A facile preparation of N-heterocyclic olefins: ring-opening polymerization of β-butyrolactone and frustrated Lewis pair reactivity

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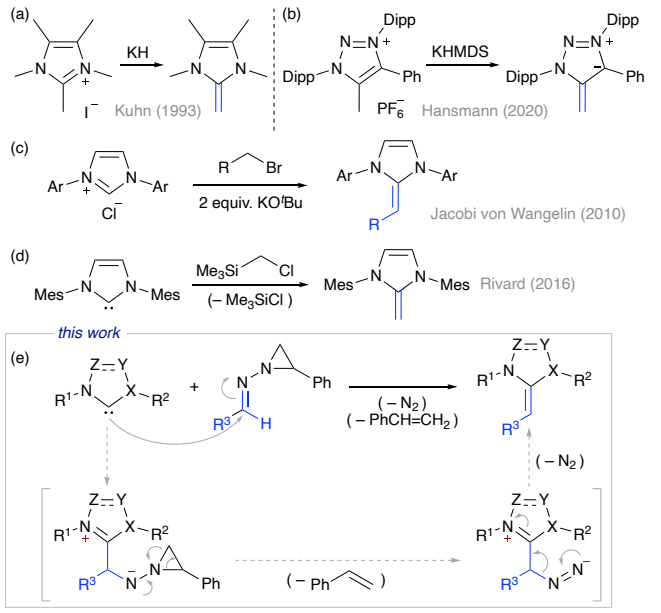
A direct synthesis of N-heterocyclic olefins (NHOs) and their mesoionic congeners from N-hererocyclic carbenes and *N*-aziridinylimines is reported. The reaction provided diverse functionalized (m)NHOs and π-extended analogues. The prepared NHOs initiated the ring-opening polymerization of β-butyrolactone, and insertion of aldehyde and nitrile into a NHO–B(C_6F_5)$_3$ adduct was demonstrated.

The term N-Heterocyclic olefin was first coined in 2011 by Rivard and co-workers[1] to refer to a family of cyclic ene-1,1-diamines[2] – also known as heterocyclic ketene aminals,[3] de(s)oxy Breslow intermediates[4] or imidazoli(ni)um ylides – whose synthesis was first reported by Kuhn et al. in 1993.[5] In the following decades,[6-10] these strongly polarized, basic and nucleophilic alkenes have found new roles as ligands for transition metals[11-14] or main-group species,[15-18] as well as organocatalysts in the activation of small molecules including CO_2.[19-24] Most notably, NHOs arose as polymerization initiators or catalysts, either on their own or as frustrated Lewis pairs (FLPs), that are suited for the ring-opening polymerization (ROP) of sustainably sourced lactones to yield biodegradable polyhydroxyalkanoates (PHAs).[25-30] NHOs are also important intermediates in catalytic transformations initiated by conjugate addition of N-heterocyclic carbenes (NHCs) leading to the umpolung of Michael acceptors.[31-33]

Despite the above, the chemistry and applications of NHOs has not proceeded as rapidly as that of NHCs, in part because their difficult preparation and isolation has impeded their study. NHOs have been prepared by the deprotonation of the corresponding 2-alkylimidazoli(ni)um salts (Scheme 1a)[5] or 5-alkyl-1,2,3-triazolium salts in the case of mesoionic NHOs (mNHOs, Scheme 1b).[34,35] Imidazolium salts have been deprotonated and alkylated in the presence of 2 equiv. of alkoxide base (Scheme 1c);[36] the same outcome can be accomplished by the direct alkylation of NHCs if an additional equivalent of the latter is consumed as a base. Finally, a direct conversion of free NHCs into methylidene NHOs was achieved with an excess of chloromethyltrimethylsilane (Scheme 1d).[37] Though several methylidene NHOs derived from either NHCs or mesoionic carbenes (MICs) have been reported, the applications of their conjugated and functionally substituted analogues are comparably rare.[6-9,38-39]



Scheme 1. Existing methods for the synthesis of (m)NHOs and our approach for the preparation of (m)NHOs.

Since NHOs may be conceived as the product of the heterodimerization of an alkylidene with a NHC, we hypothesized that a suitable carbenoid reagent would allow for their direct preparation from NHCs. Here we report a new synthesis of NHOs from readily available NHCs or MICs and *N*-

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Electronic Supplementary Information (ESI) available: Experimental and spectroscopic characterization data; X-ray crystallographic details corresponding to CCDC number 2297947 for *anti*-**6**. For ESI and crystallographic data in CIF or other electronic format, see:

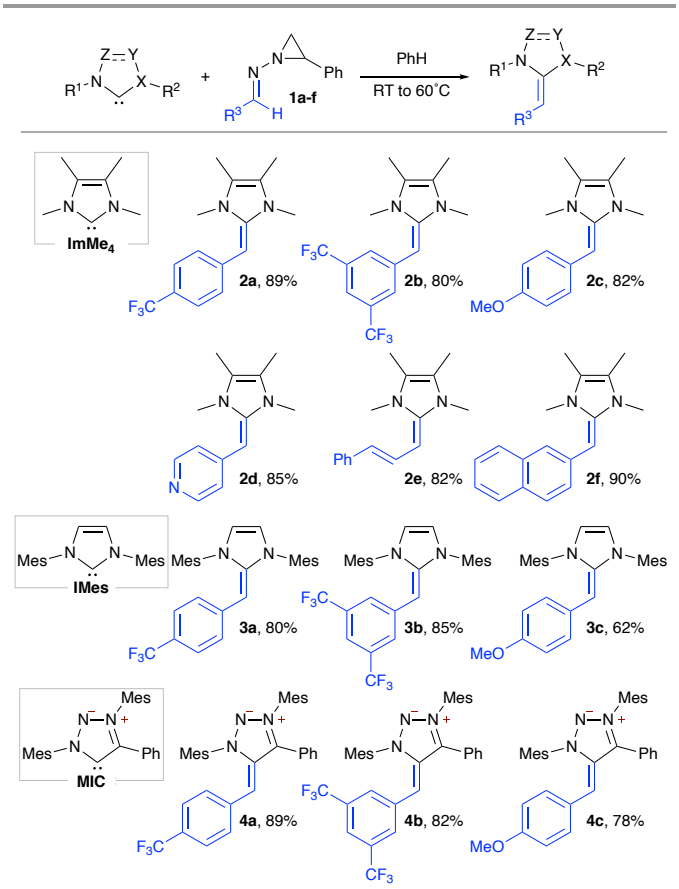
aziridinylimines (Scheme 1e). The facile synthesis also enabled an investigation of the catalytic activity of new NHOs in the ring-opening polymerization of *β*-butyrolactone (**BL**). Moreover, π-bond insertion of both aldehyde and nitrile readily occurred with a classical Lewis acid-base adduct of the NHO with $B(C_6F_5)_3$.

N-aziridinylimines **1a-f** were conveniently prepared by condensing 2-phenylaziridinamine[40] with aldehydes in toluene (Scheme S1).[41] An initial NMR survey of the reactivity of *N*-aziridinylimine **1a** with **ImMe$_4$** as a model NHC was performed at 40˚C. In the ^{1}H NMR, the imine CH signal at δ = 8.25 ppm cleanly disappeared as a new benzylidene signal appeared at δ = 4.18 ppm together with the signals of the released styrene. Similarly, in the ^{19}F NMR, the disappearance of the signal of **1a** at -62.5 ppm coincided with the rise of a new signal at δ = -59.9 ppm. In a preparative reaction, stoichiometric equivalents of **ImMe$_4$** and **1a** were simply stirred at room temperature for 8 hours to reach quantitative chemical conversion. After evaporation of the volatiles, the pure NHO **2a** was isolated in an excellent yield of 89% (Scheme 2). The exocyclic *α*-C*H* proton and *α*-carbon resonances of **2a** at δ = 4.18 and 65.0 ppm, respectively, were in line with data reported for the unsubstituted benzylidene analogue (δ = 4.36 and 65.4 ppm).[42]

The reaction was found to be compatible with both electron-poor (**1b**) and electron-rich (**1c**) benzaldimines, heterocyclic imines (**1d**), as well as α,β-unsaturated aziridinylimine (**1e**). More sterically hindered derivatives (**3a-3c**) were similarly obtained using the diaryl NHC **IMes**. In the case of the less electrophilic *N*-azirininylimine **1c**, however, two equivalents of **IMes** and longer reaction times (2 days) were required to fully consume **1c**, leading to the formation of the NHO **3c** alongside multiple unidentified side products. The saturated 1,3-dimesitylimidazolin-2-ylidene (**SIMes**) was less reactive than its unsaturated counterpart **IMes**, reacting with *N*-aziridinylimines **1a-c** to give intractable mixtures of the corresponding NHOs and unidentified side products. By comparison with reported methods for the preparation of NHOs, excellent yields were obtained without requiring a large excess of either reaction partner, and often without the need for further purification steps.[5,34,36,37]

Highly nucleophilic mesoionic N-heterocyclic olefins (mNHOs) were first reported by Hansmann and co-workers in 2020,[34] who obtained them by deprotonation of the corresponding alkyltriazolium salts. This approach unfortunately required the independent synthesis of individual heterocycles to introduce structural variations. By contrast, the reaction of the 1,3,4-triaryl **MIC** with *N*-aziridinylimines **1a-c** in benzene effortlessly gave the corresponding mNHOs **4a-c** as deep purple solids in high yields, though using a slight excess of **MIC** (1.3 equiv.) was again preferable to complete the reaction with the more electron-rich **1c**. Reactions of cyclic (alkyl)(amino)carbenes (CAACs) with *N*-aziridinylimines **1a**-**c** did not, however, produce any of the corresponding NHOs.

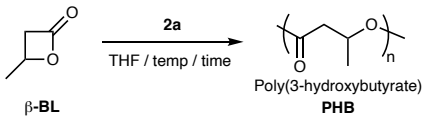
Clean reactions were obtained by reacting 1,3,4-triphenyl-1,2,4-triazol-5-ylidene (Enders' carbene) with *N*-aziridinylimines **1a-c** in benzene at elevated temperatures (60-80˚C). Interestingly, these reactions did not result in the formation of NHOs, but instead in the quantitative formation of azines (Scheme S2).[43] Enders' carbene thus failed to engage with *N*-aziridinylimines prior to their thermolysis into diazo compounds, which were subsequently trapped by the carbene.



Scheme 2. Synthesis of (m)NHOs from NHCs and *N*-aziridinylimines.

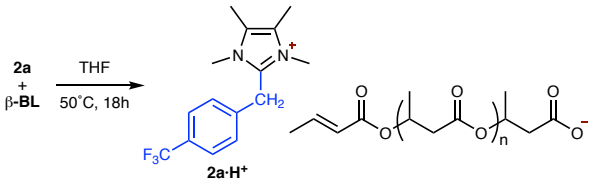
Initial investigations of the ROP of *β*-butyrolactone (**BL**) were performed using **2a**, **2c**, **4a** and **4c**. Employing the NHO **2a** without a co-initiator in THF as the solvent gave the best initial results (Table S1). The polymerizations were performed with [**BL**]/[**2a**] ratios of 100-500 at 50˚C, and representative results of these ROP experiments are summarized in Table 1. NHO **2a** provided high conversions, and the degree of polymerization, as estimated by ^{1}H-NMR analysis of the crotonate chain ends, increased in proportion to the [**BL**]/[**2a**] ratio before levelling at ca. 400 : 1 (entries 1-3 and 5). Accordingly, the number average molar mass (*M*n) obtained by GPC analysis also increased up to a [**BL**]/[**2a**] ratio of 400 : 1. Heating the reactions to 60˚C (entry 4) or lengthening the reaction time (entry 6) marginally increased monomer conversion, albeit at the expense of chain length. Moreover, increasing the **BL** feed above a 400:1 ratio (entry 7) was unproductive for conversions and polymer chain lengths alike. Overall, the performance of NHO **2a** in the ROP of **BL** was marginally improved compared to some organocatalysts such as carbenes, amidines, guanidines or phosphazenes by providing shorter polymerization times at lower optimal temperatures.[44,45]

Table 1 Polymerization of rac-**β-BL** using **2a**[a]



entry	[**BL**] / [**2a**]	Conv. (%)[b]	*Monomer : crotonate*[c]	M_n (10^3 g·mol^{-1})[d]	M_n/M_w[d]
1	100	96	42: 1	6.7	1.27
2	200	95	77: 1	9.9	1.29
3	300	92	91 : 1	15.4	1.13
4[e]	300	98	64 : 1	8.0	1.27
5	400	88	105 : 1	16.5	1.07
6[f]	400	94	86: 1	13.9	1.08
7	500	80	79 : 1	13.6	1.05

[a]All polymerization reactions performed in THF at 50˚C for 18 h (except entries 4 and 6). [b]Determined by integration of ^{1}H NMR methine resonances of ***β*-BL** and **PHB**. [c]Ratio of crotonate ends to repeating units in polymer from ^{1}H NMR. [d]Determined by gel permeation chromatography against polystyrene standards in THF. [e]Polymerization performed at 60˚C. [f]Polymerization performed for 30 h.

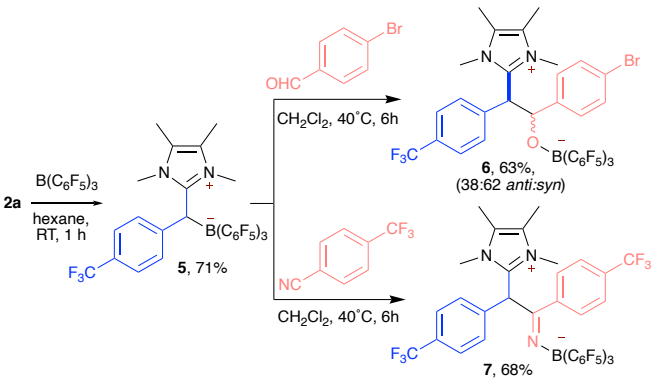


Scheme 2. Evidence for the role of **2a** as a Brønsted base initiator in the ROP of *β*-butyrolactone in the identification of the non-covalently polymer-bound **2a·H$^+$**.

^{1}H NMR analysis of low molecular weight PHB prepared using **2a** revealed the presence of the crotonate chain end and the protonated **2a** (methylene signal at δ = 4.7 ppm), whereas ^{13}C NMR was consistent with the presence of a carboxylate anion chain end (δ = 174 ppm).[45] No evidence for the covalent incorporation of **2a** within the polymer chain was found. These results suggest that **2a** initiates the polymerization by acting as a strong Brønsted base to deprotonate **BL** at the α-position, resulting in the elimination of a carboxylate anion that then propagates the ROP (Scheme 2).[46]

Upon stirring with $B(C_6F_5)_3$ in hexane at room temperature, NHO **2a** formed the Lewis acid-base adduct [**2a**·$B(C_6F_5)_3$] (**5**, Scheme 3). The orange-coloured **5** featured a benzylidene ^{1}H NMR resonance at δ = 5.84 ppm and a ^{11}B NMR signal at δ = -12.64 ppm confirming the formation of the C-B bond, as previously reported in related NHO-borane adducts.[42] Treatment of **5** with 4-bromobenzaldehyde in CD_2Cl_2 at 40˚C resulted within 6 hours in a complete conversion to **6**, the product of C=O 1,2-insertion within the C–B of **5**, which was isolated in 63% yield as 62:38 mixture of the *syn*- and *anti*-diastereomers. Suitable crystals were grown from acetonitrile solution at -20˚C; an X-ray diffraction experiment provided the solid-state structure of the *anti*-**6** diastereomer (Fig. 1). In a similar fashion, combination of **5** and 4-(trifluoromethyl)benzonitrile delivered **7**, in which 1,2-insertion of the nitrile into the C–B bond of **5** took place (Scheme 3). By contrast, no evidence for the insertion of alkenes or imines into the C–B bond of **5** was observed within 6 h at 40˚C.

The reactivity of **5** is reminiscent of that of a classical azaphosphatrane-borane Lewis acid-base adduct, $\{(C_6F_5)_3BP(MeNCH_2CH_2)_3N\}$, reported in 2018 by the Stephan group.[47] Like the latter, **5** showed no spectroscopic evidence of dissociation in solution, and yet is also able to participate in insertion reactions that are quintessential of FLPs. The results described herein suggest that the NHO-borane adduct **5** reversibly dissociated in solution in the presence of aldehydes and nitriles, and thereby mimicked FLP reactivity.



Scheme 3. Synthesis of the NHO-borane Lewis adduct **5** and insertion products from **5** and polar π-bonds.

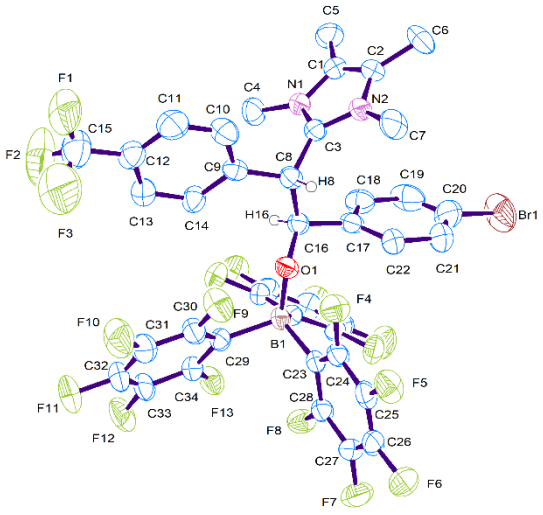


Fig. 1. Solid-state structure of *anti*-**6**. Hydrogen atoms (except H8 and H16) and a solvent molecule (CH_3CN) were omitted for clarity. Thermal ellipsoids are shown at the 40% probability level. Selected bond lengths (Å) C1-N1 1.386(5), C3-N1 1.342(5), C3-C8 1.494(5), C8-C16 1.558(5), C16-O1 1.394(4) and Br1-O1 1.471(5) and bond angles (°) N2-C3-N1 106.9(3), N1-C3-C8 126.7(3), C3-C8-C16 111.4(3), C16-O1-Br1 125.0(3).

In summary, an operationally simple protocol for the synthesis of NHOs and mNHOs by the treatment of NHCs with *N*-aziridinylimines was reported. Structurally diverse (m)NHOs could prepared by this single general approach. Screening of arylidene derivatives for their activity toward the ring-opening polymerization of *β*-butyrolactone identified **2a** as a leading candidate, and NMR studies revealed that the polymerization likely proceeded through an anionic mechanism initiated by the Brønsted basicity of **2a** rather than by a nucleophilic addition. The classical NHO-borane Lewis adduct [(**2a**)·$B(C_6F_5)_3$] (**5**) was

shown to react with aldehydes and nitriles, providing 1,2-insertion products indicative of FLP reactivity. The new synthetic method will facilitate further investigations of the chemistry of (m)NHOs, and the design of organocatalytic cycles where intermediate (m)NHOs are generated by the reaction of NHCs with *N*-aziridinylimines.

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Conflicts of interest

There are no conflicts to declare.

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