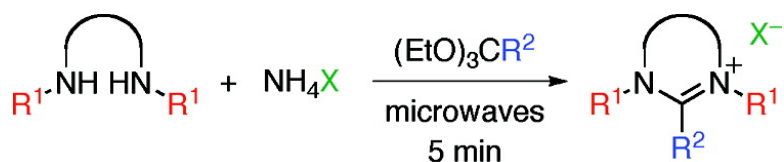Article

Facile Microwave-Assisted Synthesis of Cyclic Amidinium Salts

Adila Aidouni, Soufiane Bendahou, Albert Demonceau, and Lionel Delaude

R^1 = alkyl, aryl R^2 = H, Me, Et, Ph

X^- = F^-, Cl^-, Br^-, I^-, NO_3^-, SCN^-, BF_4^-, PF_6^-, TfO^-, Tf_2N^-

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Facile Microwave-Assisted Synthesis of Cyclic Amidinium Salts

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The cyclization of *N,N′*-dialkyl or diaryl ethane-1,2-diamines or propane-1,3-diamines with inorganic ammonium salts and orthoesters proceeds briskly under microwave irradiation to afford the corresponding imidazolinium or tetrahydropyrimidinium salts. The transformation is highly versatile and tolerates a wide range of substituents and counterions. It could be scaled from 1 to 50 mmol without any difficulty. Because the workup is equally rapid and straightforward, this experimental procedure provides fast and convenient access to an important class of heterocyclic compounds that have found numerous applications as N-heterocyclic carbene precursors, organocatalysts, and ionic liquids.

Introduction

Cyclic amidinium salts (**1**) are the most common synthetic precursors for the preparation of N-heterocyclic carbenes (NHCs, **2**). Since the first representative of these divalent carbon species was isolated and characterized by Arduengo and co-workers in 1991,[1] stable carbenes have been extensively studied.[2] Over the past 17 years, they have already afforded a whole new generation of nucleophilic reagents,[3] organocatalysts,[4] and organometallic catalysts,[5] including chiral ones,[6] that have revolutionized key areas of organic synthesis and polymer chemistry.

Most NHCs investigated so far are five- or six-membered rings derived from imidazole[1,7] or pyrimidine,[8] respectively. Because of their high sensitivity toward oxygen and moisture, they are often generated in situ by deprotonation of the corresponding cyclic amidinium salts with a strong base, such as sodium hydride or potassium *tert*-butoxide (eq 1). Thus, imidazolinium or tetrahydropyrimidinium salts bearing a hydrogen substituent at the C2 position serve de facto as stable NHC ligand precursors in many catalytic systems.[7−9]

$$\text{(1)}$$
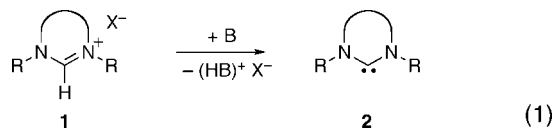
Cyclic amidinium salts have also found applications on their own as organocatalysts[10] and ionic liquids (ILs).[11,12] Both research areas are currently attracting much interest because of their importance for "greening" chemical processes. So far, applications in these fields have relied mainly on aromatic imidazolium salts. However, their saturated imidazolinium counterparts have also attracted a great deal of attention lately. In particular, imidazolinium salts incorporating a phenyl ring at the C2 position were found to be suitable catalysts for the aza Diels−Alder reaction.[13] They
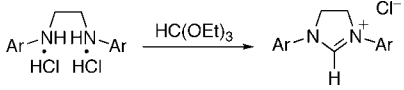
were also successfully employed as ionic liquid solvents for reactions involving medium and strong bases, such as quinuclidine and Grignard reagents.[14]

The preparation of cyclic amidinium salts with a saturated backbone is usually achieved via condensation of a N,N′-disubstituted α,ω-alkanediamine and an inorganic ammonium salt with a triethyl orthoester in the presence of a catalytic amount of formic acid (eq 2).[15] Alternatively, a suitable α,ω-alkanediammonium salt may be used as a single starting material for the heterocyclic cation and its counterion (eq 3). In all cases, the orthoester serves both as a solvent and a reagent. Numerous variations on this experimental procedure have been reported in the literature.[16] They all require prolonged heating under reflux conditions to reach satisfactory conversions. Thus, reaction times ranging between a few hours and a few days are commonly encountered, unless ethanol is distilled off the reaction mixture to drive the cyclization more rapidly to completion.[17]

$$\text{(2)}$$

$$\text{(3)}$$
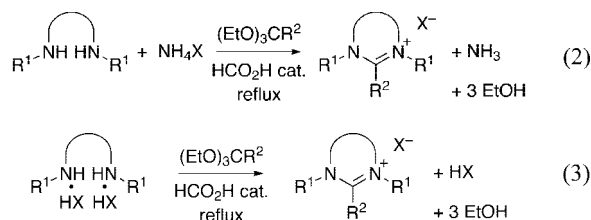
Microwave-assisted organic synthesis (MAOS) has received increasing attention in recent years as a valuable technique for acceleration of chemical reactions.[18,19] The development of safe and reliable mono- or multimodal microwave reactors specifically designed for chemical applications has significantly invigorated time-honored laboratory practices.[20] Reduction in reaction time, increase in yield, and suppression of side-product formation are often claimed when switching from conductive to microwave heating.[21] Condensation reactions leading to heterocyclic products are particularly prone to microwave irradiation enhancements.[22] Dramatic accelerations have been reported for the synthesis

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Table 1. Synthesis of 1,3-Diarylimidazolinium Chlorides Using Microwave or Conductive Heating

Ar	microwave yield (%)[a]	thermal yield (%)[b]
phenyl	62	84
4-biphenyl	82	80
1-naphthyl	91	81
2-methylphenyl (2-tolyl)	49	55
4-methylphenyl (4-tolyl)	96	79
2,6-dimethylphenyl (2,6-xylyl)	90	79
3,5-dimethylphenyl (3,5-xylyl)	93	80
2,6-diisopropylphenyl (dip)	72	59
2,4,6-trimethylphenyl (mesityl)	94	80
4-bromo-2,6-dimethylphenyl	98	50

[a] Isolated yield using microwave irradiation, 5 min at 145 °C.
[b] Isolated yield using conductive heating, up to 72 h reflux.

Table 2. Synthesis of 1,3-Dimesitylimidazolinium Salts

X^-	isolated yield (%)	X^-	isolated yield (%)
F^-	82[a]	SCN^-	82
Cl^-	68	BF_4^-	91
Br^-	36	PF_6^-	93
I^-	38	TfO^-	40
NO_3^-	66	TF_2N^-	58

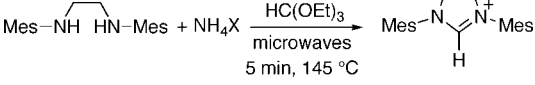[a] Starting from *N,N'*-dimesityl-1,2-ethanediamine dihydrofluoride.

of imidazoles from acyclic precursors under various experimental conditions.[23] Alkylation of nitrogen-containing heterocycles to prepare imidazolium ionic liquids under microwave irradiation has also been achieved, sometimes on a large scale.[24]

In 2006, we disclosed a very simple and efficient procedure for the microwave-assisted synthesis of 1,3-diarylimidazolinium chlorides by cyclization of *N,N'*-diaryl-1,2-ethanediamine dihydrochlorides with triethyl orthoformate.[25] In this article, we further demonstrate the generality of this method by varying the heterocyclic ring size and the nature of its various substituents or of the counteranion. We also show that the reaction can be scaled up seamlessly.

Results and Discussion

Synthesis of Imidazolinium Salts. Our initial efforts focused on optimization of the experimental conditions for the preparation of 1,3-diarylimidazolinium chlorides from the corresponding *N,N'*-diaryl-1,2-ethanediamine dihydrochlorides (1 mmol) suspended in neat triethyl orthoformate (1 mL, 6 mmol).[25] In all but two cases, isolated yields obtained after 5 min of microwave irradiation at 145 °C outperformed those reached under reflux conditions during much longer periods of time (Table 1). The most spectacular enhancement was recorded for the polar, deactivated 4-bromo-2,6-dimethylphenyl derivative. In some instances, the ionic products remained soluble in the warm reaction mixtures. They eventually precipitated during cooling or upon addition of diethyl ether. Thus, isolation was always easily carried out by simple filtration and drying. No further purification of the imidazolinium salts was required because comparison of their ¹H and ¹³C NMR chemical shifts with those of authentic samples confirmed their identity and purity (see Supporting Information).

Having set up the conditions for a fast and efficient microwave-assisted cyclization of ethylenediamine dihydrochlorides, we turned our attention to the use of an amine free base and an inorganic ammonium salt as starting materials. This simple modification provides an easy way to vary the nature of the counterion, yet it has important practical implications. Indeed, several studies have pointed

out the significant influence of the counteranion on the catalytic activity, kinetic behavior, and mesomorphic properties of imidazolium salts.[26] Currently, the most common synthetic pathways for introduction of bulky polyatomic anions, such as BF_4^-, PF_6^-, $CF_3SO_3^-$ (TfO^-), or (CF_3SO_2)$_2N^-$ (Tf_2N^-), involve metathesis reactions from halide intermediates. The ion exchange is usually achieved via liquid/liquid separation or precipitation of an inorganic halide salt, for instance AgCl. Thus, contamination of the final products with water or halide traces is a major concern because these impurities may dramatically alter the physical and chemical properties of cyclic amidinium salts[27] and interfere with their catalytic activies.[28] Hence, new, halide-free methodologies that would allow direct access to a wide range of organic and inorganic counterions are eagerly sought.[29]

N,N'-Dimesityl-1,2-ethanediamine served as a model substrate for this study. It was heated for 5 min at 145 °C with one equivalent of an ammonium salt in neat triethyl orthoformate. Although no attempts were made to further optimize the reaction conditions defined previously, decent yields were obtained in most cases (Table 2). Only ammonium fluoride did not react under the experimental conditions adopted. This is most likely caused by a side reaction of the hydrofluoric acid released upon thermal decomposition with the glass vessel, as evidenced by a clearly visible etching of the reactor walls. When *N,N'*-dimesitylethylenediamine dihydrofluoride, prepared by treating the free diamine with aqueous HF in a preliminary step, was isolated and submitted to cyclization with triethyl orthoformate, the desired imidazolinium fluoride was obtained in 82% yield. All the products were solids with melting points high above 100 °C (see Supporting Information).

It should be pointed out that for the series under examination, organic diammonium salts usually led to higher yields of product than a stoichiometric mixture of free diamine and NH₄X using the same microwave irradiation sequence. For instance, 1,3-dimesitylimidazolinium chloride was isolated in 94% yield from *N,N'*-dimesityl-1,2-ethanediammonium choride versus 68% from *N,N'*-dimesityl-1,2-ethanediamine and ammonium chloride. However, the latter method is more flexible and calls only for a single step starting from easily available starting materials.

We next investigated the formation of 1,3-dialkylimidazolinium salts from symmetrical *N,N'*-dialkyl-1,2-ethanediamines or their dihydrochlorides and triethyl orthoformate. Both experimental protocols described above for 1,3-di-

Table 3. Synthesis of 1,3-Dialkylimidazolinium Salts

R	X^-	isolated yield (%)	melting point (°C)
methyl	BF_4^-	99[a]	RTIL
ethyl	BF_4^-	92[a]	RTIL
2-hydroxyethyl	BF_4^-	93[a]	RTIL
isopropyl	BF_4^-	78[a]	151−152
tert-butyl	BF_4^-	84[a]	295−296
cyclopentyl	Cl^-	75[b]	RTIL
cyclohexyl	Cl^-	58[b]	258−259 (dec)
1-adamantyl	Cl^-	74[b]	>360 (dec)

[a] Starting from the free diamine and ammonium tetrafluoroborate (1 equiv). [b] Starting from *N,N′*-dialkyl-1,2-ethanediamine dihydrochloride.

arylimidazolinium salts were successfully applied and did not require any significant modification. Because the low molecular weight alkylamines were volatile and more prone to degradation than their arylated counterparts, the maximum microwave power applied to reach the 145 °C set temperature was reduced from 50 to 25 W. Imidazolinium tetrafluoroborates bearing methyl, ethyl, and 2-hydroxyethyl substituents on their nitrogen atoms were obtained in almost quantitative yields from commercially available diamines (Table 3). These products were isolated as viscous oils and therefore qualify as room temperature ionic liquids (RTILs). Higher molecular weight alkyl and cycloalkyl substituents led to solid products that were isolated in somewhat reduced yields. A notable exception to this tendency was observed with 1,3-dicyclopentylimidazolinium chloride that remained liquid at room temperature even after prolonged storage. Although we have no explanation for this discrepancy, it could be put in perspective with other results from our laboratory showing a significant difference of catalytic activity between ruthenium complexes bearing tricyclopentylphosphine and tricyclohexylphosphine ligands.[30]

To further expand the scope of the microwave-assisted cyclization of ethylenediamines, we investigated the preparation of C2 substituted 1,3-dimethylimidazolinium salts from various commercially available orthoesters. Replacement of triethyl orthoformate with its orthoacetate, orthopropionate, and orthobenzoate analogues led to consistently high yields of the corresponding imidazolinium tetrafluoroborates (Table 4). Substitution of H2 by methyl or ethyl groups resulted in a sharp increase of the melting point. Yet, 1,3-dimethyl-2-phenylimidazolinium tetrafluoroborate melted below 100 °C and, therefore, belongs to the ionic liquid family. Recourse to the triflate counterion (TfO$^-$) did not afford a RTIL, but the bis(trifluoromethanesulfonyl)imide (Tf$_2$N$^-$) of 1,3-dimethyl-2-phenylimidazolinium remained liquid for several weeks at room temperature and eventually afforded a solid melting at 35 °C, as previously reported by Jurčík and Wilhelm who first synthesized this compound in three steps and 71% overall yield starting from *N,N′*-dimethylethylenediamine.[14] The modest 54% yield that we obtained in our single-step procedure is mainly caused by a significant loss of material during workup, because of the non-negligible miscibility of the ionic liquid product with the other components of the reaction mixture. When the reaction was

Table 4. Synthesis of 1,3-Dimethyl-2-substituted Imidazolinium Salts

R	X^-	isolated yield (%)	melting point (°C)
hydrogen	BF_4^-	99	RTIL
methyl	BF_4^-	87	209−210
ethyl	BF_4^-	86	206−208
phenyl	BF_4^-	91	84−85
phenyl	TfO^-	85	78−79
phenyl	Tf_2N^-	54	35[a]

[a] An RTIL was initially obtained that crystallized only after several weeks.

repeated on a 4 mmol scale using a 2/1 v/v mixture of Et$_2$O and *n*-pentane instead of pure diethyl ether as washing solvent, a 76% isolated yield was obtained.

Last but not least, we have scaled up the synthesis of 1,3-dimesitylimidazolinium chloride. This salt is an immediate precursor of the important NHC nicknamed SIMes or H$_2$IMes that serves as an ancillary ligand in the second generation Grubbs[31] and Hoveyda−Grubbs[32] metathesis catalysts, among other uses. A first experiment carried out on a 10 mmol scale in 10 mL of triethyl orthoformate led to a 93% isolated yield. This result, almost identical to the one obtained on a 1 mmol scale (cf., Table 1), was deemed very gratifying, considering that a different experimental setup was employed to accommodate larger reaction vessels. A different brand of single-mode microwave reactor was also tested with no noticeable change (see Supporting Information). When the cyclization was performed on 50 mmol of starting material in 25 mL of orthoester, the microwave power had to be increased from 50 to 120 W to maintain a fast heating rate. This was the sole adjustment needed to scale up the reaction by a factor 50. Under these conditions, the yield of crude product peaked at 99% after 5 min at 145 °C and analytically pure SIMes·HCl was isolated in 80% yield after recrystallization from MeOH/Et$_2$O.

Synthesis of Tetrahydropyrimidinium Salts. In parallel with the synthesis of five-membered imidazolinium salts, we have also investigated the cyclization of *N,N′*-diaryl or dialkyl-1,3-propanediamines into six-membered tetrahydropyrimidinium salts. Thus, in a first series of experiments, we probed the condensation of triethyl orthoformate (1 mL, 6 mmol) and ammonium tetrafluoroborate (1 mmol) with two representative 1,3-propanediamine derivatives (1 mmol) bearing aromatic substituents on their nitrogen atoms, namely, mesityl (Mes) and 2,6-diisopropylphenyl (Dip) groups. Microwave irradiation for 5 min at 145 °C in neat orthoester did not afford a clean reaction. The competitive formation of a sixteen-membered azacycle (**3**), together with unidentifed oligomeric products was evidenced by ^{1}H and ^{13}C NMR, as previously established by Paulsen and Madsen using conductive heating.[33] When the cyclocondensations were conducted under milder conditions (75 °C, 10 min) using a lesser excess of triethyl orthoformate diluted with ethanol, small amounts of the desired tetrahydropyrimidinium tetrafluoroborates precipitated from the reaction media during

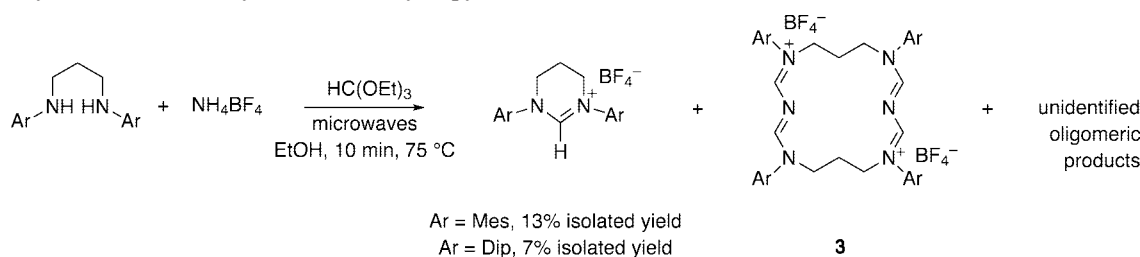**Scheme 1.** Synthesis of 1,3-Diaryl-3,4,5,6-tetrahydropyrimidium Tetrafluoroborates

Ar = Mes, 13% isolated yield
Ar = Dip, 7% isolated yield

3

Table 5. Synthesis of 1,3-Dialkyl-3,4,5,6-tetrahydropyrimidium Salts

R	X⁻	isolated yield (%)	melting point (°C)
methyl	BF_4^-	99[a]	nd[b]
ethyl	BF_4^-	93[a]	nd[b]
isopropyl	BF_4^-	88[a]	139–140
tert-butyl	BF_4^-	89[a]	197–199
cyclohexyl	BF_4^-	89[a]	106–107
methyl	PF_6^-	93[c]	58–60
ethyl	PF_6^-	93[c]	90–91
isopropyl	PF_6^-	92[c]	168–169
tert-butyl	PF_6^-	93[c]	247–248
cyclohexyl	PF_6^-	90[c]	153–154

[a] Reaction at 120 °C in EtOH. [b] Not determined, extremely hygroscopic solid that becomes deliquescent upon exposure to air. [c] Reaction in neat triethyl orthoformate at 145 °C.

workup with diethyl ether and could be isolated in high purity (Scheme 1). Attempts to further crystallize pure cycloadducts from the mother liquors using a variety of solvents failed, and we did not investigate chromatographic separations that could help improve recovery of the products.

When *N,N′*-dialkyl-1,3-propanediamines were used instead of N,N′-diarylated substrates, cyclization with triethyl orthoformate and inorganic ammonium salts proceeded cleanly and afforded only the corresponding tetrahydropyrimidinium salts, with no evidence of macrocycle formation. The experimental procedure was amenable to ample modifications, yet pure products were always isolated in high yield and purity after simple filtration and washing. For example, modification of the diamine/orthoester molar ratio, use of methanol or ethanol as solvents, and recourse to organic diammonium salts as starting materials were successfully introduced without any adverse effect (see Table 5 for selected results). In particular, we were able to switch from a 6- to 2-fold excess of orthoester compared to the diamine and ammonium salt reagents (1 equiv each), while maintaining a quantitative conversion within 5 min. Simultaneously, it was also possible to lower the reaction temperature from 145 to 120 °C and to use ethanol, a renewable, green solvent as reaction medium. This is a nontrivial result, considering that ethyl alcohol is released during the cyclocondensation and has often been distilled off in previous protocols to drive the reaction to completion.[17] Alltogether, these modifications are a good omen for future development of a truly green synthesis of cyclic amidinium salts.

It should be pointed out that 1,3-dimethyl and 1,3-diethyl-3,4,5,6-tetrahydropyrimidinium chlorides and tetrafluorobo-

Table 6. Synthesis of 1,3-Dimethyl-2-Substituted 3,4,5,6-Tetrahydropyrimidinium Salts

R	X⁻	isolated yield (%)	melting point (°C)
methyl	BF_4^-	94	205–206
ethyl	BF_4^-	92	244–245
phenyl	BF_4^-	49	84–85
phenyl	TfO⁻	95	RTIL
phenyl	Tf_2N^-	77	RTIL

rates were extremely hygroscopic salts that quickly became deliquescent upon exposure to air, thereby preventing their convenient manipulation in the laboratory. The homologous diisopropyl and di-*tert*-butyl derivatives also displayed a tendency to absorb moisture, although to a much lesser extent. Hexafluorophosphate salts of the five 1,3-dialkyltetrahydropyrimidinium cations under investigation, on the other hand, were not hygroscopic and are therefore more suitable for catalytic applications when exclusion of oxygen and moisture are mandatory.

Last but not least, we investigated the preparation of C2 substituted 1,3-dimethyltetrahydropyrimidinium salts by substituting triethyl orthoformate with its orthoacetate, orthopropionate, and orthobenzoate analogues (Table 6). The addition of an endocyclic methylene group to expand the rings of 1,3-dimethyl cyclic amidinium tetrafluoroborates bearing a methyl, ethyl or phenyl group in 2-position from five to six units did not significantly alter their melting points (cf., Table 4). A more significant deviation was observed when comparing 1,3-dimethyl-2-phenylimidazolinium and tetrahydropyrimidinium triflates. The latter salt was a RTIL, whereas the former melted at 78–79 °C. When the bis(trifluoromethanesulfonyl)imide anion served as counterion, both the five- and six-membered cyclic amidinium salts remained liquid at room temperature for extended periods of time. These results open up new vistas. Indeed, to the best of our knowledge, the use of tetrahydropyrimidinium salts as IL or RTIL has not been reported thus far.

Conclusion and Perspectives

The cyclization of N,N′-disubstituted ethane-1,2-diamines or propane-1,3-diamines with inorganic ammonium salts and orthoesters proceeds briskly under microwave irradiation to afford the corresponding imidazolinium or tetrahydropyrimidinium salts in high yields. The transformation is compatible with a wide range of aliphatic and aromatic substituents on the nitrogen and carbon atoms of the amidinium function

and a single product is formed in most cases. In addition to the halides, nitrate, and thiocyanate counterions, the reaction also permits the direct introduction of bulky polyatomic anions (BF_4^-, PF_6^-, TfO^-, and Tf_2N^-) using readily available ammonium salts as starting materials, thereby eliminating the need for subsequent ion exchange. It is noteworthy that the synthesis of the important NHC precursor 1,3-dimesitylimidazolinium chloride was scaled up seamlessly from 1 to 50 mmol.

Compared to previous methods that required prolonged heating under reflux conditions, the microwave-assisted procedure has much lower energy requirements.[34] To further improve the process in terms of green chemistry, we also showed that recourse to a large excess of orthoester was not necessary and that the cyclization could be run successfully in the environmentally friendly solvent ethanol.

Because both the reaction and its workup are equally rapid and straightforward, the whole experimental procedure could be easily automated using a robotic microwave instrument. Using high-throughput techniques, it should therefore be possible to generate libraries of imidazolinium or tetrahydropyrimidinium salts differing by their substituents and counterions for screening as NHC ligand precursors or ionic liquids in selected applications.

Experimental Section

General Information. Microvave-assisted syntheses were carried out in a CEM Discover instrument. ^{1}H and ^{13}C NMR spectra were recorded at 298 K on a Bruker DRX 400 spectrometer operating at 400.13 and 100.62 MHz, respectively. Chemical shifts are listed in parts per million downfield from TMS and are referenced from the solvent peaks or TMS. Melting points were recorded on an Electrothermal 9100 apparatus and are not corrected.

Starting Materials. N,N′-Di-R-1,2-ethanediamine dihydrochlorides (R = aryl, cyclopentyl, cyclohexyl, 1-adamantyl) were obtained by reduction of the corresponding diimines with sodium borohydride under acidic conditions.[9a] N,N′-di-*tert*-butyl-1,3-propanediamine,[35] N,N′-dimesityl-1,3-propanediamine,[8c] N,N′-bis(2,6-diisopropylphenyl)-1,3-propanediamine,[36] and ammonium bis(trifluoromethanesulfonyl)-imide (NH$_4$NTf$_2$)[37] were prepared according to literature. All the other starting materials were purchased from Aldrich or Fluka and used as received.

N,N′-Dicyclohexyl-1,3-propanediamine. A solution of cyclohexylamine (49.59 g, 0.5 mol) and water (5.40 g, 0.3 mol) was cooled in an ice−water bath before 1,3-dibromopropane (20.19 g, 0.1 mol) was slowly added. The mixture was stirred for 1 h at 0 °C and then for 1 h at room temperature. It turned into a solid mass that was melted and refluxed for 15 h in an oil bath at 125 °C. The hot reaction mixture was cooled to ∼60 °C before 2.5 M aqueous NaOH (100 mL) was added with stirring. The resulting biphasic mixture was further cooled to 0 °C and diluted with Et$_2$O (50 mL). The organic phase was washed with water (3 × 50 mL), dried over NaOH pellets, and concentrated on a rotary evaporator. The remaining brown oil was distilled under reduced pressure. Pure N,N′-dicyclohexyl-1,3-propanediamine was obtained as a colorless oil (bp 147 °C/2

mmHg) that crystallized into a pale yellow solid: mp 40 °C (17.49 g, 73%); ν_{max}(KBr)/cm^{-1} 3235, 2928, 2852, 1639, 1616, 1450, 1369, 1131; δ_H(CDCl$_3$) 0.71−0.79 (4 H, m), 0.83−1.00 (6 H, m), 1.28−1.34 (4 H, m), 1.39−1.43 (4 H, m), 1.55−1.58 (4 H, m), 2.06−2.12 (2 H, m, CHN), 2.38 (4 H, t, CH$_2$N); δ_C(CDCl$_3$) 24.6, 25.8, 30.8, 33.3, 45.3 (CH$_2$N), 56.4 (CHN).

Typical Procedure for the Microwave-Assisted Synthesis of Cyclic Amidinium Salts from N,N′-Disubstituted α,ω-Alkanediamines. A 10-mL pressure vial equipped with a stirring bar was charged with a N,N′-dialkyl- or N,N′-diarylalkane-α,ω-diamine (1 mmol), an inorganic ammonium salt (1 mmol), and a triethyl orthoester (1 mL). The vial was capped and irradiated 5 min at 145 °C (monitored by IR sensor) under stirring with a 25 W microwave power.[38] No ramp and no simultaneous cooling were applied. After rapid air cooling by the unit, the reaction mixture was diluted with Et$_2$O (2.5 mL) and filtered under vacuum. The precipitate was rinsed with Et$_2$O (2.5 mL) and dried under dynamic vacuum to afford the corresponding 1,3-dialkyl- or 1,3-diarylamidinium salt.

Typical Procedure for the Microwave-Assisted Synthesis of Cyclic Amidinium Salts from N,N′-Alkane-α,ω-diammonium Salts. A 10-mL pressure vial equipped with a stirring bar was charged with a N,N′-dialkyl- or N,N′-diarylalkane-α,ω-diammonium salt (1 mmol) and a triethyl orthoester (1 mL). The vial was capped and irradiated 5 min at 145 °C (monitored by IR sensor) under stirring with a 25 W microwave power.[38] No ramp and no simultaneous cooling were applied. After rapid air cooling by the unit, the reaction mixture was diluted with Et$_2$O (3 mL) and filtered under vacuum. The precipitate was rinsed with a few milliliters of Et$_2$O and dried under dynamic vacuum to afford the corresponding 1,3-dialkyl- or 1,3-diarylimidazolinium salt.

Scaled-Up Preparation of 1,3-Dimesitylimidazolinium Chloride. A 80-mL pressure vial equipped with a stirring bar was charged with N,N′-dimesitylethylenediamine dihydrochloride (18.47 g, 50 mmol) and triethyl orthoformate (25 mL, 0.15 mol). The vial was capped and irradiated 5 min at 145 °C (monitored by fiber optic sensor) under stirring with a 120 W microwave power.[38] No ramp and no simultaneous cooling were applied. After it was rapidly cooled in an ice bath, the reaction mixture was diluted with Et$_2$O (50 mL) and filtered under vacuum. The precipitate was rinsed with Et$_2$O (3 × 50 mL) and recrystallized from MeOH/Et$_2$O to afford pure 1,3-dimesitylimidazolinium chloride (13.72 g, 80% yield).

Supporting Information Available. Detailed experimental procedures including ^{1}H and ^{13}C NMR spectroscopy characterization of all the products. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Arduengo, A. J., III; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361–363. (b) Arduengo, A. J., III; Rasika Dias, H. V.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1992**, *114*, 5530–5534. (c) Arduengo, A. J., III; Goerlich, J. R.; Marshall, W. J. *J. Am. Chem. Soc.* **1995**, *117*, 11027–11028. (d) Arduengo, A. J., III; Goerlich, J. R.; Krafczyk, R.; Marshall, W. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1963–1965. (e) Arduengo, A. J., III *Acc. Chem. Res.* **1999**, *32*, 913–921.

(2) For monographs, see: (a) *Carbene Chemistry: From Fleeting Intermediates to Powerful Reagents*; Bertrand, G., Ed.; Marcel Dekker: New York, 2002. (b) *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, Germany, 2006. (c) *N-Heterocyclic Carbenes in Transition Metal Catalysis*; Topics in Organometallic Chemistry, Vol. 21; Glorius, F., Ed.; Springer: Berlin, 2007.

(3) Nair, V.; Bindu, S.; Sreekumar, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 5130–5135.

(4) (a) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606–5655. (b) Marion, N.; Díez-González, S.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988–3000.

(5) For reviews, see: (a) Herrmann, W. A.; Köcher, C. *Angew. Chem., Int. Ed.* **1997**, *36*, 2162–2187. (b) Jafarpour, L.; Nolan, S. P. *Adv. Organomet. Chem.* **2001**, *46*, 181–222. (c) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290–1309. (d) Herrmann, W. A.; Weskamp, T.; Böhm, V. P. W. *Adv. Organomet. Chem.* **2002**, *48*, 1–69. (e) Crudden, C. M.; Allen, D. P. *Coord. Chem. Rev.* **2004**, *248*, 2247–2273. (f) Scott, N. M.; Nolan, S. P. *Eur. J. Inorg. Chem.* **2005**, 1815–1828. (g) Garrison, J. C.; Youngs, W. J. *Chem. Rev.* **2005**, *105*, 3978–4008. (h) Dragutan, V.; Dragutan, I.; Delaude, L.; Demonceau, A. *Coord. Chem. Rev.* **2007**, *251*, 765–794.

(6) For reviews, see: (a) Perry, M. C.; Burgess, K. *Tetrahedron: Asymmetry* **2003**, *14*, 951–961. (b) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534–541. (c) César, V.; Bellemin-Laponnaz, S.; Gade, L. H. *Chem. Soc. Rev.* **2004**, *33*, 619–636.

(7) (a) Herrmann, W. A.; Elison, M.; Fischer, J.; Köcher, C.; Artus, G. R. J. *Chem.—Eur. J.* **1996**, *2*, 772–780. (b) Herrmann, W. A.; Köcher, C.; Goossen, L. J.; Artus, G. R. J. *Chem.—Eur. J.* **1996**, *2*, 1627–1636. (c) Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225–3228. (d) Dinger, M. B.; Nieczypor, P.; Mol, J. C. *Organometallics* **2003**, *22*, 5291–5296. (e) Süsner, M.; Plenio, H. *Chem. Commun.* **2005**, 5417–5419. (f) Vehlow, K.; Maechling, S.; Blechert, S. *Organometallics* **2006**, *25*, 25–28. (g) Ritter, T.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 11768–11769.

(8) (a) Mayr, M.; Wurst, K.; Ongania, K.-H.; Buchmeiser, M. R. *Chem.—Eur. J.* **2004**, *10*, 1256–1266. (b) Mayr, M.; Buchmeiser, M. R. *Macromol. Rapid Commun.* **2004**, *25*, 231–236. (c) Herrmann, W. A.; Schneider, S. K.; Öfele, K.; Sakamoto, M.; Herdtweck, E. *J. Organomet. Chem.* **2004**, *689*, 2441–2449. (d) Yun, J.; Marinez, E. R.; Grubbs, R. H. *Organometallics* **2004**, *23*, 4172–4173. (e) Yang, L.; Mayr, M.; Wurst, K.; Buchmeiser, M. R. *Chem.—Eur. J.* **2004**, *10*, 5761–5770. (f) Wang, D.; Yang, L.; Decker, U.; Findeisen, M.; Buchmeiser, M. R. *Macromol. Rapid Commun.* **2005**, *26*, 1757–1762. (g) Schneider, S. K.; Herrmann, W. A.; Herdtweck, E. *J. Mol. Catal. A: Chem.* **2006**, *245*, 248–254.

(9) (a) Delaude, L.; Szypa, M.; Demonceau, A.; Noels, A. F. *Adv. Synth. Catal.* **2002**, *344*, 749–756. (b) Grasa, G. A.; Viciu, M. S.; Huang, J.; Zhang, C.; Trudell, M. L.; Nolan, S. P. *Organometallics* **2002**, *21*, 2866–2873. (c) Nyce, G. W.; Glauser, T.; Connor, E. F.; Möck, A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 3046–3056. (d) Ma, Y.; Song, C.; Ma, C.; Sun, Z.; Chai, Q.; Andrus, M. B. *Angew. Chem., Int. Ed.* **2003**, *42*, 5871–5874. (e) Maj, A.; Delaude, L.; Demonceau, A.; Noels, A. F. *J. Organomet. Chem.* **2007**, *692*, 3048–3056.

(10) Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2004**, *43*, 5138–5175.

(11) For a monograph, see: *Ionic Liquids in Synthesis*; Wasserscheid, P., Welton, T., Eds.; Wiley-VCH: Weinheim, Germany, 2003.

(12) For reviews, see: (a) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772–3789. (b) Ranke, J.; Stolte, S.; Störmann, R.; Arning, J.; Jastorff, B. *Chem. Rev.* **2007**, *107*, 2183–2206. (c) Pâvulescu, V. I.; Hardacre, C. *Chem. Rev.* **2007**, *107*, 2615–2665. (d) Van Rantwijk, F.; Sheldon, R. A. *Chem. Rev.* **2007**, *107*, 2757–2785. (e) Greaves, T. L.; Drummond, C. J. *Chem. Rev.* **2008**, *108*, 206–237. (f) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Zanatta, N.; Bonacorso, H. G. *Chem. Rev.* **2008**, *108*, 2015–2050.

(13) Jurčík, V.; Wilhelm, R. *Org. Biomol. Chem.* **2005**, *3*, 239–244.

(14) Jurčík, V.; Wilhelm, R. *Green Chem.* **2005**, *7*, 844–848.

(15) Saba, S.; Brescia, A.; Kaloustian, M. S. *Tetrahedron Lett.* **1991**, *32*, 5031–5034.

(16) (a) Arduengo, A. J., III; Krafczyk, R.; Schmutzler, R.; Craig, H. A.; Goerlich, J. R.; Marshall, W. J.; Unverzagt, M. *Tetrahedron* **1999**, *55*, 14523–14534. (b) Ma, Y.; Song, C.; Jiang, W.; Wu, Q.; Wang, Y.; Liu, X.; Andrus, M. B. *Org. Lett.* **2003**, *5*, 3317–3319. (c) Funk, T. W.; Berlin, J. M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2006**, *128*, 1840–1846.

(17) (a) Alder, R. W.; Blake, M. E.; Bufali, S.; Butts, C. P.; Orpen, A. G.; Schütz, J.; Williams, S. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1586–1593. (b) Van Veldhuizen, J. J.; Gillingham, D. G.; Garber, S. B.; Kataoka, O.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 12502–12508.

(18) For monographs, see: (a) *Microwaves in Organic and Medicinal Chemistry*; Kappe, C. O., Stadler, A., Eds.; Methods and Principles in Medicinal Chemistry, Vol. 25; Wiley-VCH: Weinheim, Germany, 2005. (b) *Microwaves in Organic Synthesis*, 2nd ed.; Loupy, A., Ed.; Wiley-VCH: Weinheim, Germany, 2006.

(19) For reviews, see: (a) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250–6284. (b) Dallinger, D.; Kappe, C. O. *Chem. Rev.* **2007**, *107*, 2563–2591. (c) Baxendale, I. R.; Hayward, J. J.; Ley, S. V. *Comb. Chem. High Throughput Screen.* **2007**, *10*, 802–836. (d) Kappe, C. O. *Chem. Soc. Rev.* **2008**, *37*, 1127–1139. (e) Polshettiwar, V.; Varma, R. S. *Chem. Soc. Rev.* **2008**, *37*, 1546–1557.

(20) For reviews, see: (a) Hoogenboom, R.; Schubert, U. S. *Macromol. Rapid Commun.* **2007**, *28*, 368–386. (b) Coquerel, Y.; Rodriguez, J. *Eur. J. Org. Chem.* **2008**, 1125–1132. (c) Appukkuttan, P.; Van der Eycken, E. *Eur. J. Org. Chem.* **2008**, 1133–1155.

(21) For reviews, see: (a) Caddick, S. *Tetrahedron* **1995**, *51*, 10403–10432. (b) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225–9283. (c) Hayes, B. L. *Aldrichim. Acta* **2004**, *37*, 66–76. (d) de la Hoz, A.; Diaz-Ortiz, A.; Moreno, A. *Adv. Org. Synth.* **2005**, *1*, 119–171.

(22) Xu, Y.; Guo, Q.-X. *Heterocycles* **2004**, *63*, 903–974.

(23) (a) Usyatinsky, A. Y.; Khmelnitsky, Y. L. *Tetrahedron Lett.* **2000**, *41*, 5031–5034. (b) Balalaie, S.; Arabanian, A. *Green Chem.* **2000**, *2*, 274–276. (c) Wolkenberg, S. E.; Winoski, D. D.; Leister, W. H.; Wang, Y.; Zhao, Z.; Lindsley, C. W. *Org. Lett.* **2004**, *6*, 1453–1456.

(24) (a) Deetlefs, M.; Seddon, K. R. *Green Chem.* **2003**, *5*, 181–186. (b) Cravotto, G.; Boffa, L.; L'Eveque, J. M.; Estager, J.; Draye, M.; Bonrath, W. *Aust. J. Chem.* **2007**, *60*, 946–950. (c) Fang, D.; Cheng, J.; Gong, K.; Shi, Q.-R.; Zhou, X.-L.; Liu, Z.-L. *J. Fluorine Chem.* **2008**, *129*, 108–111. (d) Erdmenger, T.; Paulus, R. M.; Hoogenboom, R.; Schubert, U. S. *Aust. J. Chem.* **2008**, *61*, 197–203.

(25) Aidouni, A.; Demonceau, A.; Delaude, L. *Synlett* **2006**, 493–495.

(26) (a) Moreau, C.; Hague, C.; Weller, A. S.; Frost, C. G. *Tetrahedron Lett.* **2001**, *42*, 6957–6960. (b) Kovacevic, A.;

Gründemann, S.; Miecznikowski, J. R.; Clot, E.; Eisenstein, O.; Crabtree, R. H. *Chem. Commun.* **2002**, 2580–2581. (c) Fahlbusch, T.; Frank, M.; Schatz, J.; Schüle, D. T. *J. Org. Chem.* **2006**, *71*, 1688–1691. (d) Dobbs, W.; Douce, L.; Allouche, L.; Louati, A.; Malbosc, F.; Welter, R. *New J. Chem.* **2006**, *30*, 528–532. (e) Kouwer, P. H. J.; Swager, T. M. *J. Am. Chem. Soc.* **2007**, *129*, 14042–14052.

(27) (a) Seddon, K. R.; Stark, A.; Torres, M.-J. *Pure Appl. Chem.* **2000**, *72*, 2275–2287. (b) Thomazeau, C.; Olivier-Bourbigou, H.; Magna, L.; Luts, S.; Gilbert, B. *J. Am. Chem. Soc.* **2003**, *125*, 5264–5265.

(28) Gallo, V.; Mastrorilli, P.; Nobile, C. F.; Romanazzi, G.; Suranna, G. P. *J. Chem. Soc., Dalton Trans.* **2002**, 4339–4342.

(29) (a) Cassol, C. C.; Ebeling, G.; Ferrera, B.; Dupont, J. *Adv. Synth. Catal.* **2006**, *348*, 243–248. (b) Smiglak, M.; Holbrey, J. D.; Griffin, S. T.; Reichert, M.; Swatloski, R. P.; Katritzky, A. R.; Yang, H.; Zhang, D.; Kirichenko, K.; Rogers, R. D. *Green Chem.* **2007**, *9*, 90–98. (c) Bridges, N. J.; Hines, C. C.; Smiglak, M.; Rogers, R. D. *Chem.—Eur. J.* **2007**, *13*, 5207–5212. (d) Leclerq, L.; Suisse, I.; Nowogrocki, G.; Agbossou-Niedercorn, F. *Green Chem.* **2007**, *9*, 1097–1103.

(30) (a) Simal, F.; Demonceau, A.; Noels, A. F. *Tetrahedron Lett.* **1999**, *40*, 5689–5693. (b) Jan, D.; Delaude, L.; Simal, F.; Demonceau, A.; Noels, A. F. *J. Organomet. Chem.* **2000**, *606*, 55–64. (c) Simal, F.; Jan, D.; Delaude, L.; Demonceau, A.; Spirlet, M.-R.; Noels, A. F. *Can. J. Chem.* **2001**, *79*, 529–535.

(31) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956.

(32) (a) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179. (b) Gessler, S.; Randl, S.; Blechert, S. *Tetrahedron Lett.* **2000**, *41*, 9973–9976.

(33) Paulsen, A. L.; Madsen, R. *Heterocycles* **2004**, *63*, 2051–2056.

(34) Razzaq, T.; Kappe, C. O. *ChemSusChem* **2008**, *1*, 123–132.

(35) Denk, M. K.; Gupta, S.; Brownie, J.; Tajammul, S.; Lough, A. J. *Chem.—Eur. J.* **2001**, *7*, 4477–4486.

(36) Scollard, J. D.; McConville, D. H.; Vittal, J. J.; Payne, N. C. *J. Organomet. Chem.* **1998**, *128*, 201–214.

(37) Davidson, M. G.; Raithby, P. R.; Johnson, A. L.; Bolton, P. D. *Eur. J. Inorg. Chem.* **2003**, 3445–3452.

(38) For a discussion on the importance of internal temperature monitoring and stirring, see: Herrero, M. A.; Kremsner, J. M.; Kappe, C. O. *J. Org. Chem.* **2008**, *73*, 36–47.