

An *N,N*-Diamidocarbene: Studies in C–H Insertion, Reversible Carbonylation, and Transition-Metal Coordination Chemistry

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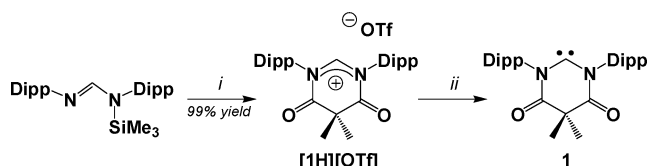
Considerable controversy has surrounded the carbenoid character of *N*-heterocyclic carbenes (NHCs) since their isolation nearly two decades ago by Arduengo.¹ Indeed, these remarkable compounds, as well as other diaminocarbenes (DACs), are termed “ylidenes” according to IUPAC nomenclature because of their ylidic reactivity.² Traditional carbenes, such as methylene, typically facilitate insertions into unactivated C–H bonds,³ activate H₂,⁴ cyclopropanate olefins,⁵ and form ketenes upon exposure to CO.⁶ In contrast, DACs do not facilitate the aforementioned chemical reactions. This disparity is primarily due to the π -donating nature of the amino substituents bonded to the carbene atom, which, in addition to stabilizing the divalent carbon nucleus, renders it nucleophilic. Moreover, DACs do not display reactivities typical of Fischer-type carbenes despite their high propensity to metalate,² presumably because of a lack of electrophilic character.^{7–9} In fact, as recently documented by Bertrand,⁹ DACs are not sufficiently electrophilic to activate H₂⁷ or fix CO to form ketenes.⁸

We sought to alter this paradigm and increase the electrophilic nature of DACs by shepherding nitrogen lone pair donation away from the empty *p* orbital on the carbon nucleus. We envisioned an *N,N'*-diamidocarbene, where significant electron density would be localized on the low-lying π^* orbitals of carbonyls attached directly to the nitrogen atoms of a DAC. As detailed below, we discovered that such a carbene is not only electrophilic but, surprisingly, displays familiar nucleophilic characteristics as well.¹⁰

As shown in Scheme 1, the pyrimidinium salt [1H][OTf] was prepared by treatment of *N,N'*-bis(2,6-diisopropylphenyl)-*N*-trimethylsilylformamidinium¹¹ with dimethylmalonyl dichloride in toluene. Immediate precipitation of the desired compound was observed upon addition of trimethylsilyl triflate (TMS·OTf), which facilitated isolation of the product in nearly quantitative yield.^{12,13} Single crystals suitable for X-ray diffraction analysis were obtained by cooling a concentrated solution of [1H][OTf] in 1:1 (v/v) CH₂Cl₂/toluene to –40 °C (Figure 1). Remarkably, [1H]⁺ exhibited minimal amide character in the solid state, presumably because of donation of the nitrogen lone pairs into the formally empty *p* orbital on the positively charged carbon center rather than to the α -carbonyl moieties. The carbonyl bond lengths [C4–O1 = 1.188(4) Å, C6–O2 = 1.183(4) Å] as well as the N1–C6 and N2–C4 distances [1.456(5) and 1.447(5) Å, respectively] deviate substantially from those of prototypical amides such as formamide [C–O = 1.193 Å, N–CO = 1.349 Å (calcd)].¹⁴ This assignment was confirmed by FT-IR spectroscopy, which revealed that [1H]⁺ exhibits a carbonyl stretching frequency (ν_{CO}) at 1760 cm^{–1} (CH₂Cl₂). These structural features, which are strikingly similar to those observed by Stoltz for 2-quinuclidone,^{14,15} suggested to us that [1H]⁺ contains functional groups that are more consistent with α -ketoimines than amides.

Treatment of [1H][OTf] with sodium hexamethyldisilazide (NaHMDS) in C₆D₆ afforded the corresponding *N,N'*-diamidocarbene **1** (Scheme 1), as determined by NMR spectroscopy. The ¹³C

Scheme 1^a



^a Conditions: (i) (1) dimethylmalonyl dichloride, toluene, 25 °C, 1 h; (2) TMS·OTf, 25 °C, 1 h. (ii) NaHMDS, C₆H₆, 25 °C, 30 min. Dipp = 2,6-diisopropylphenyl.

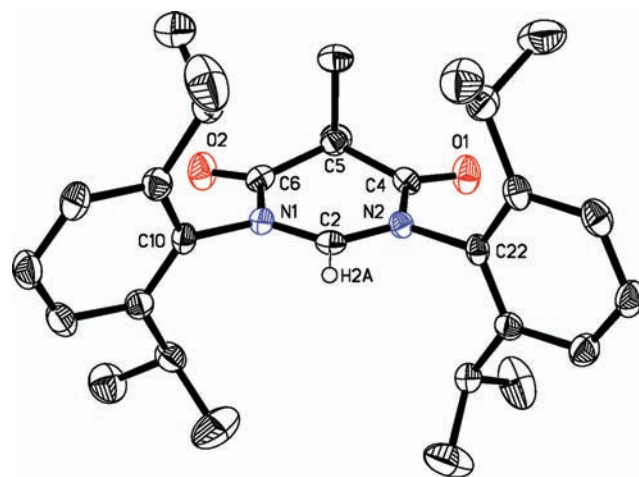


Figure 1. ORTEP representation of [1H]⁺ in [1H][OTf] (drawn as 50% thermal ellipsoids; the triflate counterion and all of the H atoms except for H2A have been omitted for clarity). Pertinent structural metrics are provided in the text.

resonance of the carbene nucleus was observed at 278.4 ppm, a value that is significantly downfield relative to those displayed by other six-membered NHCs.^{11,16} Indeed, **1** exhibits one of the most downfield-shifted carbene resonances of any NHC featuring two donor substituents¹⁰ and deficient of main-group heteroatoms.¹⁷ As expected, the carbonyl stretching frequency of **1** was shifted to lower energy (ν_{CO} = 1714 cm^{–1} in CH₂Cl₂) with respect to the analogous energy exhibited by [1H]⁺, reflecting the loss of cationic character upon deprotonation.

Upon the successful synthesis of **1**, subsequent efforts were directed toward elucidating its structure in the solid state. To our surprise, X-ray diffraction analysis of crystals obtained by cooling a concentrated 1:1 (v/v) toluene/hexane solution of the carbene to –40 °C revealed the structure of the C–H insertion product **2** (Figure 2 and Scheme 2). Unlike [1H]⁺, the NCO fragments in **2** were found to be characteristic of prototypical amides with short N–C bond lengths [N1–C2 = 1.373(2) Å, N2–C4 = 1.376(2) Å] and long C–O distances [C2–O1 = 1.216(2) Å, C4–O2 = 1.216(2) Å]. Likewise, **2** exhibited ν_{CO} values of 1690 and 1662

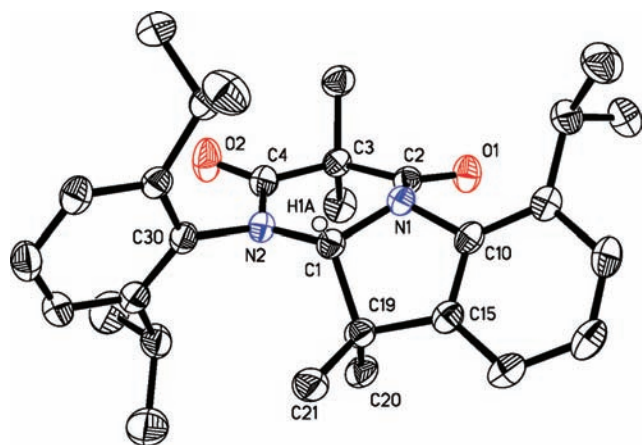
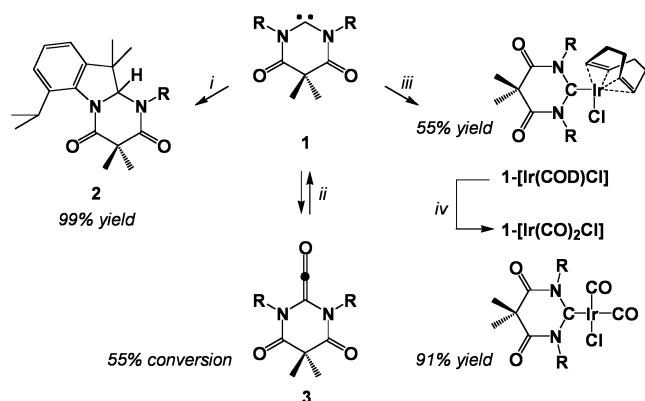


Figure 2. ORTEP representation of **2** (drawn as 50% thermal ellipsoids; H atoms except for H1A have been omitted for clarity). Pertinent structural metrics are provided in the text.

Scheme 2^a



^a Conditions: (i) C₆H₆, 50 °C, 30 h; (ii) 100 psi CO(g), C₇D₈, 25 °C; (iii) [Ir(COD)Cl]₂, C₆D₆, 25 °C, 12 h; (iv) 1 atm CO(g), CH₂Cl₂, 25 °C, 2 h. R = Dipp. Isolated yields are indicated.

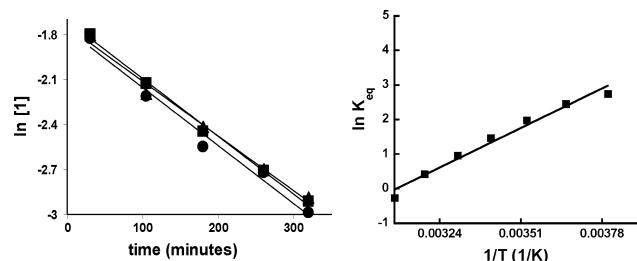


Figure 3. (left) Plot of ln [1] ([1]₀ = 1.6 × 10⁻¹ M) vs time in C₆D₆ in the presence of (circles) 1.0, (squares) 3.0, and (triangles) 10 equiv of Na⁺ at 50 °C. The Na⁺ was derived from NaHMDS. (right) Plot of ln K_{eq} vs 1/T for the reaction **1** + CO ⇌ **3** using the data summarized in Table S2 in the SI. The equation for the best-fit line is $y = 4249.3x - 13.171$ ($R^2 = 0.98$).

cm⁻¹ (CH₂Cl₂), which are at significantly lower frequencies than the analogous signals observed for [1H]⁺.

An investigation of the kinetics of this reaction revealed that the formation of **2** was first-order in carbene concentration and proceeded with a first-order rate constant $k = 3.6 \times 10^{-3} \text{ min}^{-1}$ at 50 °C [see the Supporting Information (SI)]. Additionally, the rate of this reaction did not depend on the concentration of NaHMDS, effectively eliminating the possibility of a catalyzed process (Figure 3, left).¹⁸ While it has been previously reported that stabilized singlet carbenes facilitate insertion into C–H bonds,^{18–23} the

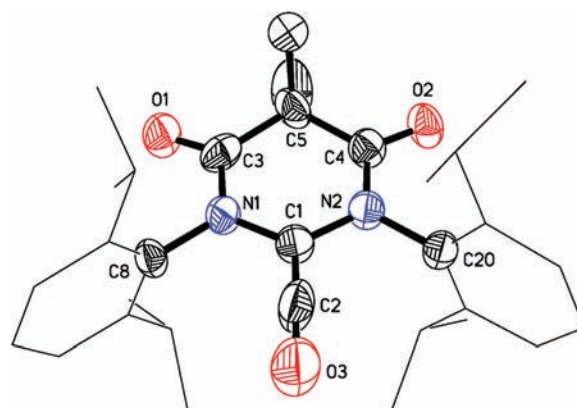


Figure 4. ORTEP representation of **3** in 3·NaHMDS (drawn as 50% thermal ellipsoids; for clarity, H atoms have been omitted and the Dipp substituents drawn as thin lines). Pertinent structural metrics are provided in the text.

substrates employed in such reactions are relatively acidic. Furthermore, the formation of **2** occurs under mild conditions²⁴ and involves a C–H insertion reaction at a tertiary alkyl group.²⁵ In a broader sense, NHCs akin to **1** are expected to find applications in C–H activation chemistry, particularly as organic alternatives to commonly employed metal-catalyzed processes.²⁶

The formation of **2** is characteristic of transformations typically exhibited by traditional (unstabilized) carbenes, indicating that **1** displays a certain degree of electrophilic character.^{7,9,10} Upon the observation of this unprecedented reactivity, subsequent efforts were focused on further investigation of the electrophilic character of **1**. Although DACs were previously reported to be incapable of affixing CO,^{7–9} an instant color change from pale-yellow to purple ($\lambda_{\text{max}} = 510 \text{ nm}$) was observed upon bubbling CO into a toluene-*d*₈ solution of **1**. A new compound that exhibited all of the signals corresponding to diamidoketene **3** (see Scheme 2) was observed by ¹H NMR spectroscopy, albeit in a 2:1 **1/3** ratio.²⁷ Regardless, the ketene CO resonance (250.5 ppm) was shifted significantly downfield relative to that for CO (184.5 ppm), and the carbene CCO resonance (98.85 ppm) was drastically upfield-shifted relative to the carbene atom signal for **1** (278.3 ppm).²⁸ Additionally, a sharp band in the IR spectrum of this purple solution centered at 2100 cm⁻¹ was also observed, consistent with the formation of a ketene.⁷ Subsequent heating of this solution resulted in an instantaneous loss of color, presumably due to expulsion of CO; in contrast, cooling the same solution resulted in a more intense purple color. The thermally reversible CO fixation process was confirmed using variable temperature (VT) NMR spectroscopy (see the SI), and from the van't Hoff plot shown in the right panel of Figure 3, the thermodynamic parameters for the carbonylation of **1** were determined to be $K_{\text{eq}} = 2.62 \text{ M}^{-1}$ at 30 °C, $\Delta H^\circ = -35.33 \text{ kJ mol}^{-1}$, and $\Delta S^\circ = -109.5 \text{ J mol}^{-1} \text{ K}^{-1}$. Although the reversible coordination of CO to metals has been well-documented,²⁹ to the best of our knowledge this is the first example of a reversible carbonylation process involving an organic substrate. Furthermore, these results expand the short list of noncatalyzed, reversible C=C bond-forming processes.^{1c,30}

Cooling a saturated solution of **3** in toluene-*d*₈ to -80 °C resulted in the formation of purple crystals of 3·NaHMDS, as determined by X-ray crystallography (Figure 4). The C=C=O fragment in the solid-state structure of **3** clearly indicated the formation of a ketene³¹ with C1–C2 and C2–O3 distances of 1.302(9) and 1.182(8) Å, respectively. Additionally, the C1–C2–O3 angle was nearly linear [177.8(9)°], as expected for a ketene functional group. The NCO

moieties were similar to those observed in **2**, demonstrating a large degree of amide character with relatively short C–N bonds [1.355(7)–1.369(7) Å] and long C–O distances [1.220(7)–1.214(7) Å].

Having demonstrated that **1** exhibits reactivity characteristic of electrophilic carbenes, our efforts shifted toward probing its intrinsic nucleophilicity. Treating a freshly prepared solution of **1** in C₆D₆ with [Ir(COD)Cl]₂ (COD = 1,5-cyclooctadiene) led to the formation of the metal complex **1**–[Ir(COD)Cl] (Scheme 2).³² Notably, the carbene's ¹³C NMR resonance was found at 231.3 ppm (C₆D₆), which is significantly downfield-shifted relative to those for other NHC complexes reported in the literature (179.6–208.2 ppm).³³ This unusual chemical shift was attributed to reduced electron density at the carbene nucleus due to delocalization between the nitrogen atoms of **1** and the adjoining carbonyl groups. In agreement with this assessment, the complex exhibited $\nu_{\text{CO}} = 1736$ and 1711 cm⁻¹ (CH₂Cl₂) and the acyl carbons resonated at 171.4 ppm (C₆D₆), indicative of carbonyls with bond orders that were effectively hybrids of those for ketones and amides.

The electronic structure of **1** was also expected to result in a significantly reduced ligand donicity compared with other NHCs. To investigate this, **1**–[Ir(CO)₂Cl] was prepared by sparging a CH₂Cl₂ solution of **1**–[Ir(COD)Cl] with CO. Salient spectroscopic features of the product included a ¹³C NMR resonance at 224.1 ppm (C₆D₆), which was assigned to the carbene nucleus. This chemical shift was shifted downfield relative to those for other NHC–[Ir(CO)₂Cl] complexes reported in the literature (176.2–204.9 ppm),³³ reflecting the electron-deficient nature of **1**. The IR spectrum of **1**–[Ir(CO)₂Cl] exhibited two strong ν_{CO} signals at 2074 and 1991 cm⁻¹ (CH₂Cl₂), which were attributed to the trans and cis CO ligands on the metal center, respectively, as well as a ν_{CO} of 1736 cm⁻¹ for the NCO groups. By Nolan's method,^{33a} the Tolman Electronic Parameter³⁴ for **1** was calculated to be 2057 cm⁻¹, a value similar to that obtained for analogous metal complexes containing tricyclohexylphosphine.³³ Hence, while **1** retains the nucleophilic reactivity typical of traditional NHCs,³⁵ the carbonyl groups adjacent to the nitrogen atoms significantly attenuate the ligand's donicity.

In conclusion, the electrophilic character of *N,N'*-diamidocarbene **1**, imparted by the strongly π -withdrawing carbonyl moieties linked to the nitrogen atoms of a DAC, has effectively opened a new vista in NHC reactivity, including an ability to insert into a tertiary C–H bond and the discovery of an unprecedented reversible carbonylation reaction. However, like other NHCs, **1** is also sufficiently nucleophilic to coordinate to transition metals. We believe these results will enable the rational design of novel classes of transition-metal complexes and enrich many stoichiometric, metal-mediated, and organocatalyzed reactions involving NHCs.^{2,36,37}

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Supporting Information Available: Synthetic details, VT NMR data, and crystallographic data for [1H]OTf, **2**, **3**•NaHMDS, and **1**–[Ir(COD)Cl] (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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