A General and Versatile Approach to Thermally Generated *N*-Heterocyclic Carbenes

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Abstract: The synthesis of *N*-heterocyclic carbene (NHC) adducts by condensation of diamines with appropriately substituted benzaldehydes is described. This simplified approach provides the NHC adduct without first having to generate the carbene followed by its protection. These adducts undergo thermal deprotection to generate *N*-heterocyclic carbene in situ. Adduct decomposition temperatures were investigated as a function of catalyst structure by using thermal analysis and spectroscopic techniques. Importantly, unlike adducts derived from chloroform, the new pentafluorobenzene-based adducts are more readily prepared and are stable at room temperature. The utility of these adducts as organic catalyst precursors for living ring-opening polymerization (ROP) of lactide, transesterification reactions, and the synthesis of *N*-heterocyclic carbene ligated organometallic complexes is also described.

Keywords: carbenes · nitrogen heterocycles · organic catalysis · organometallic complexes

Introduction

Although carbenes have historically played an important function in organic chemistry as transient intermediates,[1] significant advances in the isolation of heteroatom-substituted singlet carbenes and persistent triplet diarylcarbenes have collectively renewed interest and the scope of possibilities.[2] Wanzlick's[3] pioneering studies of the chemistry of bis-1,3-diphenyl imidazolin-2-ylidene carbenes[4] laid the groundwork for Arduengo's[5] elegant studies on the synthesis, isolation, and characterization of the first stable imidazolin-2-ylidene and imidazol-2-ylidene carbenes.[6] The chemistry of *N*-heterocyclic carbenes (NHC) has become a major area of research[7] as these stable carbenes have proven to be outstanding ligands for transition metals[8] as well as potent nucleophilic organic catalysts.[9]

Arduengo and others observed that the saturated (1,3-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene) *N*-heterocyclic carbene (SIMes) cleanly undergoes a C–H insertion reaction with compounds containing acidic C–H bonds to form stable NHC adducts, whereas the corresponding unsaturated carbenes led to more complicated mixtures of products.[10] Arduengo implicated that this adduct yielded the free carbene upon melting. Lappert[11] and Grubbs[12] have utilized the chloroform adducts to generate transition-metal carbenes and implicated that free carbenes were generated in these reactions. Enders carried out analogous investigations on the methanol adduct of the 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2,4,-triazol-5-ylidene; thermolysis of this methanol adduct cleanly liberated the free carbene and methanol.[13] The elimination of alcohols from methanol or *tert*-butanol adducts of carbenes has proven a useful strategy for generating transition-metal carbene complexes,[12–14] but the role of free carbenes in these processes has never been clearly demonstrated.

We have recently shown that NHC are potent organic catalysts for ring-opening polymerization of cyclic esters and transesterification reactions.[9g,h] As part of our interests in developing convenient methods for generating catalysts in situ,[9h,j] our attention was drawn towards NHC adducts that could be thermally activated[10,11] to form NHC for controlled organocatalytic polymerization. For this strategy to be successful, it was important to demonstrate that carbenes can be liberated from these adducts efficiently in the absence of transition metals. In this report, we describe a general strategy for generating a variety of carbene adducts

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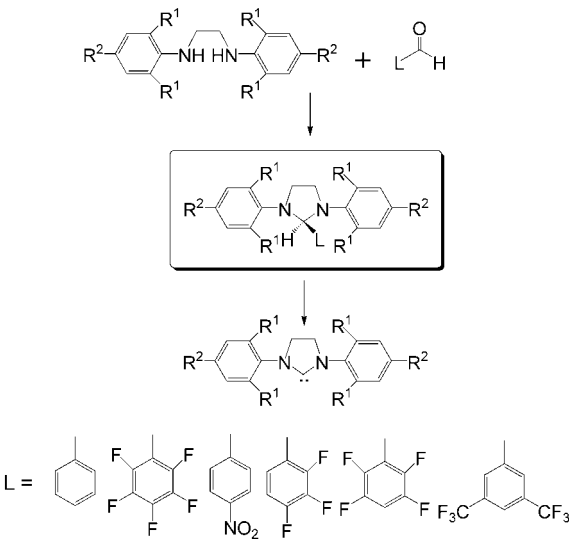
from the corresponding diamines and aldehydes (Scheme 1),[3] and show that thermolysis of these adducts provide a convenient source of carbenes in a tunable manner depending on the nature of the adduct.



Scheme 1.

Experimental Section

General methods: Commerical reagents and solvents were purchased from Aldrich and used without further purification. Deuterated NMR solvents were purchased from Cambridge Isotope Laboratories. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer. ^{1}H and ^{13}C NMR chemical shifts were referenced to the residual solvent peak. Gel permeation chromatography was performed in THF on a Waters chromatograph equipped with four 5 μm Waters columns (300× 7.7 mm) connected in series with increasing pore size (10, 100, 1000, 10^5, 10^6 Å). A Waters 410 differential refractometer and 996 photodiode array detector were employed. Modulated differential scanning calorimetry (MDSC) measurements were recorded on a TA Instruments DSC 2920 with a ramp rate of 10° min^{-1} under a nitrogen atmosphere. Thermal gravimetric analysis (TGA) measurements were recorded on a TA Instruments Hi-Res 2950 with a ramp rate of 10° min^{-1} under a nitrogen purge. 1,3-Bis(2,4,6-trimethylphenyl)-2-(trichloromethyl)imidazolidine was prepared by literature methods.[15]

1,3-Bis(2,4,6-trimethylphenyl)-2-(pentafluorophenyl)imidazolidine (4): In a 5 mL scintillation vial, 2,3,4,5,6-pentafluorobenzaldehyde (201 mg, 1.7 mmol) was dissolved in a minimal amount of glacial acetic acid. *N*,*N*′-Bis-(2,4,6-trimethylphenylamino)ethane (305 mg, 1.03 mmol) was placed into the vial. The reaction mixture was stirred, after which the reaction mixture was completely homogeneous. After 1 min the reaction mixture felt warm to the touch and within 30 min a large amount of precipitate had formed. The precipitate was washed with cold methanol. The precipitate was then dissolved in CH_2Cl_2 and forced through a short silica plug that had been previously treated with triethylamine. Evaporation of the CH_2Cl_2 solution afforded **4** as a white crystalline solid (346 mg, 71 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.3 (s, 6H), δ 2.3–2.6 (br, 12H), 3.5–3.6 (m, 2H), 3.9–3.4 (m, 2H), 6.4 (s, 1H), 6.9 ppm (br, 4H); ^{19}F NMR (376 MHz): δ = −136.3 (m, 1F), −148.6 (m, 1F), −155.8 (m, 1F), −163.1 ppm (m, 2F); ^{13}C NMR (100 MHz): δ = 19.2 (br), 20.9, 51.4, 71.8, 129.9, 130.1, 130.6 (br), 130.5, 130.6, 131.8, 135.3, 135.9, 139.3, 143.8 ppm; HRMS analysis (ESI): *m*/*z* calcd $[M+H]^+$: 475.2173; found: 475.2188.

1,3-Bisphenyl-2-(pentafluorophenyl)imidazolidine (6): *N*,*N*′-diphenylethylenediamine (200 mg, 0.94 mmol) and 2,3,4,5,6-pentafluorobenzaldehyde (230 mg, 0.94 mmol) were placed in a 20 mL scintillation vial, equipped with a stir bar, and dissolved with CH_2Cl_2 (5 mL). A catalytic amount *p*-toluenesulfonic acid and Na_2SO_4 (50 mg) were then added to the vial. The reaction mixture was stirred for 8 h; it was then filtered and the solvent evaporated under reduced pressure to yield **6** as a light brown powder (395 mg, 96 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.7–3.9 (m, 2H), 3.9–4.1 (m, 2H), 6.5 (s, 1H), 6.7–6.8 (m, 2H), 6.8–6.9 (m, 1H), 7.2–7.5 ppm (m, 2H); ^{19}F NMR (376 MHz): δ = −143.2 (brs, 2F), −153.7 (m, 1F), −161.7 ppm (m, 2F); ^{13}C NMR (100 MHz): δ = 46.9, 68.1, 112.9, 118.7, 129.9, 144.4 ppm; m.p. 140 °C; HRMS analysis (ESI): *m*/*z* calcd $[M+H]^+$: 391.1234; found: 391.1228.

1,3-Bis(2,4,6-trimethylphenyl)-2-(2,3,5,6-tetrafluorophenyl)imidazolidine (7): By Using the synthetic procedure described for **4**, the reaction of 2,3,5,6-tetrafluorobenzaldehyde (246 mg, 1.38 mmol) and *N*,*N*′-bis-(2,4,6-trimethylphenylamino)ethane (408 mg, 1.38 mmol) afforded **7** as a white crystalline solid (520 mg, 82 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.2 (s, 6H), δ 2.3–2.6 (br, 12H), 3.5–3.6 (m, 2H), 3.9–3.4 (m, 2H), 6.4 (s, 1H), 6.8 ppm (br, 4H); ^{19}F NMR (376 MHz): δ = −137.1 (m, 1F), −140.5 (m, 1F), −140.8 (m, 1F), −149.3 ppm (m, 1F); ^{13}C NMR (100 MHz): δ = 19.2 (br), 21.0, 51.4, 71.8, 104.1, 105.1 (t, *J* = 22.4 Hz), 124.1 (m), 130.2 (br), 135.7, 139.5, 144.1 (m), 145.1 (m), 146.5 (m), 147.5 ppm (m); HRMS analysis (ESI): *m*/*z* calcd $[M+H]^+$: 457.2267; found: 457.2256.

1,3-Bisphenyl-2-(2,3,5,6-tetrafluorophenyl)imidazolidine: By using the synthetic procedure described for **6**, the reaction of *N*,*N*′-diphenylethylenediamine (105 mg, 0.5 mmol) and 2,3,5,6-trifluorobenzaldehyde (89 mg, 0.5 mmol) afforded the product as an off-white powder (173 mg, 93 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.7 (m, 2H), 3.9 (m, 2H), 6.5 (s, 1H) 6.6 (d, 4H), 6.8 (t, 2H), 6.8 (m, 1H), 7.1 ppm (m, 4H); ^{19}F NMR (376 MHz): δ = −139.0 (m, 2F), −143.7 ppm (br, 2F); ^{13}C NMR (100 MHz): δ = 46.9, 68.1, 106.4 (t, *J* = 22.5 Hz), 112.7, 118.5, 120.6 (t, *J* = 14 Hz), 129.8, 143.9 (m), 144.6, 145.1 (m), 146.4 (m), 147.5 ppm (m); m.p. 172 °C.

1,3-Bis(2,4,6-trimethylphenyl)-2-(trifluoromethyl)imidazolidine:, *N*,*N*′-Bis-(2,4,6-trimethylphenylamino)ethane (205 mg, 0.69 mmol) with trifluoroacetaldehyde ethyl hemiacetal (120 mg, 0.82 mmol) were placed in a 20 mL scintillation vial equipped with a stir bar. Several drops of toluene were then added to the reaction vial with a catalytic amount of *p*-toluenesulfonic acid and anhydrous magnesium sulfate. The reaction mixture was then placed in a 40 °C oil bath and stirred for 24 h. The reaction mixture was diluted with a small amount of CH_2Cl_2 and passed through a small column of basic alumina to afford a white powder. The product was then passed through a small column of silica gel (CH_2Cl_2) to afford pure white powder (175 mg, 68 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C,): δ = 2.3 (s, 6H), 2.4 (brs, 12H), 3.4 (m, 2H) 3.8 (m, 2H), 5.0 (q, 1H, *J* = 4.1 Hz), 6.9 ppm (brs, 4H); ^{19}F NMR (376 MHz): δ = −78.1 ppm (d, *J* = 4.1 Hz, 3F); ^{13}C (100 MHz): δ = 19.1 (br), 20.3 (br), 21.1, 51.1, 74.9 (q, *J* = 33.0 Hz), 130.1, 135.9, 139.4 ppm; m.p. 177 °C.

1,3-Bisphenyl-2-(trifluoromethyl)imidazolidine: *N*,*N*′-Diphenylethylenediamine (105 mg, 0.5 mmol) and trifluoroacetaldehyde ethyl hemiacetal (80 mg, 0.55 mmol) were combined in a 20 mL scintillation vial equipped with a stir bar. Several drops of toluene were then added to the reaction vial. A catalytic amount of *p*-toluenesulfonic acid and anhydrous magnesium sulfate were then added to the reaction vial. The vial was placed in a 70 °C oil bath and stirred for 24 h. The reaction mixture was diluted with a small amount of CH_2Cl_2 and passed through a small column of basic alumina to afford a white powder. The product was then passed through a small column of silica gel (CH_2Cl_2) to afford the desired product as a pure white powder (140 mg, 89 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.7 (m, 2H), 3.8 (m, 2H), 5.7 (q, 1H, *J* = 4.7 Hz), 6.9 (m, 6H), 7.3 ppm (m, 4H); ^{19}F NMR (376 MHz): δ = −75.3 ppm (d, *J* = 4.6 Hz, 3F); ^{13}C (100 MHz): δ = 47.1, 73.9 (q, *J* = 32.7 Hz), 114.1, 119.7, 129.7, 146.0 ppm; m.p. 78 °C.

1,3-Dimethyl-2-(pentafluorophenyl)imidazolidine: A stirring solution of *N*,*N*′-dimethylethylenediamine (113 mg, 1.2 mmol) in diethyl ether (5 mL) was cooled to −78 °C. Pentafluorobenzaldehyde (248 mg, 1.2 mmol) was added to the stirring solution and was allowed to warm to room temperature. The reaction mixture was stirred at room temperature for 30 min, after which the solvent was removed under reduced pressure to yield the desired product as colorless oil (284 mg, 89 %). The product decomposed rapidly in pure isolated form, but was stable over 24 h in dilute solution. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.2 (s, 6H), 2.6

(m, 2H), 3.3 (m, 2H), 4.1 ppm (s, 1H); ^{19}F NMR (376 MHz): $\delta = -142.9$ (m, 1F), −155.2 (t, $J = 21.1$ Hz, 2F), −163.0 ppm (m, 2F).

1,3-Dimethyl-2-(2,3,5,6-tetrafluorophenyl)imidazolidine: A stirring solution of *N*,*N*′-dimethylethylenediamine (136 mg, 1.5 mmol) in diethyl ether (5 mL) was cooled to 0 °C. 2,3,5,6-Tetrafluorobenzaldehyde (267 mg, 1.5 mmol) was added and the solution was allowed to warm to room temperature. The reaction mixture was stirred at room temperature for 30 min, after which the solvent was removed under reduced pressure to yield the desired product as light yellow oil (346 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.3$ (s, 6H), 2.7 (m, 2H), 3.4 (m, 2H), 4.2 (s, 1H), 7.0 ppm (m, 1H); ^{19}F NMR (376 MHz): $\delta = -139.9$ (m, 2F), −143.6 ppm (br, 2F); ^{13}C (100 MHz): $\delta = 40.8$, 54.2, 83.4, 105.9 (t, $J =$ 84.9 Hz); 120.6 (t, $J = 44.3$); 144.8 (m), 147.3 (m), 163.4 ppm (m).

1,3-Dimethyl-2-(2,3,6 trifluorophenyl)imidazolidine: A stirring solution of *N*,*N*′-dimethylethylenediamine (144 mg, 1.6 mmol) in diethyl ether (5 mL) was cooled to 0 °C. 2, 3,6-Trifluorobenzaldehyde (256 mg, 1.6 mmol) was added and the solution was allowed to warm to room temperature. The reaction mixture was stirred at room temperature for 30 min, after which the solvent was removed under reduced pressure to yield the desired product as light yellow oil (346 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 2.3$ (s, 6H), 2.6 (m, 2H), 3.3 (m, 2H), 4.1 (s, 1H), 6.8 (m, 1H), 7.1 ppm (m, 1H); ^{19}F NMR (376 MHz): $\delta = -119.4$ (br, 1F), −137.3 (br, 1F), 142.8 ppm (m, 1F).

1,3-Bisphenyl-2-(3,5-bis(trifluoromethyl)phenyl)imidazolidine: By using the synthetic procedure described for **6**, the reaction of *N*,*N*′-diphenylethylenediamine (105 mg, 0.5 mmol) and 3,5-bis(trifluoromethyl)benzaldehyde (122 mg, 0.5 mmol) afforded the product as an off-white powder (206 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 3.8$ (m, 2H), 3.9 (m, 2H), 6.7 (s, 2H) 6.8 (s, 2H), 6.8 (m, 2H), 7.2 (m, 4H), 7.7 (m, 1H), 7.9 ppm (s, 2H); ^{19}F NMR (376 MHz): $\delta = -63.1$ ppm (s, 6F); ^{13}C NMR (100 MHz): $\delta = 46.9$, 114.4, 119.3, 122.2, 122.6 (m), 124.9, 127.9 (br), 129.7, 132.1 (q, $J = 34$ Hz), 144.6, 145.6 ppm (m); m.p. 138 °C.

1,3-Bis(2,4,6-trimethylphenyl)-2-(3,5-bis(trifluoromethyl)phenyl)imidazolidine: By using the synthetic procedure described for **4**,the reaction of 3,5-bis(trifluoromethyl)benzaldehyde (220 mg, 0.90 mmol) and *N*,*N*′-bis-(2,4,6-trimethylphenylamino)ethane (270 mg, 0.90 mmol) afforded the desired product as a white crystalline solid (407 mg, 87%). ^{1}H NMR (400 MHz, C_6D_6, 25 °C): $\delta = 2.1$ (s, 6H), 2.3 (br, 12H), 3.5–3.6 (m, 2H), 3.9–3.4 (m, 2H), 5.9 (s, 1H), 6.7 (br, 4H), 7.5 (s, 1H), 7.9 ppm (s, 2H); ^{19}F NMR (376 MHz, C_6D_6): $\delta = -62.9$ ppm (s, 6F); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 20.1$ (br), 20.9, 51.1, 80.1, 122.2 (m), 122.9, 125.7, 129.4 (br), 130.7 (br), 136.1, 136.9 (br), 139.5, 146.8 ppm; m.p. 139 °C.

Preparation of free carbene from $SImMesHCCl_3$: A solution of $SImMesHCCl_3$ (0.056 M, 150 μL 8.4 μmol) in [D_6]benzene was diluted with [D_5]chlorobenzene (500 mL) in a teflon screw-capped NMR tube (J. Young) under nitrogen, and the tube was placed to a 60 °C oil-bath. The tube was heated slowly and placed under high vacuum every minute. After 10 minutes at 100 °C, 50 μL remained and the tube was cooled to room temperature and of [D_5]chlorobenzene (250 μL) was added. Analysis of the mixture by ^{1}H NMR spectroscopy revealed a 20% conversion to the carbene SimMes; this was confirmed by charging the tube with an authentic sample (3 mg, 10 μmol). ^{1}H NMR (400 MHz, C_6D_5Cl): $\delta = 2.14$ (s, 6H, *p*-CH_3–Ar), 2.23 (s, 12H, *o*-CH_3–Ar), 3.49 (s, 4H, N–CH_2), 6.75 ppm (s, 4H, $CH_{arom.}$).

Preparation of $SImMesCS_2$ from $SImMesHCCl_3$: Carbon disulfide (10 μL, 168 μmol) was added to a solution of $SImMesHCCl_3$ (0.056 M, 300 μL, 16.8 μmol) in [D_6]benzene under nitrogen, and the solution was heated to 60 °C for 10 min. Red crystals of the zwitterion $SImMesCS_2$ precipitated. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.23$ (s, 6H, *p*-CH_3–Ar), 2.54 (s, 12H, *o*-CH_3–Ar), 4.20 (s, 4H, N–CH_2), 6.87 ppm (s, 4H, CH_{arom}); MS +ESI: *m/z*: 403.3 $[M+Na]^+$; elemental analysis calcd (%) for $C_{22}H_{24}N_2S_2$ (380.57): C 69.07, H 6.85, N 7.32; found: C 69.62, H 6.85, N 7.23.

Typical polymerization experiment: In the glove box, compound **4** (8.1 mg, 17.1 μmol), benzyl alcohol (1.8 mg, 17.1 μmol), and L-lactide (240 mg, 1.7 mmol) were combined in a 20 mL vial equipped with a stir bar. THF (10 mL) was then added to the reaction mixture. The vial was then capped and sealed with electrical tape. The vial was taken out of the glovebox and place in a 65 °C oil bath. After 10 min, the solution color changed from colorless to light yellow. After 3 h of stirring, the reaction was removed from the oil bath and quenched with several drops of water. The polymer was precipitated from cold methanol and isolated by filtration. The polymer was dried under reduced pressure to yield poly-L-lactide as a white powder (192 mg, 80%).

Kinetic measurements with $SImMesHCCl_3$: A solution of $SImMesHCCl_3$ (0.056 M, 150 μL, 8.4 μmol) [D_6]benzene was diluted with [D_6]benzene (150 μL 0.028 M) and charged into teflon screw-capped NMR tube along with carbon disulphide (5 μL, 84 μmol) and $SImMesCS_2$ (1 mg, 2.6 μmol). The NMR tube was placed into a Varian 300 MHz NMR instrument calibrated to constant temperature with ethylene glycol and the disappearance of the 2-H proton of the imidazolidine ring was monitored versus the residual proton signal of the [D_6]benzene solvent. Standard error analysis was used assuming a 10% error in proton integrals and a negligible error in the temperature (Table S2 in the Supporting Information).

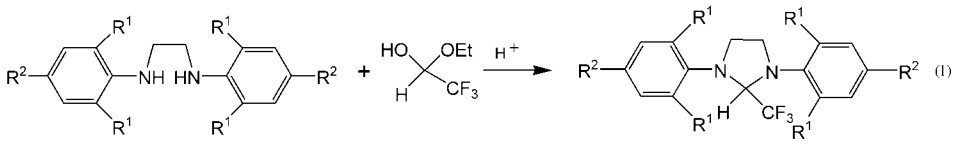
Kinetic measurements with $SImMesHC_6F_5$: Carbon disulphide (6.5 μL, 108 μmol) was injected into a solution of $SImMesHC_6F_5$ (0.036 M, 300 μL, 10.8 μmol) in [D_6]benzene in a teflon screw-capped NMR tube under nitrogen. $SImMesCS_2$ (1 mg, 2.6 μmol) was added. The NMR tube was placed into a calibrated, constant temperature Varian 300 MHz NMR instrument and the disappearance of the protons on the imidazolidine backbone was followed. The integral values were calibrated with the benzene peak.

Dependence of k_{obs} on the concentration of carbon disulphide: The reaction with a solution of $SImMesHC_6F_5$ (0.036 M, 0.3 mL, 10.8 μmol) in [D_6]benzene was repeated with 20 times (216 μmol) and 30 times (324 μmol) excess of carbon disulfide at 68.5 °C. The slight decrease in k_{obs} observed for $[CS_2] = 0.072$ M and 1.080 M is just outside our experimental error and may be indicative of an association of CS_2 with the adduct.

Dependence of k_{obs} on $[SImMesHC_6F_5]_0$: **A** solution of $SImMesHC_6F_5$ (0.036 M, 150 μL, 5.4 μmol) in [D_6]benzene was diluted to 0.016 M with [D_6]benzene (190 μL) and the kinetics were measured with 20-fold excess (108.0 μmol) of carbon disulfide at 68.5 °C. The observed k_{obs} was identical within experimental error to that obtained at $[SImMesHC_6F_5]_0 =$ 0.036 M (Table S2 in the Supporting Information).

Results and Discussion

NHC adducts were prepared by acid-catalyzed diamine/aldehyde condensation reaction from readily available starting materials, (Scheme 1). Three diamines were surveyed: *N*,*N*′-bis(2,4,6-trimethylphenylamino)ethane (**1**), *N*,*N*′-bis(phenylamino)ethane (**2**), and *N*,*N*′-bis(2,6-diisopropylphenylamino)ethane (**3**) with benzaldehyde derivatives functionalized with electron-withdrawing groups in an effort to tune the steric and electronic elements of the adduct (Scheme 1). Diamines **1** and **2** react with aldehydes to form adducts in yields of 68–96%. In the presence of a catalytic amount of acid, hemiacetals also react with **1** and **2** to form NHC adducts [Eq. (1)]; however, the reaction of **3** with aldehydes and hemiacetals/acetals did not lead to adduct formation, presumably due to the steric bulk of **3**. The X-ray crystal structure of 1,3-bis(2,4,6-trimethylphenyl)-2-(pentafluoro-



phenyl)imidazolidine (**4**) is given in Figure 1. While the quality of the data does not permit a detailed comparison of the structural features, the structure reveals the expected

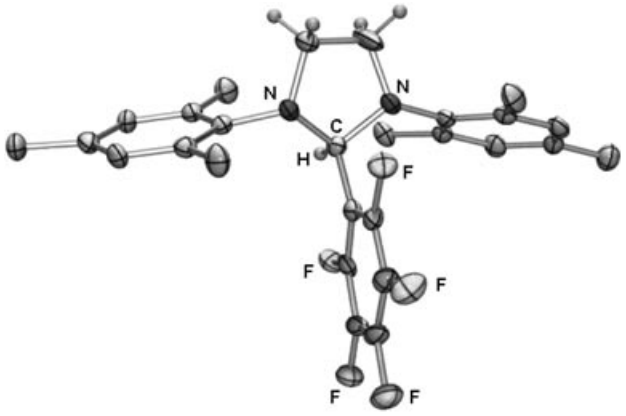


Figure 1. Plot of 1,3-bis(2,4,6-trimethylphenyl)-2-(pentafluorophenyl)imidazolidine (**4**) with thermal ellipsoids drawn at the 50% probability level.

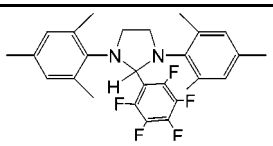
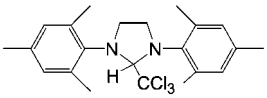
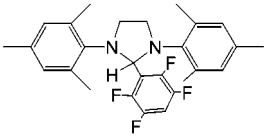
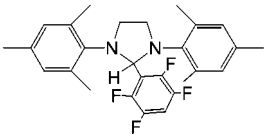
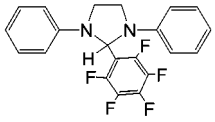
tetrahedral geometry at C1 and average bond lengths for the C1–N1 (1.47(2) Å) and C1–N2 (1.46(2) Å) bonds that are longer than those in the corresponding carbene (1.352(5) and 1.345(5) Å, respectively), as observed for analogous acetylene or alcohol adducts.[10a,7i,16]

To demonstrate the utility of the NHC adducts as versatile and effective catalyst precursors for ring-opening polymerization, the polymerization of L-lactide was performed in the presence of a benzyl alcohol initiator and 1.5 equivalents of NHC adduct relative to initiator in 1–2 M THF or toluene lactide solutions, Table 1. The molecular weights closely tracked the monomer/initiator (M/I) ratio (targeted 100), and the ^{1}H NMR spectrum clearly shows resonances associated the benzyl ester α-end group, consistent with initiation from benzyl alcohol as well as the hydroxyl ω-chain end. Compound **4** and 1,3-bis(2,4,6-trimethylphenyl)-2-(trichloromethyl)imidazolidine (**5**) effect the ring-opening polymerization (ROP) of lactide at temperatures as low as 65 °C in high yields with narrow polydispersities (Table 1, entries 1 and 2). Conversely, the adducts 1,3-bis(2,4,6-trimethylphenyl)-2-(2,3,5,6 tetrafluorophenyl)imidazolidine (**6**) and 1,3-bisphenyl-2-(pentafluorophenyl)imidazolidine (**7**) required extended reaction times and higher temperatures to effect polymerization (Table 1, entries 4 and 5), but with significant loss in control as evidenced by the generation of some low-molecular-weight oligomers. Lower polymerization temperatures (entry 3, Table 1) generated narrowly dispersed products, but with modest conversions. No ROP was observed with the trifluoromethane, benzene, 2,3,4-triflourobenzene, *p*-nitrobenzene, or (3,5-trifluoromethyl)benzene adducts, irrespective of the reaction times and temperature surveyed.[17]

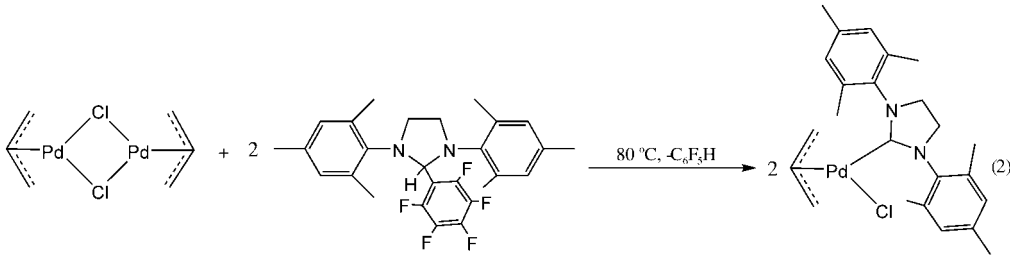
In recent reports, NHC have been shown to be effective transesterification catalysts.[18] Transesterification of dimethyl terephthalate (DMT) with excess ethylene glycol (EG) to give bis(2-hydroxyethyl) terephthalate (BHET), an important precursor to poly(ethene terephthalate) (PET), was investigated with NHC adducts (Scheme 2). The reaction of excess ethylene glycol with DMT in the presence of **4** and **5** (3.5 mol%) at 65 °C in THF generated BHET in 75% isolated yield after 3 h. The transesterification of DMT to BHET with **7** required higher temperatures (145 °C) and was carried out in *O*-xylene to yield BHET in 70% isolated yield after 12 h.

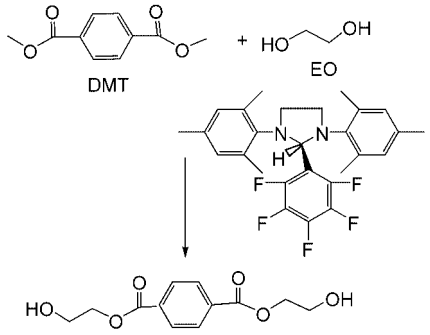
Adducts **4** and **5** are also convenient synthons for the preparation *N*-heterocyclic carbene organometallic complexes.[12] Treatment of **4** and **5** with $[(\eta^3\text{-}C_3H_5)PdCl]_2$ at 80 °C in toluene yielded [(1,3-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene)Pd(η^3-C_3H_5)Cl] in >95% isolated yield in less than 2 h [Eq. (2)]. These reactions can be carried out in air with no prior solvent purification.

Table 1. Characteristics of selected polylactides prepared from NHC adduct precatalysts. All experiments used benzyl alchohol as the initiator with a target DP of 100. M_n was determined by gel-permeation chromatography (GPC) calibrated with polystyrene standards in THF.

Entry	Precatalyst	Adduct	Polymerization conditions	% Conv.	M_n [kg mol^{-1}][a]	M_w/M_n[a]
1		**4**	65 °C, THF, 3 h	80	9890	1.13
2		**5**	65 °C, THF, 3 h	83	9980	1.15
3		**6**	65 °C, THF, 24 h	30	4030	1.10
4		**6**	110 °C, $PhCH_3$, 24 h	66	4700	1.11
5		**7**	144 °C, o-xylene, 12 h	68	3200	1.52

[a] From GPC data.





Scheme 2.

of pentafluorobenzene from **7** (43 %). The large endotherm observed at 140 °C in the MDSC experiment is assigned to the melting point of **7**, and the broad endotherm at 150–210 °C is attributed to the elimination of pentafluorobenzene. The exothermic peak observed at 180 °C, is tentatively assigned to the dimerization of (1,3-diphenyl-2-imidazolidinylidene) to form bis(1,3-diphenyl-2-imidazolidinylidene) (**9**), as this olefin is clearly observed by ^{1}H NMR analysis of the sample after thermolysis.[19] (The ^{1}H NMR spectra of **7** before and after thermolysis are shown in Figure 2.)

Several experiments were carried out to provide evidence for the reversibility of adduct formation and the intermediacy of the free carbene in solution. Thermolysis of the pentafluorobenzene adduct **4** at 65 °C in the presence of excess $HCCl_3$ or $DCCl_3$ cleanly yields **5** (or $\mathbf{5_{D1}}$) and pentafluorobenzene [Eq. (3)].[20] Evidence for the intermediacy of the free carbene was provided by thermolysis of the chloroform adduct **5** at 100 °C under vacuum in [D_5]chlorobenzene. After ten minutes, resonances attributable to free carbene, that is, (1,3-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene)

The data in Table 1 suggest that not all NHC adducts are equally efficient precatalysts for ROP and transesterification catalysis. The tetrafluorobenzene adduct **6** led to lower conversions of lactide than the pentafluorobenzene adduct **4** at 65 °C, and the 1,3-diphenyl-substituted pentafluorobenzene adduct **7** required much higher temperature than the 1,3-mesityl adduct **4** to reach comparable conversions in the ring-opening of lactide. The 1,3-bis(2,4,6-trimethylphenyl)-2-(trifluoromethyl)imidazolidine adduct (**8**) is surprisingly robust, and did not ring-open lactide after 12 h at 100 °C.[17] We attribute this behavior to the differential thermal stability of the adducts.

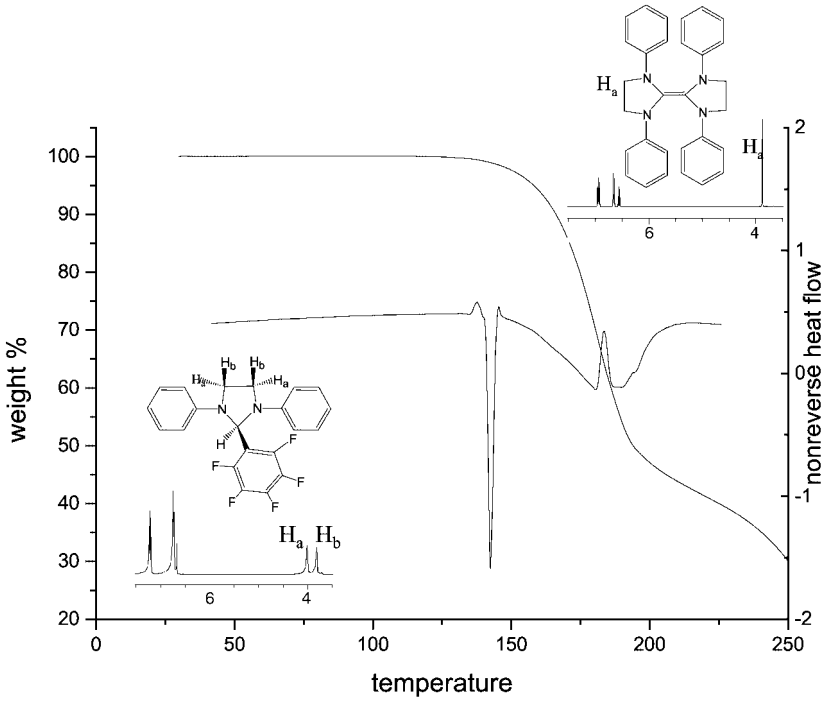
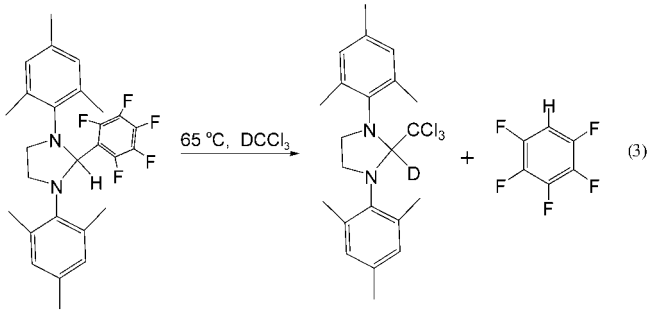


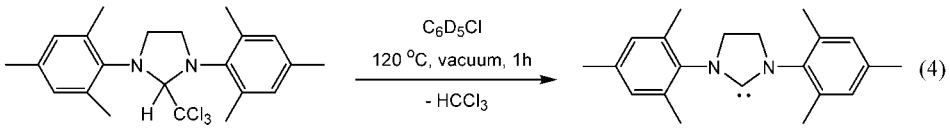
Figure 2. Thermogravimetric analysis and nonreversible heat flow of **7** as a function of temperature together with the ^{1}H NMR spectra.

This hypothesis is supported by modulated differential scanning calorimetry (MDSC) and thermal gravimetric analysis (TGA) measurements of compounds **4**–**7**. TGA analysis of powdered samples of **4** and **5** began to show weight loss at 80 °C, presumably due to loss of pentafluorobenzene or chloroform, whereas weight loss in **6** and **7** began at 130 °C and 165 °C, respectively. The MDSC and TGA experiments of **7** are shown in Figure 2. In the TGA experiment, a 45 % weight loss was observed at 165–210 °C; this correlates with the theoretical % weight loss

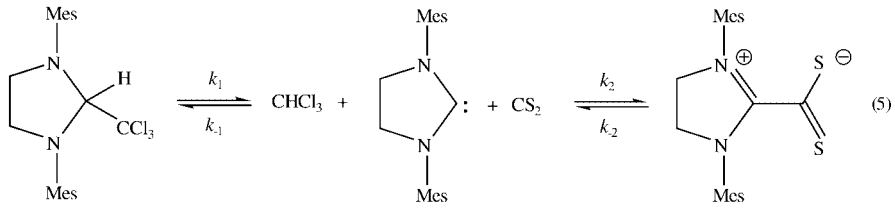


(3)

(**10**; 10% conversion), were observed, providing clear evidence that the elimination of chloroform from **5** generates the free carbene in solution even in the absence of transition metals [Eq. 4)].



(4)



5 **10** **11**

Thermomolysis of either **4** or **5** in the presence of CS_2 cleanly generates the zwitterionic CS_2 adduct **11**,[21] which rapidly precipitates from nonpolar solvents. The clean formation of the CS_2 adduct **11** and pentafluorobenzene, and absence of deuterium exchange in the **4**/$CDCl_3$ exchange experiment [Eq. (3)] is consistent with a concerted elimination of $HCCl_3$ or HC_6F_5, rather than a stepwise ionic mechanism.[10a,22]

The kinetics of carbene generation were monitored by ^1H NMR spectroscopy in [D_6]benzene in the presence of excess CS_2 and a small crystal of **11**.[23] The disappearance of the adduct followed first-order kinetics ($-\ln([A]/[A]_0 = k_{obs}t$). Experiments at several initial concentrations of the adduct **5** and CS_2 confirmed that the rates are first-order with respect to the adduct and zero-order for CS_2.[23] If we adopt the steady-state assumption for **10** [Eqs. (5) and (6)], then under conditions in which $k_2[CS_2] \gg k_{-1}[CHCl_3]$ ($k_1[\mathbf{5}] + k_{-2}[\mathbf{11}]$), the observed rate constant $k_{obs} = k_1$, which is the rate constant for the generation of the carbene.

$$-\frac{d[\mathbf{5}]}{dt} = k_1[\mathbf{5}] - k_{-1}[CHCl_3][\mathbf{10}] = k_1[\mathbf{5}]$$
$$-k_{-1}[CHCl_3]\left(\frac{k_1[\mathbf{5}] + k_{-2}[\mathbf{11}]}{k_{-1}[CHCl_3] + k_2[CS_2]}\right) - \frac{d[\mathbf{5}]}{dt} \approx k_1[\mathbf{5}] \quad (6)$$

The observed first-order rate constants for the disappearance of **4** ($k_{obs} = 1.85\ (\pm 0.84) \times 10^{-5}\ s^{-1}$ at 39.5 °C) and **5** ($k_{obs} = 8.39\ (\pm 2.74) \times 10^{-5}\ s^{-1}$ at 39.3 °C) imply that the elimination of chloroform from **5** is faster than elimination of C_6F_5H from **4**, but analysis of the temperature dependence of the rate constants reveal activation parameters for **5** ($E_a = 94.7 \pm 15.4\ kJ\,mol^{-1}$) and **4** ($E_a = 103.5 \pm 7.4\ kJ\,mol^{-1}$) that are within experimental error.

The observed differences in the rate of elimination of C_6F_5H versus $CHCl_3$ from **4** and **5**, respectively, at 39 °C also reflect the relative stabilities of the adducts in solution. While the decomposition of **4** in the presence of CS_2 in benzene can be observed after ten minutes at room temperature, **5** is stable under similar conditions. Thus, the pentafluorobenzene adduct **4** is superior in solution to the chloroform adduct **5** as an in situ carbene source both, as a consequence of its ease of synthesis and its room-temperature stability.

Conclusion

In summary, the condensation of diamines with aldehydes provides a convenient and general source of alkane adducts of saturated *N*-heterocyclic carbenes. Unlike adducts derived from chloroform, the pentafluorobenzene-based adducts are stable at room temperature. Thermolysis of these adducts generates the carbenes in solution, which we have shown are effective organic catalysts for transesterification reactions and ring-opening polymerization reactions. These adducts also provide convenient synthons for the generation of transition-metal complexes. The thermal elimination of the alkanes from the carbene adducts depends on the substitutents on the carbene and the adduct, providing a convenient method for tuning the rate of carbene generation in situ.

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