for quantifying the π-accepting character of carbenes[8,9] and complements the frequently used Tolman electronic parameters.[10-12] However, despite the critical roles of both P−H insertions in hydrophosphinylations[13-16] and phosphorus−metal ligation in catalysis,[17,18] there is only one report of P−H activation using isolable carbenes (*i.e.*, **1**[19,20] or **2**[21] in Figure 7.1).[22,23] Similarly, P→$C_{carbene}$ interactions are extremely rare.[24-26] The realization and understanding of such chemistry is not only fundamentally attractive but practical as it should facilitate access to new classes of organophosphorus and other important phosphine containing compounds[16] with high atom economy.

Building on our report[27] describing the N−H insertion chemistry of the readily available *N,N′*-diamidocarbene[28-33] (DAC) **3**, we reasoned that such carbenes may facilitate isolobal P−H insertions. Our hypothesis was inspired by a recent study[34] by

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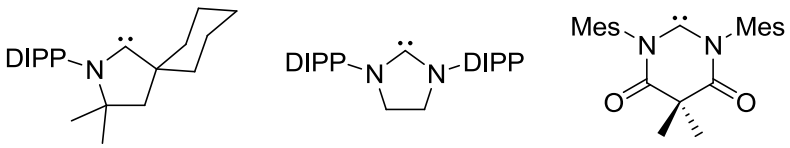


1 2 3

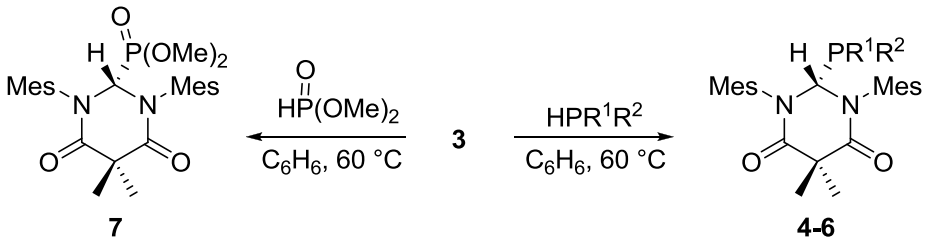
Figure 7.1: Isolable carbenes (**1** and **2**) previously reported to insert into P–H bonds and a diamidocarbene (**3**).

Hudnall who revealed that **3** stabilizes P_4 through a mechanism that likely involves the attack of the carbene by an incipient anionic phosphorus center, an intriguing result which suggested to us that DACs may be capable of accepting electron density from nucleophilic phosphines. Herein, we show that a DAC inserts into the P−H bonds of primary and secondary phosphines as well as dimethyl phosphite. Additionally, the DAC underwent ring contraction in the presence of catalytic tertiary phosphines and afforded the products expected from an Arbuzov-type reaction involving trimethyl phosphite, potentially via ylidic intermediates.

7.2 Results and Discussions

Our efforts began by adding an equimolar quantity of phenylphosphine to a C_6H_6 solution of **3** ($[\mathbf{3}]_0$ = 0.199 M). After being stirred at 23 °C for 1 h, the aforementioned mixture was analyzed by ^{13}C NMR spectroscopy (C_6D_6) which revealed a doublet (J = 11.6 Hz) at 75.5 ppm that was attributed to a diamidomethine (*c.f.*, the carbene nucleus in **3** has been reported to resonate at 277.7 ppm). Combined with the ^{1}H and ^{31}P NMR signals observed at 6.17 and −60.4 ppm, respectively, the spectroscopic data supported the formation of the P−H insertion product **4**, which was subsequently isolated in 83% yield. As summarized in Scheme 7.1 and Table 7.1, alkyl- and arylphosphines as well as a phosphonate ester were successfully treated with **3** to afford the corresponding P−H insertion products **4**−**7** in up to 83% yield.[35] The structure of **5** was unambiguously

determined via single-crystal X-ray diffraction (XRD) analysis which confirmed the expected sp^3-hybridized carbon center (*e.g.*, the sum of N1−C1−N2, N1−C1−P1, and N2−C1−P1 angles = 333.34°), and a distance typical of a carbon−phosphorus single bond was measured (1.92 Å; Figure 7.2).[36] To the best of our knowledge, these are the first examples of isolable carbenes facilitating P−H insertions into alkyl phosphines or a phosphonate ester.



Scheme 7.1: Treatment of **3** with Phosphines and Phosphites.

Product	R^1	R^2	Yield (%)
4	H	Ph	83[b]
5	Ph	Ph	48
6	Et	Et	60
7	-	-	60[c]

Table 7.1: Summary of P−H Insertion Reactions. [a] Isolated yields. Conditions unless otherwise specified: C_6H_6, 60 °C, $[\mathbf{3}]_0 = [\text{phosphine}]_0 = 0.133$ M, 3 h. [b] 23 °C, 1 h. [c] $[\mathbf{3}]_0 = [\text{phosphite}]_0 = 0.266$ M, 12 h.

We hypothesized that if the aforementioned DAC-facilitated P−H activation processes proceeded via ylidic intermediates, as observed with **3** and various N−H insertion reactions,[27] stable ylides might be obtained upon the exposure of **3** to tertiary phosphines. To test, an equimolar quantity of trimethylphosphine (1.0 M in C_7H_8) was

added to a C_6D_6 solution of **3** ($[\mathbf{3}]_0$ = 0.133 M), and then the resulting mixture was heated to 60 °C for 3 h, which resulted in the formation of a bright red solution. ^{1}H NMR spectroscopic analysis of the crude reaction mixture revealed that a new compound with lower symmetry than **3** had formed, as indicated by the presence of two sets of aryl protons in equal integration at 6.78 and 6.76 ppm. Surprisingly, the signals associated with trimethylphosphine at 0.81 and −61.9 ppm in the ^{1}H and ^{31}P NMR spectra, respectively, were unchanged, and new ^{31}P signals were not observed. Combined with the ^{13}C NMR signals assigned to keto (194.7 ppm) and amido (174.9 ppm) functional groups, the spectroscopic data were consistent with the formation of the iminopyrrolidinedione **8**. The product was subsequently isolated by silica gel chromatography in 88% yield, and the structure was unambiguously confirmed by XRD analysis (Figure 7.3).

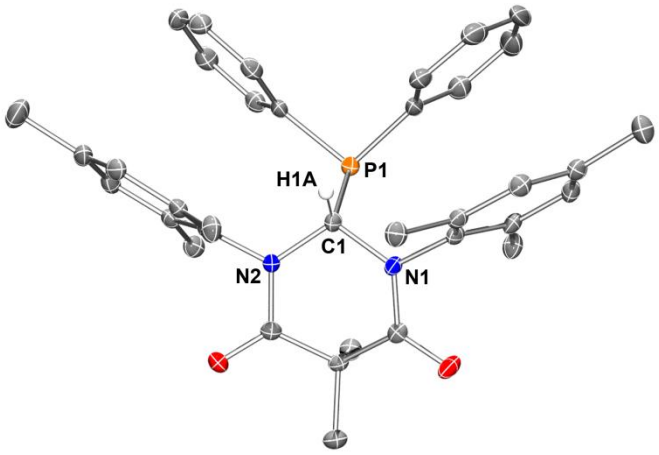


Figure 7.2: ORTEP diagram of **5** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity except at the carbenoid carbon. Selected distances (Å) and angles (°): C1-P1, 1.9176(16); C1-N1, 1.4739(19); C1-N2, 1.4690(19); P1-C1-N1, 110.26(10); P1-C1-N2, 111.96(10); N1-C1-N2, 111.12(12).

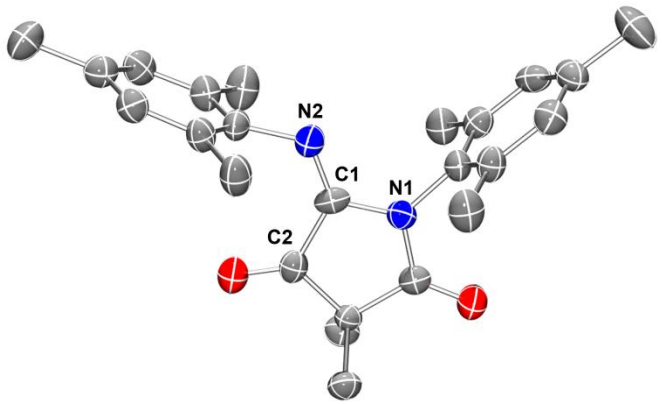
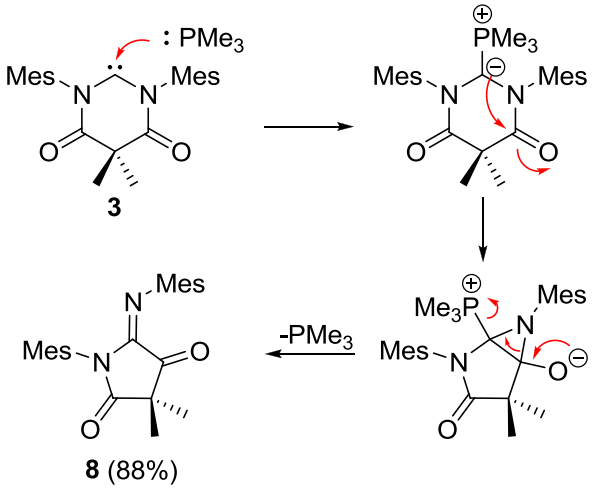


Figure 7.3: ORTEP diagram of **8** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (°): C1-N1, 1.385(5); C1-N2, 1.277(5); N1-C1-N2, 122.6(3); N1-C1-C2, 106.4(3); C2-C1-N2, 131.0(2).



Scheme 7.2: Proposed PMe_3 Catalyzed Rearrangement of **3**.

To probe the generality of the aforementioned rearrangement, **3** was treated to tertiary phosphines containing relatively bulky substituents (*e.g.*, ethyl, propyl, butyl, or phenyl). However, the formation of **8** was not observed even at elevated temperatures (*e.g.*, 100 °C), likely due to steric inhibition. Although **8** was obtained after treating **3** with chlorodiethylphosphine, larger chlorodialkyl- (*e.g.*, isopropyl or tert-butyl) or

chlorodiarylphosphines were not observed to facilitate the aforementioned rearrangement. Quantitative conversion to **8** was observed in the presence of catalytic quantities (10 mol%) of trimethyl- or chlorodiethylphosphine. Collectively, the aforementioned results suggested to us that the isomerization was initiated by nucleophilic attack of the phosphine on the carbene nucleus which generated a transient phosphonium ylide. Subsequent intramolecular addition of the carbanion into the carbonyl group of an amide would form a strained, bicyclic, and zwitterionic intermediate that expelled trimethylphosphine and yielded **8** upon collapse (Scheme 7.2).

Having examined tertiary phosphines, we next focused on the reaction of **3** with an electron-deficient phosphite (as compared to the analogous phosphine) to deconvolute the role of electronics. In an initial experiment, equimolar quantities of **3** ($[\mathbf{3}]_0$ = 0.27 M) and trimethyl phosphite were dissolved in C_6D_6 and heated to 60 °C, which resulted in the formation of a colorless precipitate after 12 h. Analysis of the crude reaction mixture by ^{1}H and ^{31}P NMR spectroscopy revealed the presence of residual phosphite as well as the formation of a new product. Considering that the spectroscopic data recorded for the precipitate were identical to those of **7** and taking mass balance into account, the new product was predicted to be the exocyclic olefin **9**. To increase the yield of this material, the aforementioned reaction was repeated using 2 equiv of **3** with respect to the trimethyl phosphite. Collection of the resultant precipitate followed by washing with pentane afforded pure **7** (76% isolated yield), whereas purification of the filtrate residue by silica gel column chromatography yielded **9** (53%), as determined by NMR spectroscopy and XRD analysis (Figure 7.4).[37,38]

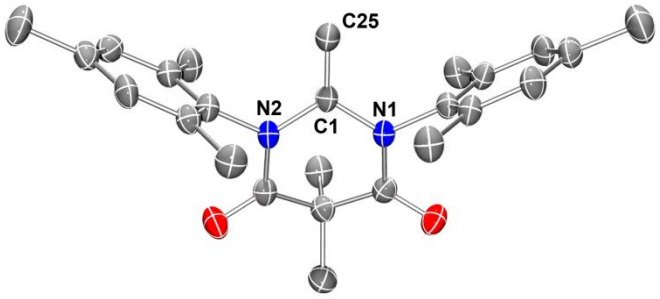
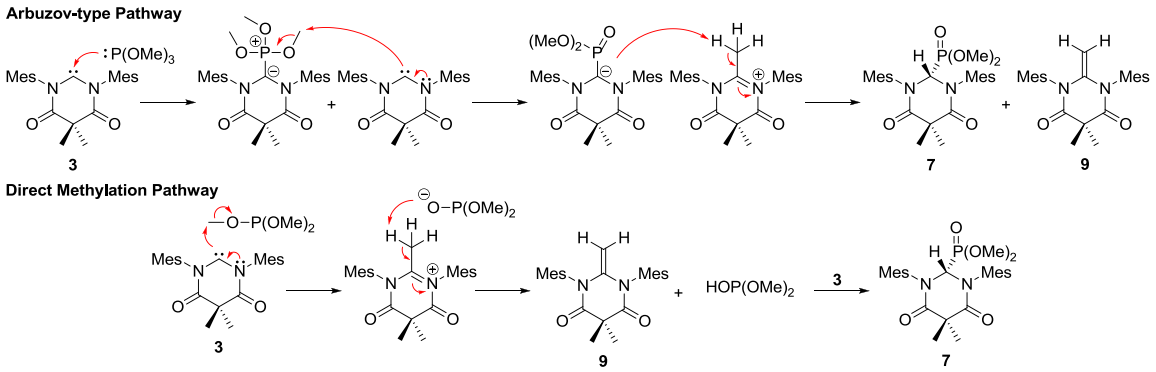


Figure 7.4: ORTEP diagram of **9** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (°): (a) C1-N1, 1.420(5); C1-N2, 1.420(5); C1-C25, 1.331(6); N1-C1-N2 = 114.9(3); N1-C1-C25 = 122.1(3); N2-C1-C25 = 122.8(3).

As summarized in Scheme 7.3, the formation of **7** and **9** may have proceeded through an Arbuzov- or a direct methylation-type pathway. In the former, **3**, acting as an electrophile, would undergo attack from trimethyl phosphite to form the corresponding ylide. Subsequent demethylation by a second equivalent of **3** followed by proton transfer between the resultant resonance-stabilized ion pair would then afford the observed products. Alternatively, the direct methylation of nucleophilic **3** by trimethyl phosphite followed by proton transfer would afford **8** and dimethyl phosphite, which was previously shown to undergo P−H insertion with **3** (see Scheme 7.1). As the ylide intermediate of the Arbuzov-type pathway may be expected to undergo intramolecular rearrangement and lead to the formation of **8**, which was not observed, the direct methylation pathway may be preferred.[39]



Scheme 7.3: Possible Mechanistic Pathways Leading to the Formation of **7** and **9**.

7.3 CONCLUSIONS

In summary, DAC-facilitated insertions were extended to encompass compounds containing a variety of P−H bonds including the first insertions of an isolable carbene into dialkylphosphines and a phosphonate ester. The rearrangement of **3** to the iminopyrrolidinone **8** catalyzed by trimethylphosphine or chlorodimethylphosphine also supported the ability of the DACs to develop negative charge at the carbenoid center and to form ylidic intermediates. Furthermore, the reaction of **3** with trimethyl phosphite afforded the products expected from an Arbuzov-type reaction, although a distinct mechanism that involves the direct methylation of the DAC may be operative. More broadly, the results extend the abilities of stable carbenes to mimic transformations typically expected from transition metals and afford access to novel organophosphorus derivatives. Moreover, the reactions presented herein effectively broaden phosphorus-carbene chemistry and are envisioned to facilitate the synthesis of new phosphine-containing compounds and ligands.

7.4 EXPERIMENTAL

General Considerations. All procedures were performed using standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen-filled glove box unless otherwise noted. *N,N′*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (**3**) was prepared according to literature procedures.[30] All commercial liquid substrates were dried over molecular sieves for 24 h prior to use. All commercial solid substrates were dried under reduced pressure for 24 h prior to use. Benzene and pentane were dried and degassed by a Vacuum Atmospheres Company solvent purification system (model number 103991-0319) and stored over molecular sieves in a nitrogen-filled glove box. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer. High-resolution mass spectra (HRMS) were obtained with a Waters Micromass Autospec-Ultima (CI) or an Agilent 6530 QTOF (ESI) mass spectrometer. NMR spectra were recorded on a Varian Unity+ 300, Varian Mercury 400, Varian Directdrive 400, or Agilent MR400 spectrometer. Chemical shifts (δ) are represented in ppm relative to residual benzene (^{1}H: 7.15 ppm, ^{13}C: 128.0 ppm) or chloroform (^{1}H: 7.24 ppm, ^{13}C: 77.0 ppm) as reference or against an external standard of 85% H_3PO_4 (^{31}P: 0.0 ppm). Elemental analyses were performed at Midwest Microlab, LLC (Indianapolis, IN). Melting points were obtained using a Stanford Research Systems MPA100 OptiMelt automated melting point apparatus (ramp rate: 1 °C·min^{-1}) and are uncorrected.

Synthesis of 4. An 8 mL vial was charged with **3** (0.150 g, 0.398 mmol), benzene (2 mL), and a stir bar. To this vial, phenylphosphine (43.8 μL, 0.398 mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 1 h. Concentration of the crude reaction mixture under reduced pressure followed by washing with pentane and drying under reduced pressure afforded **4** (0.161 g, 83%) as a colorless solid. m.p. 215-216 °C. ^{1}H NMR (C_6D_6, 399.68 MHz): δ 6.80 (m, 1H), 6.75 (s, 2H), 6.64-6.70 (s

overlapping m, 3H), 6.55 (m, 2H), 6.17 (m, 3H), 4.12 (dd, J = 222.6, 1.4 Hz, 1H), 2.57 (s, 3H), 2.39 (s, 3H), 2.18 (s, 3H), 2.09 (s, 3H), 1.98 (s, 3H), 1.92 (s, 3H), 1.72 (s, 3H), 1.66 (s, 3H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 170.6, 170.0 (d, J = 1.5 Hz), 138.4, 138.2 (d, J = 1.7 Hz), 138.1, 136.3, 135.8, 135.5, 135.2 (d, J = 2.2 Hz), 134.4 (d), 131.1 (d, J = 11.6 Hz), 130.0 (d, J = 18.1 Hz), 129.8 (d, J = 16.6 Hz), 129.0, 127.9 (d, J = 7.2 Hz), 75.5 (d, J = 11.6 Hz), 47.3, 25.4, 22.2, 20.9, 20.7, 20.4 (d, J = 14.0 Hz), 19.7 (d, J = 6.0 Hz), 18.8, 18.4. ^{31}P NMR (C_6D_6, 121.50 MHz): δ -60.4. IR (KBr): ν = 2978, 2919, 2845, 1685, 1659, 1608, 1481, 1458, 1436, 1399, 1369, 1351, 1268, 1213, 1195, 1169, 1090, 1033 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{30}H_{36}N_2O_2P$: 487.2509; Found 487.2510. Anal. calcd. for $C_{30}H_{35}N_2O_2P$: C, 74.05; H, 7.25; N, 5.76; Found: C, 73.87; H, 7.20; N, 5.59.

Synthesis of 5. An 8 mL vial was charged with **3** (0.100 g, 0.266 mmol), benzene (2 mL), and a stir bar. To this vial, diphenylphosphine (42.3 μL, 0.266 mmol, 1 eq) was added and the resultant mixture heated at 60 °C for 3 h. Concentration of the crude reaction mixture under reduced pressure followed by washing with pentane and drying under reduced pressure afforded **5** (0.072 g, 0.128 mmol, 48%) as a colorless solid. m.p. 198-200 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 7.01 (dt, J = 8.2, 1.4 Hz, 4H), 6.91 (dt, J = 7.2, 1.4 Hz, 2H), 6.75 (t, J = 7.2 Hz, 4H), 6.67 (s, 4H), 5.94 (s, 1H), 2.43 (s, 6H), 2.08 (d, J = 2.0 Hz, 3H), 2.05 (s, 6H), 1.98 (s, 6H), 1.58 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 170.5, 137.6, 137.6, 136.5 (d, J = 15.9 Hz), 134.5, 132.8, 131.5 (d, J = 22.5 Hz), 129.2, 129.0, 127.4 (d, J = 8.8 Hz), 127.4, 71.4 (d, J = 22.0 Hz), 46.8, 27.2 (d, J = 8.6 Hz), 21.1 (d, J = 1.3 Hz), 20.6 (d, J = 9.2 Hz) 20.5, 19.4. ^{31}P NMR ($CDCl_3$, 121.50 MHz): δ -13.2. IR (KBr): ν = 3072, 3045, 3004, 2974, 2919, 2858, 1682, 1656, 1610, 1481, 1460, 1412, 1372, 1357, 1231, 1217, 1189, 1161, 1090, 1029 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{36}H_{40}N_2O_2P$: 563.2822; Found 563.2820. Anal. calcd. for $C_{36}H_{39}N_2O_2P$: C, 76.84; H, 6.99; N, 4.98; Found: C, 76.71; H, 6.71.; N, 5.09.

Synthesis of 6. An 8 mL vial was charged with **3** (0.100 g, 0.266 mmol), benzene (2 mL) and a stir bar. To this vial, diethylphosphine (24.0 μL, 0.266 mmol, 1 eq) was added and the resultant mixture heated at 60 °C for 3 h. Concentration of the crude reaction mixture under reduced pressure followed by washing with pentane and drying under reduced pressure afforded **6** (0.075 g, 0.161 mmol, 60%) as a colorless solid. m.p. = 139-141 °C. ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 6.89 (s, 2H), 6.88 (s, 2H), 5.73 (d, *J* = 6.0 Hz, 2H), 2.29 (s, 6H), 2.27 (overlapping s, 12H), 1.80 (s, 3H), 1.56 (s, 3H), 1.09-1.01 (m, 2H), 0.97-0.90 (m, 2H), 0.63 (overlapping t, 6H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 170.8, 138.0, 137.9 134.9, 134.5, 129.7, 129.6, 72.4 (d, *J* = 36.0 Hz), 46.3, 26.4 (d, *J* = 3.9 Hz), 21.7, 20.9, 19.8 (d, *J* = 6.4 Hz), 19.5, 15.7 (d, *J* = 17.9 Hz), 9.5 (d, *J* = 16.0 Hz). ^{31}P NMR ($CDCl_3$, 121.50 MHz): δ 1.85. IR (KBr): ν = 2981, 2925, 2873, 1686, 1655, 1654, 1607, 1482, 1459, 1414, 1354, 1214, 1187, 1176, 1089, 1033, 940, 859 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{28}H_{40}N_2O_2P$: 467.2827; Found 467.2827. Anal. calcd. for $C_{28}H_{39}N_2O_2P$: C, 72.08; H, 8.42; N, 6.00; Found: C, 72.18; H, 8.31; N, 6.16.

Synthesis of 7. *Method A*: An 8 mL vial was charged with **3** (0.200 g, 0.53 mmol, 2 eq), benzene (2 mL), and a stir bar. To this vial, trimethylphosphite (0.033 g, 31.3 μL, 0.266 mmol, 1 eq) was added and the resultant mixture heated at 60 °C for 12 h during which time a white precipitate accumulated. Upon cooling to ambient temperature, the precipitate was collected via vacuum filtration using a medium porosity fritted funnel. Subsequent washing with pentane (3 × 1 mL) followed by drying under reduced pressure afforded **7** as a white solid (0.099 g, 0.203 mmol, 76%). *Method B*: An 8 mL vial was charged with **3** (0.500 g, 1.33 mmol), benzene (5 mL) and a stir bar. To this vial, dimethylphosphite (122 μL, 1.33 mmol, 1 eq) was added and the resultant mixture heated at 60 °C for 3 h. After evaporating the yellow product mixture to dryness, the resulting solid was triturated with pentane. The solid was then collected using a medium porosity

frit and rinsed with pentane until the washings were colorless. Drying the solid under reduced pressure afforded **7** (0.390 g, 0.80 mmol, 60%) as a white solid. m.p. 229-230 °C. ^{1}H NMR ($CDCl_3$, 300.14 MHz): δ 6.92 (s, 2H), 6.88 (s, 2H), 5.26 (d, *J* = 2.4 Hz, 1H), 3.11 (d, *J* = 10.8 Hz, 6H), 2.30 (s, 12H), 2.26 (s, 6H), 1.91 (s, 3H), 1.57 (s, 3H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 170.4, 139.6, 137.8, 134.2, 133.2, 129.5, 129.3, 68.3 (d, *J* = 175.0 Hz), 52.3 (d, *J* = 8.0 Hz), 46.5, 26.5, 26.4, 22.3, 20.8, 19.2, 18.8. ^{31}P NMR ($CDCl_3$, 121.50 MHz): δ 15.7. IR (KBr): ν = 3005, 2982, 2939, 2875, 1691, 1663, 1606, 1461, 1419, 1383, 1361, 1279, 1245, 1225, 1202, 1182, 1162, 1098, 1061, 1045 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{26}H_{26}N_2O_5P$: 487.2352. Found: 487.2356. Anal. calcd. for $C_{26}H_{25}N_2O_5P$: C, 64.18; H, 7.25; N, 5.76; Found: C, 64.12; H, 7.30; N, 5.77.

Synthesis of 8. An 8 mL vial was charged with **3** (0.100 g, 0.266 mmol), benzene (2 mL) and a stir bar. To this vial, trimethylphosphine (1.0 M, C_7H_8, 0.27 mL, 0.27 mmol, 1 eq) was added and the mixture heated at 60 °C for 3 h. The red solution was evaporated to dryness and the crude product was purified by silica gel column chromatography (eluent = CH_2Cl_2) to afford **8** (0.088 g, 0.234 mmol, 88%) as a red solid. Similar results were observed when using catalytic quantities of trimethylphosphine or chlorodiethylphosphine (10 mol%) under identical conditions. m.p. 181-182 °C. ^{1}H NMR (C_6D_6, 400.27 MHz): δ 6.78 (s, 2H), 6.76 (s, 2H), 2.16 (s, 3H), 2.15 (s, 6H), 2.08 (s, 3H), 2.01 (s, 6H), 1.11 (s, 6H). (C_6D_6, 75.47 MHz): δ 194.7, 174.9, 145.2, 143.6, 139.0, 135.5, 132.3, 129.6, 129.4, 129.1, 125.57, 47.1, 21.0, 20.9, 18.6, 17.9. IR (KBr): ν = 2968, 2928, 2866, 1774, 1747, 1667, 1480, 1463, 1390, 1368, 1303, 1291, 1192, 1178, 1142, 1129, 1060, 1032 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{24}H_{29}N_2O_2$: 377.2224; Found: 377.2224. Anal. calcd. for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44; Found: C, 76.06; H, 7.39; N, 7.44.

Synthesis of 9. An 8 mL vial was charged with **3** (0.200 g, 0.53 mmol, 2 eq), benzene (2 mL), and a stir bar. To this vial, trimethylphosphite (0.033 g, 31.3 μL, 0.266 mmol, 1 eq) was added and the resultant mixture heated at 60 °C for 12 h during which time a white precipitate accumulated. Upon cooling to ambient temperature, the precipitate was collected via vacuum filtration using a medium porosity fritted funnel and washed with pentane (3 × 1 mL). The filtrate was concentrated under reduced pressure and the resulting crude solid was purified by silica gel column chromatography (eluent = ethyl acetate). Concentration of the resultant fractions afforded **9** as an off white solid (0.055 g, 0.141 mmol, 53%). m.p. 220-222 °C (decomp). ^{1}H NMR ($CDCl_3$, 300.14 MHz): δ 6.95 (s, 4H), 3.25 (s, 2H), 2.29 (s, 6H), 2.15 (s, 12H), 1.67 (s, 6H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ 169.0, 138.9, 138.5, 135.2, 132.7, 129.7, 78.2, 46.7, 24.4, 21.0, 17.4. IR (KBr): ν = 2982, 2920, 1711, 1690, 1664, 1607, 1462, 1417, 1393, 1381, 1361, 1346, 1307, 1279, 1246, 1226, 1202, 1195, 1098, 1059, 1043 cm^{-1}. HRMS (ESI): $[M+H]^+$ calcd. for $C_{25}H_{31}N_2O_2$: 391.2378; Found: 391.2380. Anal. calcd. for $C_{25}H_{30}N_2O_2$: C, 76.89; H, 7.74; N, 7.17; Found: C, 76.53; H, 7.55; N, 6.92.

7.5 Acknowledgements

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Chapter 8: Reductive Generation of Stable Five-Membered *N,N′*-Diamidocarbenes*

8.1 INTRODUCTION

Over the past few years, our group[1-4] and others[5-14] have explored modulating the chemistry displayed by *N*-heterocyclic carbenes (NHCs)[15-18] through the attachment of carbonyl groups to the nitrogen atoms adjoining the carbene nucleus. The *N,N′*-diamidocarbenes (DACs),[2,3,9] in particular, were found to be relatively electrophilic and effectively expanded NHC chemistry to include [2+1] cycloadditions,[12,19,20] carbon monoxide or isonitrile couplings,[2,9,21] intermolecular C–H insertions,[22] and other useful reactions[23,24] as discussed in earlier chapters and elsewhere. We had also shown that certain six-[2] and seven-membered[3] DACs (*i.e.*, **6DAC** and **7DAC**, respectively; Figure 8.1) were stable and isolable. However, the analogous five-membered derivative (**5DAC**) pioneered by Ganter[9,10] was observed to undergo rapid dimerization. Unfortunately, attempts to prevent dimerization through the introduction of increased steric bulk were unsuccessful as an HCl adduct of the corresponding *N,N′*-diadamantyl precursor failed to undergo deprotonation.[10] Thus, the development of new approaches for accessing stable, five-membered DACs and other carbenes is warranted.

Despite the extraordinary diversity of NHC scaffolds reported in the literature, the methods used to generate carbenes are relatively few and generally limited to: (1) deprotonation of the conjugate acids of the corresponding carbenes,[17] (2) extrusion of volatile small molecules (*e.g.*, ammonia, methanol, CO_2, etc.) from an appropriate precursor,[25-30] (3) reduction of thioureas,[31-33] and (4) reduction of chloroiminium or

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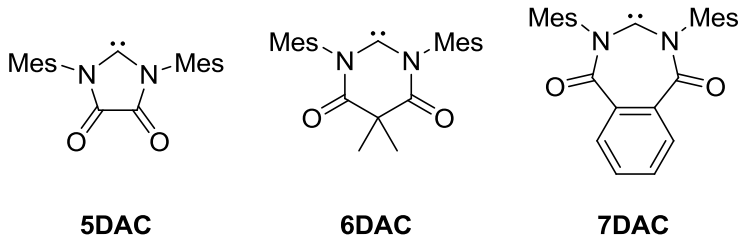
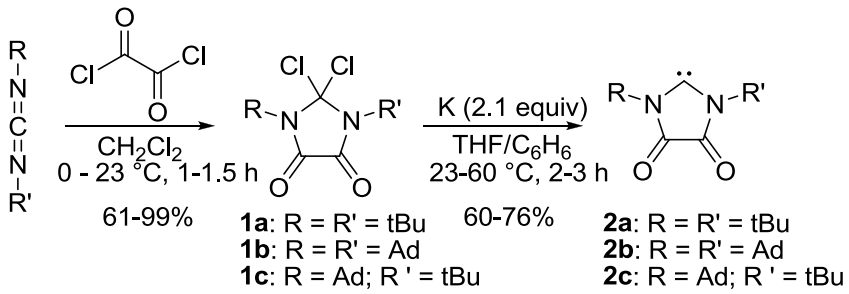


Figure 8.1: Structures of various *N,N*′-diamidocarbenes.[2,3,9] **5DAC** is not isolable. Mes = 2,4,6-trimethylphenyl.

chloroamidinium salts using bis(trimethylsilyl)mercury.[34] Although the first two methods are the most widely used, we reasoned that the utility of the latter may be expanded through the reduction of readily-accessible geminal dichlorides. Herein, we report the synthesis of the first stable, five-membered DACs, including a differentially *N,N*'-substituted derivative, through the treatment of dichloroimidazolidinediones with potassium. The reactivity displayed by the five-membered DACs was also explored and compared to that of six-membered and other DACs.

8.2 Results and Discussion

Following a modified procedure reported by Zinner in 1970,[35] the dichloroimidazolidine-4,5-dione **1a** was synthesized via the condensation of *N,N*′-di-*tert*-butylcarbodiimide with oxalyl chloride in CH_2Cl_2 at 0 °C. A signal was recorded at 101.7 ppm ($CDCl_3$) upon ^{13}C NMR analysis of the isolated product and assigned to the geminal dichlorocarbon nucleus. The structure of **1a** was later confirmed by single crystal X-ray diffraction (XRD) analysis, which revealed an average C–Cl distance (1.80 Å) that was nearly identical to that measured by Roesler (1.79 Å) in the solid state structure of an analogous five-membered DAC·HCl adduct.[8]



Scheme 8.1: Synthesis of DACs **2a-c**. Ad = 1-adamantyl.

Initial efforts to reduce **1a** were directed toward the use of one-electron reductants, such as sodium or potassium, expected to form readily removable inorganic byproducts (*i.e.*, NaCl or KCl). While no reaction was observed between **1a** and sodium in THF at 23 °C after 6 h, the addition of potassium (2.1 equiv) to a solution of **1a** at the same temperature immediately turned red and grew darker in colour over time. After 3 h, the solvent was removed and ^{1}H NMR analysis of the residue revealed the expected upfield shift of the singlet, from 1.52 ppm recorded for **1a** to 1.37 ppm (C_6D_6). The free carbene **2a** was isolated as a red solid in 76% yield via extraction of the crude product with pentane followed by filtration. Compared to the analogous signal recorded for **6DAC** (277.7 ppm),[2] the ^{13}C NMR resonance measured for the carbene carbon in **2a** was slightly downfield (287.2 ppm). The solid state structure of **2a** was also determined via XRD analysis, as shown in Figure 8.2. When compared to the solid state structure of **6DAC**, that of **2a** displayed a relatively acute N-C-N bond angle (106.45° vs 127.7°) although similar average N–$C_{carbene}$ distances were measured (1.377(2) vs 1.371(3) Å).[2]

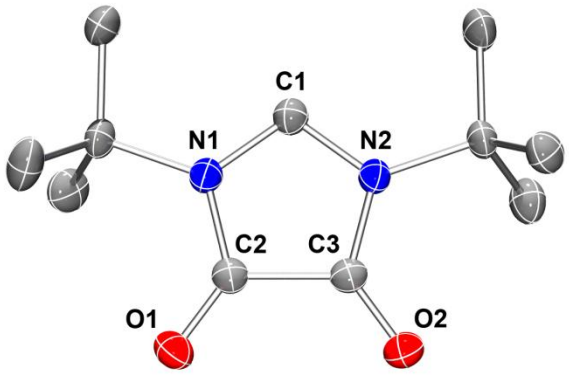
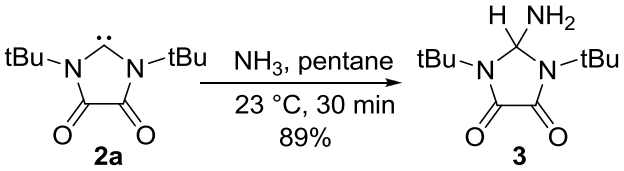


Figure 8.2: ORTEP diagram of **2a** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): C1-N1, 1.377(2); C1-N2, 1.376(2); N1-C2, 1.385(2); N2-C3, 1.383(2); C2-C3, 1.535(2), O1-C2, 1.2068(19); O2-C3, 1.2048(19); N1-C1-N2, 106.45(13).

Using methodology similar to that described above, the 1,3-bis(*N*-adamantyl) DAC **2b** and the differentially substituted *N*-adamantyl-*N'*-*tert*-butyl DAC **2c** were synthesized and found to display ^{13}C NMR signals similar to that recorded for **2a** (287.5-288.0 ppm; C_6D_6). Previous attempts to generate **2b** from its HCl adduct were unsuccessful,[10] thus highlighting an advantage of the aforementioned reductive methodology. Moreover, given the ready availability of various carbodiimides, the reductive route reported herein may facilitate access to a wide variety of DACs and other stable carbenes, particularly differentially substituted derivatives that may be challenging to prepare via other routes.[36]

With DACs **2** in hand, subsequent attention shifted to exploring their abilities to activate ammonia[37] and carbon monoxide[38] as previously observed with other known DACs.[1-3] Stirring a solution of **2a** in pentane under an atmosphere of NH_3 resulted in the rapid formation of a white precipitate that was later identified via NMR spectroscopy and XRD analysis as the N–H inserted product **3** (Scheme 8.2). While the insertion reaction may have been predicted based on similar results reported for **6DAC**,[2] a different

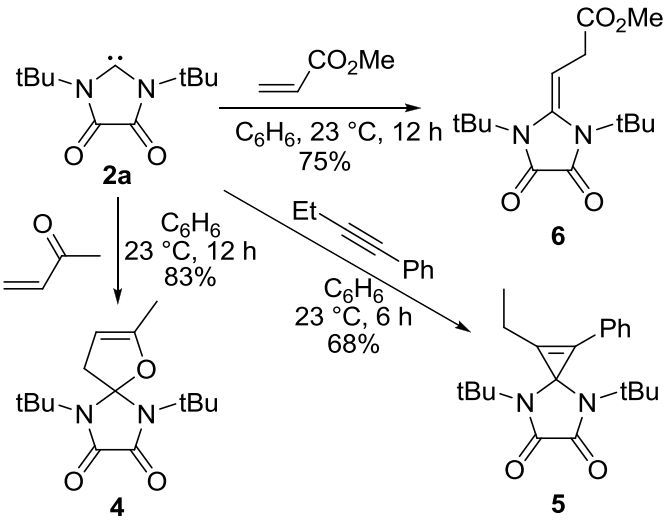
outcome was obtained with carbon monoxide. The addition of 1 atm of CO to a medium pressure NMR tube containing **2a** in C_6D_6 (0.14 M) showed no change in the ^{1}H NMR spectrum nor a change in colour indicative of ketene formation. While ketene formation may be reversible,[1,2] variable temperature NMR spectroscopy conducted as low as -78 °C (C_7D_8) showed no discernible changes.



Scheme 8.2: Activation of ammonia by **2a**.

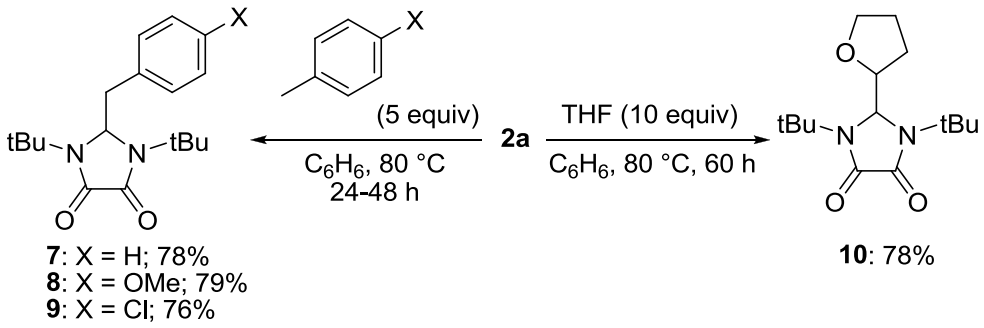
To further compare the chemistry of **2** with other DACs, the former were treated to a range of unsaturated substrates. As summarized in Scheme 8.3, products analogous to those obtained with analogous six-membered DACs were observed in several cases.[19,20] For example, stirring **2a** and methyl vinyl ketone in C_6H_6 at 23 °C afforded the dihydrofuran derivative **4**. Similarly, the expected[20] formal [2+1] cycloaddition product **5** was obtained as a crystalline solid upon treating **2a** with 1-phenyl-1-butyne. However, despite the overlapping reactivity profile, key differences between **2a** and other DACs were observed. For example, treating **2a** with methyl acrylate afforded the exocyclic olefin **6** as the exclusive product (75%), as evidenced by the downfield ^{1}H NMR (3.87 ppm) and ^{13}C NMR spectroscopic (106.3 ppm) signals. For comparison, a cyclopropane derivative was isolated when known five- or six-membered DACs were treated with methyl acrylate.[10,19] In light of the aforementioned observations and the apparent lack of reactivity between **2a** and diethyl maleate, even at 80 °C (24 h), the results suggested to

us that differences observed may be due to the sterically-demanding *N*-substituents of **2a**.¶



Scheme 8.3: Exposure of **2a** to various unsaturated substrates.

To further probe the reactivity differential, the ability of **2** to activate C–H bonds was also explored (Scheme 8.4). Heating a solution of **2a** and toluene (5 equiv) in C_6H_6 at 80 °C resulted in the gradual loss of the red colour associated with **2**. After 40 h, the reaction mixture was concentrated and the resulting residue was washed with pentane to afford **7** as a crystalline solid in 78% yield. The aforementioned insertion process appeared to be general as electron-rich as well as electron-deficient tolyl derivatives underwent C–H insertion to afford the expected products in 76-79% yield. Additionally, **2a** was found to insert into the C–H bond located at the 2-position of tetrahydrofuran affording the resulting product **10** in good yield (78%). The latter result constituted the least acidic C–H bond to undergo insertion with a stable DAC to date[21] and may be facilitated by a relatively high electrophilicity associated with **2a**.



Scheme 8.4: Intermolecular insertion of **2a** into C–H bonds.

8.3 CONCLUSIONS

In summary, we report the synthesis of the first stable, five-membered DACs as well as the first DAC of any ring size with differing *N*- and *N′*-substituents. The aforementioned carbenes were accessed using a novel method that employs readily accessible geminal dichloroimidazolidindiones in conjunction with strong reductants. Although the five-membered DACs **2** were generally found to react in a similar manner to six-membered analogues (*e.g.*, ammonia activation, benzylic C–H activation, formal [2+1] cycloadditions with alkynes, etc.), the former appeared to be more electrophilic and was observed to insert into the C–H bond of an electron-rich (*i.e.*, non-acidic) substrate. We expect that the methodology reported herein will facilitate access to new carbene derivatives and that an ability to use isolable forms of **2** will inspire new applications for this relatively electrophilic class of stable carbene.

8.4 EXPERIMENTAL

General Considerations. All procedures were performed using standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen-filled glove box unless otherwise noted. Compounds **1** and **2** are highly moisture sensitive. *N*,*N′*-di-*tert*-butylcarbodiimide was purchased from Sigma Aldrich. Bromotriphenylphosphonium bromide[37] was synthesized according to literature procedures. *N*-adamantyl-*N′*-*tert*-

butylcarbodiimide[38] was prepared using the methods reported by Palomo.[39] Methyl acrylate, methyl vinyl ketone, 1-phenyl-1-butyne, 4-methyl anisole, and 4-chlorotoluene were dried over molecular sieves for at least 24 h prior to use. Toluene, tetrahydrofuran, benzene, diethyl ether, and pentane were dried and degassed using a Vacuum Atmospheres Company solvent purification system and stored over molecular sieves. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer. High resolution mass spectra (HRMS) were obtained with a Waters Micromass Autospec-Ultima (CI). UV-vis spectra were acquired on a Perkin Elmer Lambda 35 UV-vis spectrometer. NMR spectra were recorded on a Varian Mercury 400, a Varian Directdrive 400, or an Agilent MR400 spectrometer. Chemical shifts (δ) are reported in ppm relative to the residual solvent (benzene: ^{1}H: 7.15 ppm, ^{13}C: 128.0 ppm; chloroform: ^{1}H: 7.24 ppm, ^{13}C: 77.0 ppm). Elemental analyses were performed with a ThermoScientific Flash 2000 Organic Elemental Analyzer. Melting points were obtained using a Stanford Research Systems MPA100 OptiMelt automated melting point apparatus (ramp rate: 1 °C·min^{-1}) and are uncorrected.

Synthesis of *N*,*N*′-bis(1-adamantyl)carbodiimide. A 100 mL Schlenk flask was charged with bromotriphenylphosphonium bromide (1.93 g, 4.57 mmol, 1.5 equiv), triethylamine (1.5 mL, 10.65 mmol, 3.5 equiv), dichloromethane (20 mL) and a stir bar. The heterogeneous mixture was cooled to 0 °C and *N*,*N*′-bis(1-adamantyl)urea (1.0 g, 3.0 mmol) added in four portions over 30 min. The resultant mixture was heated at 40 °C for 14 h during which time the solution became homogenous. After adding water (60 mL) to the red solution, the two layers were separated, and the aqueous layer was washed with dichloromethane (10 mL). The combined organic layers were dried over sodium sulfate and filtered. After removing the residual solvent under reduced pressure, the crude solid was extracted with diethyl ether and passed through a plug of silica gel using diethyl

ether as the eluent. Concentration of the resultant solution afforded *N*,*N*′-bis(1-adamantyl)carbodiimide as a white solid (0.828 g, 2.67 mmol, 88%). m.p. = 310-312 °C. ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.57-1.65 (m, 12 H), 1.75 (overlapping s, 12 H), 2.05 (bs, 6H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 29.8, 36.0, 44.7, 54.9, 139.4. IR (KBr): 2901.8, 2848.8, 2108.3, 2037.5, 1352.7, 1300.5, 1079.8, 633.9 cm^{-1}. HRMS (CI): $[M-H]^+$ calcd. for $C_{21}H_{29}N_2$: 309.2331; Found: 309.2330. Anal. calcd. for $C_{21}H_{30}N_2$: C, 81.24; H, 9.74; N, 9.02; Found: C, 80.97; H, 9.99; N, 9.15.

Synthesis of 1a. Using a modified procedure reported by Zinner,[40] a 100 mL Schlenk flask outfitted with a septum was charged with *N*,*N*′-di-*tert*-butylcarbodiimide (2.00 g, 12.96 mmol), dichloromethane (60 mL) and a stir bar. The resultant solution was cooled to 0 °C for 15 min whereupon oxalyl chloride (1.73 g, 1.17 mL, 13.6 mmol, 1.05 equiv) was added dropwise. The ice bath was removed and the solution was stirred for 1 h. Removal of the residual solvent under reduced pressure afforded **1a** as a white solid (3.63 g, 12.91 mmol, 99%). m.p. = 129-130 °C (decomp.) ^{1}H NMR ($CDCl_3$, 400.27 MHz): δ 1.75 (s, 18H). ^{1}H NMR (C_6D_6, 400.09 MHz): δ 1.52 (s, 18H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 28.0, 62.2, 101.7, 154.9. IR (KBr): 3458.9, 3002.5, 2975.8, 2940.1, 1757.7, 1483.3, 1368.8, 1295.4, 1174.1, 1129.7, 1019.9, 873.0, 771.4, 552.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{11}H_{19}N_2O_2{}^{35}Cl_2$: 281.0824; Found: 281.0827. Anal. calcd. for $C_{11}H_{18}Cl_2N_2O_2$: C, 46.99; H, 6.45; N, 9.96; Found: C, 46.96; H, 6.58; N, 10.23.

Synthesis of 1b. Using an adapted procedure reported by Zinner,[S4] a 25 mL Schlenk flask outfitted with a septum was charged with *N*,*N*′-bis(1-adamantyl)carbodiimide (0.500 g, 1.61 mmol), dichloromethane (10 mL) and a stir bar. To this solution, oxalyl chloride (0.225 g, 0.15 mL, 1.77 mmol, 1.1 eq) was added dropwise and the resultant mixture was stirred at ambient temperature for 1.5 h. After removing the residual solvent under reduced pressure, the resulting solid was washed

with a minimal quantity of cold diethyl ether followed by a minimal quantity of pentane. Subsequent drying under reduced pressure afforded **1b** as a white solid (0.630 g, 1.44 mmol, 89%). m.p. = 200-202 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.68 (m, 6H), 1.78 (m, 6H), 2.17 (bs, 6H), 2.63 (overlapping s, 12H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 30.1, 36.0, 38.7, 65.5, 101.8, 155.0. IR (KBr): 2914.9, 2851.9, 1758.0, 1457.1, 1376.8, 1359.0, 1343.2, 1263.8, 1200.8, 1124.5, 978.6, 866.3, 749.6 cm^{-1}. HRMS (CI): $[M-H]^+$ calcd. for $C_{23}H_{29}N_2O_2{}^{35}Cl_2$: 435.1606; Found: 435.1610. Anal. calcd. for $C_{23}H_{30}N_2O_2Cl_2$: C, 63.16; H, 6.91; N, 6.40; Found: C, 63.45; H, 6.78; N, 6.41.

Synthesis of 1c. Using an adapted procedure reported by Zinner,[S4] a 50 mL Schlenk flask outfitted with a septum was charged with *N*-adamantyl-*N'*-*tert*-butylcarbodiimide (0.450 g, 1.94 mmol), dichloromethane (10 mL) and a stir bar. To the resulting solution was added dropwise oxalyl chloride (0.18 mL, 2.13 mmol, 1.1 equiv). After stirring the resulting mixture at ambient temperature for 1.5 h, the residual solvent was removed under reduced pressure. The resulting crude residue was washed twice with a minimal quantity of cold diethyl ether followed by minimal quantity of pentane (×2). Subsequent drying of the product under reduced pressure afforded **1c** as an off-white solid (0.427 g, 1.19 mmol, 61%). m.p. = 141-143 °C (decomp.) ^{1}H NMR ($CDCl_3$, 399.68 MHz): δ 1.72 (m, 3H), 1.77-1.80 (m overlapping s, 12H), 2.18 (bs, 3H), 2.64 (overlapping s, 6H). ^{13}C NMR ($CDCl_3$, 100.50 MHz): δ 28.2, 30.07, 35.97, 38.65, 62.35, 65.48, 101.78, 154.90, 155.13. IR (KBr): 2917.4, 2852.3, 1756.8, 1374.3, 1368.6, 1345.2, 1276.3, 1123.9, 741.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{17}H_{25}N_2O_2{}^{35}Cl_2$: 359.1293; Found: 359.1289. Anal. calcd. for $C_{17}H_{24}N_2O_2Cl_2$: C, 56.83; H, 6.73; N, 7.80; Found: C, 56.99; H, 6.74; N, 7.47.

Synthesis of 2a. A 30 mL vial was charged with **1a** (1.0 g, 3.56 mmol), tetrahydrofuran (10 mL), potassium metal (0.292 g, 7.47 mmol, 2.1 equiv) and a stir bar.

The resulting solution was observed to rapidly turn red and form a precipitate over time at ambient temperature. After 3 h, the residual solvent was removed under reduced pressure and the crude solid was extracted with pentane (4 mL), filtered through a medium porosity fritted funnel, and then washed with pentane (2 × 2 mL). Concentration of the filtrate afforded **2a** as a bright red solid (0.567 g, 2.70 mmol, 76%). m.p. = 73-75 °C. ^{1}H NMR (C_6D_6, 400.09 MHz): δ 1.37 (s, 18H). ^{13}C NMR (C_6D_6, 100.60 MHz): δ 28.6, 58.6, 154.2, 287.2. IR (KBr): 2979.5, 2935.2, 1780.1, 1754.9, 1395.4, 1325.6, 1205.0, 1066.3, 996.6, 770.9, 572.3 cm^{-1}. UV-vis (C_5H_{12}): λ_{max} = 489 nm. HRMS (CI): $[M+H]^+$ calcd. for $C_{11}H_{19}N_2O_2$: 211.1447; Found: 211.1448. Anal. calcd. for $C_{11}H_{18}N_2O_2$: C, 62.83; H, 8.63; N, 13.32; Found: C, 62.76; H, 8.82; N, 13.50.

Synthesis of 2b. An 8 mL vial was charged with **1b** (0.200 g, 0.457 mmol), tetrahydrofuran (2 mL), potassium metal (0.038 g, 0.96 mmol, 2.1 equiv) and a stir bar. Stirring the resultant mixture at ambient temperature for 2 h afforded a red solution that was accompanied by the formation of a precipitate. The reaction mixture was concentrated under reduced pressure, and the crude solid was extracted with benzene (5 mL), filtered through a medium fritted funnel, and washed with benzene (2 × 2 mL). Concentration of the filtrate afforded **2b** as a pale purple-red solid (0.103 g, 0.281 mmol, 61%). m.p. = 197-199 °C (decomp.) ^{1}H NMR (C_6D_6, 400.09 MHz): δ 1.49 (m, 6H), 1.55 (m, 6H), 1.95 (bs, 6H), 2.24 (overlapping s, 12H). ^{13}C NMR (C_6D_6, 400.09 MHz): δ 29.9, 36.3, 41.4, 59.5, 154.2, 288.0. IR (KBr): 2906.0, 2851.2, 1777.9, 1756.4, 1342.3, 1300.6, 1222.9, 1025.1, 668.0 cm^{-1}. UV-vis (C_5H_{12}): λ_{max} = 492 nm. HRMS (CI): $[M+H]^+$ calcd. for $C_{23}H_{31}N_2O_2$: 367.2386; Found: 367.2381. Anal. calcd. for $C_{23}H_{30}N_2O_2$: C, 75.37; H, 8.25; N, 7.64; Found: C, 75.50; H, 8.47; N, 7.83.

Synthesis of 2c. An 8 mL vial was charged with **1c** (0.150 g, 0.417 mmol), benzene (2 mL), potassium metal (0.035 g, 0.090 mmol, 2.1 equiv) and a stir bar. The

reaction vessel was sealed and then heated at 60 °C for 2 h. After cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. The resulting red-purple residue was extracted with pentane, filtered through a 0.2 μm PTFE filter and the residual solvent removed under reduced pressure to afford **2c** as a purple-red solid (0.072 g, 0.250 mmol, 60%). m.p. = 96-98 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.39 (s, 9H), 1.46-1.54 (m, 6H), 1.93 (bs, 3H), 2.20-2.21 (overlapping s, 6H). ^{13}C NMR (C_6D_6, 100.60 MHz): δ 28.6, 29.9, 36.2, 41.3, 58.6, 59.5, 154.1, 154.3, 287.5. IR (KBr): 2910.2, 1855.4, 1770.8, 1756.0, 1729.7, 1357.3, 1303.7, 1007.6 cm^{-1}. UV-vis (C_5H_{12}): λ_{max} = 491 nm. HRMS (CI): $[M+H]^+$ calcd. for $C_{17}H_{25}N_2O_2$: 289.1916; Found: 289.1913. Anal. calcd. for $C_{17}H_{24}N_2O_2$: C, 70.80; H, 8.39; N, 9.71; Found: C, 70.73; H, 8.53; N, 9.43.

Synthesis of 3. A 50 mL Schlenk flask was charged with **2a** (0.075 g, 0.36 mmol), pentane (10 mL) and a stir bar. The flask was cooled to -78 °C and the atmosphere was removed from the flask under reduced pressure prior to warming back to ambient temperature. Ammonia gas was then added to the flask via a balloon which resulted in the formation of a pale yellow solution that was accompanied with a white precipitate. After stirring for 30 min at ambient temperature, the residual solvent was removed under reduced pressure and the crude solid was washed with a minimal quantity of pentane to afford **3** as a white solid (0.072 g, 0.317 mmol, 89%). m.p. = 162-165 °C (decomp.) ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.53 (s, 18H), 1.86 (bs, 2H), 5.64 (s, 1H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 27.8, 55.8, 76.1, 157.9. IR (KBr): 3438.5, 3405.5, 3312.0, 2979.2, 1717.1, 1413.5, 1366.6, 1218.7, 1128.7, 598.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{11}H_{22}N_3O_2$: 228.1712; Found: 228.1712. Anal. calcd. for $C_{11}H_{21}N_3O_2$: C, 58.12; H, 9.31; N, 18.49; Found: C, 57.93; H, 9.36; N, 18.31.

Synthesis of 4. An 8 mL vial was charged with **2a** (0.075 g, 0.36 mmol), benzene (1 mL), methyl vinyl ketone (0.025 g, 0.36 mmol, 1 equiv) and a stir bar. The resultant mixture was stirred at ambient temperature for 12 h after which the residual solvent was removed under reduced pressure. Subsequent washing of the residue with a minimal quantity of pentane followed by drying under reduced pressure afforded **4** as a white solid (0.083 g, 0.296 mmol, 83%). m.p. = 159-161°C (decomp.) ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.52 (s, 18H), 1.82 (s, 3H), 3.07 (t, *J* = 2 Hz, 2H), 4.88 (s, 1H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 14.2, 28.0, 41.5, 58.6, 97.3, 108.5, 154.5, 157.4. IR (KBr): 3115.1, 2999.6, 2964.7, 2917.3, 1739.9, 1691.8, 1407.2, 1394.8, 1368.4, 1195.0, 1158.8, 955.9, 909.2, 751.5, 584.9 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{15}H_{25}N_2O_3$: 281.1865; Found: 281.1860. Anal. calcd. for $C_{15}H_{24}N_2O_3$: C, 64.26; H, 8.63; N, 9.99; Found: C, 64.64; H, 8.56; N, 10.01.

Synthesis of 5. An 8 mL vial was charged with **2a** (0.075 g, 0.36 mmol), benzene (1 mL), 1-phenyl-1-butyne (0.046 g, 0.36 mmol, 1 equiv) and a stir bar. The resultant mixture was stirred at ambient temperature for 6 h after which the residual solvent was removed under reduced pressure. Subsequent washing of the residue with pentane followed by drying under reduced pressure afforded **5** as a white solid (0.083 g, 0.243 mmol, 68%). m.p. = 161-163 °C (decomp.) ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.34 (s, 18H), 1.45 (t, *J* = 7.4 Hz, 3H), 2.70 (q, *J* = 7.4 Hz, 2H), 7.41-7.49 (m, 5H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 12.0, 19.64, 28.8, 57.4, 62.3, 122.1, 124.2, 126.4, 129.4, 129.6, 130.5, 159.82. IR (KBr): 3384.6, 3064.7, 3005.9, 2977.3, 2932.2, 1716.1, 1388.4, 1362.0, 1223.8, 1133.7, 766.8, 693.0, 559.6 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{21}H_{29}N_2O_2$: 341.2229; Found: 341.2235. Anal. calcd. for $C_{21}H_{28}N_2O_2$: C, 74.08; H, 8.29; N, 8.23; Found: C, 73.75; H, 8.26; N, 7.95.

Synthesis of 6. An 8 mL vial was charged with **2a** (0.075 g, 0.36 mmol), benzene (1 mL), methyl acrylate (0.031 g, 0.36 mmol, 1 equiv) and a stir bar. The resultant mixture was stirred at ambient temperature for 12 h after which the residual solvent was removed under reduced pressure. Subsequent washing of the resulting residue with a minimal quantity of pentane followed by drying under reduced pressure afforded **6** as a white solid (0.079 g, 0.267 mmol, 75%). m.p. = 129-131 °C (decomp.) ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.55 (s, 18H), 3.15 (s, 2H), 3.73 (s, 3H), 3.87 (s, 1H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 28.0, 40.4, 56.8, 58.9, 65.7, 106.3, 157.3, 160.9. IR (KBr): 3126.7, 2991.6, 2967.6, 2945.7, 1740.4, 1689.6, 1409.4, 1333.7, 1317.9, 1279.7, 1244.2, 1194.7, 1163.8, 1005.3, 954.5, 922.5, 781.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{15}H_{25}N_2O_4$: 297.1814; Found: 297.1817. Anal. calcd. for $C_{15}H_{24}N_2O_4$: C, 60.79; H, 8.16; N, 9.45; Found: C, 60.51; H, 8.02; N, 9.09.

Synthesis of 7. An 8 mL vial was charged with **2a** (0.075 g, 0.36 mmol), benzene (1 mL), toluene (0.164 g, 1.78 mmol, 5 equiv) and a stir bar. The resultant mixture was stirred at 80 °C for 40 h after which the reaction mixture was cooled and the residual solvent was removed under reduced pressure. Subsequent washing of the residue with a minimal quantity of pentane followed by drying under reduced pressure afforded **7** as a white solid (0.084 g, 0.278 mmol, 78%). m.p. = 149-151 °C. ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.46 (s, 18H), 3.28 (d, J = 3.1 Hz, 2H), 5.32 (t, J = 3.1 Hz, 1H), 7.09 (m, 2H), 7.21-7.27 (m overlapping solvent, 3H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 27.7, 42.0, 56.5, 67.7, 127.7, 128.9, 129.7, 133.0, 159.5. IR (KBr): 2981.6, 2965.9, 1716.3, 1396.2, 1371.2, 1361.6, 1207.6, 700.7, 632.6 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{18}H_{27}N_2O_2$: 303.2073; Found: 303.2076. Anal. calcd. for $C_{18}H_{26}N_2O_2$: C, 71.49; H, 8.67; N, 9.26; Found: C, 71.48; H, 8.69; N, 9.15.

Synthesis of 8. An 8 mL vial was charged with **2a** (0.075 g, 0.36 mmol), benzene (1 mL), 4-methyl anisole (0.218 g, 1.78 mmol, 5 equiv) and a stir bar. The resultant mixture was stirred at 80 °C for 24 h after which the reaction mixture was cooled and the residual solvent was removed under reduced pressure. Subsequent washing of the residue with a minimal quantity of pentane followed by drying under reduced pressure afforded **8** as a white solid (0.094 g, 0.283 mmol, 79%). m.p. = 143-145 °C. ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.46 (s, 18H), 3.21 (d, *J* = 2.7 Hz, 2H), 3.72 (s, 3H), 5.28 (t, *J* = 3.1 Hz, 1H), 6.78 (d, *J* = 8.6 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 27.7, 40.9, 55.1, 56.5, 67.7, 114.2, 124.5, 130.9, 158.9, 159.6. IR (KBr): 2981.5, 2912.6, 1717.0, 1513.8, 1407.6, 1366.0, 1244.4, 1217.6, 1032.2, 802.6, 564.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{19}H_{29}N_2O_3$: 333.2178; Found: 333.2183. Anal. calcd. for $C_{19}H_{28}N_2O_3$: C, 68.65; H, 8.49; N, 8.43; Found: C, 68.33; H, 8.55; N, 8.39.

Synthesis of 9. An 8 mL vial was charged with **2a** (0.075 g, 0.36 mmol), benzene (1 mL), 4-chlorotoluene (0.226 g, 1.78 mmol, 5 equiv) and a stir bar. The resultant mixture was stirred at 80 °C for 48 h after which the reaction mixture was cooled and the residual solvent was removed under reduced pressure. Subsequent washing of the residue with a minimal quantity of pentane followed by drying under reduced pressure afforded **9** as a white solid (0.091 g, 0.270 mmol, 76%). m.p. = 183-185 °C (decomp.) ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.47 (s, 12H), 3.25 (d, *J* = 3.1 Hz, 2H), 5.31 (t, *J* = 3.1 Hz, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 7.24 (d overlapping solvent, *J* = 8.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 27.7, 41.1, 56.7, 67.3, 129.0, 131.1, 131.3, 133.7, 159.5. IR (KBr): 2968.8, 2934.6, 1713.9, 1493.3, 1403.3, 1215.8, 1090.3, 809.4, 766.5, 603.7 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{18}H_{26}N_2O_2{}^{35}Cl$: 337.1683; Found: 337.1687. Anal. calcd. for $C_{18}H_{25}ClN_2O_2$: C, 64.18; H, 7.48; N, 8.32; Found: C, 64.08; H, 7.43; N, 8.39.

Synthesis of 10. An 8 mL vial was charged with **2a** (0.075 g, 0.36 mmol), benzene (0.3 mL), tetrahydrofuran (0.257 g, 3.6 mmol, 10 equiv) and a stir bar. The resultant mixture was stirred at 80 °C for 60 h after which the reaction mixture was cooled and the residual solvent was removed under reduced pressure. Subsequent washing of the residue with a minimal quantity of pentane followed by drying under reduced pressure afforded **10** as a white solid (0.079 g, 0.280 mmol, 78%). m.p. = 110-112 °C (decomp.) ^{1}H NMR ($CDCl_3$, 400.09 MHz): δ 1.29-1.38 (m, 1H), 1.45 (s, 9H), 1.46 (s, 9H), 1.57-1.66 (m, 1H), 1.76-1.90 (m, 2H), 3.72 (q, *J* = 7.8 Hz, 1H), 3.99 (m, 1H), 4.20 (m, 1H), 5.25 (d, *J* = 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100.60 MHz): δ 22.9, 23.9, 27.4, 27.7, 56.0, 57.2, 68.0, 68.6, 82.0, 159.0, 160.6. IR (KBr): 2980.1, 2877.9, 1725.5, 1705.9, 1402.0, 1204.3, 1076.2 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{15}H_{27}N_2O_3$: 283.2022; Found:283.2029. Anal. calcd. for $C_{15}H_{26}N_2O_3$: C, 63.80; H, 9.28; N, 9.92; Found: C, 63.86; H, 9.60; N, 10.31.

8.5 Acknowledgements

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Appendix A: Supporting Information

CHAPTER 2: AMMONIA N–H ACTIVATION BY AN *N,N′*-DIAMIDOCARBENE

X-Ray Crystallography. Single crystals of **2**·HCl were obtained by slow vapor diffusion of *n*-pentane into a saturated CH_2Cl_2 solution. This compound crystallized in the primitive monoclinic space group $P2_1/c$ with four molecules in the asymmetric unit. Colorless single crystals of **2** were grown by slow diffusion of hexanes vapor into a saturated toluene solution. This compound crystallized in the primitive monoclinic space group $P2_1/c$ with four molecules in the asymmetric unit. The NH_3 adduct **5** was crystallized at –30 °C from a concentrated hexanes:CH_2Cl_2 (2:1 v/v) solution as colorless elongated blocks. This compound crystallized in the centrosymmetric monoclinic space group $C2/c$ with 8 molecules in the asymmetric unit and solvated with 0.5 molecules of CH_2Cl_2. All crystallographic measurements were carried out on a Rigaku Mini CCD area detector diffractometer using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) at 150 K using an Oxford Cryostream low temperature device. A sample of suitable size and quality was selected and mounted onto a nylon loop. Data reductions were performed using DENZO-SMN. The structures were solved by direct methods which successfully located most of the non-hydrogen atoms. Subsequent refinements on F_2 using the SHELXTL/PC package (version 5.1) allowed location of the remaining non-hydrogen atoms. Key details of the crystal and structure refinement data are summarized in Table A1. Further crystallographic details may be found in the respective CIF files which were deposited at the Cambridge Crystallographic Data Centre, Cambridge, UK. The CCDC reference numbers for **2**·HCl, **2**, **5**·0.5(CH_2Cl_2), **7** and **9**·(C_7H_8) were assigned as 770147, 770148, 770149, 770150 and 770151, respectively.

	2·HCl	**2**	**5**·(0.5 CH_2Cl_2)
Formula	$C_{24}H_{29}ClN_2O_2$	$C_{24}H_{28}N_2O_2$	$C_{24.50}H_{32}ClN_3O_2$
M_r	412.94	376.48	435.98
crystal size (mm^3)	0.28 × 0.22 × 0.08	0.30 × 0.21 × 0.14	0.62 × 0.13 × 0.11
crystal system	monoclinic	monoclinic	monoclinic
space group	$P2_1/c$	$P2_1/c$	C_2/c
a (Å)	8.3918(12)	17.7632(14)	15.7619(11)
b (Å)	17.082(2)	16.2017(12)	25.7674(18)
c (Å)	15.992(2)	7.6426(6)	11.6636(9)
α (°)	90	90	90
β (°)	102.394(2)	97.686(2)	92.970(2)
γ (°)	90	90	90
V ($Å^3$)	2239.0(6)	2179.7(3)	4730.7(6)
Z	4	4	8
ρ_{calc} (g cm^{-3})	1.225	1.147	1.224
μ (mm^{-1})	0.192	0.073	0.187
F(000)	880	808	1864
T (K)	150(2)	150(2)	150(2)
scan mode	ω	ω	ω
hkl range	-9 → 9 -20 → 20 -19 → 19	-21 → 21 -19 → 19 -9 → 9	-18 → 18 -30 → 30 -13 → 13
measd reflns	19164	18370	20564
unique reflns [R_{int}]	3926 [0.0315]	3830 [0.0307]	4162 [0.0373]
refinement reflns	3926	3830	4162
refined parameters	262	253	287
GOF on F^2	1.006	1.008	1.008
R1[a] (all data)	0.0544 (0.0608)	0.0586 (0.0701)	0.0578 (0.0700)
wR2[b] (all data)	0.1696 (0.1772)	0.1543 (0.1640)	0.1528 (0.1637)
ρ_{fin} (max/min)	0.420	0.380	0.680
(e $Å^{-3}$)	-0.313	-0.363	-0.573

Table A1: Crystal Data, Data Collection, and Structure Refinement for **2**·HCl, **2**, and **5**·(0.5 CH_2Cl_2). [a] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$

CHAPTER 3: DIAMIDOCARBENES AS VERSATILE AND REVERSIBLE [2+1] CYCLOADDITION REAGENTS

X-Ray Crystallography. Colorless, single crystals of **2e** were obtained by evaporation of a saturated chloroform solution; this compound crystallized in the monoclinic space group $P2_1$. Colorless single crystals of **2j** were grown by slow diffusion of pentane vapor into a saturated benzene solution; this compound crystallized in the monoclinic space

group $P2_1/c$. Colorless, single crystals of **2k** were obtained by slow evaporation of a pentane/benzene solution; this compound crystallized in the monoclinic $P2_1/n$ space group. Colorless single crystals of **2m** were obtained by the slow diffusion of pentane into a saturated benzene solution; this compound crystallized in the monoclinic $P2_1/n$ space group. Colorless, single crystals of **2o** were obtained by the slow diffusion of pentane into a saturated toluene solution; this compound crystallized in the triclinic *P*-1 space group. Colorless, single crystals of **3a** were obtained by the slow evaporation of a hexanes/toluene solution; this compound crystallized in the triclinic *P*-1 space group. Colorless, single crystals of **4b** were obtained by slow diffusion of pentane vapor into a saturated benzene solution. This compound crystallized in the monoclinic $P2_1/c$ space group. Crystallographic measurements were carried out on a Rigaku Mini CCD, Enraf-Nonius Kappa CCD, or Rigaku AFC-12 with Saturn 724+ CCD area detector diffractometer using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) at 120 K using an Oxford Cryostream low temperature device. A sample of suitable size and quality was selected and mounted onto a nylon loop. Data reductions were performed using DENZO-SMN. The structures were solved by direct methods which successfully located most of the non-hydrogen atoms. Subsequent refinements on F_2 using the SHELXTL/PC package (version 5.1) allowed location of the remaining non-hydrogen atoms. Key details of the crystal and structure refinement data are summarized in Table A2,A3 Further crystallographic details may be found in the respective CIFs which were deposited at the Cambridge Crystallographic Data Centre, Cambridge, UK. The CCDC reference numbers for **2e**, **2j**, **2k**, **2m**, **2o**, **3a**, and **4b** were assigned as 831412, 831413, 831414, 831415, 831416, 831417, and 831418, respectively.

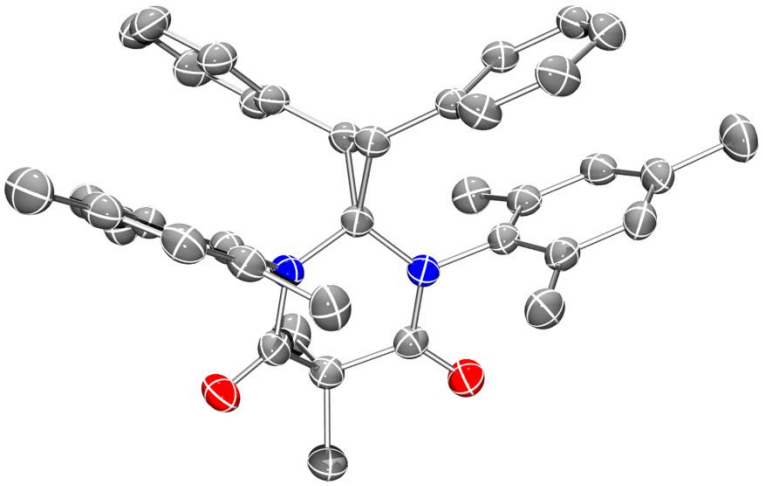


Figure A1: ORTEP diagram of **2k** with thermal ellipsoids drawn at 50% probability. H-atoms have been omitted for clarity.

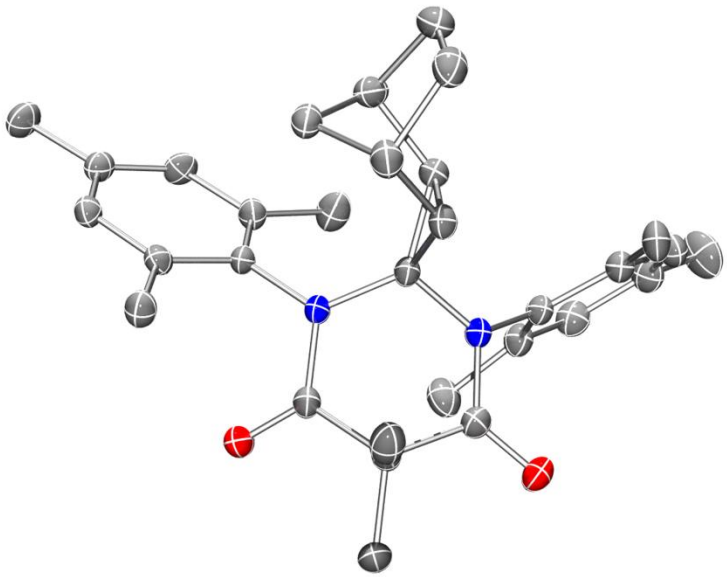


Figure A2: ORTEP diagram of **2o** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

	2e	**2j**	**2k**	**2m**
Formula	$C_{33}H_{35}F_3N_2O_2$	$C_{32}H_{40}N_2O_6$	$C_{38}H_{40}N_2O_2$	$C_{28}H_{30}N_4O_2$
M_r	548.63	548.66	556.72	454.56
crystal size (mm^3)	0.20 × 0.18 × 0.04	0.44 × 0.14 × 0.05	0.23 x 0.19 x 0.16	0.26 x 0.24 x 0.19
crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
space group	$P2_1$	$P2_1/c$	$P2_1/n$	$P2_1/n$
a (Å)	7.995(5)	16.1030(7)	10.8230(2)	15.3430(2)
b (Å)	12.695(5)	10.4950(5)	16.6860(3)	10.75550(2)
c (Å)	14.100(5)	17.6230(7)	34.9640(5)	15.6115(3)
α (°)	90.000(5)	90	90	90
β (°)	103.650(5)	101.349(3)	94.5760(7)	101.1470(10)
γ (°)	90.000(5)	90	90	90
V ($Å^3$)	1390.7(11)	2920.1(2)	6294.11(19)	2527.52(8)
Z	2	4	8	4
ρ_{calc} (g cm^{-3})	1.310	1.248	1.175	1.195
μ (mm^{-1})	0.095	0.086	0.072	0.077
F(000)	580	1176	2384	968
T (K)	120(2)	120(2)	120(2)	120(2)
scan mode	ω	ω	ω	ω
hkl range	-9 → 9 -15 → 15 -16 → 16	-19 → 19 -12 → 12 -20 → 20	-14 → 14 -20 → 21 -45 → 45	-19 → 19 -13 → 12 -20 → 20
measd reflns	4516	9408	26311	9766
unique reflns	4516 [0]	5035 [0.0876]	14329 [0.0456]	5687 [0.0291]
refinement reflns	4516	5035	14329	5687
refined	368	371	775	315
GOF on F^2	1.006	1.006	1.006	1.006
R1[a] (all) data)	0.0605 (0.0961)	0.0617 (0.1588)	0.0577 (0.1308)	0.0561 (0.0982)
wR2 (all) data)	0.1422 (0.1762)	0.1246 (0.1683)	0.1126 (0.1680)	0.1159 (0.1402)
ρ_{fin} (max/min) (e $Å^{-3}$)	0.210 -0.240	0.252 -0.224	0.242 -0.262	0.213 -0.201

Table A2: Summary of crystal data, data collection, and structure refinement details.[a] R1 = $\sum||Fo| - |Fc||/\sum|Fo|$. [b] wR2 = $\{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

	2o	**3a**	**4b**
Formula	$C_{31}H_{38}N_2O_2$	$C_{28}H_{34}N_2O_3$	$C_{31}H_{33}N_3O_5$
M_r	470.63	446.57	527.60
crystal size (mm^3)	0.28 x 0.21 x 0.18	0.38 x 0.21 x 0.02	0.22 x 0.21 x 0.18
crystal system	Triclinic	Triclinic	Monoclinic
space group	*P*-1	*P*-1	*P2₁*/c
a (Å)	12.2790(2)	8.1786(9)	15.9318(6)
b (Å)	12.38100(10)	10.2957(11)	14.2492(5)
c (Å)	18.1480(2)	14.8635(16)	24.1259(9)
α (°)	76.1480(8)	85.453(2)	90
β (°)	82.4690(7)	81.396(2)	93.8000(10)
γ (°)	76.3420(7)	80.662(2)	90
V ($Å^3$)	2594.85	1219.1(2)	5464.9(3)
Z	4	2	8
ρ_{calc} (g cm^{-3})	1.205	1.217	1.283
μ (mm^{-1})	0.075	0.079	0.088
F(000)	1016	480	2240
T (K)	120(2)	150(2)	150(2)
scan mode	ω	ω	ω
hkl range	-15 → 15 -15 → 16 -23 → 23	-9 → 9 -12 → 12 -17 → 15	-18 → 18 -16 → 16 -28 → 28
measd reflns	20306	8150	63095
unique reflns [R_{int}]	11672 [0.0358]	4278 [0.0451]	9604 [0.0821]
refinement reflns	11672	4278	9604
refined parameters	647	307	719
GOF on F^2	1.006	1.006	1.009
R1[a] (all) data)	0.0702 (0.1189)	0.0528 (0.0759)	0.0544 (0.0835)
wR2 (all) data)	0.1511 (0.1926)	0.1294 (0.1460)	0.1244 (0.1415)
ρ_{fin} (max/min) (e $Å^{-3}$)	0.324 -0.325	0.213 -0.270	0.222 -0.256

Table A3: Summary of crystal data, data collection, and structure refinement details. [a] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

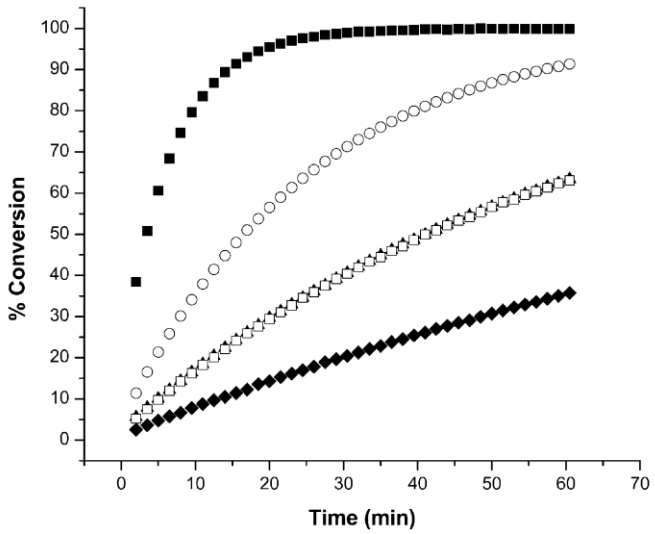


Figure A3: Plots of percent conversion versus time for the [2+1] cycloaddition of **1** with 10 equivalents of 4-methoxystyrene (solid diamonds), styrene (open squares), 4-fluorostyrene (solid triangles), 4-chlorostyrene (open circles), or 4-(trifluoromethyl)styrene (solid squares). Conditions: 15 °C, C_7D_8.

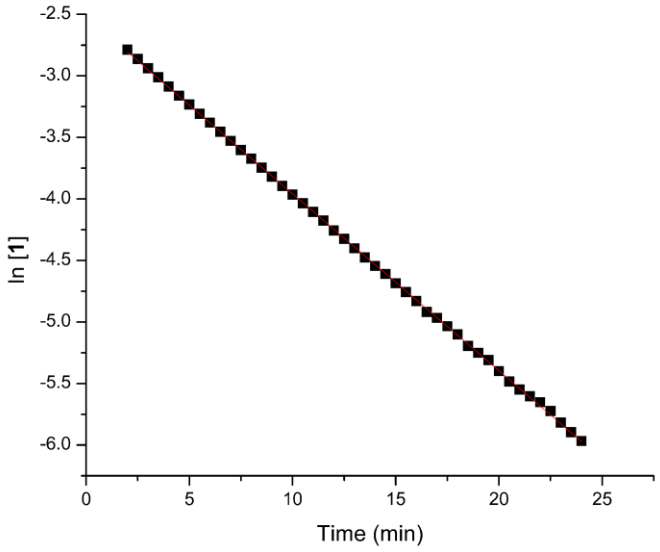


Figure A4: Plot of ln [**1**] versus time. Conditions: $[\mathbf{1}]_0$ = 0.1 M, [4-(trifluoromethyl)styrene]$_0$ = 1 M (10 eq), C_7D_8, 15 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.1439 ± 0.0003 min^{-1} and b = –2.519 ± 0.004.

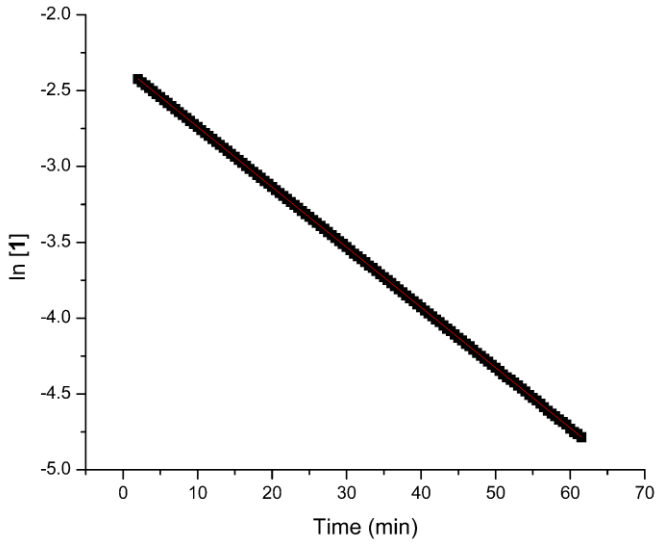


Figure A5: Plot of ln [**1**] versus time. Conditions: [**1**]$_0$ = 0.1 M, [4-chlorostyrene]$_0$ = 1 M (10 eq), C_7D_8, 15 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.03970 ± 0.00001 min^{-1} and b = –2.3418 ± 0.0004.

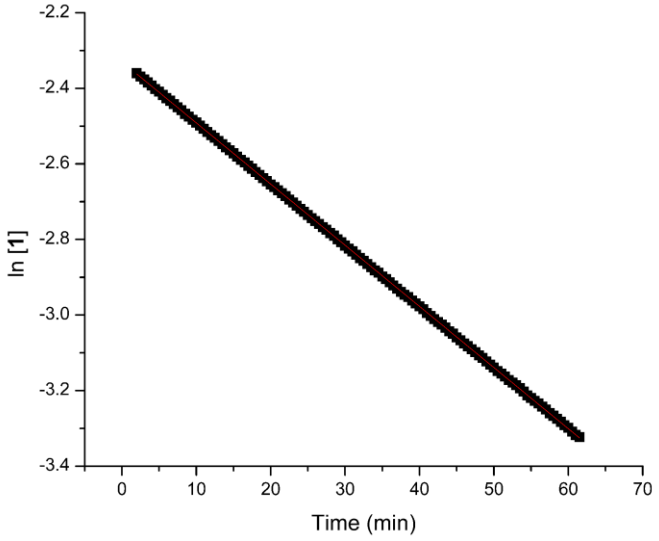


Figure A6: Plot of ln [**1**] versus time. Conditions: [**1**]$_0$ = 0.1 M, [4-fluorostyrene]$_0$ = 1 M (10 eq), C_7D_8, 15 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.01619 ± 0.000006 min^{-1} and b = –2.3295 ± 0.0002.

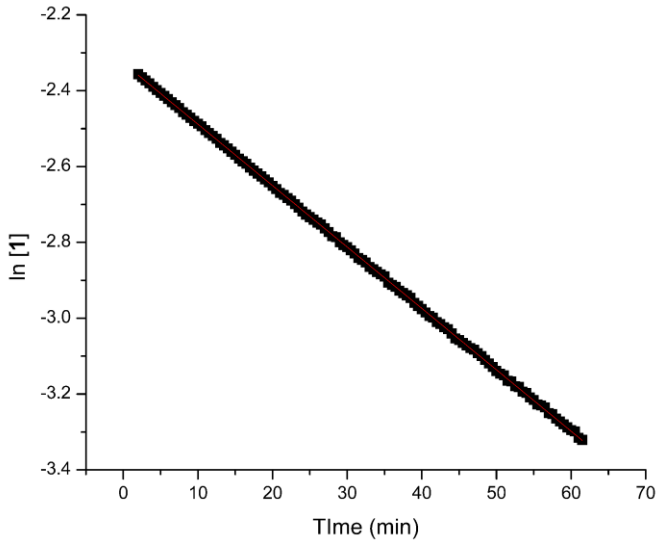


Figure A7: Plot of ln [**1**] versus time. Conditions: [**1**]$_0$ = 0.1 M, [styrene]$_0$ = 1 M (10 eq), C_7D_8, 15 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.01619 ± 0.00001 min^{-1} and b = –2.3265 ± 0.0005.

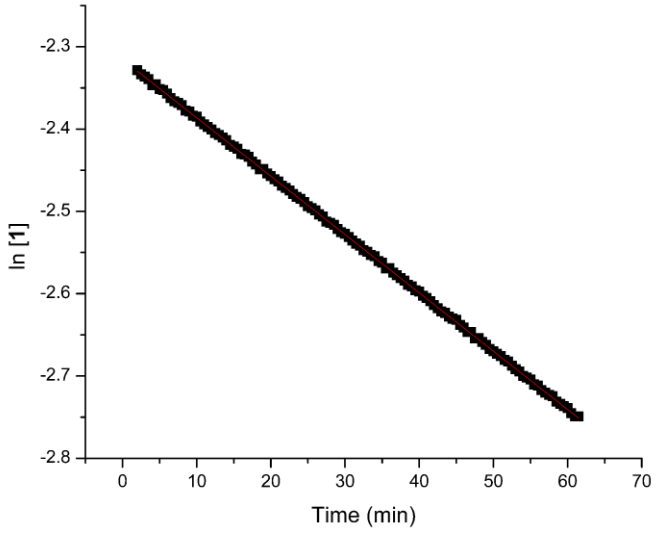


Figure A8: Plot of ln [**1**] versus time. Conditions: [**1**]$_0$ = 0.1 M, [4-methoxystyrene]$_0$ = 1 M (10 eq), C_7D_8, 15 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.00709 ± 0.00006 min^{-1} and b = –2.3154 ± 0.0002.

R	σ[a]	Rate (M^{-1})	Relative rate[b]
OMe	-0.27	0.00709	0.44
H	0	0.01619	1
F	0.06	0.01619	1
Cl	0.23	0.03970	2.45
CF_3	0.54	0.1439	8.89

Table A4: Hammett σ values and experimentally determined reaction rates for the cyclopropanation of **1** with various p-substituted styrene derivatives (10 eq) at 15 °C in C_7D_8. [a]Literature values. [b]Relative to the rate observed in the reaction of **1** with 10 eq of styrene at 15 °C.

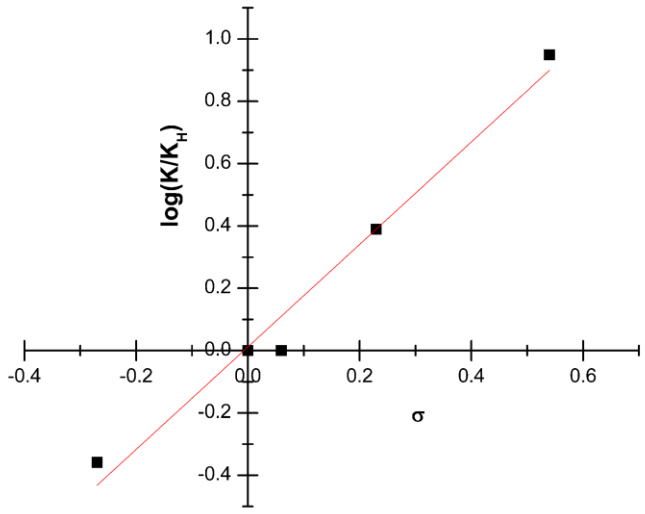


Figure A9: Hammett plot derived from the cyclopropanation of **1** and various p-substituted styrene derivatives. The equation for the best fit line is as follows: y = mx + b, where m = 1.64 ± 0.14 and b = 0.01 ± 0.04.

Evaluation of the Reactions Involving 1 and Various Nitriles. For **5a-c**: An 8 mL vial was charged with **1** (0.025 g, 0.066 mmol, 1 eq), C_7D_8 (0.6 mL), and a stir bar. To this vial, an aryl nitrile (1 eq) was added. **For 5d**: An 8 mL vial was charged with **1** (0.015 g, 0.066 mmol, 1 eq), C_7D_8 (1.6 mL), a stir bar, followed by acetonitrile (10 eq). In all cases, the resultant mixture was stirred for 45 min at 23 °C prior to being transferred to an NMR tube. The sample was then inserted into the NMR spectrometer and equilibrated at 0 °C. A ^{1}H NMR spectrum was taken at 10 °C intervals from 0-60 °C. The percent conversion was determined by the ratio of the methyl singlet of **1** at 1.34-1.49 ppm with the methyl singlet of **5a-d** at 2.25-2.46 ppm. The equilibrium constant K_{eq} was then calculated using the equation:

$$K_{eq} = [\mathbf{5}]/([\mathbf{1}][RCN])$$

The K_{eq} values calculated for **5a-d** at each 10 °C interval from 0-60 °C were used to generate a van't Hoff plot by plotting ln K_{eq} versus 1/T and fit to a linear regression (Figures A10-A13). Using the following equations, ΔH and ΔS were calculated for each reaction investigated. The standard deviations are calculated from the linear regression fit.

$$\text{slope} = -\Delta H/R$$

$$\text{y-intercept} = \Delta S/R$$

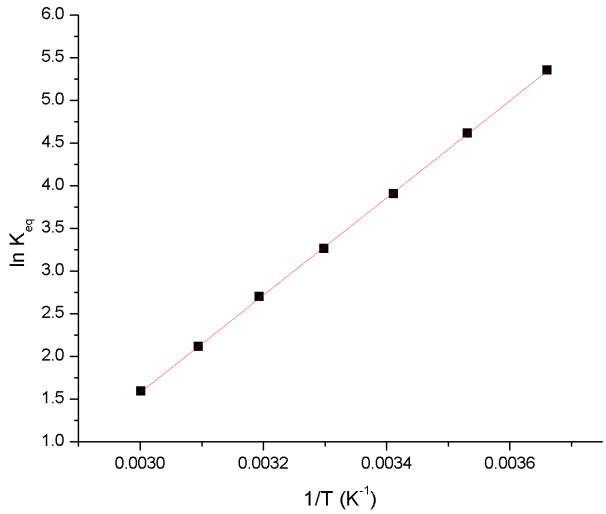


Figure A10: Plot of ln K_{eq} versus 1/T for the reaction **1** + benzonitrile → **5a**. The equation for the best fit line is as follows: y = mx + b, where m = 5700 ± 30 K^{-1} and b = -15.52 ± 0.1.

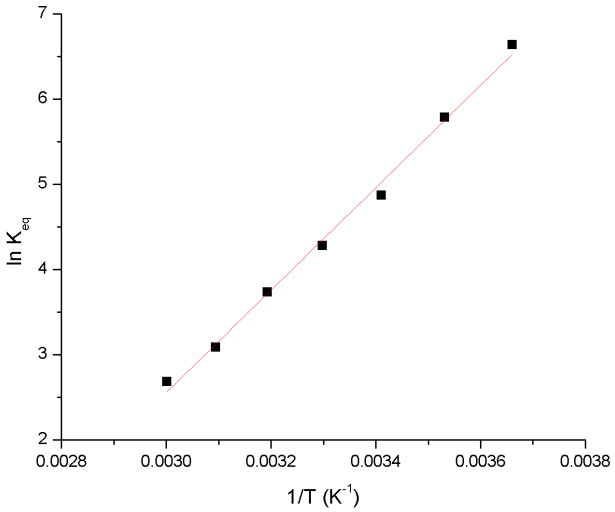


Figure A11: Plot of ln K_{eq} versus 1/T for the reaction **1** + 4-nitrobenzonitrile → **5b**. The equation for the best fit line is as follows: y = mx + b, where m = 6010 ± 190 K^{-1} and b = -15.5 ± 0.6.

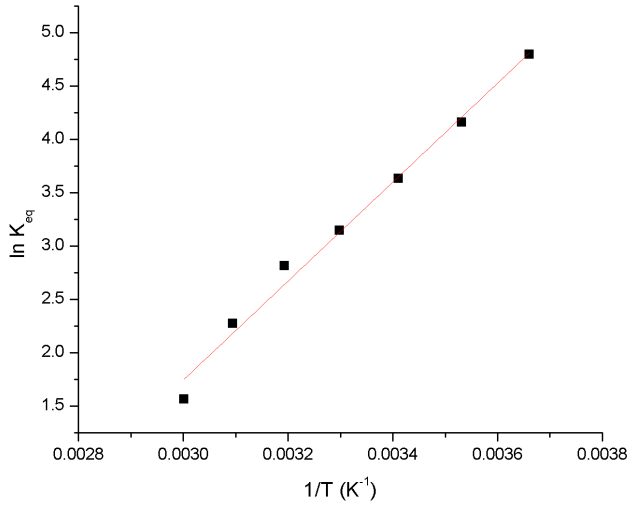


Figure A12: Plot of ln K_{eq} versus 1/T for the reaction **1** + 4-methoxybenzonitrile → **5c**. The equation for the best fit line is as follows: y = mx + b, where m = 4600 ± 200 K^{-1} and b = -12.2 ± 0.7.

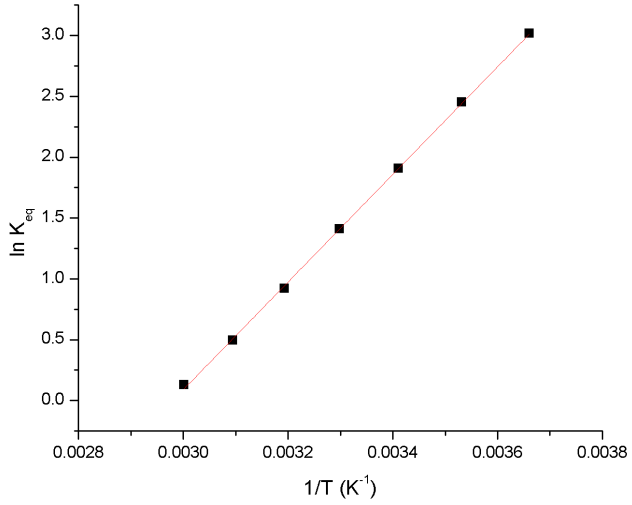


Figure A13: Plot of ln K_{eq} versus 1/T for the reaction **1** + acetonitrile → **5d**. The equation for the best fit line is as follows: y = mx + b, where m = 4420 ± 34 K^{-1} and b = -13.2 ± 0.11.

Evaluation of the Reactions Involving 1 and Various Alkynes. A 0.089 M stock solution of **1** was prepared by dissolving **1** (0.120 g, 0.319 mmol) in C_6D_6 (3.6 mL). An NMR tube equipped with a screw-cap septum was then charged inside of a glove box with the stock solution of **1** (0.6 mL, 0.053 mmol) and a sufficient quantity of C_6D_6 such that the total volume equaled 0.8 mL upon the addition of 10 eq of the alkyne analyzed. The sample was then equilibrated in an NMR probe at 50 °C. Upon equilibration, the sample was ejected from the instrument and 0.53 mmol (10 eq) of an alkyne was added via syringe. The NMR tube was then vigorously shaken to ensure proper mixing, and the sample reinserted into the NMR probe. After shimming, spectra (four scans each) were run every 30 sec for 1 h. The conversion to the cyclopropene product (**2b**,**d-f**, Figure S14) was measured by comparing the ratio of the ^{1}H NMR integrals assigned to the aryl protons of **1** (δ = 6.78 ppm; s, 4H) with the corresponding aryl protons attributed to the respective product (**2b**: 6.50 ppm, s, 2H; **2d**: 6.63 ppm, s, 2H; **2e**: 6.65 ppm; overlapping singlets, 4H; **2f**: 6.48 ppm, s, 2H). To account for the differing number of hydrogen atoms in each compound, the integrals for **2b**, **2d** and **2f** were doubled prior to calculating the integral ratio. Pseudo-first order rate constants were determined for these reactions by plotting the ln [**1**] versus time (Figures S15-S18). Linear fits of all data points collected for conversions < 90% were used to calculate the observed rate constants from the corresponding slopes.

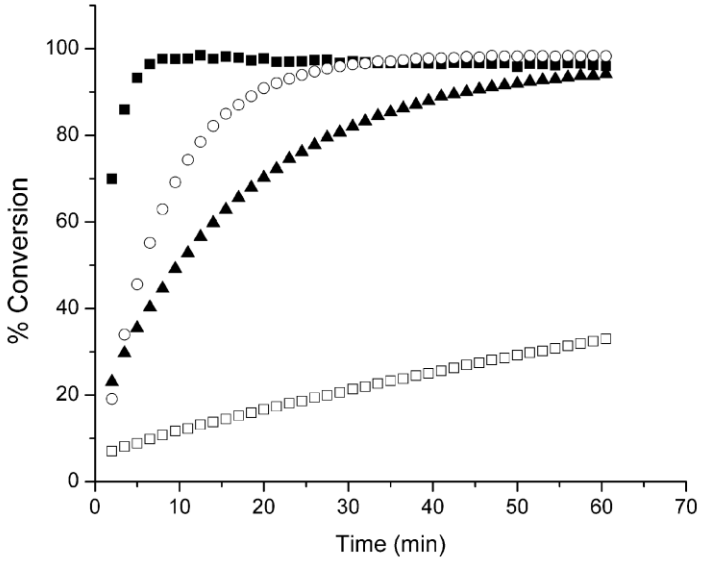


Figure A14: Plot of percent conversion versus time for the [2+1] cycloaddition of **1** with 2-hexyne (open squares), 1-phenyl-1-butyne (solid triangles), 1-hexyne (open circles), or 4-tert-butylphenylacetylene (solid squares). Conditions: $[\mathbf{1}]_0$ = 0.066 M, 10 eq of alkyne, 50 °C, C_6D_6. Every third data point is plotted for visual clarity.

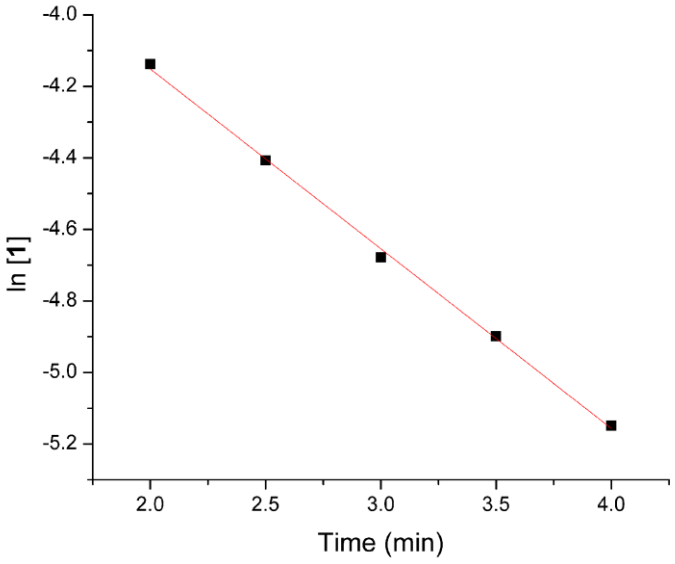


Figure A15: Plot of ln [**1**] versus time. Conditions: $[\mathbf{1}]_0$ = 0.066 M, [4-tert-butylphenylacetylene]$_0$ = 0.66 M (10 eq), C_6D_6, 50 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.502 ± 0.011 min^{-1} and b = –3.15 ± 0.03.

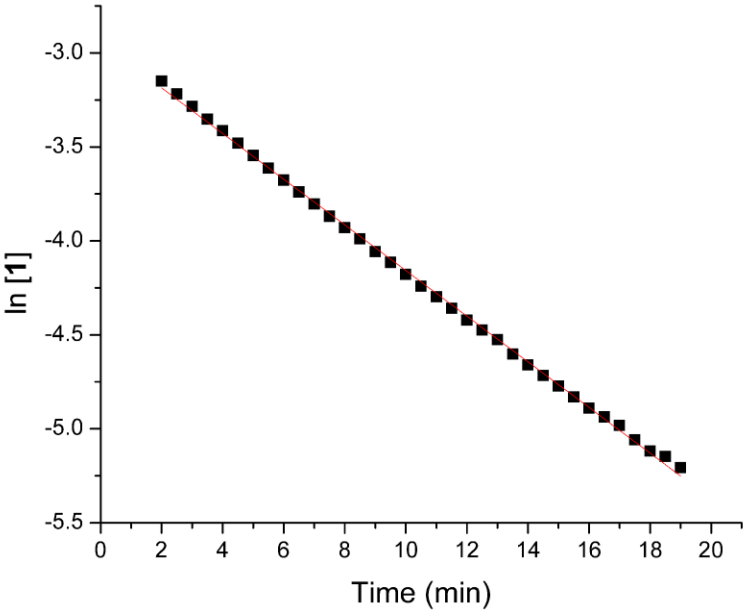


Figure A16: Plot of ln [**1**] versus time. Conditions: [**1**]$_0$ = 0.066 M, [1-hexyne]$_0$ = 0.66 M (10 eq), C_6D_6, 50 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.1215 ± 0.0007 min^{-1} and b = –2.943 ± 0.008.

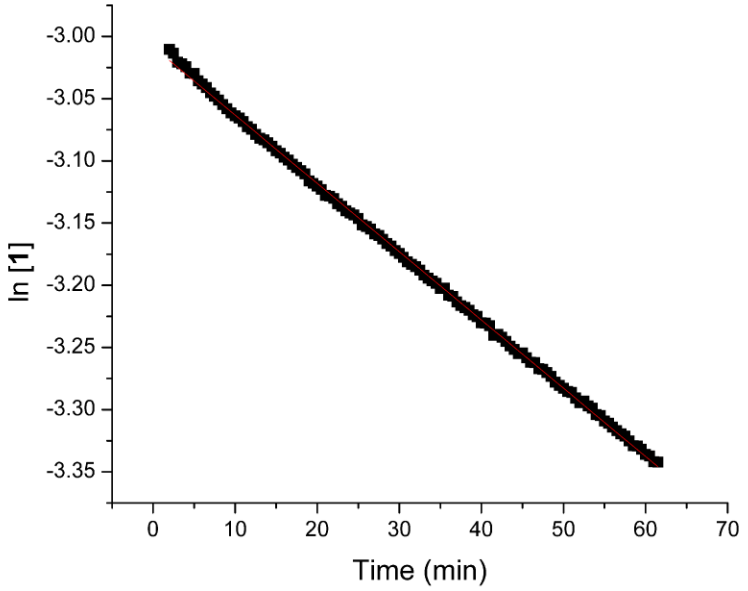


Figure A17: Plot of ln [**1**] versus time. Conditions: [**1**]$_0$ = 0.066 M, [2-hexyne]$_0$ = 0.66 M (10 eq), C_6D_6, 50 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.00549 ± 0.00001 min^{-1} and b = –3.0083 ± 0.0004.

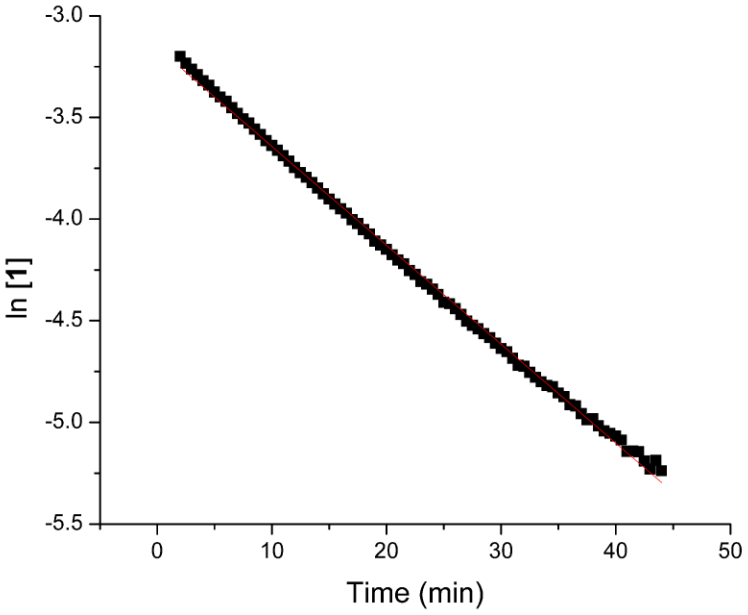


Figure A18: Plot of ln [**1**] versus time. Conditions: $[\mathbf{1}]_0$ = 0.066 M, $[\text{1-phenyl-1-butyne}]_0$ = 0.66 M (10 eq), C_6D_6, 50 °C. The equation for the best fit line is as follows: y = mx + b, where m = –0.0487 ± 0.0002 min^{-1} and b = –3.156 ± 0.005.

X-Ray Crystallography. Colorless, single crystals of **2a** were obtained by the slow diffusion of pentane into a saturated benzene solution; this compound crystallized in the monoclinic space group $P2_1/c$. Colorless single crystals of **2b** were grown by the slow evaporation of a benzene solution; this compound co-crystallized with a molecule of benzene in the monoclinic space group $P2_1/n$. Colorless, single crystals of **2c** were obtained by the slow evaporation of a benzene solution; this compound co-crystallized with a molecule of benzene in the monoclinic $P2_1/c$ space group. Colorless single crystals of **3** were obtained by the slow diffusion of pentane into a saturated benzene solution; this compound crystallized in the triclinic *P*-1 space group. Colorless, single crystals of **4** were obtained by the slow diffusion of pentane into a saturated benzene solution; this compound crystallized in the monoclinic I_2/a space group. Colorless, single crystals of **5c**

were obtained by the slow diffusion of pentane into a benzene solution; this compound crystallized in the monoclinic $P2_1/n$ space group. Colorless, single crystals of **6** were obtained by the slow evaporation of a saturated chloroform solution; this compound co-crystallized with a molecule of chloroform in the triclinic *P*-1 space group. Crystallographic measurements were carried out on a Rigaku Mini CCD, Enraf-Nonius Kappa CCD, or Rigaku AFC-12 with Saturn 724+ CCD area detector diffractometer using graphite-monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å) at 120 K or 140 K using an Oxford Cryostream low temperature device. A sample of suitable size and quality was selected and mounted onto a nylon loop. Data reductions were performed using DENZO-SMN. The structures were solved by direct methods which successfully located most of the non-hydrogen atoms. Subsequent refinements on F_2 using the SHELXTL/PC package (version 5.1) allowed the location of the remaining non-hydrogen atoms. Key details of the crystal and structure refinement data are summarized in Table A5, A6 Further crystallographic details may be found in the respective CIFs which were deposited at the Cambridge Crystallographic Data Centre, Cambridge, UK. The CCDC reference numbers for **2a**, **2b**, **2c**, **3**, **4**, **5c** and **6** were assigned as 859318, 859319, 859320, 859321, 859322, 859323, and 859324, respectively.

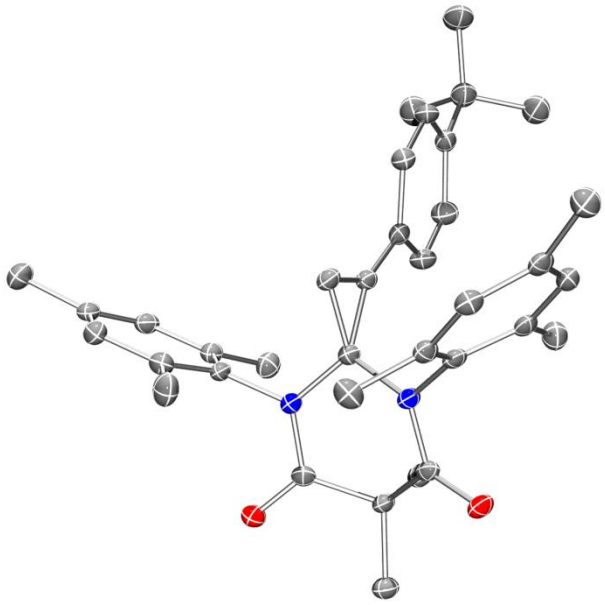


Figure A19: ORTEP diagram of **2b** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

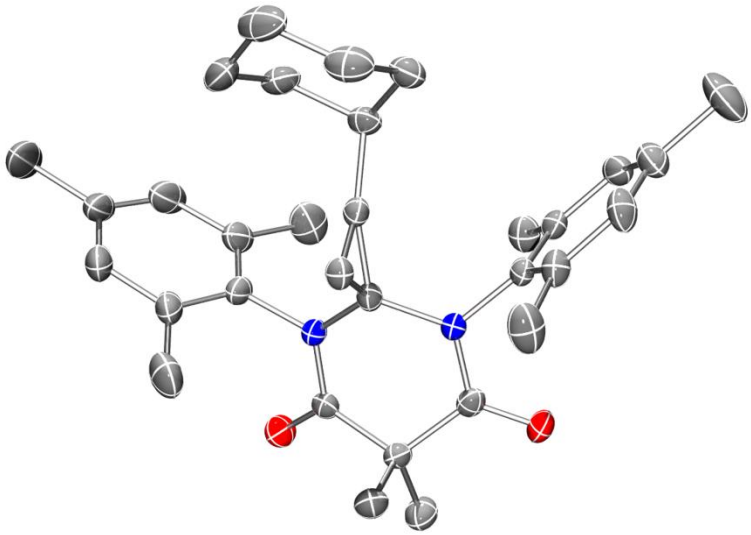


Figure A20: ORTEP diagram of **2c** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

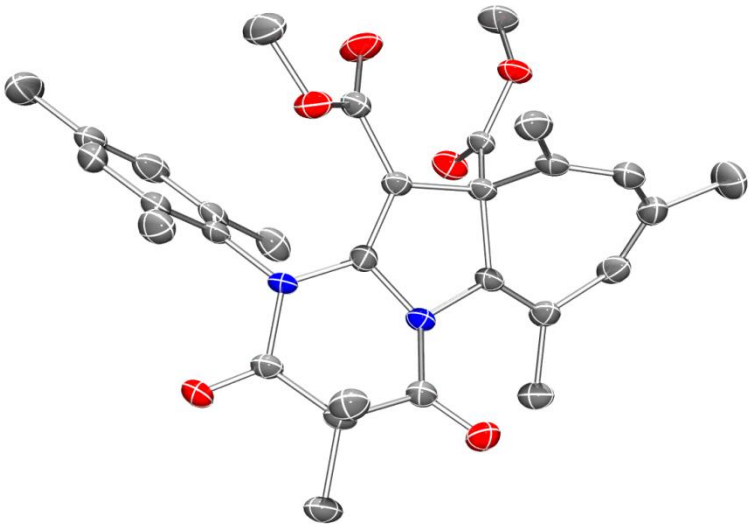


Figure A21: ORTEP diagram of **3** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

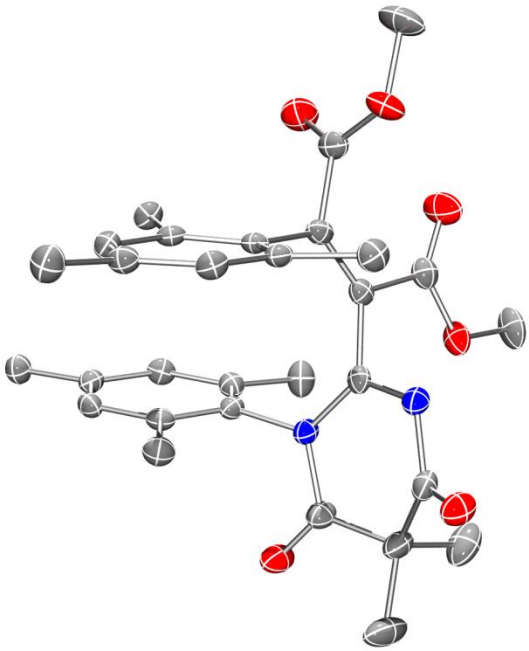


Figure A22: ORTEP diagram of **4** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

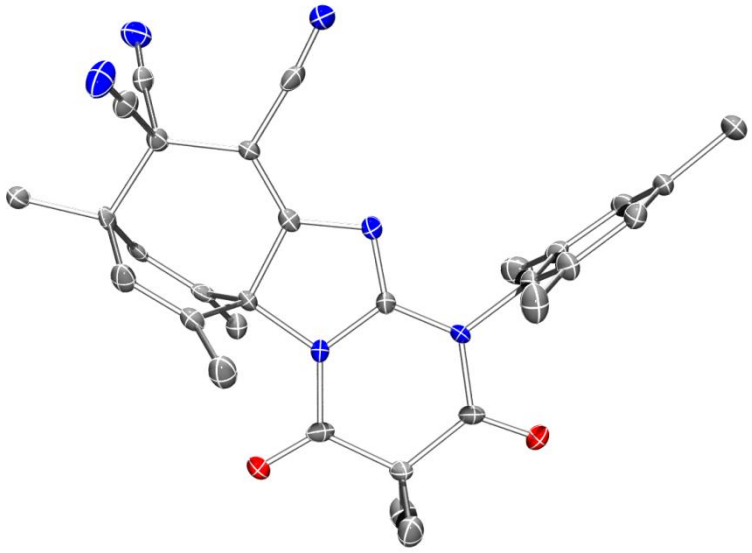


Figure A23: ORTEP diagram of **6** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

	2[a]	**2b**·C_6H_6	**2c**·C_6H_6	**3**
Formula	$C_{26}H_{30}N_2O_2$	$C_{42}H_{48}N_2O_2$	$C_{38}H_{46}N_2O_2$	$C_{30}H_{34}N_2O_6$
M_r	402.52	612.82	562.77	518.59
crystal size (mm^3)	0.19 × 0.16 × 0.04	0.18 × 0.14 × 0.03	0.38 × 0.20 × 0.07	0.14 × 0.10 × 0.09
crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
space group	$P2_1/c$	$P2_1/n$	$P2_1/c$	P-1
a (Å)	8.3627(3)	16.8334(16)	12.0444(9)	9.2245(14)
b (Å)	16.4334(6)	8.7348(8)	23.2835(17)	11.6531(18)
c (Å)	15.9457(6)	24.305(2)	11.9648(9)	14.266(2)
α (°)	90	90	90	97.528(4)
β (°)	99.6680(10)	100.763(2)	103.659(2)	104.301(4)
γ (°)	90	90	90	108.506(3)
V ($Å^3$)	2160.26(14)	3510.9(6)	3260.5(4)	1372.1(4)
Z	4	4	4	2
ρ_{calc} ($g\ cm^{-3}$)	1.238	1.159	1.146	1.255
μ (mm^{-1})	0.078	0.070	0.070	0.088
F(000)	864	1320	1216	552
T (K)	120(2)	120(2)	150(2)	150(2)
scan mode	ω	ω	ω	ω
hkl range	-9 → 9 -19 → 19 -18 → 18	-20 → 20 -10 → 10 -28 → 28	-14 → 13 -27 → 27 -14 → 14	-10 → 10 -13 → 13 -16 → 16
measd reflns	42443	67264	34255	19559
unique reflns [R_{int}]	3787 [0.0524]	6176 [0.0726]	5739 [0.1303]	4810 [0.0990]
refinement reflns	3787	6176	5739	4810
refined parameters	279	426	387	353
GOF on F^2	1.006	1.006	1.006	1.006
R1[a] (all data)	0.0419 (0.0466)	0.0561 (0.0713)	0.0647 (0.0989)	0.0642 (0.1061)
wR2 (all data)	0.1141 (0.1182)	0.1446 (0.1553)	0.1534 (0.1775)	0.1400 (0.1672)
ρ_{fin} (max/min) (e $Å^{-3}$)	0.311 -0.197	0.312 -0.287	0.232 -0.389	0.241 -0.306

Table A5: Summary of crystal data, data collection, and structure refinement details. [a] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

	4	**5c**	**6**·$CHCl_3$
Formula	$C_{30}H_{34}N_2O_6$	$C_{32}H_{35}N_3O_3$	$C_{30}H_{28}N_6O_2 \cdot CHCl_3$
M_r	518.59	509.63	623.95
crystal size (mm^3)	0.20 × 0.09 × 0.02	0.19 × 0.06 × 0.05	0.08 × 0.08 × 0.02
crystal system	Monoclinic	Monoclinic	Triclinic
space group	*I*2/a	$P2_1/n$	*P*-1
a (Å)	20.1337(10)	8.7238(3)	11.880(3)
b (Å)	8.1571(4)	17.0451(7)	12.278(3)
c (Å)	33.9244(17)	18.8797(7)	12.464(3)
α (°)	90	90	70.128(5)
β (°)	93.899(3)	95.1970(10)	61.921(4)
γ (°)	90	90	73.727(5)
V ($Å^3$)	5558.6(5)	2795.83(18)	1492.6(6)
Z	8	4	2
ρ_{calc} (g cm^{-3})	1.239	1.211	1.388
μ (mm^{-1})	0.086	0.078	0.347
F(000)	2208	1088	648
T (K)	120(2)	120(2)	150(2)
scan mode	ω	ω	ω
hkl range	-23 → 23 -9 → 9 -40 → 40	-10 → 10 -20 → 20 -22 → 22	-20 → 20 -10 → 10 -28 → 28
measd reflns	38508	55292	21392
unique reflns	4882 [0.0903]	4909[0.0621]	5161 [0.1077]
refinement reflns	4882	4909	5161
refined	353	352	387
GOF on F^2	1.006	1.006	1.006
R1[a] (all data)	0.0563 (0.0806)	0.0398 (0.0440)	0.0863 (0.1580)
wR2 (all data)	0.1178 (0.1296)	0.1033 (0.1062)	0.1811 (0.2205)
ρ_{fin} (max/min) (e $Å^{-3}$)	0.225 -0.228	0.280 -0.169	1.653 -0.820

Table A6: Summary of crystal data, data collection, and structure refinement details. [a] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

X-Ray Crystallography. Colorless single crystals of **3** were obtained by slow evaporation of a concentrated chloroform solution; this compound crystallized in the orthorhombic space group $Pna2_1$. Colorless single crystals of **5b** were obtained by slow vapor diffusion of pentane into a saturated benzene solution; this compound crystallized in the monoclinic space group $P2_1/n$.Colorless single crystals of **6a** were obtained by slow vapor diffusion of pentane into a saturated benzene solution; this compound crystallized in the monoclinic space group $P2_1/c$. Colorless single crystals of **6l** were obtained by the slow evaporation of a concentrated benzene solution; this compound crystallized in the triclinic space group *P*-1. Crystallographic measurements were carried out on a Rigaku Mini or Rigaku Saturn CCD area detector diffractometer using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) at 150 or 120 K using a Rigaku XStream low temperature device. A sample of suitable size and quality was selected and mounted onto a nylon loop. Data reductions were performed using CrystalClear. The structures were solved by direct methods which successfully located most of the non-hydrogen atoms. Subsequent refinements on F2 using the SHELXTL/PC package (version 5.1) allowed location of the remaining non-hydrogen atoms. Key details of the crystal and structure refinement data are summarized in Table A7. Further crystallographic details may be found in the respective CIFs which were deposited at the Cambridge Crystallographic Data Centre, Cambridge, UK. The CCDC reference numbers for **3, 5b, 6a**, and **6l** were assigned as 943779, 943780, 943781 and 943782, respectively.

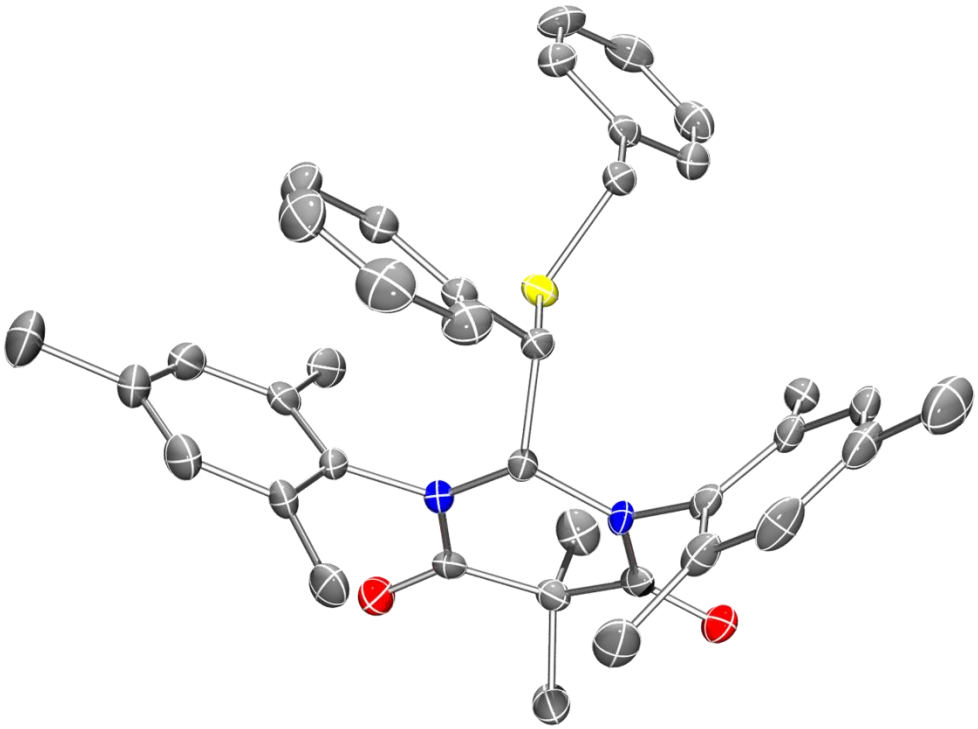


Figure A24: ORTEP diagram of **6l** with thermal ellipsoids drawn at the 50% probability. H-atoms except at the diamidomethine nucleus are omitted for clarity.

	3	**5b**	**6a**	**6l**
Formula	$C_{24}H_{28}N_2O_2$	$C_{26}H_{32}N_2O_2$	$C_{32}H_{38}N_2O_2S$	$C_{38}H_{42}N_2O_2S$
M_r	376.48	404.54	514.70	590.80
crystal size (mm^3)	0.26×0.15×0.12	0.35×0.12×0.11	0.22×0.12×0.08	0.20×0.07×0.04
crystal system	Orthorhombic	Monoclinic	Monoclinic	Triclinic
space group	*Pna*2$_1$	*P*2$_1$/*n*	*P*2$_1$/*c*	*P*-1
a (Å)	11.5813(13)	16.6531(11)	13.2597(6)	12.5664(11)
b (Å)	11.0742(12)	8.7573(6)	8.3147(4)	13.1794(12)
c (Å)	16.0796(17)	16.7688(11)	26.1388(12)	20.2275(18)
α (°)	90	90	90	77.086(2)
β (°)	90	113.7050(10)	100.6260(10)	85.650(2)
γ (°)	90	90	90	89.676(2)
V ($Å^3$)	2062.3(4)	2239.2(3)	2832.4	3255.7(5)
Z	4	4	4	4
ρ_{calc} (g cm^{-3})	1.213	1.200	1.207	1.205
μ (mm^{-1})	0.077	0.076	0.145	0.135
F(000)	808	872	1104	1264
T (K)	150	150	150	120
scan mode	ω	ω	ω	ω
hkl range	-7 → 13 -11 → 13 -18 → 18	-19 → 19 -10 → 10 -19 → 19	-15 → 15 -9 → 9 -31 → 31	-14 → 14 -15 → 15 -24 → 24
measd reflns	5713	25362	31776	43919
unique reflns [R_{int}]	3410 [0.0443]	3936 [0.0762]	4979 [0.0753]	11427 [0.0855]
refinement reflns	3410	3936	4979	11427
refined parameters	260	279	343	791
GOF on F^2	1.006	1.006	1.006	1.006
R1[a] (all data)	0.0486 (0.0583)	0.0517 (0.0724)	0.0512 (0.0729)	0.0702 (0.1162)
wR2 (all data)	0.1149 (0.1206)	0.1153 (0.1261)	0.1174 (0.1299)	0.1347 (0.1556)
ρ_{fin} (max/min) (e $Å^{-3}$)	0.157 -0.172	0.163 -0.189	0.410 -0.352	0.356 -0.293

Table A7: Summary of crystal data, data collection, and structure refinement details. [a] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

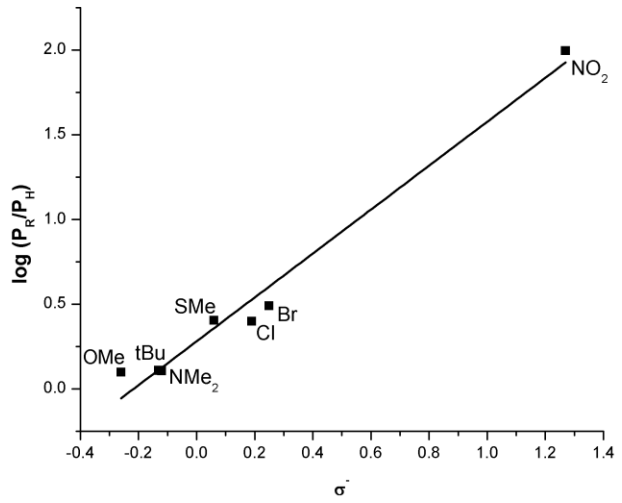


Figure A25: Plot of the logarithm of the product ratio (P_R/P_H) versus σ^- for the competitive reaction of **2** with toluene and the indicated para-substituted toluene derivative (10 equiv. each). The equation for the best fit line shown in black is as follows: y = mx + b, where m = 1.30 ± 0.09 and b = 0.28 ± 0.04.

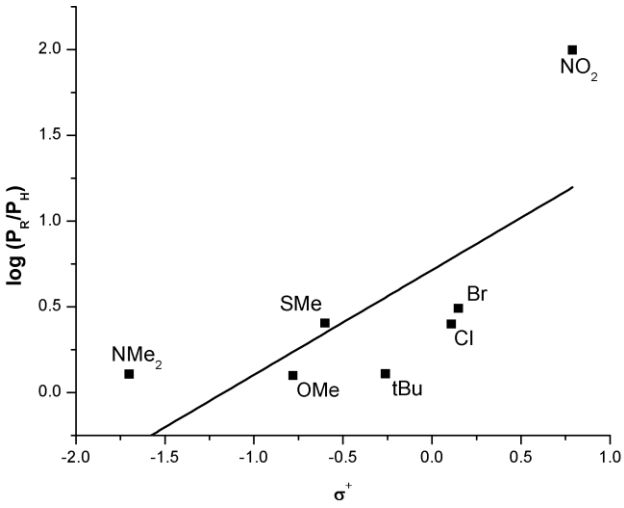


Figure A26: Plot of the logarithm of the product ratios (P_R/P_H) versus σ^+ for the competitive reaction of **2** with toluene and the indicated para-substituted toluene derivative (10 equiv. each). The equation for the best fit line shown in black is as follows: y = mx + b, where m = 0.6 ± 0.3 and b = 0.7 ± 0.2.

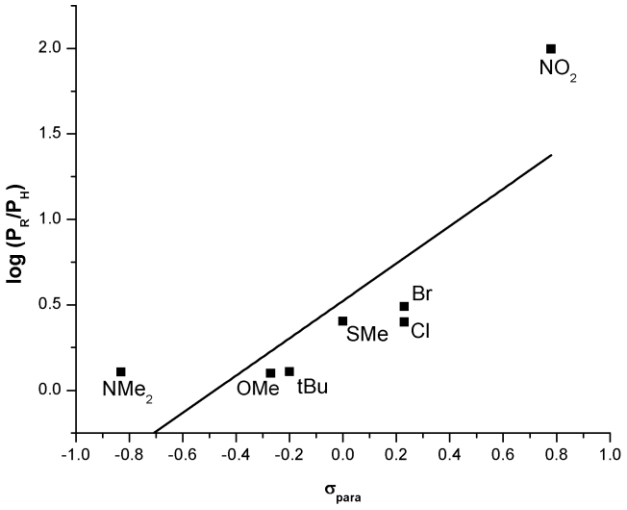


Figure A27: Plot of the logarithm of the product ratios (P_R/P_H) versus σ_{para} for the competitive reaction of **2** with toluene and the indicated para-substituted toluene derivative (10 equiv. each). The equation for the best fit line shown in black is as follows: y = mx + b, where m = 1.1 ± 0.3 and b = 0.52 ± 0.16.

CHAPTER 6: ELUCIDATION OF CARBENE AMBIPHILICITY LEADING TO THE DISCOVERY OF REVERSIBLE AMMONIA ACTIVATION

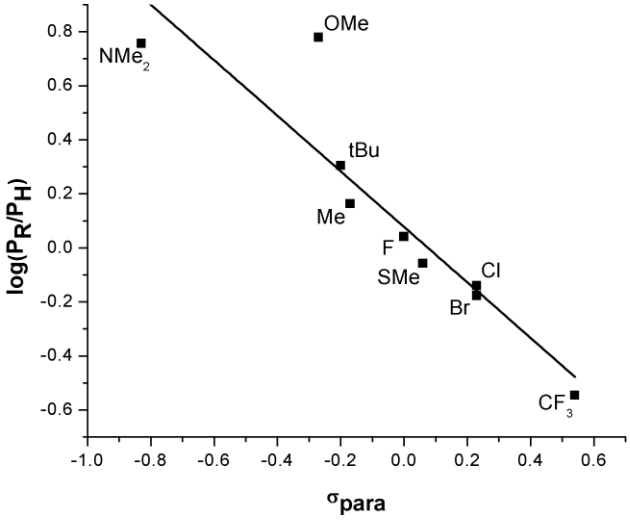


Figure A28: Plot of the logarithm of the product ratios (P_R/P_H) versus σ_{para} for the reaction of **2** with 5 equiv. of aniline and the indicated para-substituted aniline. The equation for the best fit line shown is as follows: y = mx + b, where m = -1.02 ± 0.16 and b = 0.08 ± 0.06.

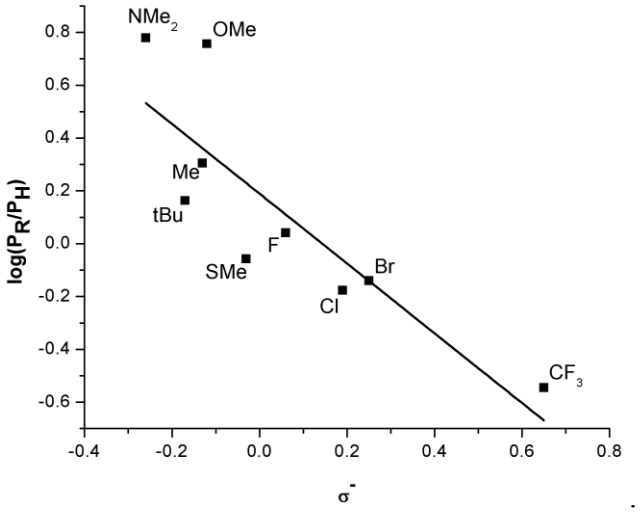


Figure A29: Plot of the logarithm of the product ratios (P_R/P_H) versus σ^- for the reaction of **2** with 5 equiv. of aniline and the indicated para-substituted aniline. The equation for the best fit line shown is as follows: y = mx + b, where m = -1.3 ± 0.3 and b = 0.19 ± 0.08.

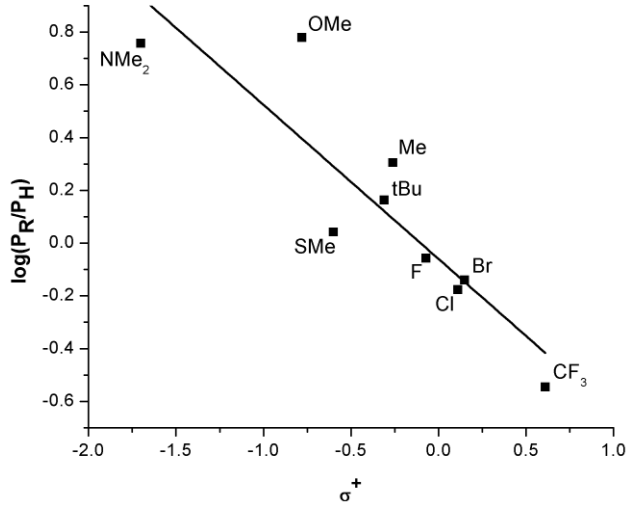


Figure A30: Plot of the logarithm of the product ratios (P_R/P_H) versus σ^+ for the reaction of **2** with 5 equiv. of aniline and the indicated para-substituted aniline. The equation for the best fit line shown is as follows: y = mx + b, where m = -0.58 ± 0.11 and b = -0.06 ± 0.08.

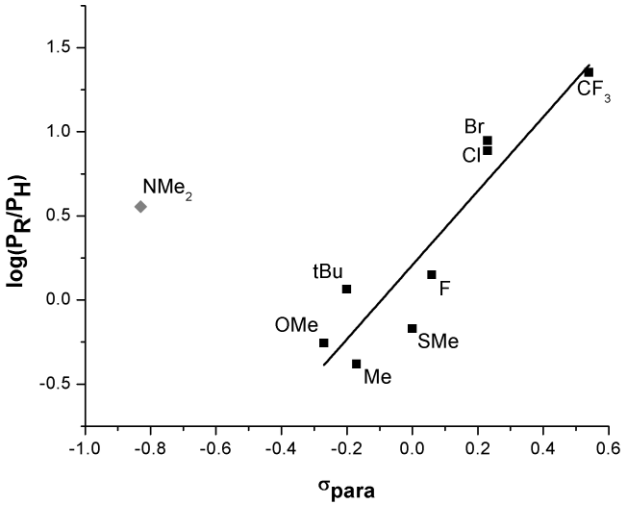


Figure A31: Plot of the logarithm of the product ratios (P_R/P_H) versus σ_{para} for the reaction of **4** with 5 equiv. of aniline and the indicated para-substituted aniline. The equation for the best fit line shown is as follows: y = mx + b, where m = 2.2 ± 0.4 and b = 0.21 ± 0.09.

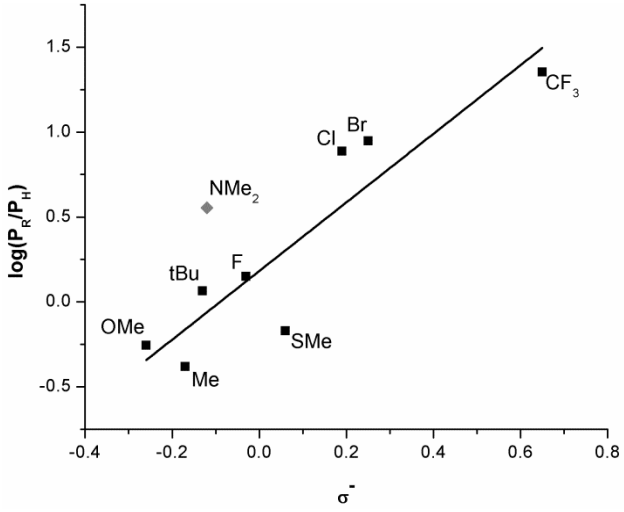


Figure A32: Plot of the logarithm of the product ratios (P_R/P_H) versus σ^- for the reaction of **4** with 5 equiv. of aniline and the indicated para-substituted aniline. The equation for the best fit line shown is as follows: y = mx + b, where m = 2.0 ± 0.4 and b = 0.18 ± 0.10. The equation for the best fit of all data points is as follows: y = mx + b, where m = 1.9 ± 0.4 and b = 0.26 ± 0.12.

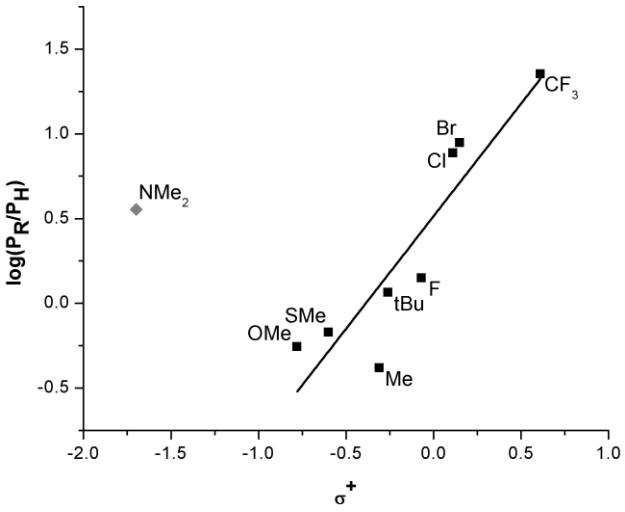
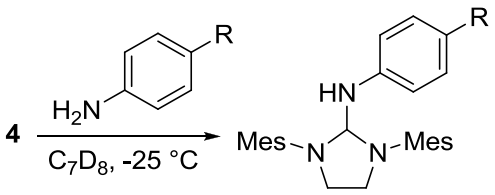


Figure A33: Plot of the logarithm of the product ratios (k_R/k_H) versus σ^+ for the reaction of **4** with 5 equiv. of aniline and the indicated para-substituted aniline. The equation for the best fit line shown in black is as follows: y = mx + b, where m = 1.3 ± 0.2 and b = 0.51 ± 0.11.



Product	R	k ($M^{-1}\cdot min^{-1}$)
22	H	0.0245
23	NMe2	0.0331
24	OMe	0.0186
25	tBu	0.127
26	Me	0.0061
27	SMe	0.431
28	F	0.140
29	Cl	0.450
30	Br	0.659

Table A8: Observed second-order rate constants (k) for the reaction of **4** and *p*-substituted anilines. [a]Conditions: C_7D_8, –25 °C.

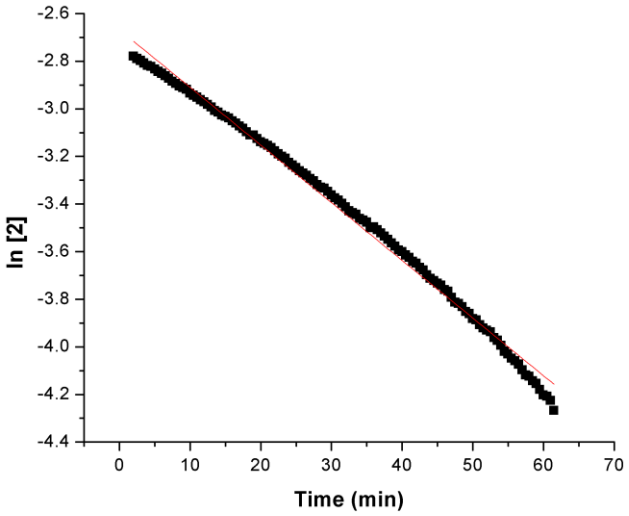


Figure A34: Plot of ln [**2**] versus time. Conditions: $[\mathbf{2}]_0$ = 0.066 M, $[\text{diethylamine}]_0$ = 0.66 M, C_6D_6, 30 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.0242 ± 0.0002 min^{-1} and b = -2.667 ± 0.007.

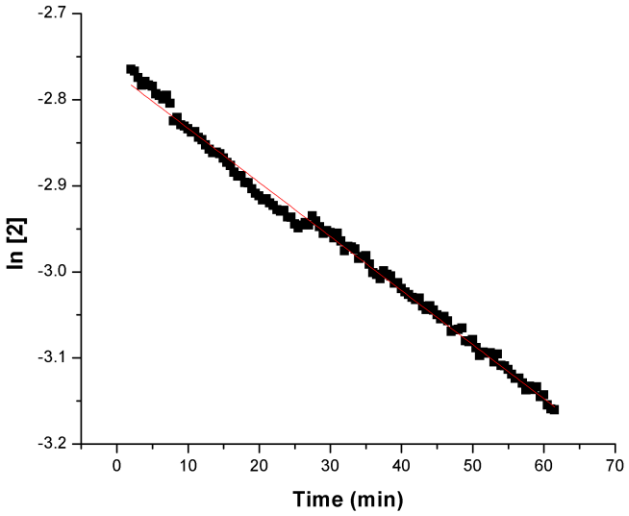


Figure A35: Plot of ln [**2**] versus time. Conditions: $[\mathbf{2}]_0$ = 0.066 M, $[\text{dibutylamine}]_0$ = 0.66 M, C_6D_6, 30 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.00628 ± 0.00004 min^{-1} and b = -2.7704 ± 0.0016.

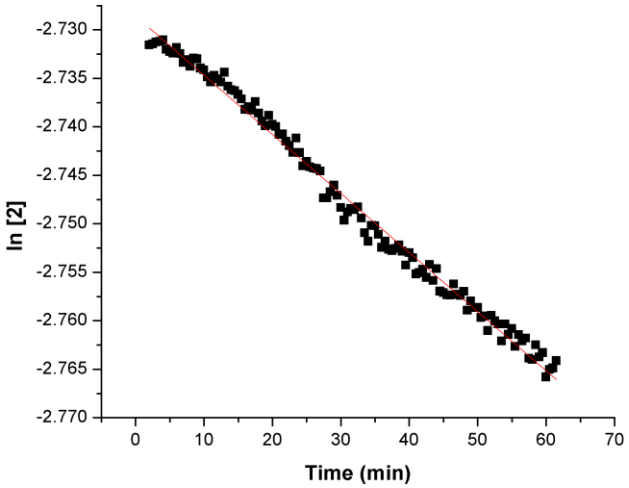


Figure A36: Plot of ln [**2**] versus time. Conditions: [**2**]$_0$ = 0.066 M, [*N*-methylaniline]$_0$ = 0.66 M, C_6D_6, 30 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.00061 ± 0.000005 min^{-1} and b = -2.7286 ± 0.00019.

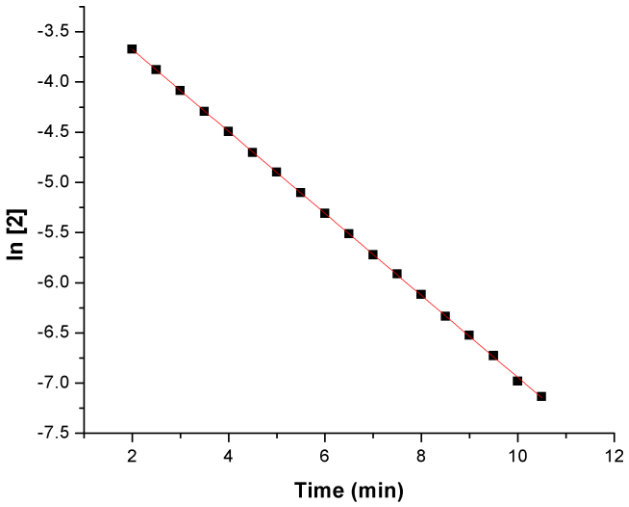


Figure A37: Plot of ln [**2**] versus time. Conditions: [**2**]$_0$ = 0.066 M, [4,4'-dimethoxyldiphenylamine]$_0$ = 0.66 M, C_6D_6, 30 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.4083 ± 0.0011 min^{-1} and b = -2.860 ± 0.007.

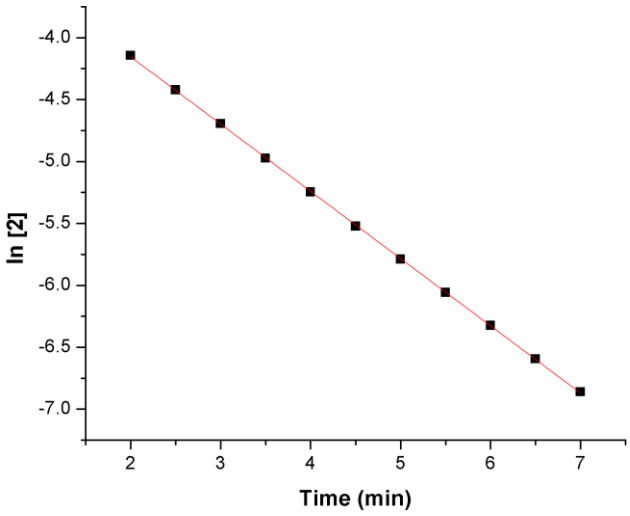


Figure A38: Plot of ln [**2**] versus time. Conditions: $[\mathbf{2}]_0$ = 0.066 M, $[\text{diphenylamine}]_0$ = 0.66 M, C_6D_6, 30 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.5430 ± 0.0013 min^{-1} and b = -3.068 ± 0.006.

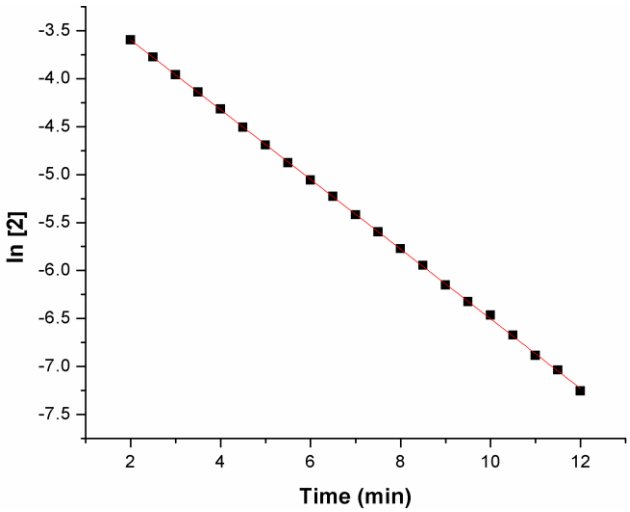


Figure A39: Plot of ln [**2**] versus time. Conditions: $[\mathbf{2}]_0$ = 0.066 M, $[\text{diphenylamine-}d_1]_0$ = 0.66 M, C_6D_6, 30 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.3635 ± 0.0010 min^{-1} and b = -2.870 ± 0.007.

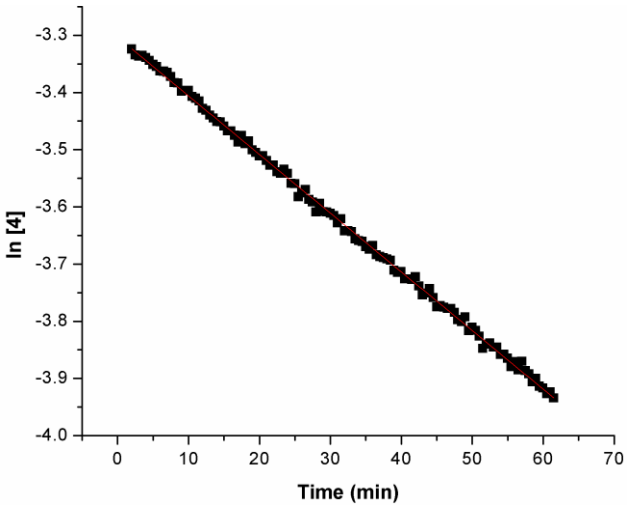


Figure A40: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.035 M, [aniline]$_0$ = 0.42 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.01026 ± 0.00003 min^{-1} and b = -3.3035 ± 0.0012.

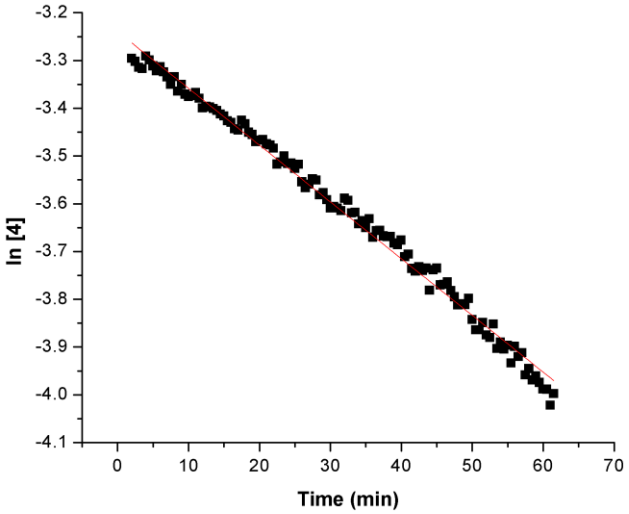


Figure A41: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.035 M, [*N,N*-dimethyl-*p*-phenylenediamine]$_0$ = 0.36 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.01188 ± 0.00010 min^{-1} and b = -3.240 ± 0.003.

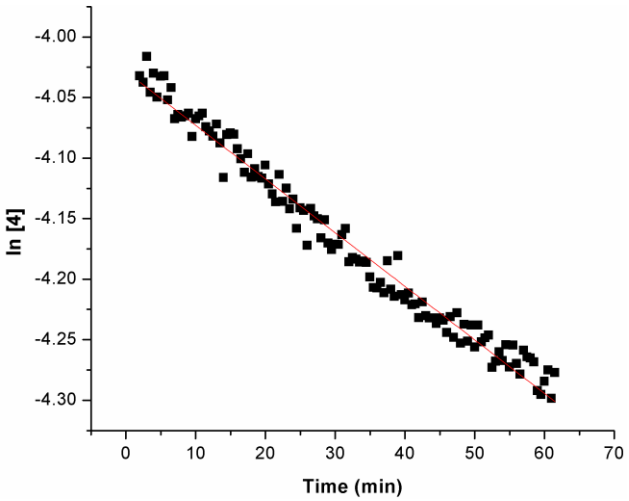


Figure A42: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.0175 M, [*p*-anisidine]$_0$ = 0.175 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.00443 ± 0.00006 min^{-1} and b = -4.029 ± 0.002.

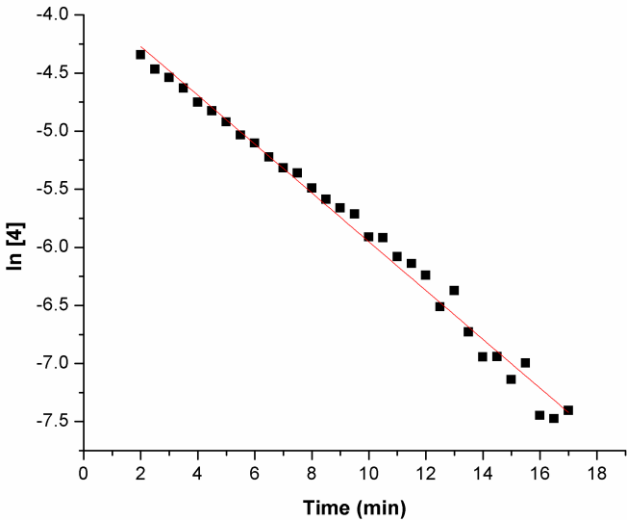


Figure A43: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.035 M, [4-*tert*-butylaniline]$_0$ = 0.47 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.0604 ± 0.0016 min^{-1} and b = -3.308 ± 0.019.

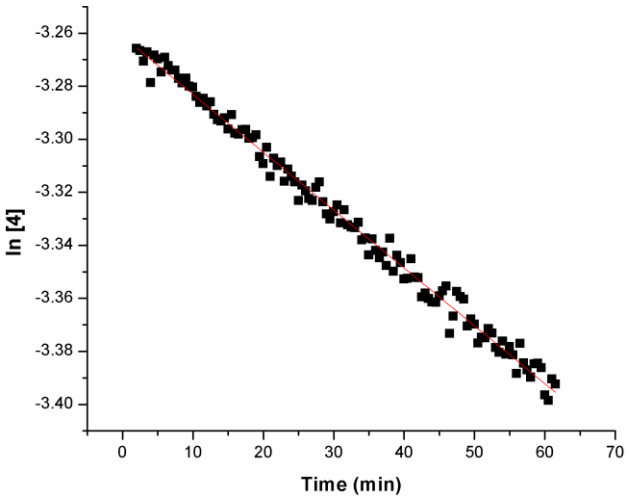


Figure A44: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.035 M, [*p*-toluidine]$_0$ = 0.36 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.00218 ± 0.00002 min^{-1} and b = -3.2612 ± 0.0007.

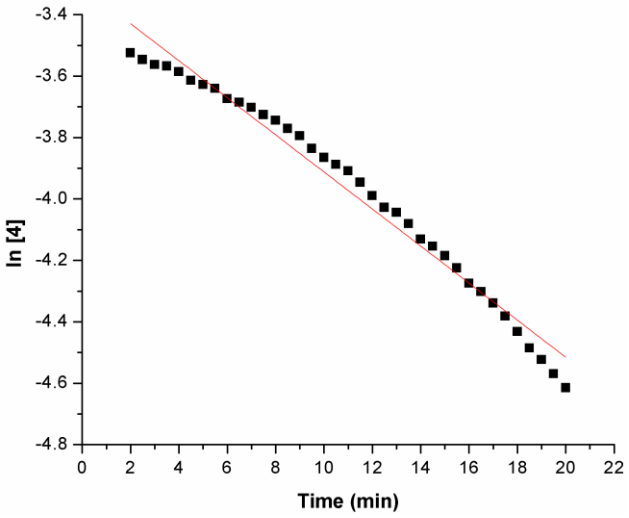


Figure A45: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.035 M, [4-(thiomethyl)aniline]$_0$ = 0.49 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.210 ± 0.004 min^{-1} and b = -3.85 ± 0.04.

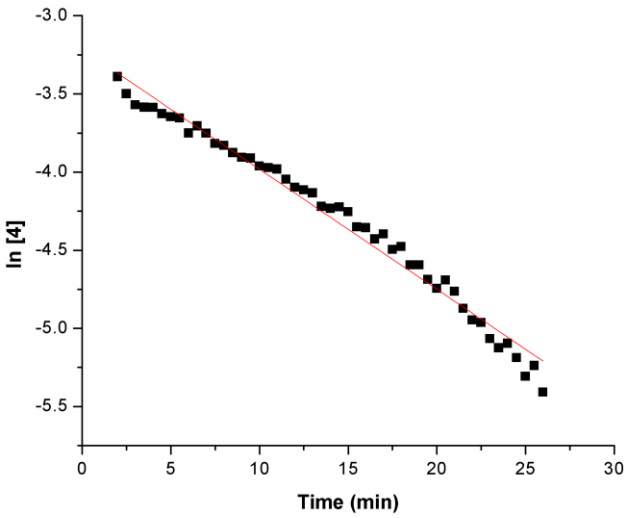


Figure A46: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.035 M, [4-fluoroaniline]$_0$ = 0.55 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.0767 ± 0.0016 min^{-1} and b = -3.21 ± 0.02.

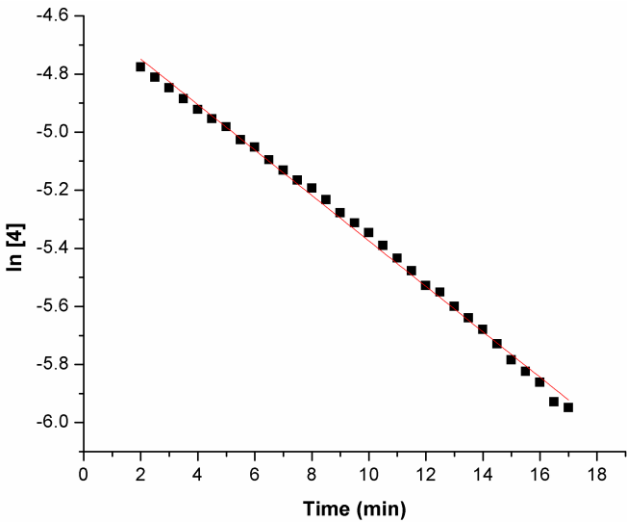


Figure A47: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.0175 M, [4-chloroaniline]$_0$ = 0.175 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.0782 ± 0.0008 min^{-1} and b = -4.592 ± 0.008.

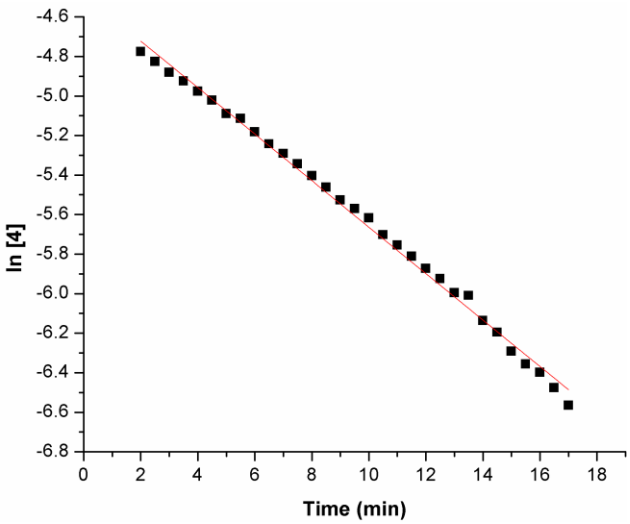


Figure A48: Plot of ln [**4**] versus time. Conditions: [**4**]$_0$ = 0.0175 M, [4-bromoaniline]$_0$ = 0.18 M, C_7D_8, –25 °C. The equation for the best fit line is as follows: y = mx + b, where m = -0.1176 ± 0.0014 min^{-1} and b = -4.487 ± 0.015.

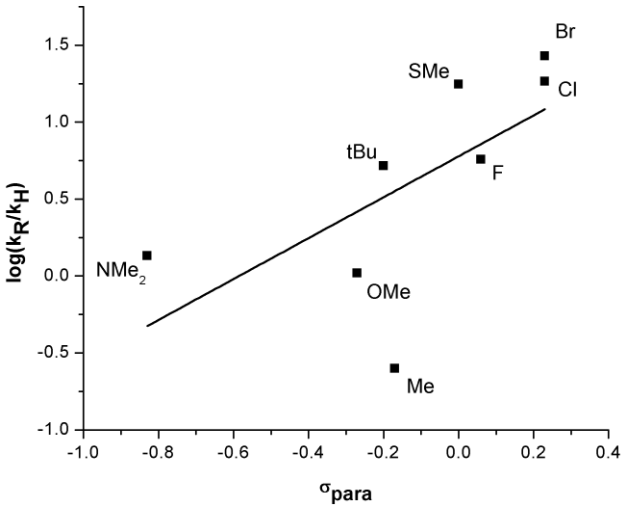


Figure A49: Plot of the logarithm of the ratio of the rate constants for the reaction of **4** with the indicated para-substituted aniline or aniline (k_R/k_H) versus σ_{para}. The equation for the best fit line shown in black is as follows: y = mx + b, where m = 1.3 ± 0.7 and b = 0.8 ± 0.2.

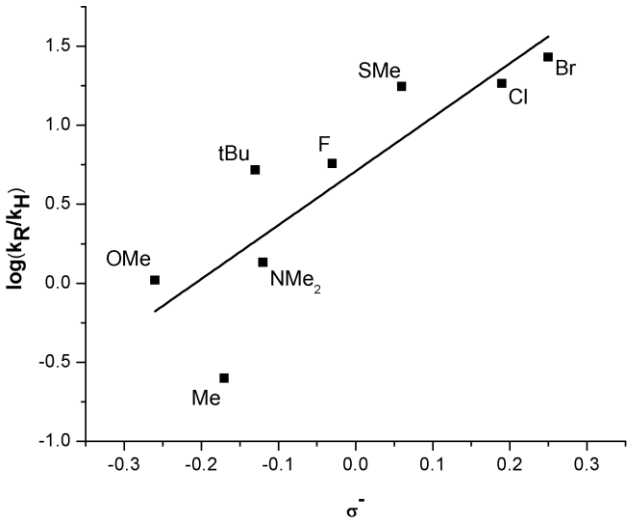


Figure A50: Plot of the logarithm of the ratio of the rate constants for the reaction of **4** with the indicated para-substituted aniline or aniline (k_R/k_H) versus σ^-. The equation for the best fit line shown in black is as follows: y = mx + b, where m = 3.4 ± 0.8 and b = 0.71 ± 0.14.

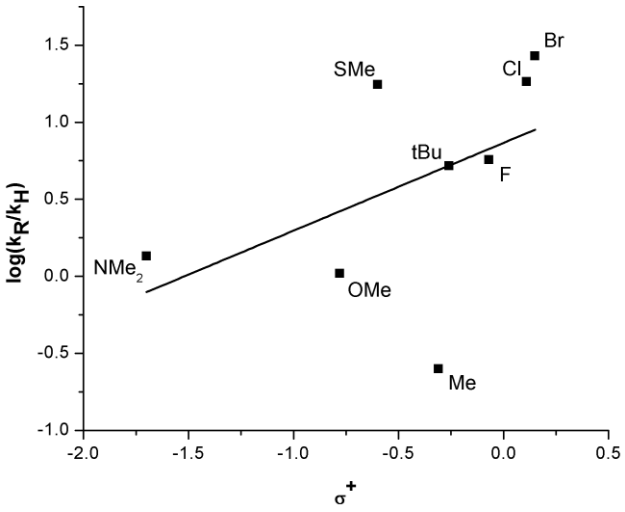


Figure A51: Plot of the logarithm of the ratio of the rate constants for the reaction of **4** with the indicated para-substituted aniline or aniline (k_R/k_H) versus σ^+. The equation for the best fit line shown in black is as follows: y = mx + b, where m = 0.6 ± 0.4 and b = 0.9 ± 0.3.

Analysis of the Reversible Ammonia Activation Reaction

NMR Spectroscopy: An NMR tube with a PTFE screw-cap was charged with **42** (0.100 g, 0.31 mmol) and C_6D_6 (0.5 mL). The solution was frozen at –30 °C. Elemental sulfur (0.010 g, 0.31 mmol, 1 equiv.) suspended in C_6D_6 (0.2 mL) was layered on top of the frozen solution and the NMR tube sealed. The sample was allowed to warm to ambient temperature and shaken to ensure mixing. A ^{1}H NMR spectrum revealed peaks consistent with **43** and a broad triplet at -0.17 ppm indicative of free ammonia.

GC: Gas chromatography analyses were performed using an Agilent 7890A GC system equipped with a thermal conductivity detector and an Agilent PoraPLOT Q GC column (25 m × 0.53 mm × 20 μm) under the following conditions: Front Inlet = 250 °C; Pressure = 7.7 psi; Flow = 140 mL/min; TCD temperature = 300 °C; Column Flow = 12 mL/min; Oven Temperature: 40 °C for 4 min, ramp 20 °C/min to 90 °C and then hold for 2 min.

Sample A: A 25 mL Schlenk flask was charged with **42** (0.150 g, 0.464 mmol), elemental sulfur (0.015 g, 0.468 mmol, 1.01 equiv.), and a stir bar. Through a septum, 5 mL of benzene was added and the mixture in the sealed flask was allowed to stir for 15 min at ambient temperature. Subsequently, 250 μL of the reaction headspace was removed via syringe and manually injected into the gas chromatograph. Comparison to an authentic sample of ammonia confirmed the presence of this compound in the headspace above the reaction mixture.

Sample B: A 10 mL Schlenk flask was charged with **42** (0.200 g, 0.618 mmol) and a stir bar. Through a septum, 5 mL of benzene was added and the solution stirred at ambient temperature for 2 h. Subsequently, 500 μL of the reaction headspace was removed via syringe and manually injected into the gas chromatograph. Comparison to an authentic sample of ammonia confirmed the presence of this compound in the headspace above the reaction mixture.

HRMS: Analyses of the headspace above the reaction mixtures described above for Sample A and Sample B using a Waters Micromass Autospec-Ultima (CI) mass spectrometer resulted in signals that corresponded to masses of 17.0265 Da and 17.0264 Da respectively, confirming the presence of ammonia in the corresponding headspaces of the aforementioned reaction mixtures (theoretical mass for NH_3 = 17.0265 Da).

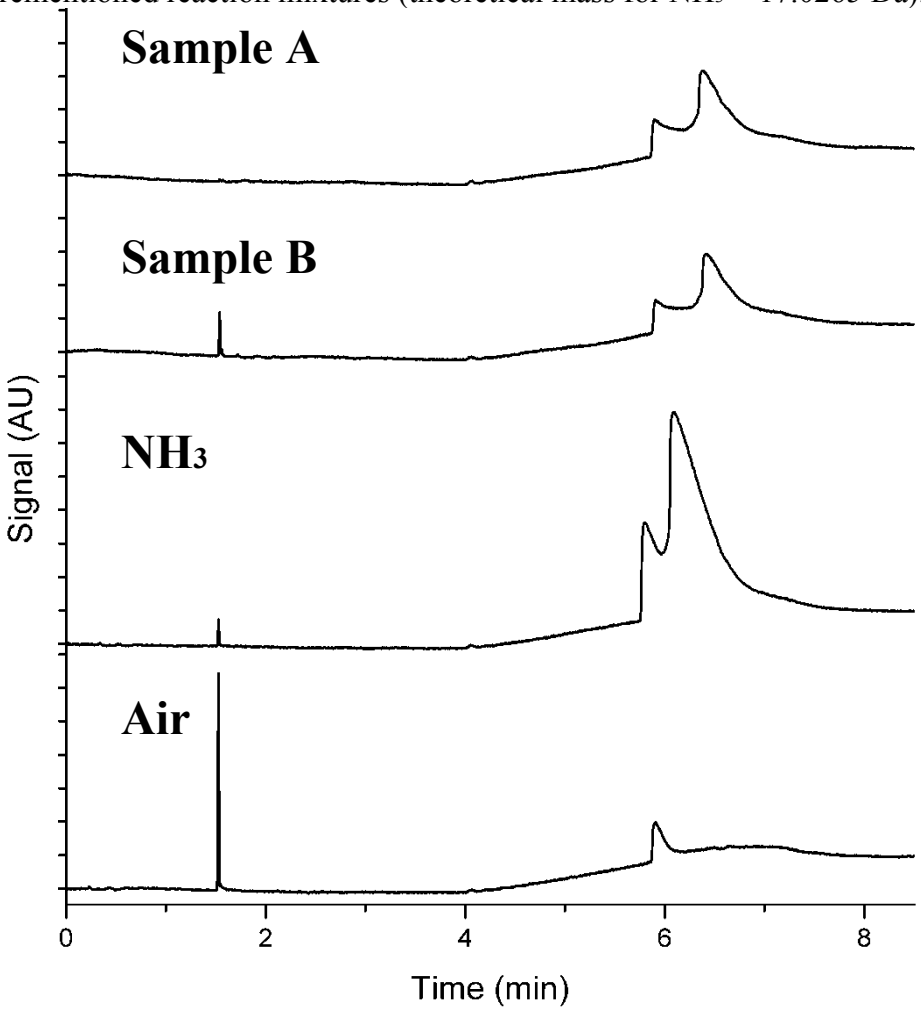


Figure A52: Stacked GC traces of the headspace following the reaction of **42** with elemental sulfur (Sample A), the headspace after stirring **42** in benzene for 2 h (Sample B), an authentic sample of ammonia, and the ambient atmosphere.

X-Ray Crystallography. Colorless, single crystals of **5** were obtained by the slow diffusion of pentane into a saturated benzene solution; this compound co-crystallized with a molecule of benzene in the monoclinic space group $P2_1/n$. Orange, single crystals of **8** were obtained by the slow diffusion of pentane into a saturated benzene solution; this compound crystallized in the monoclinic space group $P2_1/c$. Colorless, single crystals of **9** were obtained by the slow diffusion of pentane into a saturated benzene solution; this compound crystallized in the monoclinic space group $P2_1/c$. Crystallographic measurements were carried out on a Rigaku Mini CCD or Rigaku AFC-12 with Saturn 724+ CCD area detector diffractometer using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) at 120 K or 150 K using a Rigaku XStream low temperature device. A sample of suitable size and quality was selected and mounted onto a nylon loop. Data reductions were performed using CrystalClear. The structures were solved by direct methods which successfully located most of the non-hydrogen atoms. Subsequent refinements on F_2 using the SHELXTL/PC package (version 5.1) allowed the location of the remaining non-hydrogen atoms. Key details of the crystal and structure refinement data are summarized in Table A9. Additional crystallographic details may be found in the respective CIFs which were deposited at the Cambridge Crystallographic Data Centre, Cambridge, UK. The CCDC reference numbers for **5**, **8**, and **9** were assigned as 945042, 945043, and 945044, respectively.

	5·C_6H_6	**8**	**9**
Formula	$C_{42}H_{45}N_2O_2P$	$C_{24}H_{28}N_2O_2$	$C_{25}H_{30}N_2O_2$
M_r	640.77	376.48	390.51
crystal size (mm^3)	0.26× 0.16 × 0.15	0.21× 0.14 × 0.06	0.23 × 0.17 × 0.04
crystal system	Monoclinic	Monoclinic	Monoclinic
space group	$P2_1/n$	$P2_1/c$	$P2_1/c$
a (Å)	14.3562(8)	17.070(4)	8.441(7)
b (Å)	14.8127(8)	16.146(4)	16.218(13)
c (Å)	17.4328(9)	7.7572(17)	15.825(13)
α (°)	90	90	90
β (°)	110.316(2)	91.011(5)	96.725(13)
γ (°)	90	90	90
V ($Å^3$)	3476.5(3)	2137.5(8)	2151(3)
Z	4	4	4
ρ_{calc} (g cm^{-3})	1.224	1.170	1.206
μ (mm^{-1})	0.118	0.074	0.076
F(000)	1368	808	840
T (K)	120(2)	150(2)	150(2)
scan mode	ω	ω	ω
	-17 → 17	-20 → 20	-10 → 10
hkl range	-17 → 17	-19 → 19	-19 → 19
	-20 → 20	-9 → 9	-18 → 18
measd reflns	52626	18113	24428
unique reflns [R_{int}]	6108 [0.0502]	3710 [0.1031]	3780 [0.1297]
refinement reflns	6108	3710	3780
refined parameters	432	261	270
GOF on F^2	1.006	1.006	1.006
R1[a] (all data)	0.0425 (0.0451)	0.0942 (0.1198)	0.0889 (0.1377)
wR2 (all data)	0.1124 (0.1148)	0.2249 (0.2434)	0.2025 (0.2377)
ρ_{fin} (max/min) (e $Å^{-3}$)	1.245 -0.490	0.630 -0.277	0.244 -0.309

Table A9: Summary of the crystal data, data collection, and structure refinement details for **5**, **8**, and **9**. [a] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

CHAPTER 8: REDUCTIVE GENERATION OF STABLE FIVE-MEMBERED *N,N'*-DIAMIDOCARBENES

X-Ray Crystallography. Colorless, single crystals of **1a** were obtained by the slow diffusion of pentane into a concentrated benzene solution; this compound crystallized in the monoclinic $P2_1/c$ space group. Colorless, single crystals of **1b** were

obtained by the slow diffusion of pentane into a concentrated chloroform solution; this compound crystallized in the monoclinic $P2_1/c$ space group. Red-orange single crystals of **2a** were grown by cooling a concentrated pentane solution to -20 °C; this compound crystallized in the monoclinic $P2_1/n$ space group. Colorless, single crystals of **3** were obtained by the slow diffusion of pentane into a concentrated chloroform solution; this compound crystallized with two molecules of **3** in the asymmetric cell in the orthorhombic $P2_12_12_1$ space group. Colorless single crystals of **4** were obtained by the slow diffusion of pentane into a concentrated benzene solution; this compound crystallized in the monoclinic $P2_1$ space group. Colorless, single crystals of **5** were obtained by the slow diffusion of pentane into a saturated benzene solution; this compound crystallized with two molecules of **5** in the asymmetric cell in the monoclinic $P2_1/c$ space group. Colorless, single crystals of **7** were obtained by the slow diffusion of pentane into a benzene solution; two molecules of **7** co-crystallized with a solvent benzene molecule in the monoclinic $P2_1/c$ space group. Crystallographic measurements were carried out on a Rigaku Mini CCD, Enraf-Nonius Kappa CCD, or Rigaku AFC-12 with Saturn 724+ CCD area detector diffractometer using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) at 120 K or 150 K using an Oxford Cryostream low temperature device. A sample of suitable size and quality was selected and mounted onto a nylon loop. Data reductions were performed using DENZO-SMN. The structures were solved by direct methods which successfully located most of the non-hydrogen atoms. Subsequent refinements on F_2 using the SHELXTL/PC package (version 5.1) allowed the location of the remaining non-hydrogen atoms. Key details of the crystal and structure refinement data are summarized in Table A10-A11. Further crystallographic details may be found in the respective CIFs which were deposited at the Cambridge Crystallographic Data Centre, Cambridge, UK. The CCDC reference numbers for **1a**, **1b**, **2a**, **3**, **4**, **5**, and **7**

were assigned as 983770, 983771, 983772, 983773, 983774, 983775, and 983776, respectively.

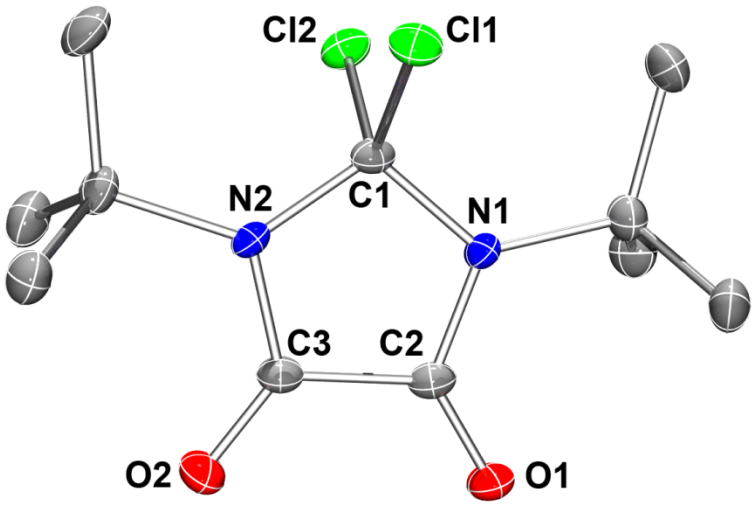


Figure A53: ORTEP diagram of **1a** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

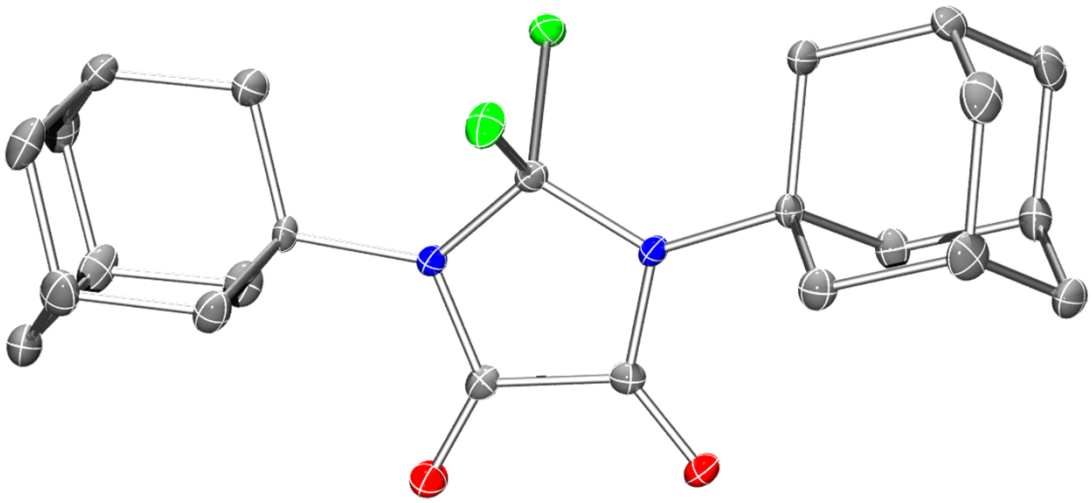


Figure A54: ORTEP diagram of **1b** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

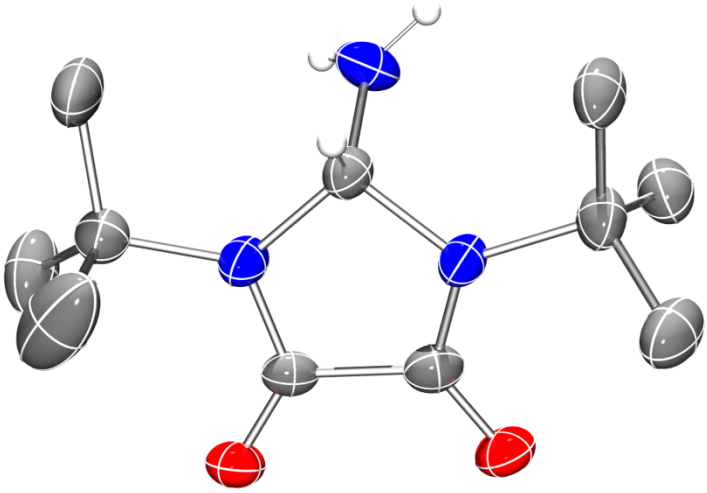


Figure A55: ORTEP diagram of **3** with thermal ellipsoids drawn at 50% probability and H-atoms, except at the nitrogens and carbenoid carbon, and a second molecule of **3** omitted for clarity.

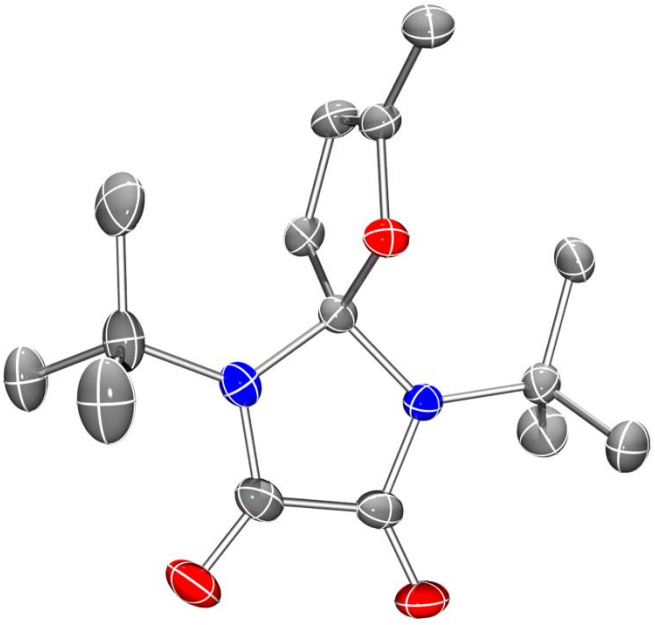


Figure A56: ORTEP diagram of **4** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity.

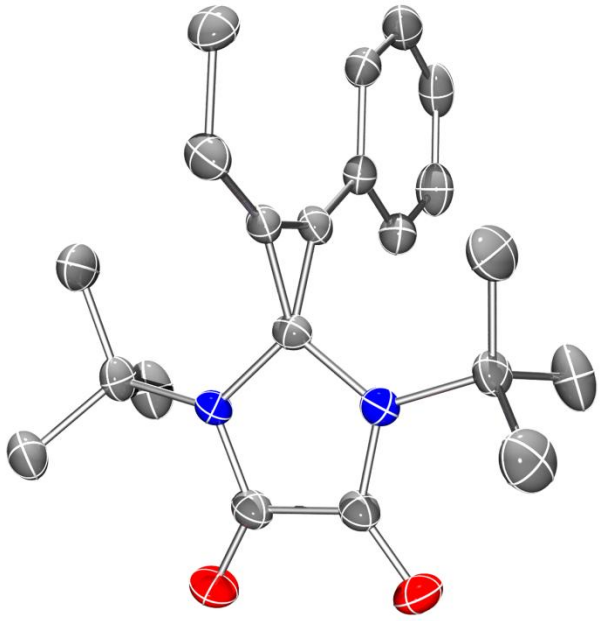


Figure A57: ORTEP diagram of **5** with thermal ellipsoids drawn at 50% probability and H-atoms and a second molecule of **5** omitted for clarity.

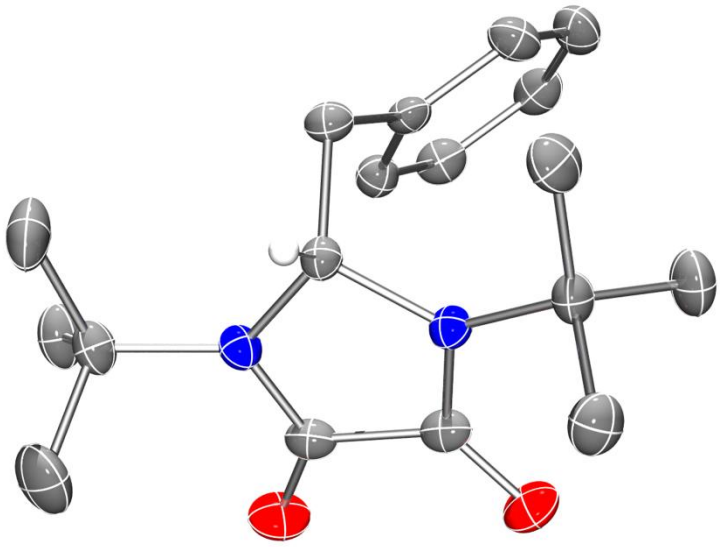


Figure A58: ORTEP diagram of **7** with thermal ellipsoids drawn at 50% probability and H-atoms, except at the carbenoid carbon, a second molecule of **7**, and a solvent benzene molecule omitted for clarity.

	1a	**1b**	**2a**	**3**
Formula	$C_{11}H_{18}Cl_2N_2O_2$	$C_{23}H_{30}Cl_2N_2O_2$	$C_{11}H_{18}N_2O_2$	$C_{11}H_{21}N_3O_2$
M_r	281.17	437.39	210.27	227.31
crystal size (mm^3)	0.14 × 0.09 × 0.08	0.29× 0.26 × 0.22	0.18 × 0.13 × 0.07	0.12 × 0.07 × 0.04
crystal system	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
space group	$P2_1/c$	$P2_1/c$	$P2_1/n$	$P2_12_12_1$
a (Å)	8.3148(19)	14.331(4)	13.3310(12)	9.102(3)
b (Å)	14.215(3)	11.335(4)	5.9383(5)	12.188(4)
c (Å)	11.639(3)	12.768(4)	15.6507(14)	23.505(8)
α (°)	90	90	90	90
β (°)	99.688(5)	103.063(6)	105.521(3)	90
γ (°)	90	90	90	90
V ($Å^3$)	1356.1(5)	2020.3(11)	1193.78(18)	2607.5(16)
Z	4	4	4	8
ρ_{calc} ($g\ cm^{-3}$)	1.377	1.438	1.170	1.158
μ (mm^{-1})	0.471	0.345	0.081	0.081
F(000)	592	928	456	992
T (K)	120(2)	120(2)	120(2)	150(2)
scan mode	ω	ω	ω	ω
hkl range	-9 → 9 -16 → 16 -13 → 13	-16 → 17 -13 → 13 -15 → 15	-15 → 15 -7 → 6 -18 → 18	-10 → 10 -14 → 14 -27 → 27
measd reflns	19296	13343	11792	34428
unique reflns [R_{int}]	2373[0.0989]	3550 [0.0356]	2089 [0.0416]	4584[0.0919]
refinement reflns	2373	3550	2089	4584
refined parameters	160	262	142	301
GOF on F^2	1.006	1.006	1.006	1.006
R1[a] (all data)	0.0449 (0.0598)	0.0366 (0.0937)	0.0452 (0.0546)	0.0851 (0.0897)
wR2 (all data)	0.0982 (0.1055)	0.0393 (0.0958)	0.1137 (0.1211)	0.1985 (0.2025)
ρ_{fin} (max/min) ($e\ Å^{-3}$)	0.307 -0.261	0.506 -0.299	0.305 -0.187	0.337 -0.336

Table A10: Summary of crystal data, data collection, and structure refinement details for **1a**, **1b**, **2a**, and **3**. [a] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

	4	**5**	**7**·C_6H_6
Formula	$C_{15}H_{24}N_2O_3$	$C_{21}H_{28}N_2O_2$	$C_{42}H_{58}N_4O_4$
M_r	280.36	340.45	682.92
crystal size (mm^3)	0.26 × 0.24 × 0.07	0.14 × 0.09 × 0.05	0.31 × 0.26 × 0.23
crystal system	Monoclinic	Monoclinic	Monoclinic
space group	$P2_1$	$P2_1/c$	$P2_1/c$
a (Å)	6.1949(2)	9.1753(6)	17.9469(10)
b (Å)	13.0960(3)	22.7039(14)	17.5630(8)
c (Å)	9.5555(3)	18.5417(13)	12.2414(7)
α (°)	90	90	90
β (°)	93.800(2)	97.125(5)	90.152(2)
γ (°)	90	90	90
V ($Å^3$)	773.52(4)	3832.7(4)	3858.5(4)
Z	2	8	4
ρ_{calc} (g cm^{-3})	1.204	1.180	1.176
μ (mm^{-1})	0.084	0.076	0.075
F(000)	304	1472	1480
T (K)	150(2)	120(2)	120(2)
scan mode	ω	ω	ω
hkl range	-7 → 7 -15 → 15 -11 → 11	-10 → 10 -27 → 27 -22 → 22	-21 → 19 -14 → 20 -13 → 14
measd reflns	20735	144570	18906
unique reflns [R_{int}]	2727 [0.0346]	6729 [0.2417]	6694[0.0313]
refinement reflns	2727	6729	6694
refined parameters	188	465	463
GOF on F^2	1.006	1.006	1.006
R1[a] (all data)	0.0285 (0.0303)	0.0594 (0.1175)	0.0422 (0.0986)
wR2 (all data)	0.0781 (0.0798)	0.1462 (0.1648)	0.0590 (0.1113)
ρ_{fin} (max/min) (e $Å^{-3}$)	0.197 -0.217	0.224 -0.335	0.263 -0.256

Table A11: Summary of crystal data, data collection, and structure refinement details for **4**, **5**, and **7**.[a] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

Appendix B: Olefin Metathesis Catalysts Containing *N,N′*-Diamidocarbenes*

B1. Introduction

Previously, we discovered that *N,N′*-diamidocarbenes (DACs), such as **1** (Figure B1), exhibit a unique combination of electrophilic and nucleophilic characteristics similar to the alkylamino carbenes pioneered by Bertrand).[1-5] For example, DACs were found to display reactivities typical of nucleophilic *N*-heterocyclic carbenes (NHCs),[6-8] including the ability to coordinate to various transition metals and condense with electrophilic agents, such as CS_2.[1] However, the DACs were also found to facilitate reactions atypical of NHCs, including ammonia N–H[2] and intramolecular C–H activation,[1] reversible coupling with carbon monoxide,[1,2] and irreversible coupling with isocyanides.[2,3] Beyond their unique reactivity, DACs have been calculated from their respective $[M(CO)_2Cl]$ complexes (M = Ir or Rh)[1,9] to display unusually high Tolman electronic parameters (2056 – 2057 cm^{-1}) suggesting that these ligands are relatively weak donors compared to prototypical NHCs, such as 1,3-dimesitylimidazol-2-ylidene (2051 cm^{-1}) or 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene (SIMes; 2052 cm^{-1}), and similar to tricyclohexylphosphine (PCy_3) (2056 cm^{-1}).[10] Since Grubbs-type Ru olefin metathesis catalysts[11,12] are well-known to be strongly influenced by the donating abilities of their ligands,[13,14] one may predict that (DAC)(L)Cl_2Ru=CHPh type complexes (L = phosphine or pyridine) should exhibit catalytic activities similar to that of (PCy_3)(L)Cl_2Ru=CHPh type complexes. However, as described herein, we found that such DAC-supported complexes exhibit high catalytic activities and relatively broad reactivities, particularly

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compared to phosphine-containing complexes as well as those supported by 1,3-dimesityl-4,5-tetrahydropyrimidin-2-ylidene (**2**), a saturated and strongly donating analogue of **1**.[15]

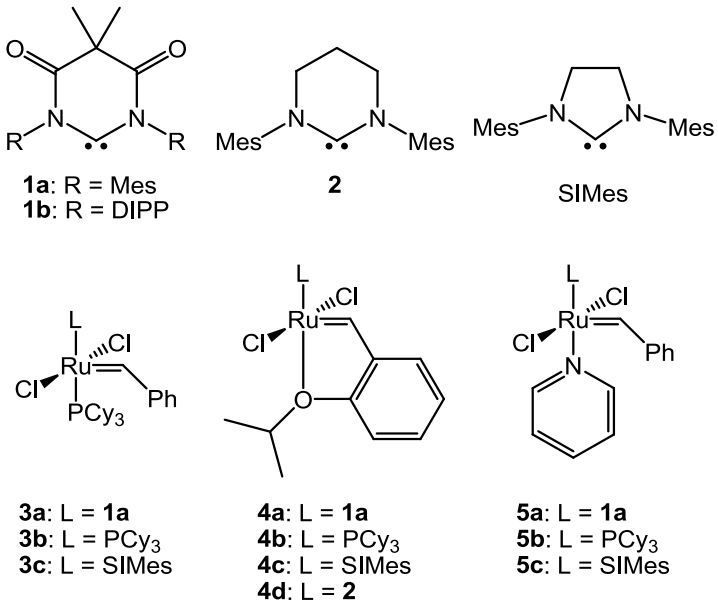


Figure B1: Structures of various *N,N′*-diamidocarbenes (DACs) (**1**), 1,3-dimesityl-3,4,5,6-tetrahydropyrimidin-2-ylidene (**2**), and Ru complexes which contain these ligands (**3** – **5**). SIMes = 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene (shown). Mes = 2,4,6-trimethylphenyl. DIPP = 2,6-diisopropylphenyl. Cy = cyclohexyl.

B2. Results and Discussion

Initial efforts were focused on the synthesis of (**1a**)(PCy_3)Cl_2Ru=CHPh (**3a**). Treatment of **1a**, as its stable free carbene,[2] with (PCy_3)$_2Cl_2$Ru=CHPh (**3b**) (0.67 equiv) for 4 h in C_6D_6 at ambient temperature generated new NMR spectroscopic signals that were consistent with the desired product.[16] However, the isolation of this complex was challenged by its high solubility in organic solvents and decomposition upon exposure to either silica or alumina. Considering that Hoveyda-Grubbs-type complexes often exhibit relatively high stabilities and may be conveniently isolated using chromatographic

techniques,[17] efforts shifted toward the synthesis of **4a**. Treatment of **4b** with **1a** (1.2 equiv) for 5 h in benzene at ambient temperature followed by purification via silica gel chromatography (eluent = 2:1 v/v hexanes/ethyl acetate) afforded **4a** in 48% yield as a crystalline solid. The complex exhibited a ^{1}H NMR signal at δ = 15.55 ppm (C_6D_6) that was diagnostic of a benzylidene moiety, though the signal was observed at a frequency that was upfield compared to analogous complexes reported in the literature (15.9 – 17.5 ppm),[18-23] which may be attributed to increased steric shielding on account of the DAC's wide N–C–N bond angle (vide infra). The ^{13}C NMR resonance assigned to the DAC's carbene nucleus (δ = 312.3 ppm; C_6D_6) was observed at a frequency that was downfield compared to related NHC complexes (287.5 – 298.3 ppm),[18-23] presumably due to the DAC's relatively electron deficient character. IR spectroscopy revealed that **4a** exhibited two carbonyl stretching frequencies (ν_{CO}) at 1707.6 and 1733.9 cm^{-1} (KBr) which were ascribed to ketone-like functionality based on the analogous values recorded for a related six-membered bisamide, 1,3-di-*p*-tolyldihydropyrimidine-4,6-dione (1690 cm^{-1}),[24] and 2,2-dimethyl-1,3-cyclohexanedione (1702 and 1730 cm^{-1}).[25]

Additional structural support for **4a** was obtained via X-ray diffraction analysis of single crystals grown from the slow diffusion of pentane into a saturated benzene solution. As shown in Figure B2 (left), the complex adopted a square-pyramidal geometry with an apically positioned alkylidene moiety. Inequivalent N–C_{acyl} and O–C_{acyl} distances (1.422(7) versus 1.403(7) Å and 1.197(7) versus 1.206(7) Å, respectively) were measured, and the C1–Ru distance (1.938(5) Å) in **4a** was measured to be significantly shorter than the corresponding distances in **4d** (2.048(6) Å) (see Figure B2; right), a saturated analogue of **4a**, and SIMes supported **4c** (1.981(5) Å; structure not shown).[26] The contracted bond distance was consistent with the formation of increased multiple-bond character, potentially due to π-backbonding[27] on account of the DAC's relatively

low-lying LUMO[3] although coulombic attractions between the metal center and relatively electron deficient carbene may also be important contributors.

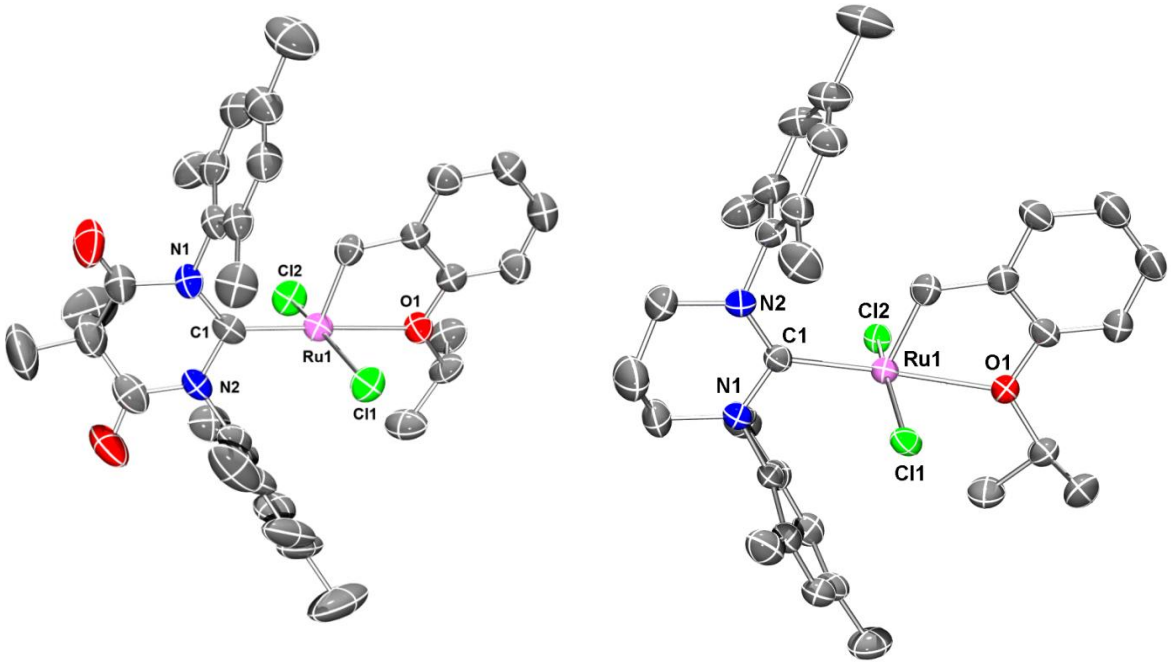


Figure B2: (left) ORTEP diagram of **4a** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): Ru1–C1, 1.938(5); Ru1–O1, 2.297(3); N1–C1–N2, 114.4(4); C1–Ru1–Cl1, 101.39(15); C1–Ru1–Cl2, 89.97(14). (right) ORTEP diagram of **4d** with thermal ellipsoids drawn at 50% probability and H-atoms omitted for clarity. Selected distances (Å) and angles (deg): Ru1–C1, 2.048(6); Ru1–O1, 2.357(4); N1–C1–N2, 113.8(5); C1–Ru1–Cl1, 92.26(16); C1–Ru1–Cl2, 96.49(16).

Efforts were also directed toward the synthesis of **5a**, as Ru complexes containing pyridine ligands are known to initiate olefin metathesis reactions at relatively low temperatures.[28] Generation of **3a** in situ via the method described above followed by dilution with pentane and addition of excess pyridine (200 equiv.) resulted in the precipitation of the desired complex as a brown solid, which was collected via filtration in 41% isolated yield. Whereas hexacoordinate Ru complexes bearing two pyridine

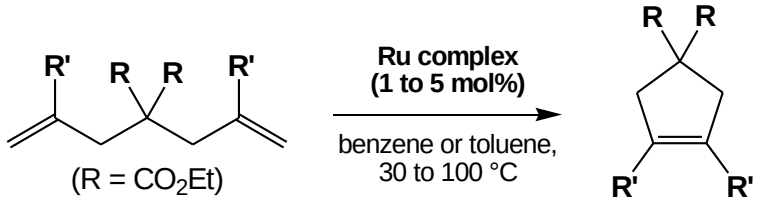
ligands are often obtained under similar conditions,[28,29] complex **5a** featured only one pyridine ligand[30] in solution, as determined by ^{1}H NMR spectroscopy, as well as in the solid state (see Figure B6). The carbonyl stretching frequencies recorded for this complex (1710.6 and 1735.2 cm^{-1}; KBr) were higher than those recorded for **4a**, consistent with an increased donation from the nitrogen atoms on the DAC to the metal center as a means to compensate for the weakly donating pyridine ligand.

Upon the synthesis and characterization of **4a** and **5a**, efforts were directed toward comparing their catalytic activities with other complexes in a variety of ring-closing metathesis (RCM) reactions (Scheme B1). Using modified literature procedures,[31] the conversion of diethyldiallyl malonate (**6**) to its respective cyclic olefin (**7**) was monitored via ^{1}H NMR spectroscopy using 1 mol% catalyst loading at various temperatures. As summarized in Table B1, complex **4a** facilitated an 83% conversion of **6** to **7** after 20 h at 30 °C, although significantly enhanced activity was observed when the same reaction was repeated at 60 °C where an 85% conversion was measured after 20 min. Similarly, complex **4d**, which contained a saturated NHC analogue of the DAC ligand, slowly converted **6** to **7** at room temperature but exhibited significantly enhanced catalytic activity at 60 °C (e.g., 74% conversion after 30 min) under otherwise identical reaction conditions. To better compare the catalytic activities exhibited by **4a** and **4d**, the conversion of **6** to **7** was monitored over time by ^{1}H NMR spectroscopy (C_6D_6) at 45 °C using a 1 mol% loading of the aforementioned complexes (see Figure B4, B9). The pseudo-first order rate constant measured for the RCM reaction catalyzed by **4a** (k_{obs} = 0.031 s^{-1}) was nearly four times greater than the analogous reaction catalyzed by **4d** (k_{obs} = 0.007 s^{-1}). Moreover, the former catalyst afforded a significantly higher yield of product after 75 min than the latter (88% vs 48%, respectively). However, the phosphine complex **4b** displayed improved activity (k_{obs} = 0.133 s^{-1}; 95% conversion after 30 min) over **4a**

under identical conditions. Similarly, the catalytic activities of phosphine complex **3b** and SIMes-supported complexes **3c** and **4c** were also measured to be greater than that of **4a**. While **5a** afforded a 60% conversion of **6** to **7** after only 10 min at 60 °C, presumably due to an enhanced initiation rate, high conversions were not observed as the corresponding catalyst may suffer from premature decomposition over the course of the reaction.

Next, our efforts shifted toward exploring the abilities of the aforementioned catalysts to facilitate the RCM of diethyldimethallyl malonate (**8**) to its respective tetrasubstituted olefin **9**, a relatively challenging reaction.[11d] As summarized in Table B1, a 29% conversion was measured after 20 h at 100 °C in toluene when **4a** (5 mol%) was used as the catalyst. Slightly lower activity was observed when **4d** was utilized as the catalyst as a 19% conversion was measured after 24 h under otherwise identical conditions. The phosphine catalysts **3b** and **4b** did not facilitate the conversion of **8** to product, even over extended periods of time at 100 °C, whereas the SIMes-supported catalyst **4c** exhibited a significantly higher activity than the other complexes studied, as expected.[31]

Collectively, these RCM results were surprising: based on the TEP values, the DAC-containing complexes were expected to exhibit similar catalytic activities as their PCy_3 analogues; yet, the latter appeared to convert **6** to **7** at higher rates under otherwise identical conditions. While these activity differences may be rationalized by initiation phenomena, the DAC- and NHC-supported complexes were found to be more reactive and capable of converting **8** to **9**. More unexpectedly, the DAC containing complex **4a** was more active than its NHC analogue **4d**, even though the TEP measured for DAC **1a** was significantly higher than that measured for **2** (2056 versus 2035 cm^{-1}, respectively).



6 R' = H
8 R' = Me

7 R' = H
9 R' = Me

Scheme B1: The RCM of **6** and **8** to their corresponding cyclic olefins **7** and **9**, respectively.

Complex	Temp. (°C)	% Conversion of 6 to 7 (time)[a]	Temp. (°C)	% Conversion of 8 to 9 (time)[b]
3b	30	53 (30 min)	100	NC
3c	30	97 (30 min)	100	26 (1 h)
4a	30	10 (30 min)	100	29 (20 h)
	30	83 (20 h)		
	45	88 (75 min)		
	60	85 (20 min)		
4b	30	69 (30 min)	100	NC
	45	95 (30 min)		
4c	30	98 (30 min)	100	64 (1 h)
4d	30	11 (30 min)	100	19 (24 h)
	30	15 (20 h)		
	45	48 (75 min)		
	60	74 (30 min)		
5a	30	21 (30 min)	100	3 (4 d)
	60	60 (10 min)		

Table B1: Summary of the various RCM reactions investigated. [a]Performed in C_6D_6 using a 1 mol% catalyst loading. [b] Performed in C_7D_8 using a 5 mol% catalyst loading. NC = no conversion was observed by ^{1}H NMR spectroscopy.

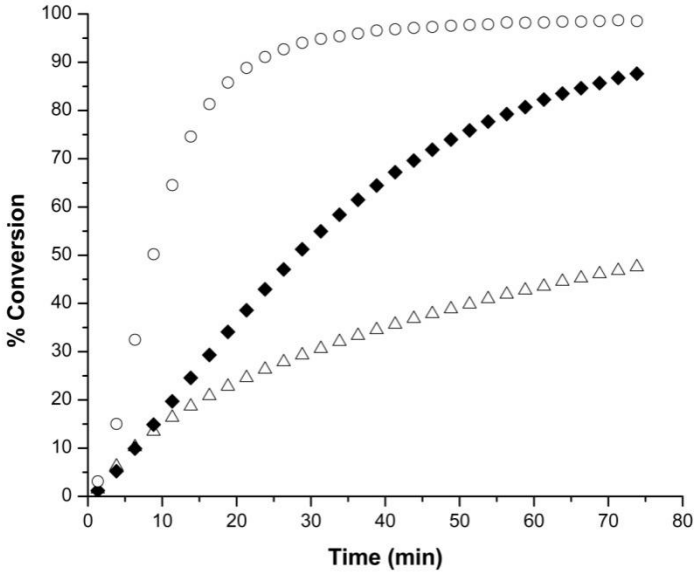


Figure B3: Conversion to the disubstituted olefin product **7** using **4a** (solid diamonds), **4b** (open circles), and **4d** (open triangles). Conversion was determined by ^{1}H NMR. Every fifth data point is plotted for visual clarity.

Despite its common utilization for the quantification of NHC electron donating ability, the TEP scale is an indirect measure of ligand donicity as it relies on the measurement of the ν_{CO} exhibited by $LM(CO)_2Cl$ complexes (M = Ni, Rh or Ir).[32] To obtain a direct measurement of the electronic state of the metal center for the aforementioned complexes and to gain greater insight into how their electronic properties may be influencing their respective catalytic activities, a series of cyclic voltammetry (CV) and differential pulse voltammetry (DPV) experiments were performed (see B5 and Figures B11 – B36).[19,33] The redox processes associated with each complex analyzed were found to be quasi-reversible in CH_2Cl_2, except for **3b**, **5b**,[29] and **5c**[29] which were irreversible.[34] Although **3a** could not be isolated, the complex was generated in situ and measured to exhibit an anodic peak potential (E_{pa}) of 0.99 V, which was >300 mV higher

than the E_{pa} measured for its phosphine analogue **3b** (0.63 V). Likewise, **4a** also underwent oxidation at significantly higher potential than **4b** as did **5a** when compared to **5b**. These data conflict with the TEP values measured for the DAC and phosphine ligands of these complexes: the TEP values indicate that the respective Ru centers exhibit similar electronic properties whereas the electrochemical data reveal that they are significantly different.[35] In contrast, the E_{pa} values measured for **4c**, **4d** and **5c** were significantly lower (up to 0.5 V) than **4a** and **5a** respectively, consistent with the TEP-derived donicities of DACs compared to NHCs.

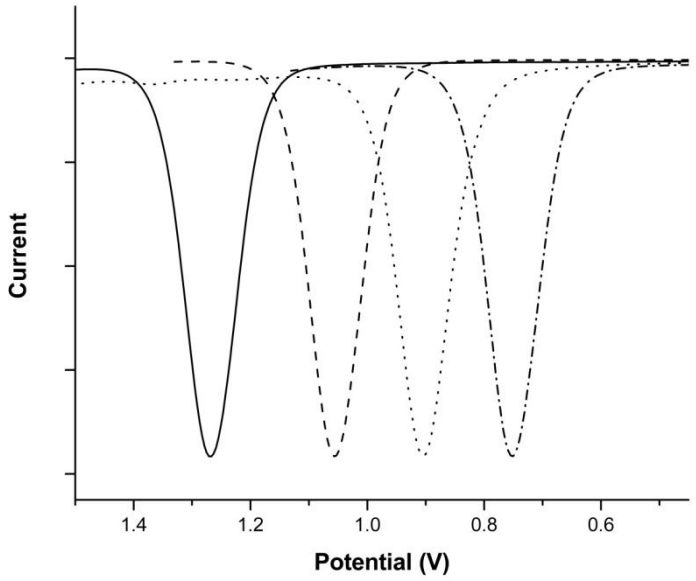


Figure B4: Normalized differential pulse voltammograms of **4a** (solid), **4b** (dash), **4c** (dot), and **4d** (dash-dot). Measurements were performed in CH_2Cl_2 containing 0.1 M $[Bu_4N][PF_6]$ at 100 mV s^{-1} scan rate and were referenced to decamethylferrocene (Fc*) (internal standard adjusted to –0.057 V vs SCE).[36]

Complex	E_{pa} (V)[a]	TEP (cm^{-1})[b]
3a	0.99	2056
3b	0.63	2056
3c	0.51	2052
4a	1.27	2056
4b	1.06	2056
4c	0.90	2052
4d	0.75	2035
5a	1.01	2056
5b	0.80	2056
5c	0.68	2052

Table B2: Summary of oxidation potentials and TEP values. [a]Measurements were performed in CH_2Cl_2 containing 0.1 M $[Bu_4N][PF_6]$ at 100 mV s^{-1} scan rate and were referenced to decamethylferrocene (Fc*) (internal standard adjusted to –0.057 V vs SCE).[36] Complexes **3b**, **5b**, and **5c** exhibited irreversible oxidation processes whereas all the other complexes studied exhibited quasi-reversible oxidation processes. [b] The Tolman electronic parameter of **1a** was calculated using Nolan's method[10] from its respective Ir carbonyl complexes as was **2** after converting the carbonyl stretching frequencies of the known Rh analogue[15] to the Ir scale using the following equation: $\nu_{av}(CO)Ir = 0.8695 \times \nu_{av}(CO)Rh + 250.7\ cm^{-1}$.[37] The TEP values of PCy_3 and SIMes were obtained from their literature values.[10]

Considering no general correlations were observed between either (1) the E_{pa} values of these complexes and the TEP values of their respective ligands or (2) the E_{pa} values of these complexes and their catalytic activities, we reasoned that sterics may play a relatively large role in governing the activities exhibited by these Ru-type olefin metathesis catalysts.[38] To investigate, the steric properties associated with the aforementioned phosphine, NHC, and DAC ligands were quantified by measuring the

respective ligand's percent buried volume (%V_{bur}) from the crystallographic data[39-41] of complexes **4** using methods described by Nolan and Cavallo.[42] Consistent with their relatively wide N–C–N bond angles (113.8 – 114.4°), the six-membered **1a** (37.8%) and **2** (38.1%) exhibited the largest %V_{bur} values of the ligands studied and were similar in magnitude. The relatively large sizes of the aforementioned ligands may account for the slower catalytic rates exhibited by **4a** and **4d** as compared to **4c** which features a relatively small five-membered NHC ligand (%V_{bur} = 33.7%).[41] Consistent with this analysis, catalysts containing PCy_3 (%V_{bur} = 37.1%)[41] were also more active than **4a** and **4d** in the conversion of **6** to **7**.[43-45] While ligand size may inversely correlate with catalytic activity in certain reactions, it does not explain the unusual reactivities displayed by **4a**. Despite being a weak donor, the DAC ligand in **4a** may enhance the metal's affinity toward olefins, particularly compared to its phosphine based analogue (*i.e.*, **4b**), and facilitate the RCM of **8**.[46,47] However, considering that **4a** and **4d** exhibited significantly different electronic properties, we conclude that the comparable catalytic activities displayed by these two complexes were largely due to the unique steric constraints imposed by their similarly sized NHC and DAC ligands, respectively.[48,49]

B3. CONCLUSIONS

In sum, we report the synthesis and characterization of the first olefin metathesis complexes containing DACs and evaluate their catalytic activities in various ring-closing metathesis reactions. While the DACs exhibit similar TEP values as PCy_3, the Ru complexes containing the former effected the RCM of diethyldiallyl malonate at a relatively slow rate. However, unlike the phosphine complexes, the DAC-supported complexes were found to be capable of catalyzing the RCM of diethyldimethallyl malonate to its respective tetrasubstituted olefin, a result that effectively expands the

limited range of catalysts known to facilitate this challenging reaction.[11d] Although the DAC was found to be a significantly weaker donor than a saturated NHC analogue, as determined by a series of IR and electrochemical measurements, a Ru complex containing the former ligand was found to exhibit only slightly higher catalytic activities in various RCM reactions than an analogous complex containing the latter. The comparable performances of these catalysts were attributed to the similar steric properties of the two aforementioned DAC and NHC ligands.

B4. EXPERIMENTAL

General Considerations. All procedures were performed using standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen-filled glove box unless otherwise noted. The following compounds were synthesized according to literature procedures: 2-chloro-1,3-dimesityl-4,6-diketo-5,5-dimethylpyrimidine,[2] *N,N′*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (**1a**),[2] *N,N′*-bis(2,6-di-isopropylphenyl)-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (**1b**),[1] *N,N*'-dimesityl-3,4,5,6-tetrahydropyrimidin-1-ium bromide,[50] (pyridine)(tricyclohexylphosphine)Cl_2RuCHPh (**5b**),[29] (pyridine)(1,3-dimesityl-4,5-dihydroimidazole-2-ylidene)Cl_2RuCHPh (**5c**),[29] diethyldimethallyl malonate (**8**),[51] and chloro(1,5-cyclooctadiene)iridium(I) dimer. The complexes **3b**, **3c**, **4b**, and **4c** were generously donated by Materia, Inc. and used as received. Pyridine was purchased from Fisher, diethyldiallyl malonate (**6**) from Sigma-Aldrich, and sodium bis(trimethylsilyl)amide (NaHMDS) from Acros and used as received. Pentane and benzene were dried over 3Å molecular sieves and distilled prior to use. Dichloromethane (CH_2Cl_2) and hexanes were dried and degassed by a Vacuum Atmospheres Company solvent purification system (model number 103991-0319) and

stored over molecular sieves in a nitrogen-filled glove box. Electrochemical experiments were performed on a Series 660D CH Instruments Electrochemical Workstation using a gas-tight, three-electrode cell under an atmosphere of dry nitrogen. The cell was equipped with gold working, tungsten counter, and silver quasi-reference electrodes. The electrochemical measurements were performed in dry CH_2Cl_2 with 0.1 M [tetra-*n*-butylammonium][PF_6] (TBAP) as the electrolyte and decamethylferrocene (Fc*) as the internal standard. All potentials were measured at 100 mV s^{-1} scan rates and referenced to saturated calomel electrode (SCE) by shifting $(Fc^*)^{0/+}$ to –0.057 V.[36] Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrophotometer. High resolution mass spectra (HRMS) were obtained with a VG analytical ZAB2-E instrument (CI or ESI). NMR spectra were recorded on Varian Unity+ 300, Varian Mercury 400, or Varian Inova 500. Chemical shifts (δ) are given in ppm and are referenced to the residual solvent (^{1}H: $CDCl_3$, 7.24 ppm; C_6D_6, 7.15 ppm; ^{13}C: $CDCl_3$, 77.0 ppm; C_6D_6, 128.0 ppm). Elemental analyses were performed at Midwest Microlab, LLC (Indianapolis, IN). Melting points were obtained using a Mel-Temp apparatus and are uncorrected.

Synthesis of (*N*,*N*′-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene)Cl_2Ru=CH(*o*-^{i}Pr-Ph) (4a). An 8 mL vial was charged with a stir bar, **4b** (0.200 g, 0.333 mmol, 1 equiv), **1a** (0.150 g, 0.398 mmol, 1.2 equiv), and benzene (5 mL). After stirring the resulting mixture at ambient temperature for 5 h, the residual solvent was removed under reduced pressure. The resultant solid was purified via column chromatography using silica gel as the stationary media and a 2:1 v/v hexanes/ethyl acetate solution as the eluent. Removal of residual solvent under reduced pressure afforded the desired compound as a brown solid (0.111 g, 0.159 mmol, 48% yield). Single crystals suitable for X-ray diffraction analysis were grown via the slow diffusion of pentane into a benzene solution saturated with **4a**. mp = 206–208 °C (decomp.) IR

(KBr): ν_{CO} = 1707.6, 1733.9 cm^{-1}. ^{1}H NMR (C_6D_6, 300.14 MHz): δ 1.03 (d, J = 6.0 Hz, 6H, $CH(CH_3)_2$), 1.64 (s, 6H, Ar-CH_3), 2.14 (s, 3H, CCH_3), 2.16 (s, 3H, CCH_3), 2.31 (s, 6H, Ar-CH_3), 2.63 (s, 6H, Ar-CH_3), 4.42 (sept, J = 6.15 Hz, 1H, $CH(CH_3)_2$), 6.27 (d, J = 8.1 Hz, 1H), 6.60 (t, J = 7.5 Hz, 1H), 6.76 (s, 2H), 6.91 (s, 2H), 6.94 (d, J = 7.5 Hz, 1H), 15.55 (s, 1H, Ru=C*H*-Ar). ^{13}C NMR (C_6D_6, 125.60 MHz): δ 18.87, 20.97, 21.07, 21.53, 21.66, 24.97, 30.17, 49.47, 76.00, 113.34, 121.93, 124.57, 130.32, 133.11, 138.02, 138.79, 139.43, 141.10, 143.21, 145.89, 153.38, 166.76, 168.04, 240.96, 312.34 (d, 18.21 Hz). HRMS $[M]^+$ (CI): Calcd. for $C_{34}H_{40}N_2O_3Cl_2Ru$: 696.1459. Found: 696.1466. Anal. Calcd. for $C_{34}H_{40}N_2O_3Cl_2Ru$: C, 58.62; H, 5.79; N, 4.02. Found: C, 59.12; H, 6.16; N, 4.27.

Synthesis of (*N,N′*-dimesityl-3,4,5,6-tetrahydropyrimidin-2-ylidene)Cl_2Ru=CH(*o*-^{i}Pr-Ph) (4d). An 8 mL vial was charged with a stir bar, *N,N′*-dimesityl-3,4,5,6-tetrahydropyrimidin-1-ium bromide (0.050 g, 0.125 mmol, 1.3 equiv), sodium hexamethyldisilazide (0.025 g, 0.134 mmol, 1.4 equiv), and C_6D_6 (1 mL). The complex **4b** (0.058 g, 0.096 mmol) was added after stirring the aforementioned mixture at ambient temperature for 30 min and filtering through a PTFE filter. The resulting mixture was then stirred for an additional 16 h at ambient temperature. A green precipitate formed, which was collected via filtration and washed with hexanes (2 × 0.5 mL). Subsequent removal of residual solvent under reduced pressure afforded the desired compound as a green solid (0.046 g, 0.072 mmol, 75% yield). Single crystals suitable for X-ray diffraction analysis were grown from the slow diffusion of pentane into a benzene solution saturated with **4b**. mp = 200-201 °C (decomp.) IR (KBr): 2965.8, 2901.8, 1481.1, 1274.2 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300.14 MHz): δ 1.03 (d, J = 6.00 Hz, 6H, $CH(CH_3)_2$), 2.31 (s, 12 H, Ar-CH_3), 2.45 (s, 2H, $CH_2CH_2CH_2$), 2.56 (s, 6H, Ar-CH_3), 3.61 (t, J = 5.80 Hz, 4H, NCH_2CH_2), 4.70 (sept, J = 6.00 Hz, 1H, $CH(CH_3)_2$), 6.67 (d, J = 8.01

Hz, 1H, Ar-*H*), 6.81 (t, J = 7.40 Hz, 1H, Ar-*H*), 6.93 (dd, J = 1.60 Hz, 7.61 Hz, 1H, Ar-*H*), 7.02 (s, 2H, Ar-*H*), 7.06 (s, 2H, Ar-*H*), 7.47 (dt, J = 1.2 Hz, 7.40 Hz), 16.46 (s, 1H, Ru=C*H*). ^{13}C NMR ($CDCl_3$, 125.71 MHz): δ 18.40, 20.96, 21.10, 21.15, 21.42, 21.89, 49.84, 49.96, 74.19, 112.95, 122.19, 122.89, 129.52, 129.56, 129.85, 137.14, 137.21, 137.93, 139.37, 141.46, 144.67, 146.59, 146.61, 151.36, 203.75, 303.35. HRMS [M – Cl]$^+$ (ESI): Calcd. for $C_{34}H_{40}N_2OClRu$: 605.1873. Found: 605.1872. Anal. Calcd for $C_{34}H_{40}N_2OCl_2Ru$: C, 59.99; H, 6.29; N 4.37. Found: C, 59.78; H, 5.96; N, 3.90.

Synthesis of (Pyridine)(*N,N′*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene)Cl_2Ru=CHPh (5a). An 8 mL vial was charged with a stir bar, 2-chloro-1,3-dimesityl-4,6-diketo-5,5-dimethylpyrimidine (75 mg, 0.182 mmol, 1.5 equiv), sodium hexamethyldisilazide (0.035 g, 0.191 mmol, 1.6 equiv), benzene (2 mL), and a stir bar. The solution was stirred for 1 h at ambient temperature and then filtered through a PTFE filter into an 8 mL vial that was previous charged with **3b** (0.100 g, 0.122 mmol, 1 equiv) and a stir bar. After stirring the resulting mixture for 2 h at ambient temperature, 40 mL of pentane and 2 mL pyridine (1.964 g, 24.8 mmol, 203 equiv) were added. A brown precipitate formed after 2 h of additional stirring at ambient temperature. The supernatant was decanted and the residual solid washed with pentane until the supernatant was clear. Removal of residual solvent under reduced pressure afforded the desired compound as a brown solid (0.036 g, 0.050 mmol, 41% yield). Single crystals suitable for X-ray diffraction analysis were grown by the slow diffusion of hexanes into a toluene solution saturated with **5a**. mp = 191–193 °C (decomp.) IR (KBr): ν_{CO} = 1710.6, 1735.2 cm^{-1}. ^{1}H NMR (C_6D_6, 400.27 MHz): δ 1.67 (s, 6H, Ar-CH_3), 1.96 (s, 3H, CCH_3), 2.02 (s, 3H,CCH_3), 2.40 (s, 6H, Ar-CH_3), 2.71 (s, 6H, Ar-CH_3), 6.19 (t, J = 7.2 Hz, 2H, Ar-H), 6.55 (s, 2H, Ar-H), 6.55 (m overlapping with singlet, 1H, Ar-H), 6.78 (s, 2H, Ar-H), 6.85 (t, J = 7.8 Hz, 2H, Ar-H), 7.11 (m overlapping solvent, 1H, Ar-*H*), 7.95 (d of d, J = 6.4

Hz, 2H, Ar-H), 8.01 (d, J = 7.2 Hz, 2H, Ar-H), 19.01 (s, 1H, C=C*H*-Ar). ^{13}C NMR (C_6D_6, 125.71 MHz): δ 19.07, 20.96, 22.01. 24.96, 50.01, 123.06, 130.02, 130.23, 132.03, 132.32, 136.94, 137.06, 137.20, 137.54, 138.89, 140.96, 143.77, 151.64, 152.97, 166.76, 168.88, 247.64, 324.88. HRMS $[M]^+$ (CI): Calcd. for $C_{36}H_{39}Cl_2N_3O_2Ru$: 717.1463. Found: 717.1481. Anal. Calcd. for $C_{36}H_{39}Cl_2N_3O_2Ru$: C, 60.25; H, 5.48; N, 5.85. Found: C, 60.32; H, 5.45; N, 5.61.

RCM of 6 to 7. An NMR tube equipped with a screw-cap septum was charged with a stock solution of catalyst (0.016 M in C_6D_6, 50 μL, 1 mol%) and C_6D_6 (0.75 mL) inside a glove box. After equilibrating the sample at 30 or 60 °C in a temperature controlled oil bath, diethyldiallyl malonate (**6**; 19.3 μL, 19.2 mg, 0.08 mmol, 0.1 M) was added via syringe and the conversion of **6** to **7** determined by comparing the ^{1}H NMR ratio of the integration of the methylene protons in the starting material (δ = 2.87 ppm, dt) with those in the product (δ = 3.16 ppm, s) over an appropriate time period. The kinetic analyses were performed in an analogous manner, with the exception that the NMR tube containing the reaction mixture was equilibrated at 45 °C for 15 minutes in an oil bath prior to injection of **6** and immediate insertion of the tube into an spectrometer with the probe equilibrated at 45 °C. After shimming, spectra were acquired every 30 sec using the Varian array function for 75 min. The observed reaction rate was determined from the slope of the plot of ln [**6**] versus time using all data points after an induction period of 20 min for complexes **4a**,**d** (Figure B9,10). Due to the rapidity of the conversion at this temperature, the rate for **4b** was determined from the data points between 8 and 15 minutes (Figure B9,10).

RCM of 8 to 9. An NMR tube equipped with a screw-cap septum was charged with a stock solution of catalyst (0.016 M in C_7D_8, 250 μL, 5 mol%) and C_7D_8 (0.55 mL) inside a glove box. After equilibrating the sample at 100 °C in a temperature controlled

oil bath, diethyldimethallyl malonate (**8**; 21.6 μL, 21.5 mg, 0.08 mmol, 0.1 M) was added via syringe and the conversion of **8** to **9** determined by comparing the ^{1}H NMR ratio of the integration of the methylene protons in the starting material (δ = 2.94 ppm) with those in the product (δ = 3.11 ppm) over an appropriate time period.

Synthesis of 1,3-Bis(dimesityl)-5,5-dimethyl-4,6-diketo-pyrimidinyl iridium(I) (1,5-cyclooctadiene) chloride (10). An 8 mL vial was charged with $[Ir(COD)Cl]_2$ (0.050 g, 0.074 mmol, 1 equiv), **1a** (0.056 g, 0.149 mmol, 1 equiv), benzene (2 mL), and a stir bar. After stirring the resulting solution at ambient temperature for 16 h, the residual solvent was removed under reduced pressure. Purification of the crude product by column chromatography using silica gel as the separation medium and 1:9 v/v ethyl acetate/hexanes as the eluent afforded the desired compound as a red solid (0.063 g, 0.088 mmol, 59% yield). Single crystals suitable for X-ray diffraction analysis were grown from the slow diffusion of hexanes into a toluene solution saturated with **10**. mp = 221 – 222 °C (decomp.) E_{pa} (vs SCE) = 0.94 V. IR (KBr): ν_{CO} = 1711.4, 1741.6 cm^{-1}. ^{1}H NMR (C_6D_6, 400.27 MHz): δ 1.2-1.45 (m, 8H, CCH_2CH_2C), 1.52 (s, 3H, $C(CH_3)$), 1.87 (s, 3H, $C(CH_3)$), 1.91 (s, 6H, Ar-CH_3), 2.14 (s, 6H, Ar-CH_3), 2.69 (s, 6H, Ar-CH_3), 2.96 (m, 2H, C=CH), 4.81 (m, 2H, C=CH), 6.69 (s, 2H, Ar-H), 6.83 (s, 2H, Ar-H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 19.02, 19.65, 20.34, 20.86, 27.79, 29.89, 33.43, 50.79, 57.62, 89.92, 130.65, 135.38, 136.22, 137.65, 138.61, 170.46, 230.33. HRMS $[M]^+$ (CI): Calcd. for $C_{32}H_{40}N_2O_2ClIr$: 712.2408. Found: 712.2404. Anal. Calcd. for $C_{32}H_{40}ClIrN_2O_2$: C, 53.95; H, 5.66; N, 3.93. Found: C, 53.84; H, 5.59; N, 3.89.

Synthesis of 1,3-Bis(dimesityl)-5,5-dimethyl-4,6-diketo-pyrimidinyl iridium(I) (dicarbonyl) chloride (11). Under ambient conditions, an 8 mL vial was charged with **10** (0.025 g, 0.035 mmol, 1 equiv) and CH_2Cl_2 (5 mL) and capped with a septum pierced with a needle. Carbon monoxide was bubbled through a needle into the

solution of **10** until the solvent had evaporated to dryness. Fresh CH_2Cl_2 (5 mL) was added to the vial and the aforementioned process was repeated (2×). After removing the residual solvent under reduced pressure, the crude product was washed with cold pentane, and then dried to afford the desired compound as a yellow solid (0.021 g, 0.032 mmol, 91% yield). Single crystals suitable for X-ray diffraction analysis were grown from the slow evaporation of pentane saturated with **11**. mp = 128 – 130 °C. E_{pa} (vs SCE) = ca. 1.6 V. IR (CH_2Cl_2): ν_{CO} = 1988.8, 2072.1 cm^{-1}. ^1H NMR (C_6D_6, 300.14 MHz): δ 1.37 (s, 3H, C(CH_3)), 1.46 (s, 3H, C(CH_3), 1.99 (s, 6H, Ar-CH_3), 2.18 (s, 6H, Ar-CH_3), 2.42 (s, 6H, Ar-CH_3), 6.74 (s, 2H, Ar-H), 6.76 (s, 2H, Ar-H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 18.65, 19.86, 20.97, 28.40, 51.68, 129.60, 130.65, 134.80, 135.15, 136.27, 140.02, 169.70, 170.92, 178.89, 221.90. HRMS $[M]^+$ (CI): Calcd. for $C_{26}H_{28}N_2O_4ClIr$: 660.1337. Found: 660.1314, 660.1367 (corresponds to $^{37}Cl^{191}Ir$ and $^{35}Cl^{193}Ir$, respectively). Anal. Calcd. for $C_{26}H_{28}ClIrN_2O_4$: C, 47.30; H, 4.27; N, 4.24. Found: C, 47.29; H, 4.37; N, 3.99.

X-Ray Crystallography. Brown, single crystals of **4a** were grown by slow diffusion of pentane vapor into a saturated benzene solution; this compound crystallized in the primitive triclinic space group *P*-1 with two molecules in the asymmetric unit. Single crystals of **4d** were obtained by slow vapor diffusion of pentane into a saturated benzene solution; this compound crystallized in the primitive monoclinic cell $P2_{1/a}$ with four molecules in the asymmetric unit and was solvated by four molecules of C_6H_6. Single crystals of **5a** were obtained by slow vapor diffusion of hexanes into a saturated toluene solution; this compound crystallized in the primitive triclinic space group *P*-1 with two molecules in the asymmetric unit. Red, single crystals of **10** were obtained by the slow diffusion of hexanes into a saturated toluene solution; this compound crystallized in the primitive monoclinic space group $P2_{1/n}$ with four molecules in the asymmetric unit. Yellow, single crystals of **11** were obtained by slow evaporation of the

solvent from a pentane solution; this compound crystallized in the primitive monoclinic space group $P2_{1/n}$ with four molecules in the asymmetric unit. Crystallographic measurements were carried out on a Rigaku Mini CCD area detector diffractometer using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) at 150 K using an Oxford Cryostream low temperature device. A sample of suitable size and quality was selected and mounted onto a nylon loop. Data reductions were performed using DENZO-SMN. The structures were solved by direct methods which successfully located most of the non-hydrogen atoms. Subsequent refinements on F_2 using the SHELXTL/PC package (version 5.1) allowed location of the remaining non-hydrogen atoms. Key details of the crystal and structure refinement data are summarized in Table B3,B4. Further crystallographic details may be found in the respective CIFs which were deposited at the Cambridge Crystallographic Data Centre, Cambridge, UK. The CCDC reference numbers for **4a**, **4d**, **5a**, **10**, and **11** were assigned as 806315, 806314, 806316, 806317, and 806318, respectively.

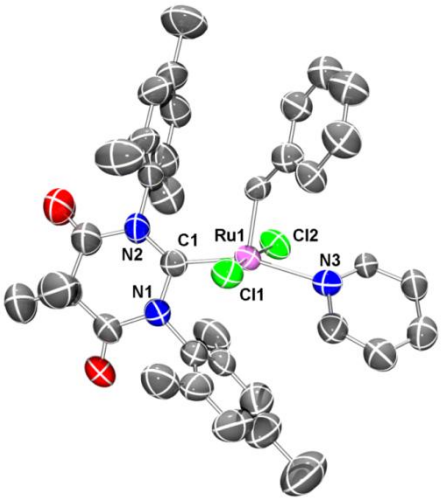


Figure B5: ORTEP diagram of **5a** with thermal ellipsoids drawn at 50% probability. H-atoms have been omitted for clarity.

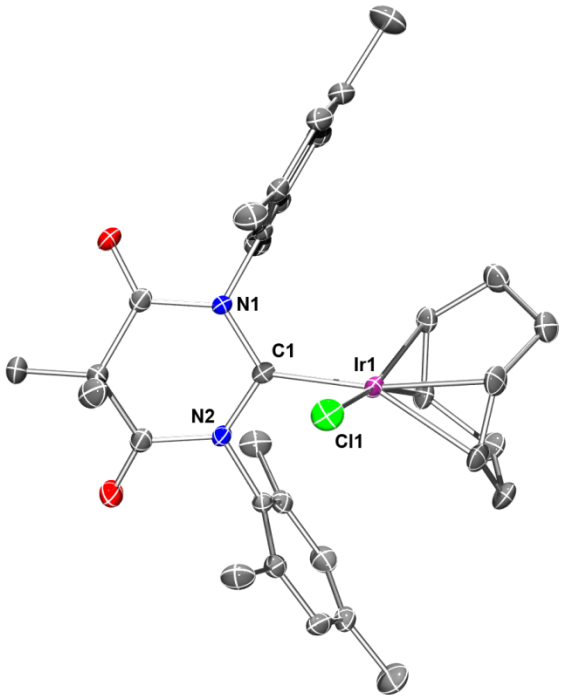


Figure B6: ORTEP diagram of **10** with thermal ellipsoids drawn at 50% probability. H-atoms have been omitted for clarity.

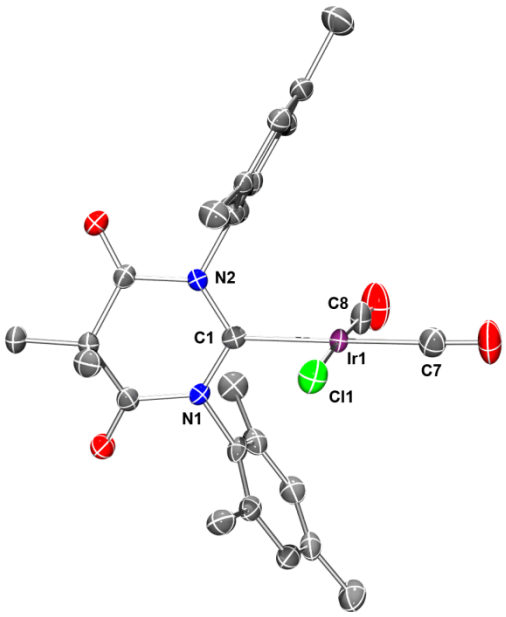


Figure B7: ORTEP diagram of **11** with thermal ellipsoids drawn at 50% probability. H-atoms have been omitted for clarity.

	4a	**4d**·(C_6H_6)	**5a**
Formula	$C_{34}H_{40}Cl_2N_2O_3Ru$	$C_{38}H_{46}Cl_2N_2ORu$	$C_{36}H_{39}Cl_2N_3O_2Ru$
M_r	696.65	718.74	717.67
crystal size (mm^3)	0.08 × 0.035 × 0.02	0.09 x 0.08 x 0.03	0.12 × 0.10 × 0.03
crystal system	triclinic	monoclinic	triclinic
space group	*P*	$P2_{1/a}$	*P*
a (Å)	10.166(2)	9.035(5)	9.3797(16)
b (Å)	11.320(2)	36.801(5)	9.8430(16)
c (Å)	15.196(3)	10.840(5)	19.455(3)
α (°)	75.51(3)	90	77.608(4)
β (°)	84.09(3)	99.370(5)	84.921(4)
γ (°)	87.83(3)	90	82.834(5)
V ($Å^3$)	1684.0(6)	3556(3)	1737.1(5)
Z	2	4	2
ρ_{calc} (g cm^{-3})	1.374	1.342	1.372
μ (mm^{-1})	0.659	0.622	0.640
F(000)	720	1496	740
T (K)	223(2)	223(2)	223(2)
scan mode	ω	ω	ω
hkl range	-12 → +12 -13 → +13 -18 → +18	-10 → 10 0 → 43 0 → 12	-11 → 11 -11 → 11 -23 → 23
measd reflns	14787	6194	15143
unique reflns [R_{int}]	5915[0.0682]	6194[0.0000][a]	6097[0.0670]
refinement reflns	5915	6194	6097
refined parameters	389	397	551
GOF on F^2	1.003	1.006	1.006
R1[a] (all data)	0.0577 (0.0952)	0.0624 (0.0768)	0.0794 (0.1295)
wR2 (all data)	0.0979 (0.1114)	0.1596 (0.1766)	0.1701 (0.1967)
ρ_{fin} (max/min)	0.428	1.166	0.430
(e $Å^{-3}$)	-0.320	-0.813	-0.287

Table B3: Summary of crystal data, data collection, and structure refinement details.[a] The low temperature control stopped partway through the run causing the crystal to move slightly. Thus, the framesets were solved separately and merged to obtain the final dataset. [b] $R1 = \sum||Fo| - |Fc||/\sum|Fo|$. [b] $wR2 = \{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

	10	**11**
Formula	$C_{32}H_{40}ClIrN_2O_2$	$C_{26}H_{28}ClIrN_2O_4$
M_r	712.31	660.15
crystal size (mm^3)	$0.20 \times 0.20 \times 0.20$	$0.31 \times 0.14 \times 0.14$
crystal system	monoclinic	monoclinic
space group	$P2_{1/n}$	$P2_{1/n}$
a (Å)	11.75290(10)	14.801(3)
b (Å)	9.43090(10)	8.9845(18)
c (Å)	26.6821(2)	19.229(4)
α (°)	90	90
β (°)	98.0040(10)	95.39(3)
γ (°)	90	90
V ($Å^3$)	2928.64(5)	2545.7(9)
Z	4	4
ρ_{calc} (g cm^{-3})	1.616	1.722
μ (mm^{-1})	4.681	5.384
F(000)	1424	1296
T (K)	150(2)	150(2)
scan mode	ω	ω
hkl range	$-13 \rightarrow +13$ $-11 \rightarrow +11$ $-31 \rightarrow +31$	$-17 \rightarrow +17$ $-10 \rightarrow +10$ $-22 \rightarrow +22$
measd reflns	16922	8247
unique reflns [R_{int}]	5118[0.0222]	4452 [0.0185]
refinement reflns	5118	4452
refined parameters	351	315
GOF on F^2	1.006	1.008
R1[a] (all data)	0.0155 (0.0162)	0.0210 (0.0269)
wR2 (all data)	0.0426 (0.0431)	0.0644 (0.0808)
ρ_{fin} (max/min)	0.458	0.874
(e $Å^{-3}$)	-0.695	-1.597

Table B4: Summary of crystal data, data collection, and structure refinement details. R1 = $\sum||Fo| - |Fc||/\sum|Fo|$. [b] wR2 = $\{[\sum w(Fo^2 - Fc^2)^2]/[\sum w(Fo^2)^2]\}^{1/2}$.

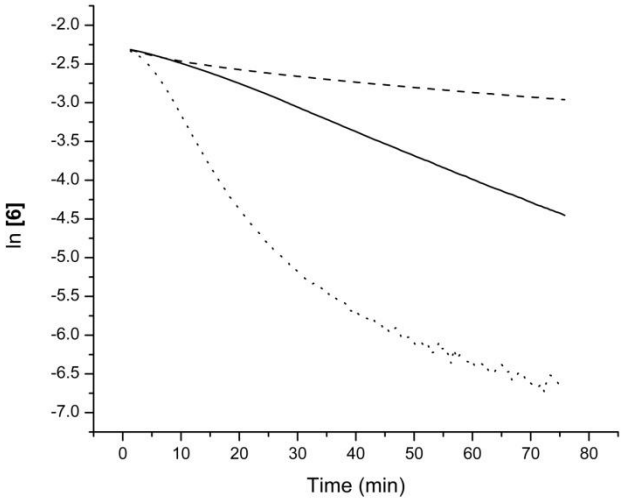


Figure B8: Plot of ln [**6**] versus time in the presence of **4a** (solid line), **4b** (dotted line), or **4d** (dashed line) as determined by ^{1}H NMR spectroscopy. Conditions: C_6D_6, 45 °C, 1 mol% catalyst loading. See text for additional details.

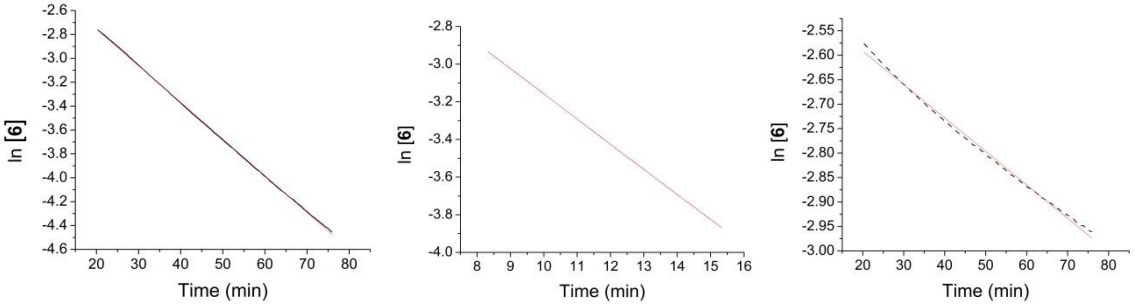


Figure B9: (left) Plot of ln [**6**] versus time in the presence of **4a** (black line) after a 20 min induction period. The equation for the best fit line is as follows: y = mx + b, where m = –0.03071 ± 0.00004 s^{-1} and b = –2.141 ± 0.002. (middle) Plot of ln [**6**] versus time in the presence of **4b** (dotted black line) after an 8 min induction period. The equation for the best fit line is as follows: y = mx + b, where m = –0.1336 ± 0.0004 s^{-1} and b = –1.822 ± 0.005. (right) Plot of ln [**6**] versus time in the presence of **4d** (dashed black line) after a 20 min induction period. The equation for the best fit line is as follows: y = mx + b, where m = –0.00684 ± 0.00004 s^{-1} and b = –2.455 ± 0.002.

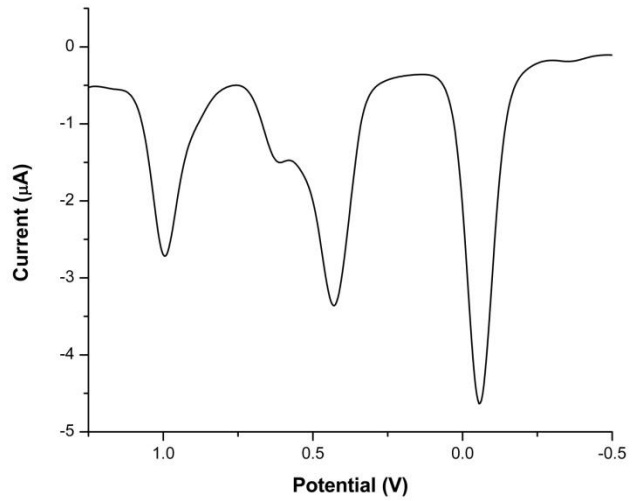


Figure B10: DPV of **3a** (generated in situ; see main text) in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard. The signals recorded at 0.43 and 0.61 V are consistent with the oxidation of free phosphine and residual **3b** (used for the synthesis of **3a**), respectively.

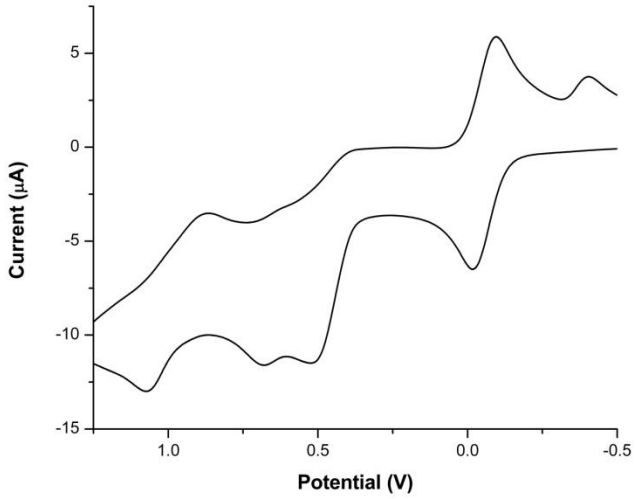


Figure B11: CV of **3a** (generated in situ; see main text) in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

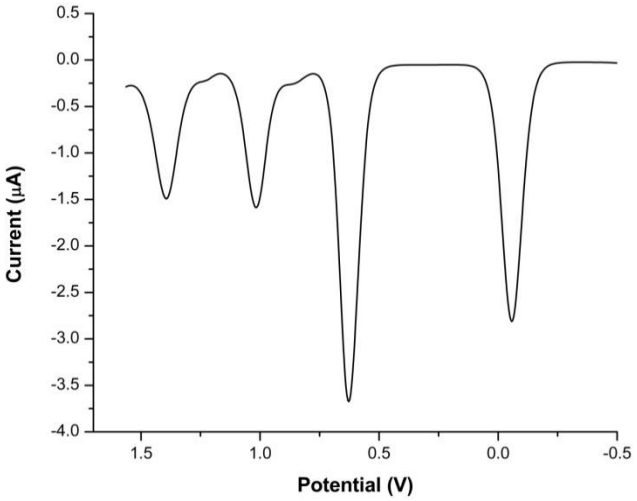


Figure B12: DPV of **3b** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

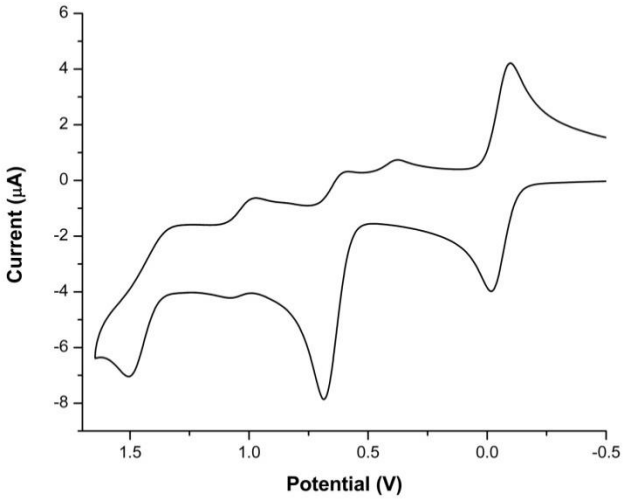


Figure B13: CV of **3b** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

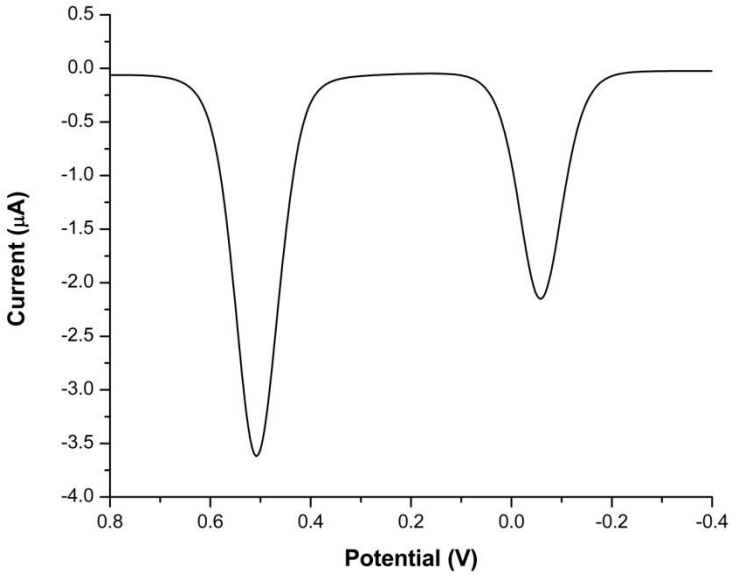


Figure B14: DPV of **3c** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

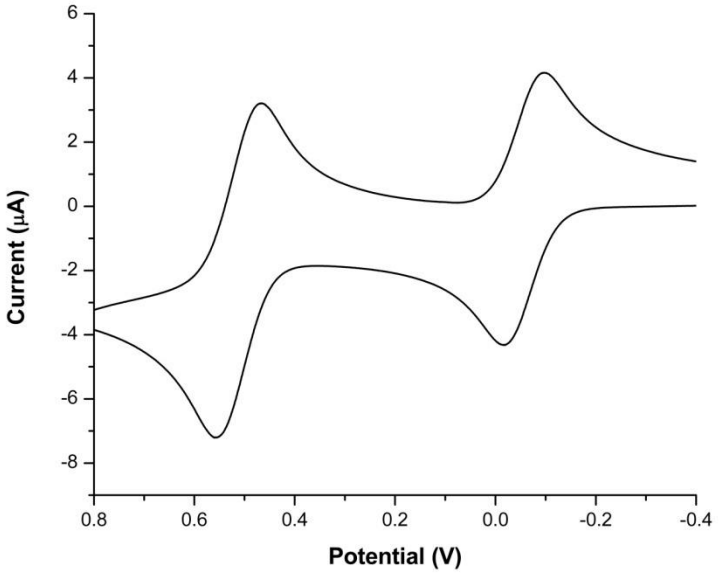


Figure B15: CV of **3c** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

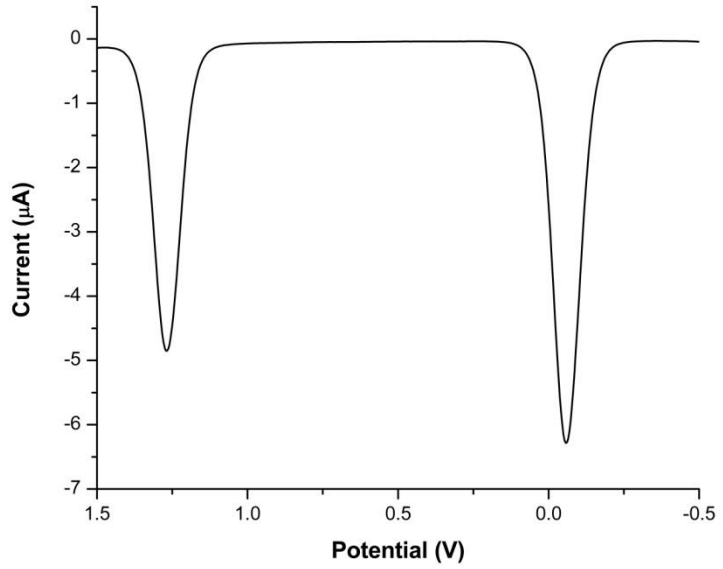


Figure B16: DPV of **4a** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

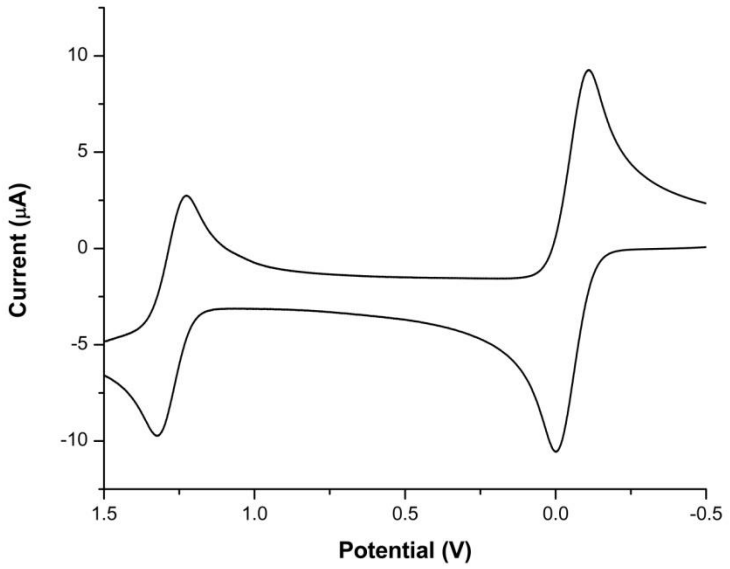


Figure B17: CV of **4a** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

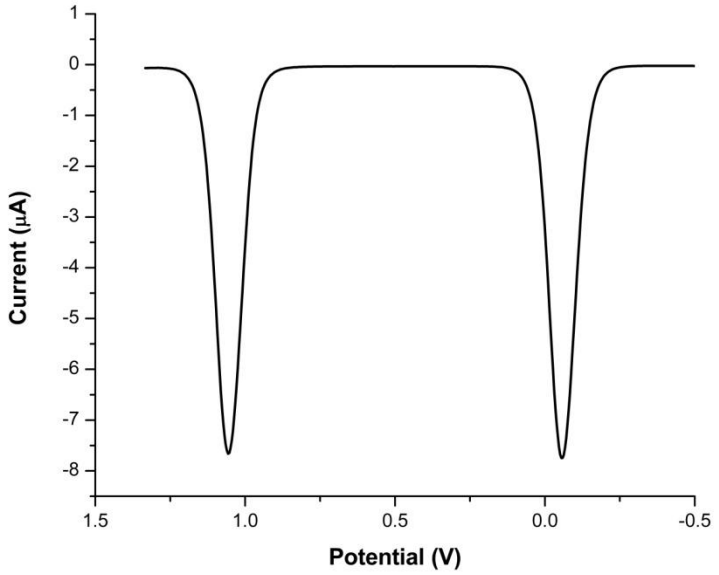


Figure B18: DPV of **4b** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

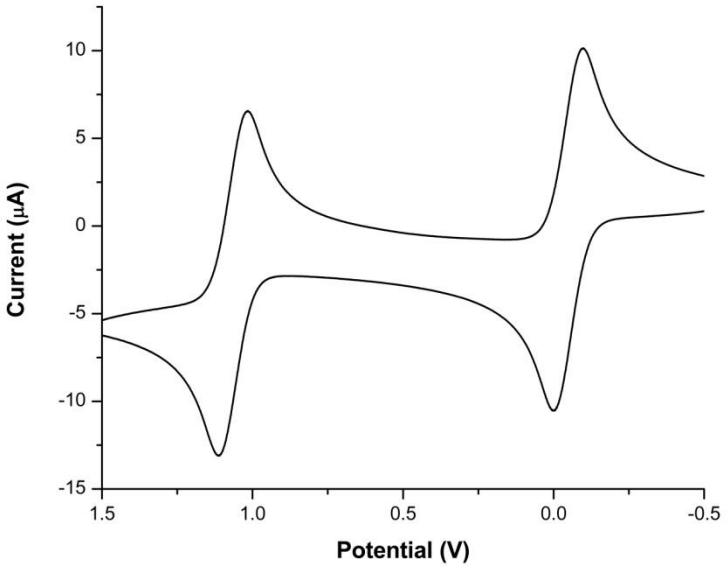


Figure B19: CV of **4b** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

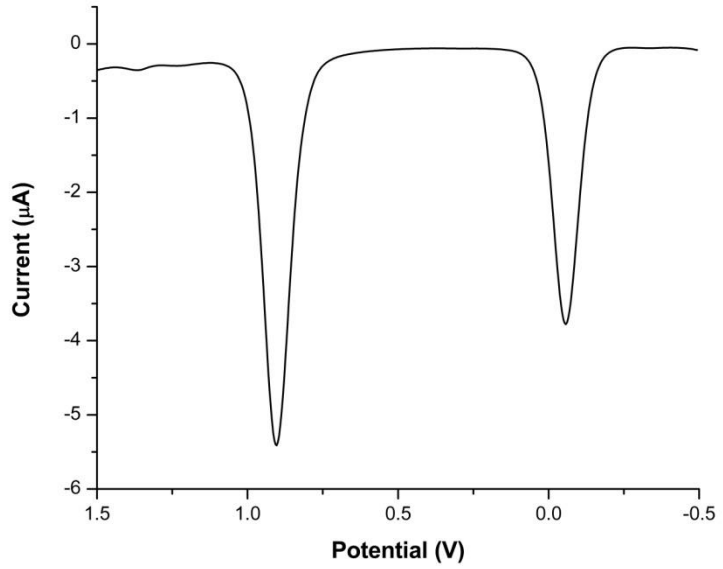


Figure B20: DPV of **4c** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

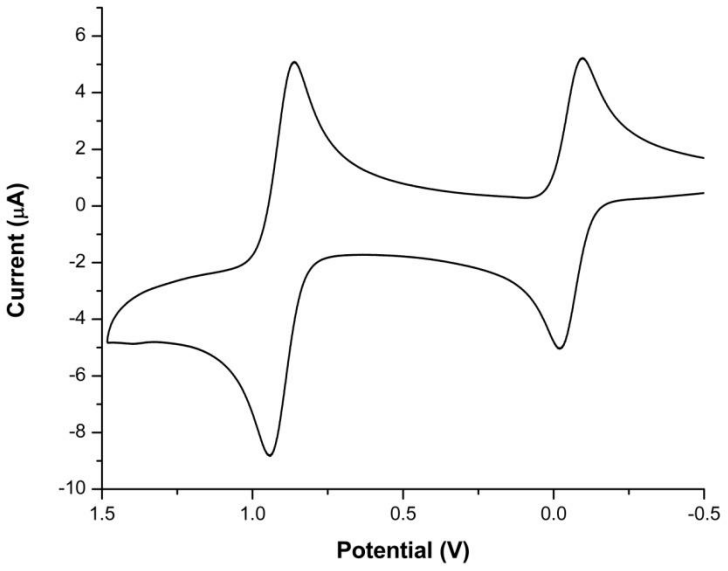


Figure B21: CV of **4c** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

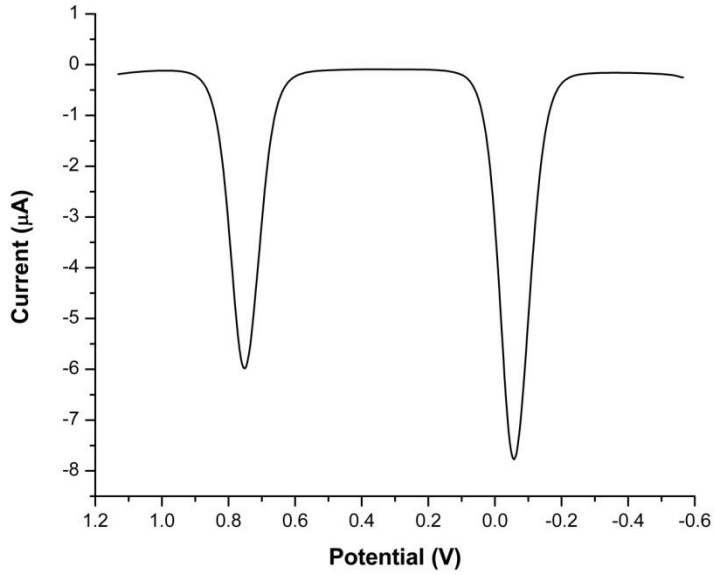


Figure B22: DPV of **4d** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

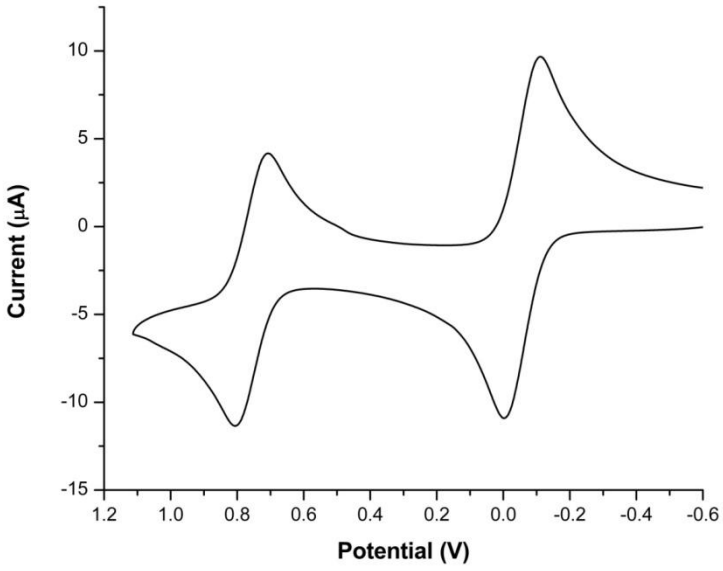


Figure B23: CV of **4d** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

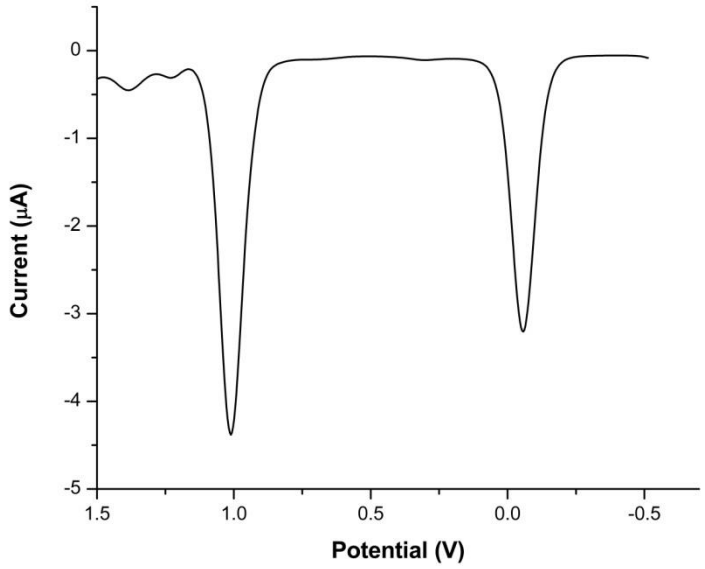


Figure B24: DPV of **5a** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

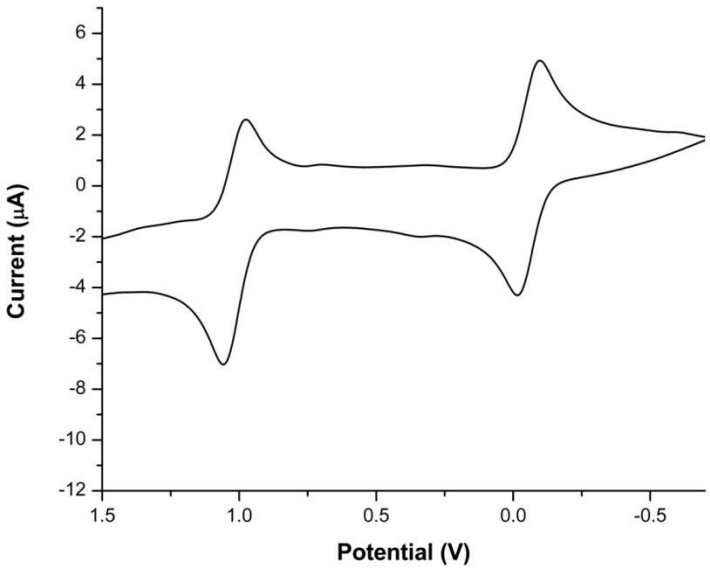


Figure B25: CV of **5a** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

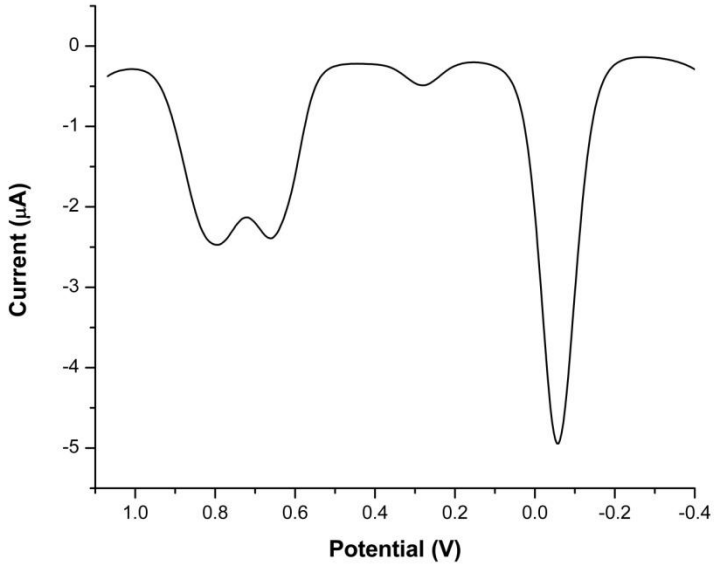


Figure B26: DPV of **5b** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

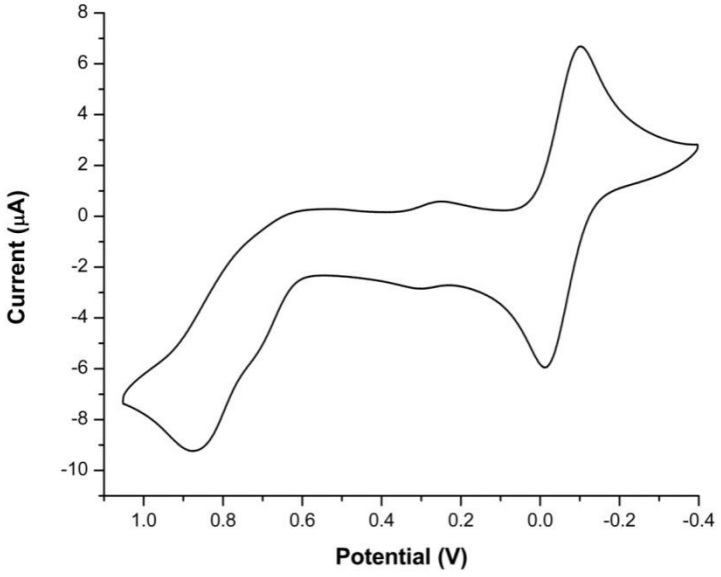


Figure B27: CV of **5b** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

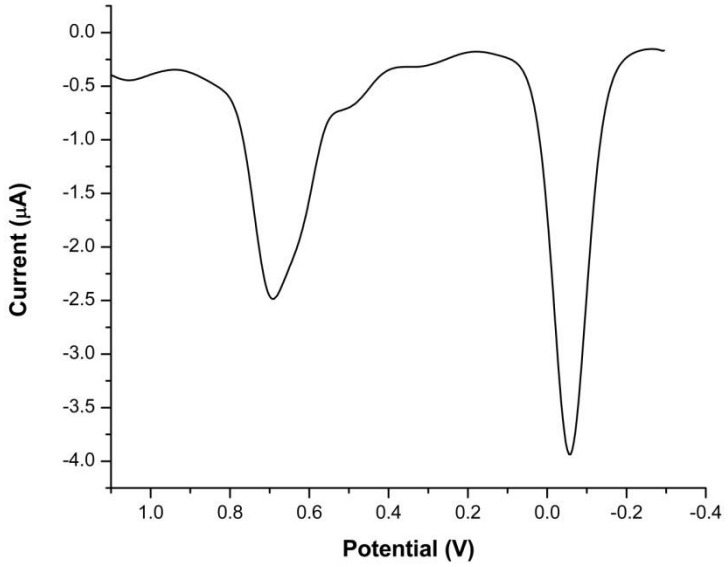


Figure B28: DPV of **5c** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

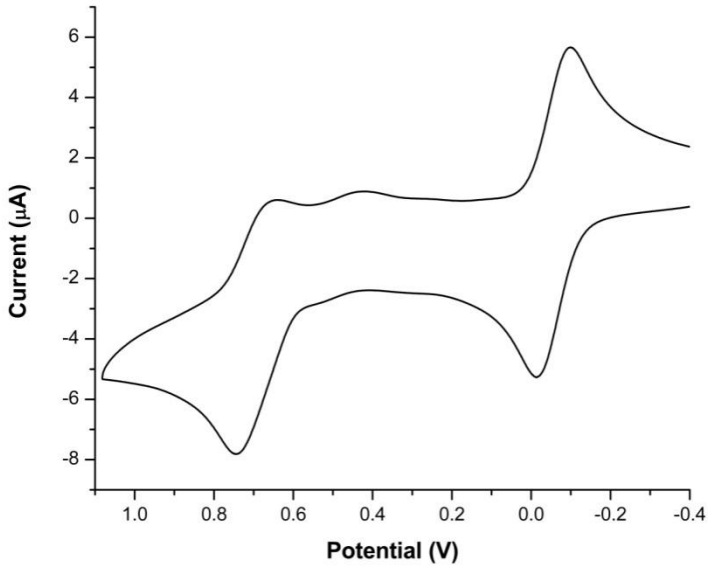


Figure B29: CV of **5c** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

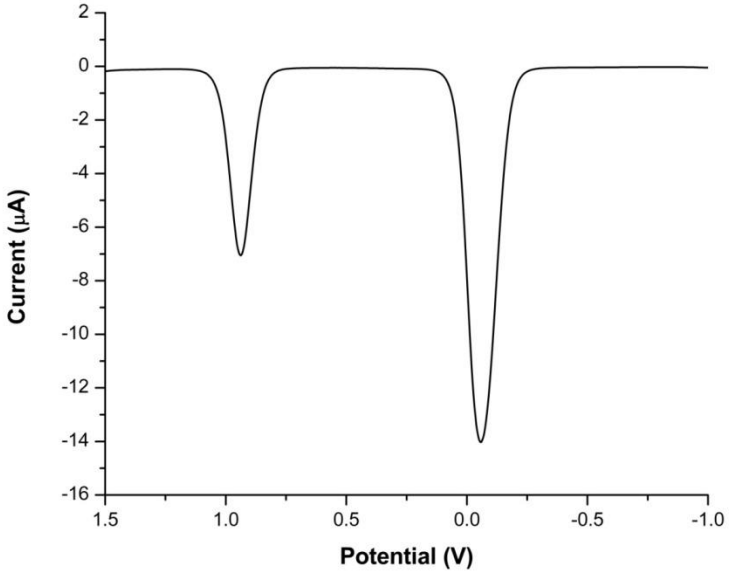


Figure B30: DPV of **10** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

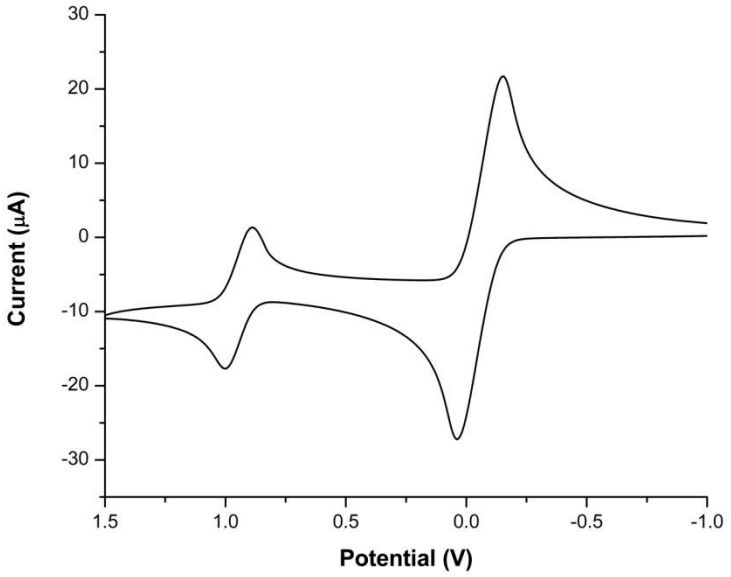


Figure B31: CV of **10** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

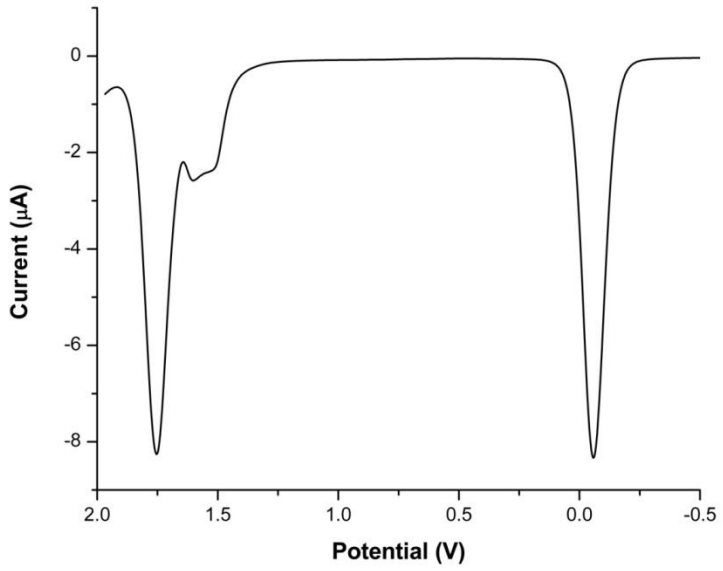


Figure B32: DPV of **11** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

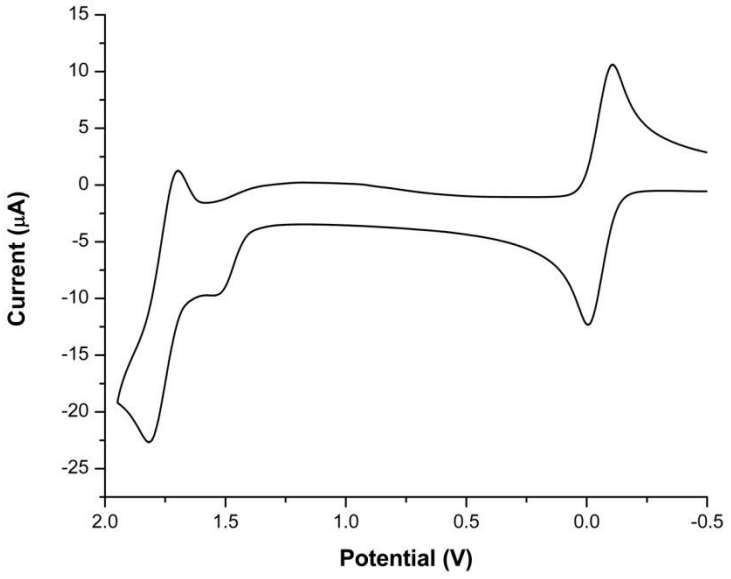


Figure B33: CV of **11** in CH_2Cl_2 with 0.1 M $[Bu_4N][PF_6]$ and Fc* internal standard.

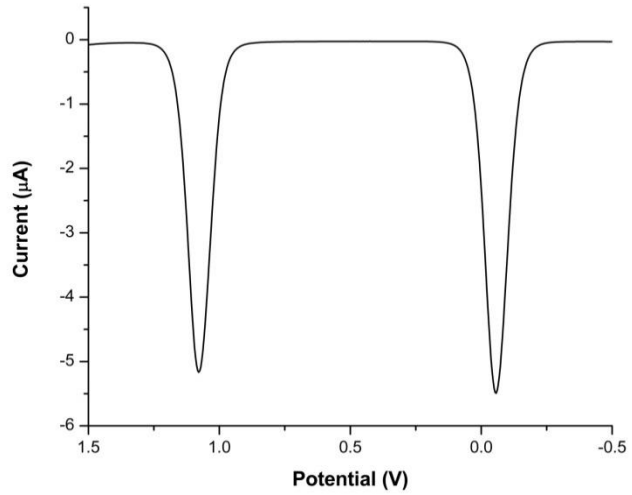


Figure B34: DPV of [2-[2,6-bis(diisopropylphenyl)]-3,3-dimethyl-2-azaspiro[4.5]dec-1-ylidene]Cl_2Ru=CH(*o*-^{i}Pr-Ph) in CH_2Cl_2 with 0.1 M [Bu_4N][PF_6] and Fc* internal standard.

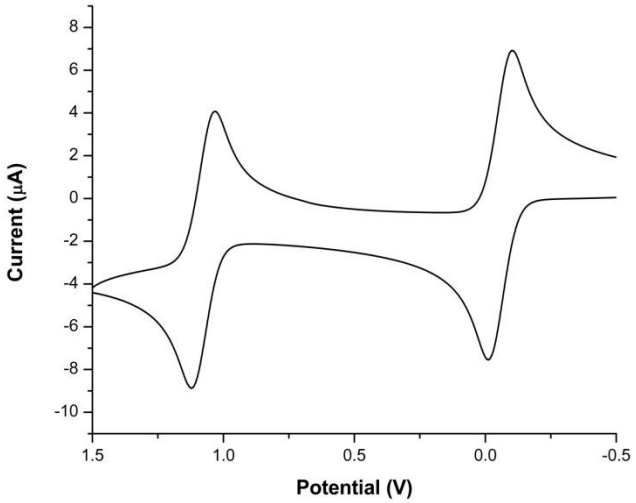


Figure B35: CV of [2-[2,6-bis(diisopropylphenyl)]-3,3-dimethyl-2-azaspiro[4.5]dec-1-ylidene]Cl_2Ru=CH(*o*-^{i}Pr-Ph) in CH_2Cl_2 with 0.1 M [Bu_4N][PF_6] and Fc* internal standard.

B5. Acknowledgements

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43) The fictive M-L bond distance of 2.00 Å commonly employed for calculating $\%V_{bur}$ (see ref. 26) is near that of the DAC- and NHC-Ru bond lengths as determined via X-ray crystallography for **4a**,**d** (1.938 and 2.048 Å, respectively) but is significantly shorter than the Ru-P distance reported for **4b** (2.242 Å; ref. 11). The $\%V_{bur}$ for PCy_3 is therefore likely closer to 31.8% calculated using a M-P distance of 2.28 Å (ref. 26c) and significantly less bulky than **4a**,**d**. Using the Ru-ligand distances determined experimentally by X-ray crystallography for **4a** (1.938 Å) and **4d** (2.048 Å) a $\%V_{bur}$ of 39.0% and 37.2% was calculated for **4a**,**d**, respectively. With a computed $\%V_{bur}$ of 37.1% at 2.00 Å and 31.8% at 2.28 Å (ref 26c), the reported P-Ru distance of 2.242 Å for **4b** (see ref. 11) indicates the latter value may be more accurate. Thus, the $\%V_{bur}$ difference between **1a**/**2** and PCy_3 is likely greater than indicated from the numbers obtained from the fictive, but commonly employed, M-L distance of 2.00 Å for all three ligands.

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Appendix C: Elucidating the Mechanism of Reversible Oxiranations via Magentization Transfer Spectroscopy*

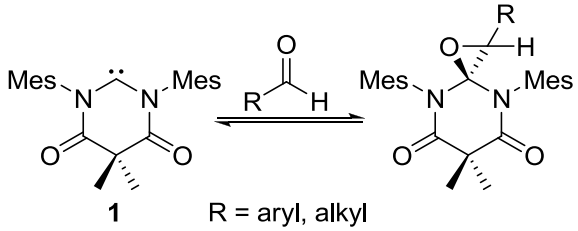
C1. INTRODUCTION

Due to their high ring strain, oxiranes are important precursors to a broad range of valuable small molecules and polymers.[1-3] Such three-membered cyclic ethers are typically synthesized via one of four routes: (1) the ring closure of an appropriately substituted alcohol, (2) the monooxidation of an olefin, (3) the Corey-Chaykovsky reaction, or (4) the [2+1] cycloaddition of a carbene with an aldehyde.[4-8] Despite its high atom economy and the availability of a wide range of aldehydes, the latter process remains largely underdeveloped, mainly because carbenes frequently react with carbonyl groups to give the corresponding ylides rather than the desired cycloadducts.[9-11] Moreover, most carbenes used in known oxiranation reactions (*e.g.*, dimethoxycarbene[4]) must be generated *in situ* from unstable precursors.[9,13-15] As such, the mechanistic details of the aldehyde/carbene cycloaddition process are relatively unrefined and derived mainly from time-resolved spectroscopic[11] and computational studies.[16-18]

To expand the scope of the carbene/aldehyde cycloaddition reaction and to gain additional insight into the corresponding mechanism, the use of an isolable carbene[19] as a cycloaddition partner is desirable. However, for the past 20 years, the only known isolable carbenes capable of reacting with aldehydes to give the corresponding oxiranes were Bertrand's phosphinosilyl carbenes.[16-18,20,21] Earlier, we reported that diamidocarbenes (DACs; *e.g.*, **1**)[22-24] undergo [2+1] cycloadditions with a wide range of

* Portions of this appendix were reproduced with permission from Chase, D. T.; Moerdyk, J. P.; Bielawski, C. W. *Org. Lett.* **2012**, *14*, 5510. Copyright 2012 the American Chemical Society. The author acknowledges the contributions of D. T. Chase in the synthetic characterization of the oxirations and elucidation of the equilibria constants as well as for helpful discussions. The author is also grateful to D. T. Chase and C. W. Bielawski, for their roles in writing the original manuscript.

alkyl and aryl aldehydes (Scheme C1).[25] Moreover, the corresponding reactions were found to be rapid and reversible under mild conditions (< 80 °C). We reasoned that additional insight into the [2+1] cycloaddition mechanism as well as the corresponding activation parameters may be obtained by probing the equilibration process.



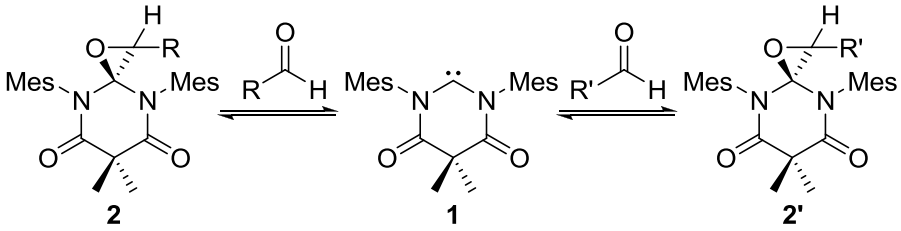
Scheme C1: Known [2+1] cycloadditions of **1** with aldehydes.

C2. Results and Discussion

Building upon our previous results,[25] a range of aryl and alkyl substituted diamidooxiranes (**2**) were first synthesized by combining **1** with the appropriate aldehyde at 23 °C. The formation of **2a**–**g** was complete within 30 min, as determined by NMR spectroscopy, and the new oxirane products **2b**,**c** were isolated in good yield (76-83%) in a manner similar to that used for previously reported **2a**,**d-f**.[25,26] However, incomplete (<85%) conversion was observed for **2h** even in the presence of excess pivaldehyde (10 equiv), presumably due to steric inhibition.[27]

With **2** in hand, subsequent efforts were directed toward probing the oxiranation equilibria. Two different aldehydes (1.05 equiv. ea) were mixed with **1** in C_6D_6 ($[\mathbf{1}]_0$ = 0.066 M) and the product ratios were measured by ^{1}H NMR spectroscopy over time. For every combination of aldehydes studied (Figure C1), three separate experiments were performed: (1) the addition of one aldehyde followed by the other, (2) vice versa, and (3) the simultaneous addition of both aldehydes to **1**. Afterward, the mixture was allowed to stir for 20 min at room temperature. Following ^{1}H NMR analysis, each solution was then

heated to 60 °C for 2 h, cooled to room temperature, and then re-analyzed. Similar product ratios were observed regardless of the order of aldehyde addition which indicated that the reactions were reaching equilibrium.



2a: R = 4-NO_2-C_6H_4
2b: R = 4-Br-C_6H_4
2c: R = 4-F-C_6H_4
2d: R = C_6H_6
2e: R = 4-MeO-C_6H_4
2f: R = C_6H_{11}
2g: R = C_8H_{17}
2h: R = $C(CH_3)_3$

Figure C1: Competitive oxiranation equilibria. Conditions: $[\mathbf{1}]_0$ = 0.066 M, $[\text{aldehyde}]_0$ = $[\text{aldehyde}']_0$ = 0.07 M, C_6D_6, 60 °C, 2 h.

entry	**2**	**2′**	**2**:**2′**	K_{eq}/K'_{eq}[b]
1	**2a**	**2d**	76:24	8.9×10^{0}
2	**2b**	**2d**	55:45	1.4×10^{0}
3	**2c**	**2d**	55:45	1.4×10^{0}
4	**2e**	**2d**	29:71	1.9×10^{-1}
5	**2f**	**2d**	71:29	5.6×10^{0}
6	**2g**	**2d**	68:32	4.3×10^{0}
7	**2h**	**2d**	<1:>99	$<6.7 \times 10^{-4}$

Table C1: Selected product and equilibrium constant ratios compared to **2d**. [a]The product ratios and equilibrium constants shown were calculated from an average of three separate experiments. Conditions: $[\mathbf{1}]_0$ = 0.066 M, $[\text{aldehyde}]_0$ = $[\text{aldehyde}']_0$ = 0.07 M, C_6D_6, 60 °C, 2 h. [b] K_{eq}/K'_{eq} = ([**2**][aldehyde′])/([**2′**][aldehyde]). Representative aldehyde combinations shown; see the experimental section for the results obtained from all other possible combinations.

Inspection of the results obtained from the aforementioned experiments (see Table C1,C3) revealed the following trend in stability: **2f** ≈ **2a** > **2g** ≈ **2b** ≈ **2c** > **2d** > **2e** >> **2h**. While the DAC **1** appeared to favor electron-deficient aryl aldehydes, the formation of **2f** (from **1** and cyclohexanecarboxaldehyde) was similarly favored[28] as **2a** which we believe stemmed from a slow dissociation process (see below). In addition to electronics, sterics also prominently influenced the stability of the diamidooxiranes (*c.f.*, entries 5 or 6 to 7).

Unfortunately, due to the rapid rate of cycloaddition, all attempts to expand upon the aforementioned equilibrium studies and obtain the corresponding pseudo first order rate constants (k_{obs}) by variable temperature ^{1}H NMR spectroscopy were unsuccessful. For example, treating a C_7D_8 solution of **1** ($[\mathbf{1}]_0$ = 0.066 M) with 10 equiv. of benzaldehyde was found to quantitatively form **2b** within 60 sec at -80 °C ($k_{obs} > 1.9 \times 10^{-1}$ $M^{-1}\cdot s^{-1}$ at 99.9% conversion).

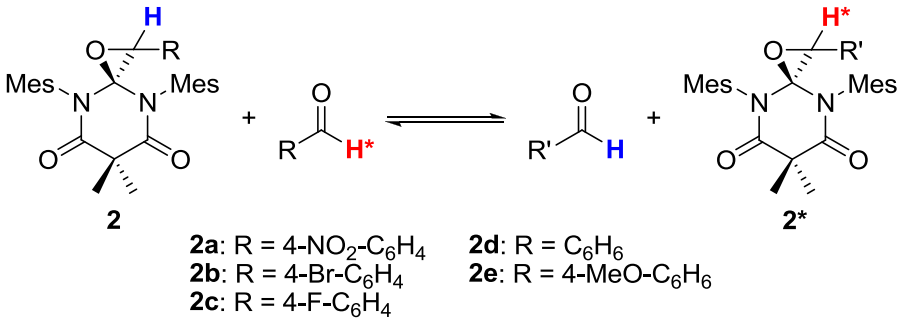


Figure C2: Substrates used in the magnetization transfer spectroscopy experiments. Conditions: $[\mathbf{1}]_0$ = 0.066 M, $[\text{aldehyde}]_0$ = 0.199 M, C_7D_8. The asterisk denotes the ^{1}H NMR resonances monitored during the magnetization transfer process. The rate determining step is the cycloreversion of the oxirane.

To circumvent this limitation and to measure the rates of the exchange processes at equilibrium, we considered magnetization transfer spectroscopy.[29] This one-

dimensional NMR technique involves the monitoring of a nucleus undergoing chemical exchange as it relaxes from a selective 180° pulse. While magnetization transfer has been previously utilized in biological,[30,31] organometallic,[32-34] and other physical chemistry[35-38] studies, it has not been employed to study C-C bond forming reactions to the best of our knowledge.

To test the viability of the magnetization transfer technique as a means to measure the exchange rates of the reactions summarized in Figure C2, a C_7D_8 solution of **1** ($[\mathbf{1}]_0$ = 0.066 M) and 3 equiv. of an aldehyde were heated to a predetermined temperature in the NMR probe. Next, a selective 180° pulse was applied to the equilibrated sample at the ^{1}H NMR resonance frequency assigned to the aldehyde (9.4-9.6 ppm) and the corresponding nucleus was allowed to relax over time (see Figure C3 for an illustrative example). The areas of the signals assigned to the pulsed aldehyde starting material as well as the oxirane product were monitored at various relaxation delays that ranged between 0.001 and 30 s. Using the software program CIFIT,[39] the areas of the oxirane and aldehyde signals were fitted to a nonlinear, least squares equation and an exchange rate, k_{ald}, was calculated for each aldehyde studied.

The aforementioned experiments were then repeated with the exception that the ^{1}H NMR resonance assigned to the oxirane (2.61-3.9 ppm) was selectively inverted instead of the aldehyde. Likewise, monitoring the signal areas over time provided the corresponding exchange rate, k_{ox}. The overall exchange rate, k_{exc}, was taken as the numerical average of k_{ald} and k_{ox}. As shown in Figure C4 and summarized in Table C2 (as well as Table C4), the exchange rates for **2a-e** were measured at 5 °C intervals from 85 – 100 °C; the exchange rates for **2f-h** were not measured due to premature decomposition observed at elevated temperatures.

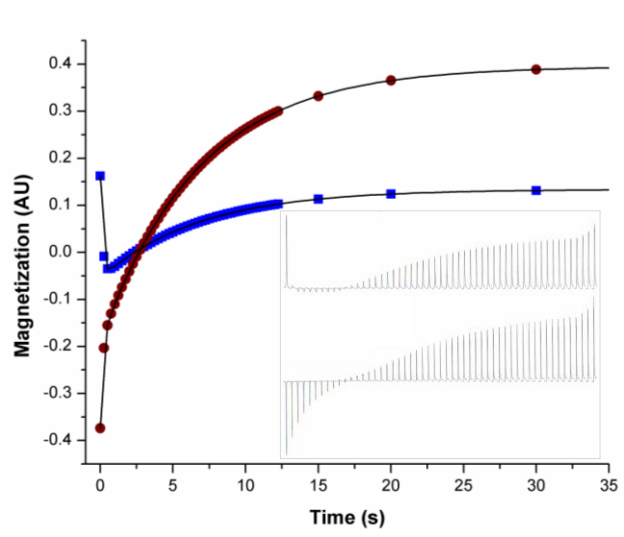


Figure C3: Plot of the measured magnetization signal versus time for **2a** (monitored at 3.9 ppm, blue squares) and 4-nitrobenzaldehyde (monitored at 9.45 ppm, red circles) and their magnetization values calculated from the best-fit parameters (black lines). Inset: Representative NMR spectra for (top) **2a** (monitored at 3.9 ppm) and (bottom) 4-nitrobenzaldehyde (monitored at 9.45 ppm) over time. Conditions: $[\mathbf{1}]_0$ = 0.066 M, [4-nitrobenzaldehyde]$_0$ = 0.199 M, C_7D_8, 100 °C.

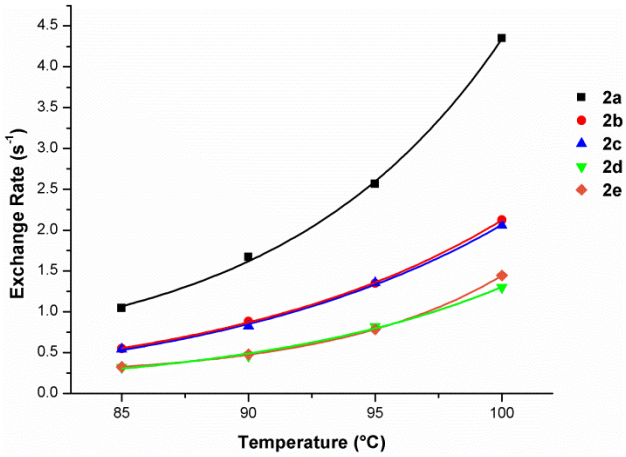
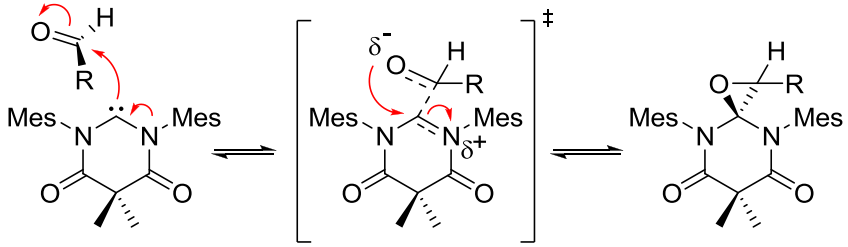


Figure C4: Measured exchange rates versus temperature. Conditions: $[\mathbf{1}]_0$ = 0.066 M, [aldehyde]$_0$ = 0.199 M, C_7D_8.

oxirane	k_{exc} (s^{-1}) (100 °C)	$\Delta H^{\ddagger}$ (kcal·mol^{-1})	$\Delta S^{\ddagger}$ (cal·mol^{-1}·K^{-1})	$\Delta G^{\ddagger}$ (298 K) (kcal·mol^{-1})
2a	4.4	23.9 ± 1.9	8 ± 5	22 ± 2
2b	2.13	23.0 ± 1.4	4 ± 4	21.7 ± 1.8
2c	2.06	23.1 ± 0.9	4 ± 2	21.8 ± 1.1
2d	1.3	26.2 ± 1.4	12 ± 4	22.6 ± 1.9
2e	1.45	23.8 ± 1.9	5 ± 5	22 ± 2

Table C2: Summary of the activation parameters.

Using the VT NMR data, Eyring plots were constructed to determine the activation energies for the cycloreversion reactions of **2a**–**e**. The $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values were calculated to be large and positive, and the exchange rate was found to be independent of the aldehyde concentration (Table C2). These data indicated that the dissociative cycloreversion was the rate limiting step of the equilibration process. Additionally, the more electron-deficient **2a** exchanged at nearly triple the rate as those measured for **2d** and **2e** at 100 °C. The higher exchange rates and slightly lower $\Delta G^{\ddagger}$ for the more electron-deficient derivatives reflected a partial buildup of negative charge in the transition state stabilized by the proximal electron-withdrawing aryl substituents (Scheme C2). Based on these results, the mechanism of the oxiranation was consistent with a process wherein the aldehyde underwent attack by the nucleophilic carbene in an asynchronous manner.



Scheme C2: Proposed mechanism for the reversible oxiranation.

C3. Conclusion

In summary, the dynamic equilibria of **1** with various aryl and alkyl aldehydes was investigated and the corresponding thermodynamic parameters were measured. Competitive equilibrium studies revealed a thermodynamic preference for electron-deficient aryl aldehydes **2a**,**b** and sterically unhindered alkyl aldehydes **2f**,**g** while the formation of sterically hindered oxiranes was strongly disfavored. Similarly, magnetization transfer experiments showed that the electron-deficient oxiranes underwent faster exchange than their electron-rich analogues. Collectively, the exchange rates and activation energies were consistent with an asynchronous mechanism that involved the buildup of partial negative charge at the aldehyde oxygen (and, by extension, buildup of partial positive charge within the *N*-heterocycle) in the transition state.[40] With knowledge of the exchange rates and thermodynamic equilibria in hand, we believe the DAC/aldehyde cycloaddition reaction is poised for use in dynamic covalent[41,42] applications (*e.g.*, sensing[43-47]) wherein the rapid, reversible oxiranation process may be advantageous.[48-50] Beyond elucidating the mechanism of the aforementioned [2+1] cycloaddition reaction, magnetization transfer spectroscopy was applied for the first time to a dynamic covalent organic reaction.

C4. Experimental

General Considerations. All procedures were performed using standard Schlenk techniques under an atmosphere of nitrogen or in a nitrogen filled glove box unless otherwise noted. *N,N′*-dimesityl-4,6-diketo-5,5-dimethylpyrimidin-2-ylidene (**1**)[23] and **2a,d-f**[25] were synthesized according to literature procedures. All commercial liquid substrates were dried over molecular sieves prior to use. All commercial solid substrates were dried under reduced pressure for 24 h prior to use. Benzene and pentane were dried and degassed using a Vacuum Atmospheres Company solvent purification system (model

number 103991-0319) and stored over molecular sieves in a nitrogen-filled glove box. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrophotometer. High resolution mass spectra (HRMS) were obtained with a Waters Micromass Autospec-Ultima (CI) mass spectrometer. NMR spectra were recorded on Varian Unity+ 300, Varian Mercury 400, Varian Directdrive 400, or Varian Inova 500 spectrometers. Chemical shifts (δ) are given in ppm and are referenced to the residual solvent (^{1}H: C_6D_6, 7.15 ppm; C_7D_8, 7.09 ppm; ^{13}C: C_6D_6, 128.0 ppm) or an external standard (^{19}F: 0.00 ppm; $CFCl_3$). Elemental analyses were performed at Midwest Microlab, LLC (Indianapolis, IN). Melting points were obtained using a Stanford Research Systems automated melting point appartus and are uncorrected.

Synthesis of 2b. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol), benzene (1 mL), and a stir bar. To this vial, 4-bromobenzaldehyde (0.037 g, 0.200 mmol, 1 eq) was added and the resultant mixture stirred at ambient temperature for 15 min. Removal of the residual solvent under reduced pressure, washing with pentane, and drying under reduced pressure afforded the desired compound as a white solid (0.085 g, 0.151 mmol, 76% yield). mp = 157-159 °C (decomp.) ^{1}H NMR (C_6D_6, 399.68 MHz): δ 1.79 (s, 3H), 1.82 (s, 3H), 1.87 (s, 3H), 1.99 (s, 3H), 2.05 (s, 3H), 2.26 (overlapping s, 6H), 2.40 (s, 3H), 3.85 (s, 1H), 5.93 (s, 1H), 6.22 (d, J = 8.4 Hz, 2H), 6.41 (s, 1H), 6.70-6.74 (overlapping d and s, 4H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 18.77, 18.78, 18.85, 18.93, 20.76, 20.88, 21.86, 27.02, 48.01, 64.33, 83.01, 120.62, 126.38, 129.00, 129.54, 130.35, 130.51, 130.53, 131.50, 132.78, 136.26, 137.26, 138.32, 138.66, 139.00, 171.99, 172.35. IR (KBr): ν = 2975.7, 2920.2, 1705.8, 1674.3, 1484.7, 1429.1, 1397.7, 1345.5, 1254.9, 1241.0, 854.1, 786.1, 612.3 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{34}N_2O_3{}^{81}Br$: 563.1732; Found: 563.1727. Anal. calcd. for $C_{31}H_{34}N_2O_3Br$: C, 66.31; H, 5.92; N, 4.99; Found: C, 65.99; H, 5.94; N, 4.92.

Synthesis of 2c. An 8 mL vial was charged with **1** (0.075 g, 0.199 mmol), benzene (1 mL), and a stir bar. To this vial, 4-fluorobenzaldehyde (0.025 g, 21.4 μL, 0.199 mmol, 1 eq) was added and the resultant mixture stirred at room temperature for 15 min. Removal of the residual solvent under reduced pressure, washing with pentane, and drying under reduced pressure afforded the desired compound as a white solid (0.083 g, 0.166 mmol, 83% yield). mp = 107-110 °C (decomp.) ^{1}H NMR (C_6D_6, 400.27 MHz): δ 1.79 (s, 3H), 1.84 (s, 3H), 1.89 (overlapping s, 6H), 2.06 (s, 3H), 2.29 (s, 3H), 2.30 (s, 3H), 2.42 (s, 3H), 3.92 (s, 1H), 5.92 (s, 1H), 6.25-6.35 (m, 4H), 6.41 (s, 1H), 6.71 (s, 1H), 6.76 (s, 1H). ^{13}C NMR (C_6D_6, 100.50 MHz): δ 18.81, 18.85, 18.87, 18.93, 20.51, 20.88, 22.02, 26.88, 47.98, 64.33, 83.03, 114.20 (J = 22.0 Hz), 126.45, 126.57, 127.29 (J = 2.7 Hz), 128.53, 128.85, 129.53, 129.58, 130.48, 131.63, 132.81, 136.41 (J = 5.5 Hz), 137.36, 138.37, 138.47, 138.63, 161.95 (J = 245.1 Hz), 172.00, 172.37. ^{19}F NMR (C_6D_6, 282.41 MHz): δ -115.63. IR (KBr): ν = 2988.7, 2919.1, 1711.3, 1678.6, 1606.8, 1511.7, 1463.7, 1431.9, 1410.0, 1388.0, 1346.2, 1225.1, 1157.8, 840.8, 750.7, 688.4, 610.6, 562.8 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{31}H_{34}N_2O_3F$: 501.2553; Found: 501.2542. Anal. calcd. for $C_{31}H_{33}N_2O_3F$: C, 74.38; H, 6.64; N, 5.60; Found: C, 74.80; H, 6.69; N, 5.23.

In situ formation of 2g. An 8 mL vial was charged with **1** (0.025 g, 0.066 mmol), C_6D_6 (0.7 mL), and a stir bar. To this vial, octanal (0.0085 g, 10.4 μL, 0.066 mmol, 1 eq) was added and the resultant mixture stirred at room temperature for 15 min to generate the desired compound in situ. ^{1}H NMR (C_6D_6, 400.27 MHz): δ 0.4-1.35 (m, 15H), 1.88 (s, 3H), 1.93 (s, 3H), 2.05-2.06 (overlapping s, 6H), 2.22 (s, 6H), 2.37 (s, 3H), 2.42 (s, 3H), 2.90 (dd, J = 6.4 Hz, 1H), 6.66 (s, 1H), 6.69 (s, 1H), 6.73 (s, 2H). ^{13}C NMR (C_6D_6, 100.65 MHz): δ 14.21, 18.91, 19.00, 19.19, 20.85, 21.30, 22.82, 26.96, 27.42, 28.76, 29.13, 31.84, 48.51, 66.02, 82.04, 129.35, 129.43, 130.00, 130.40, 133.20, 133.49, 136.59, 137.02, 138.24, 138.30, 138.47, 138.54. IR (CaF_2, C_6D_6): ν = 2955.4, 1926.1,

2856.4, 1711.5, 1680.3, 1465.6, 1393.7, 135.4, 1343.9, 1236.2, 1185.5 cm^{-1}. HRMS (CI): $[M-H]^+$ calcd. for $C_{32}H_{43}N_2O_3$: 503.3274; Found: 503.3275. Unfortunately, recrystallization or concentration of **2g** followed by washing with pentane returned **1** and precluded isolation.

In situ formation of 2h. An 8 mL vial was charged with **1** (0.025 g, 0.066 mmol), C_6D_6 (0.7 mL), and a stir bar. To this vial, pivaldehyde (0.017 g, 21.6 μL, 0.199 mmol, 3 eq) was added and the resultant mixture stirred at room temperature for 15 min to generate the deisred compound in situ. ^1H NMR (C_6D_6, 300.14 MHz): δ 0.32 (s, 9H), 1.82 (s, 3H), 1.93 (s, 3H), 2.02 (s, 3H), 2.05 (s, 3H), 2.24 (s, 6H), 2.33 (s, 3H), 2.40 (s, 3H), 3.00 (s, 1H), 6.66 (s, 1H), 6.69 (s, 1H), 6.73 (s, 2H). ^{13}C NMR (C_6D_6, 75.47 MHz): δ 18.99, 19.06, 19.24, 19.67, 20.86, 21.45, 26.53, 27.11, 32.63, 48.52, 74.69, 86.13, 130.23, 130.29, 134.44, 135.33, 136.28, 137.30, 138.14, 138.22, 138.95, 140.47, 172.52, 173.27. IR (CaF_2, C_6D_6): ν = 2965.9, 2867.8, 2806.8, 2698.5, 1767.3, 1723.4, 1682.6, 1476.7, 1401.5, 1365.2, 1216.0 cm^{-1}. HRMS (CI): $[M+H]^+$ calcd. for $C_{29}H_{39}N_2O_3$: 463.2961; Found: 463.2961. Unfortunately, recrystallization or concentration of **2h** followed by washing with pentane returned **1** and precluded isolation.

Calculation of the Product and Equilibrium Constant Ratios. Stock solutions of **1** (0.089 M), an aldehyde (0.56 M), and 1:1 mixtures of two different aldehydes (0.28 M each) were prepared in C_6D_6.

Method A: An 8 mL vial was charged with 0.6 mL of the stock solution of **1** (0.066 mmol), 0.1 mL of the stock solution of aldehyde #1 (0.070 mmol, 1.05 eq), and a stir bar. This mixture was stirred at ambient temperature for 15 min prior to addition of 0.1 mL of the stock solution of aldehyde #2 (0.070 mmol, 1.05 eq). The resulting mixture was then stirred for 20 min at ambient temperature prior to being transferred to an NMR tube. A ^1H NMR spectrum was acquired and the NMR tube was then placed in an oil bath

thermostatted to 60 °C. After 2 h, a ^{1}H NMR spectrum was acquired and the equilibrium ratio was determined from the relative integrals of the signals assigned to the starting materials and products.

Method B: An 8 mL vial was charged with 0.6 mL of the stock solution of **1** (0.066 mmol), 0.1 mL of the stock solution of aldehyde #2 (0.070 mmol, 1.05 eq), and a stir bar. This mixture was stirred at ambient temperature for 15 min prior to addition of 0.1 mL of the stock solution of aldehyde #2 (0.070 mmol, 1.05 eq). The mixture was stirred for 20 min at ambient temperature prior to being transferred to an NMR tube. A ^{1}H NMR spectrum was acquired, and the NMR tube then was placed in an oil bath thermostatted to 60 °C. After 2 h, a ^{1}H NMR spectrum was acquired and the equilibrium ratio was determined from the relative integrals of the signals assigned to the starting materials and products.

Method C: An 8 mL vial was charged with 0.6 mL of the stock solution of **1** (0.066 mmol), 0.2 mL of the stock solution of the 1:1 mixture of two aldehydes (0.070 mmol, 1.05 eq of each aldehyde), and a stir bar. This mixture was stirred at ambient temperature for 20 min prior to being transferred to an NMR tube. A ^{1}H NMR spectrum was acquired, and the NMR tube was then placed in an oil bath thermostatted to 60 °C. After 2 h, a ^{1}H NMR spectrum was acquired and the equilibrium ratio was determined from the relative integrals of the signals assigned to the starting materials and products.

Calculations. Product ratios were determined from the relative integrals of the signals assigned to the oxirane products, **2** and **2′**. For the reaction **1** + aldehyde → **2** the associated equilibrium constant, K_{eq}, may be represented as

$$K_{eq} = [\mathbf{2}]/([\mathbf{1}][\text{aldehyde}])$$

Similarly, for the reaction **1** + aldehyde′ → **2′** the associated equilibrium constant, K'_{eq}, may be represented as

$$K'_{eq} = [\mathbf{2'}]/([\mathbf{1}][\text{aldehyde'}])$$

The inability to observe a signal corresponding to **1** by NMR spectroscopy prevented the determination of [**1**] and thus, K_{eq} and K'_{eq} were not individually calculated. However, the ratios of equilibrium constants are independent of [**1**] and were calculated using the following equation:

$$K_{eq}/K'_{eq} = ([\mathbf{2}][\text{aldehyde'}]/([\mathbf{2'}][\text{aldehyde}])$$

The calculated equilibrium constant ratios summarized in Tables C3 are the average of the three experiments described above (*Method A*, *Method B*, and *Method C*).

2	2′	2:2′	K_{eq}/K'_{eq}	2	2′	2:2′	K_{eq}/K'_{eq}
2a	**2b**	73:27	6.6×10^{0}	**2c**	**2e**	65:35	3.3×10^{0}
2a	**2c**	74:26	7.0×10^{0}	**2c**	**2f**	30:70	2.0×10^{-1}
2a	**2d**	76:24	8.9×10^{0}	**2c**	**2g**	48:52	8.8×10^{-1}
2a	**2e**	85:15	2.5×10^{1}	**2c**	**2h**	>99:<1	$>1.5 \times 10^{3}$
2a	**2f**	48:52	8.8×10^{-1}	**2d**	**2e**	71:29	5.4×10^{0}
2a	**2g**	51:49	1.1×10^{0}	**2d**	**2f**	29:71	1.8×10^{-1}
2a	**2h**	>99:<1	$>1.5 \times 10^{3}$	**2d**	**2g**	32:68	2.3×10^{-1}
2b	**2c**	54:46	1.3×10^{0}	**2d**	**2h**	>99:<1	$>1.5 \times 10^{3}$
2b	**2d**	55:45	1.4×10^{0}	**2e**	**2f**	19:81	6.7×10^{-2}
2b	**2e**	75:25	7.6×10^{0}	**2e**	**2g**	23:77	1.0×10^{-1}
2b	**2f**	30:70	2.0×10^{-1}	**2e**	**2h**	>99:<1	$>1.5 \times 10^{3}$
2b	**2g**	51:49	1.1×10^{0}	**2f**	**2g**	52:48	1.2×10^{0}
2b	**2h**	>99:<1	$>1.5 \times 10^{3}$	**2f**	**2h**	>99:<1	$>1.5 \times 10^{3}$
2c	**2d**	55:45	1.4×10^{0}	**2g**	**2h**	>99:<1	$>1.5 \times 10^{3}$

Table C3. A summary of the product ratios and equilibrium constant ratios. [a]The product ratios and K_{eq}s are represented as an average of three separate mixing experiments.

Evaluating the Reaction of 1 + Pivaldehyde. An 8 mL vial was charged with **1** (0.025 g, 0.066 mmol, 1 equiv.), C_7D_8 (2.0 mL), and a stir bar. To this vial, pivaldehyde (0.0057 g, 7.2 μL, 1 eq) was added. The resultant mixture was stirred for 30 min at ambient temperature prior to being transferred to an NMR tube. The sample was then inserted into the NMR spectrometer and equilibrated at 0 °C. A ^{1}H NMR spectrum was taken at 10 °C intervals from 0-60 °C. The percent conversion was determined by the

ratio of the methyl singlet of **1** at 1.47-1.52 ppm with the methyl singlet of **2h** at 1.73-1.79 ppm. Note: to account for the differing number of hydrogens, the integral for **1** was divided by two prior to determining the ratio of the integrals. The equilibrium constant K_{eq} was then calculated using the equation:

$$K_{eq} = [\mathbf{2h}]/([\mathbf{1}][\text{pivaldehyde}])$$

The K_{eq} values calculated for **2h** at each 10 °C interval from 0-60 °C were used to generate a van't Hoff plot by plotting ln K_{eq} versus 1/T and fit to a linear regression (Figure C5). Using the following equations, ΔH and ΔS were calculated, and the standard deviations were calculated from the linear regression fit.

$$\text{slope} = -\Delta H/R$$

$$\text{y-intercept} = \Delta S/R$$

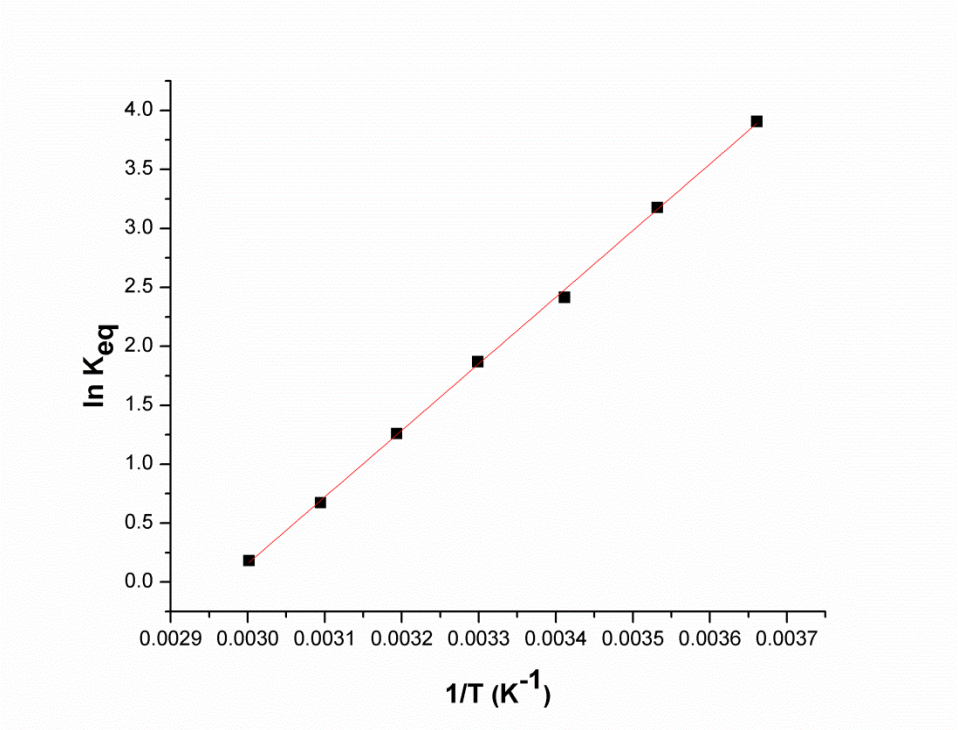


Figure C5. Plot of ln K_{eq} vs 1/T for the reaction **1** + pivaldehyde → **2h**. The equation for the best fit line is as follows: y = mx + b, where m = 5650 ± 60 K and b = -16.8 ± 0.2.

Magnetization Transfer Spectroscopy. An 8 mL vial was charged with **1** (0.020 g, 0.053 mmol) and C_7D_8 (0.8 mL). To this mixture was added the appropriate aldehyde (2-5 eq). The resultant mixture was stirred at ambient temperature for 15 min. Then, 0.5 mL of this solution was transferred to a Wilmad Labglass medium wall, quick pressure valve NMR tube and sealed with a screw cap. The sample was inserted into the NMR spectrometer and equilibrated at the appropriate temperature (85-100 °C). The free aldehyde resonance at 9.45-9.6 ppm was inverted using a selective 180° pulse and, after variable mixing times (0.001-30 s), a non-selective 90° pulse was applied and an FID recorded (4 transients). The peak areas of the aldehyde signal at 9.45-9.6 and corresponding signal for **2** at 3.8-3.9 ppm at variable mixing times were analyzed using

the computer program CIFIT[39] in order to obtain an exchange rate for the free aldehyde and the corresponding fragment in **2**. In a similar manner, the **2** resonance at 3.8-9 ppm was inverted using a selective 180° pulse and, after variable mixing times (0.001-30 s), a non-selective 90° pulse was applied. Analysis of these signal areas using CIFIT[3] afforded a second value for the exchange rate of the free aldehyde and the corresponding fragment in **2**. The reported exchange rates (k_{exc}) summarized in Table C4 are the numerical average of the two aforementioned experiments.

Oxirane	Eq. of free aldehyde[b]	Temperature (°C)	k_{exc} (s^{-1})
2a	4	100	4.0 ± 0.6
2a	2	100	4.4 ± 0.5
2a	1	100	4.3 ± 0.4
2a	2	95	2.6 ± 0.2
2a	2	90	1.67 ± 0.09
2a	2	85	1.05 ± 0.06
2b	2	100	2.13 ± 0.14
2b	2	95	1.35 ± 0.07
2b	2	90	0.89 ± 0.05
2b	2	85	0.55 ± 0.03
2c	2	100	2.06 ± 0.07
2c	2	95	1.36 ± 0.07
2c	2	90	0.82 ± 0.07
2c	2	85	0.54 ± 0.02
2d	2	100	1.30 ± 0.11
2d	2	95	0.82 ± 0.07

2d	2	90	0.46 ± 0.03
2d	2	85	0.32 ± 0.02
2e	2	100	1.45 ± 0.18
2e	2	95	0.79 ± 0.05
2e	2	90	0.48 ± 0.03
2e	2	85	0.33 ± 0.02

Table C4. A summary of the rates (k_{exc}) between various **2** and various aldehydes. [a]Conditions: $[\mathbf{1}]_0 = 0.066$ M, C_7D_8. [b] With respect to **2**.

The k_{exc} values calculated for **2a-e** at each 5 °C interval from 85-100 °C were used to generate Eyring plots by plotting ln (k_{exc}/T) versus 1/T and fit to a linear regression (see Figures C6-C10). Using the following equations, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were calculated for each exchange process investigated, and te standard deviations were calculated from the linear regression fit.

$$\text{slope} = -\Delta H^{\ddagger}/R$$

$$\text{y-intercept} = \Delta S^{\ddagger}/R$$

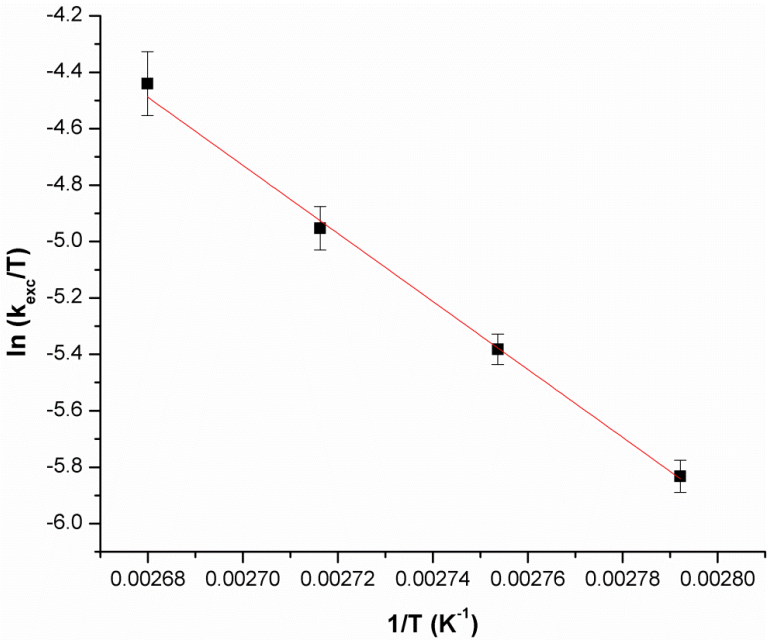


Figure C6. Plot of ln (k_{exc}/T) vs 1/T for the exchange of **2a** and 4-nitrobenzaldehyde. The equation for the best fit line is as follows: y = mx + b, where m = -12,100 ± 900 K and b = 28 ± 3.

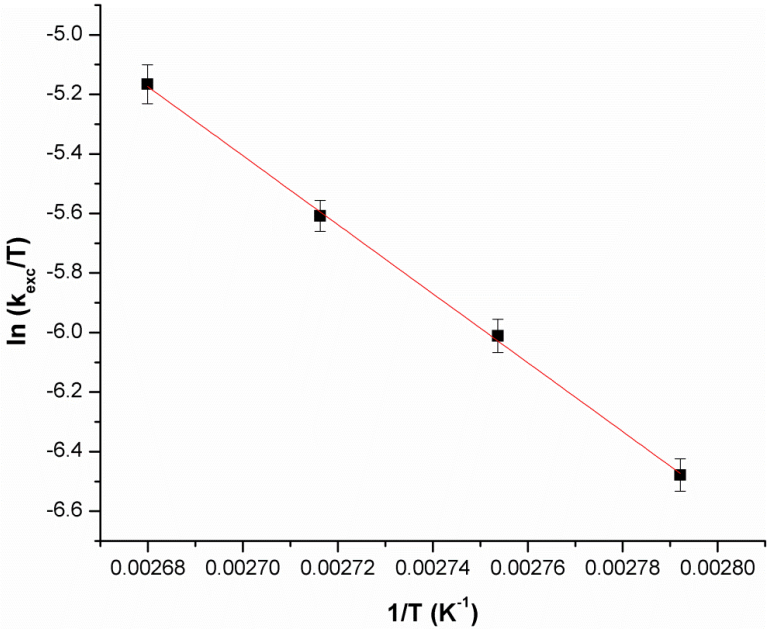


Figure C7. Plot of ln (k_{exc}/T) vs 1/T for the exchange of **2b** and 4-bromobenzaldehyde. The equation for the best fit line is as follows: y = mx + b, where m = -11,600 ± 700 K and b = 26 ± 2.

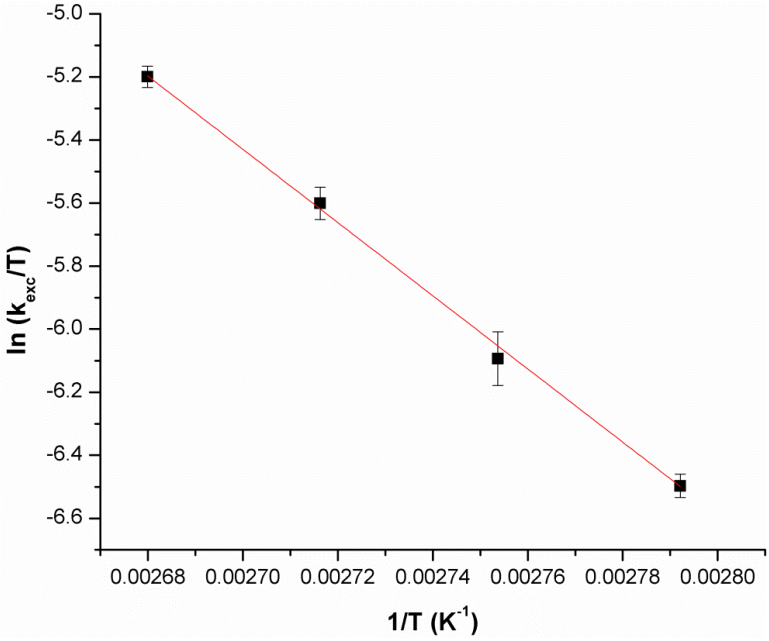


Figure C8. Plot of ln (k_{exc}/T) vs 1/T for the exchange of **2c** and 4-fluorobenzaldehyde. The equation for the best fit line is as follows: y = mx + b, where m = -11,600 ± 440 K and b = 25.9 ± 1.2.

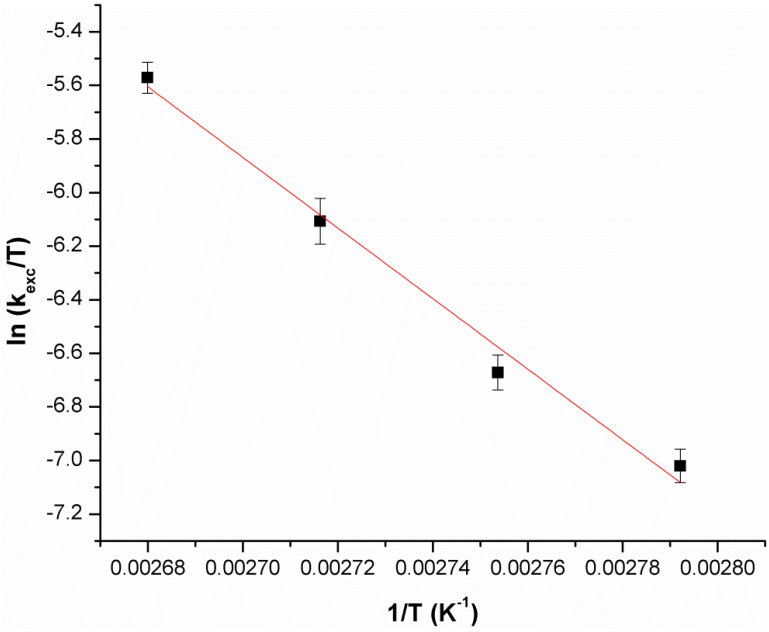


Figure C9. Plot of ln (k_{exc}/T) vs 1/T for the exchange of **2d** and benzaldehyde. The equation for the best fit line is as follows: y = mx + b, where m = -13,200 ± 700 K and b = 30 ± 2.

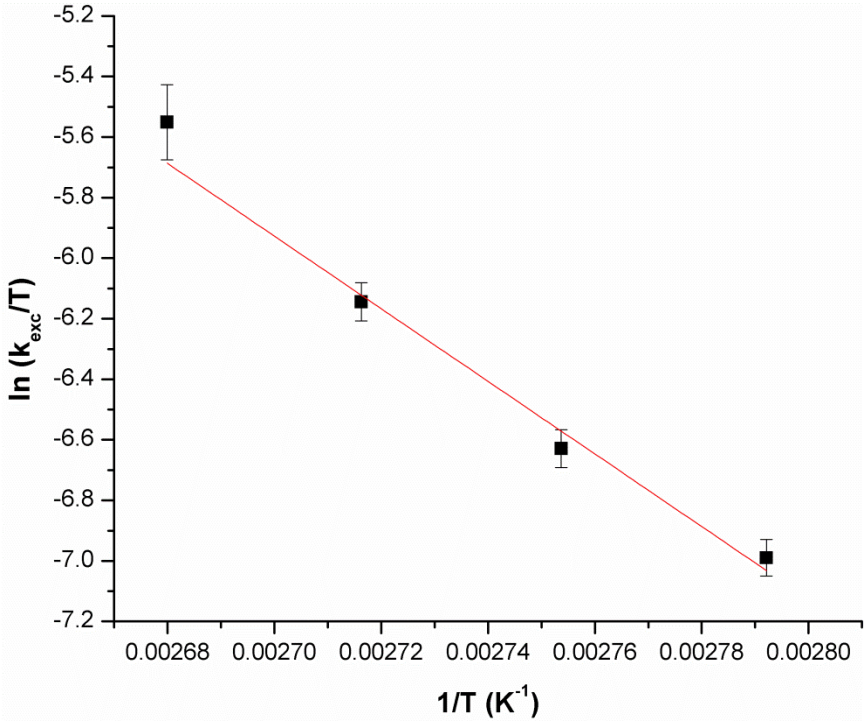


Figure C10. Plot of ln (k_{exc}/T) vs 1/T for the exchange of **2e** and 4-methoxybenzaldehyde. The equation for the best fit line is as follows: y = mx + b, where m = -12,000 ± 1000 K and b = 26 ± 3.

C5. ACKNOWLEDGEMENTS

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27) Analysis of the equilibrium between **2h** and pivaldehyde/**1** between 0° and 60 °C using VT ^{1}H NMR spectroscopy revealed ΔH and ΔS values of -11.2 kcal·mol^{-1} and -33.4 cal·mol^{-1}·K^{-1}, respectively.

28) Likewise, a 48:52 mixture of **2a**:**2f** was obtained by combining 4-nitrobenzaldehyde and cyclohexanecarboxaldehyde (1.05 equiv. ea) with a C_6D_6 solution of **1** ([**1**]$_0$ = 0.066 M) followed by heating to 60 °C for 2 h.

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