Zitierweise: *Angew. Chem. Int. Ed.* **2021**, *60*, 13559–13563
Internationale Ausgabe: doi.org/10.1002/anie.202100576
Deutsche Ausgabe: doi.org/10.1002/ange.202100576

Mechanochemistry

# Mechanochemical Release of *N*-Heterocyclic Carbenes from Flex-Activated Mechanophores

*Hang Shen, Michael B. Larsen, Allison G. Roessler, Paul M. Zimmerman, and Andrew J. Boydston**

***Abstract:*** *We have discovered a new flex-activated mechanophore that releases an N-heterocyclic carbene (NHC) under mechanical load. The mechanophore design is based upon NHC-carbodiimide (NHC-CDI) adducts and demonstrates an important first step toward flex-activated designs capable of further downstream reactivities. Since the flex-activation is non-destructive to the main polymer chains, the material can be subjected to multiple compression cycles to achieve iterative increases in the activation percentage of mechanophores. Two different NHC structures were demonstrated, signifying the potential modularity of the mechanophore design.*

Polymer mechanochemistry harnesses mechanical energy to drive chemical reactions within polymeric materials. The ability to translate between macroscopic and microscopic energy surfaces, combined with evolving mechanophore designs, has fueled impressive growth in this nascent area.[1–5] Compared to conventional reaction pathways, the potential energy surfaces of related mechanochemical reactions are altered by mechanical force. This consequently changes the overall activation energy[6,7] and in some cases alters the reaction products.[8–10] Mechanophores serve as a focal point for studying how mechanical force can be transduced to the molecular level, since these functional groups are intended to undergo predictable chemical reactions upon geometric distortions.[11] Through judicious design, mechanophores can collectively achieve changes in topology such as polymer chain extension[12,13] or cross-linking,[14–17] shifts in glass transition temperature ($T_g$),[18] enhancement of electrical conductivity,[19] photophysical changes,[20–26] and the release of small molecule cargo.[27–33]

To date, the vast majority of mechanophore designs focus on bond elongation to achieve activation, resulting in cleavage of specific bonds within polymer backbones. Alternatively, flex-activated mechanophores mainly leverage bond bending to facilitate mechanochemical reactions.[28–30,34] Therefore, flex-activation is non-destructive to the overall macromolecular architecture and polymer backbones can survive multiple activation cycles.[35] Flex-activation is also accompanied by release of small molecules owing to bond scission within pendant groups. For example, an oxanorbornadiene motif incorporated into a poly(methyl acrylate) (PMA)[28] or polyurethane matrix[29] can release a furan derivative upon compression (Figure 1a). Within the elastomeric polyurethane network, successive release of furan over multiple load cycles was observed. In addition to oxanorbornadienes, phenyltriazolinedione-anthracene adducts embedded in a poly(dimethylsiloxane) (PDMS) elastomer released phenyltriazolinedione under pressure, with nearly full shape recovery of the material after activation.[30]

Despite this progress, there is a need for further development of flex-activated mechanophores, particularly those capable of releasing other small molecules that have the ability to trigger secondary reactions or polymerizations. Since flex-activation does not require degradation of the polymer main chain, it could be employed in drug delivery,[36] damage detection,[33] self-healing,[37,38] or remodeling materials.[39] Herein, we report a new type of flex-activated mechanophore based upon *N*-heterocyclic carbene-carbodiimide (NHC-CDI) adducts, a class of zwitterionic betaine-type

[*] Dr. H. Shen, Prof. Dr. A. J. Boydston
Department of Chemistry, University of Wisconsin-Madison
1101 University Avenue, Madison, WI 53706 (USA)
E-mail: aboydston@wisc.edu
Prof. Dr. M. B. Larsen, Prof. Dr. A. J. Boydston
Department of Materials Science and Engineering
Department of Chemical and Biological Engineering
University of Wisconsin-Madison, Madison, WI 53706 (USA)
and
Department of Chemistry, Western Washington University
Bellingham, WA 98225 (USA)
Prof. Dr. A. G. Roessler, Prof. Dr. P. M. Zimmerman
Department of Chemistry, University of Michigan
930 N. University Ave, Ann Arbor, MI 48109 (USA)
Prof. Dr. A. G. Roessler
Department of Chemistry, Oglethorpe University
4484 Peachtree Rd, Atlanta, GA 30319 (USA)
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.202100576.

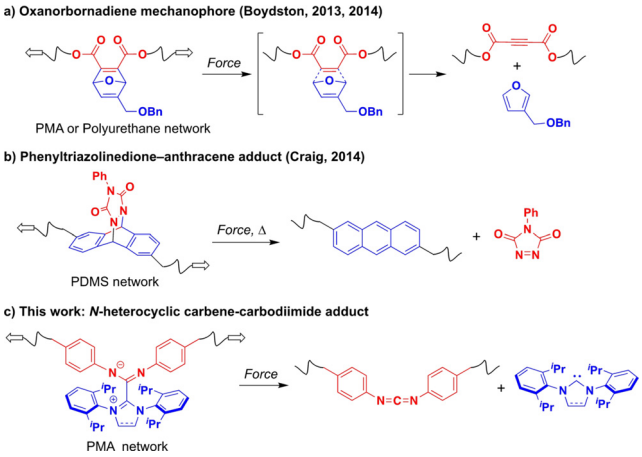


***Figure 1.*** Flex-activated mechanophores.

  

amidinates.[40,41] Related structures have attracted attention across a variety of fields including nanocatalysis,[42,43] organometallic chemistry,[44–46] and polyzwitterionic materials.[47] NHC-CDIs based on aryl carbodiimides are bench-stable and cleavage of the C–C bond between the NHC and CDI is kinetically accessible at elevated temperatures.[47] Thus, we hypothesized that bond scission could be mechanically facilitated. Furthermore, the NHCs released from this mechanophore represent widely used and powerful organocatalysts,[48–50] which provides opportunities to make diverse mechanoresponsive materials by triggering varied reactions upon activation. Different from previously reported mechanophores that use chain scission to generate NHCs at the chain ends of the daughter fragments,[51–55] the NHC-CDI mechanically releases a small molecule NHC without requiring destruction of the network linkages. The flex activation design could therefore be used as a platform to release various classes of NHCs, potentially with queued mechanochemical preference.

To gain an atomistic understanding of NHC-CDI flex-activation, quantum chemical calculations were applied using density functional theory and the force-biased growing string method.[34,56] Transition states (TSs), reaction paths (RPs), and product geometries for mechanophore activation were calculated at varying magnitudes of applied force (see SI for full computational details). Figure 2a and 2b shows how increasing tensile force lowers the activation energy for NHC release in the mechanophore model. Applying force to the reactant (Figure 2c (i→ii)) results in mechanophore stretching which effectively lowers the thermal energy required for subsequent activation. As activation occurs (i→iii or ii→iv), the overall length of the mechanophore increases, despite the central CDI contracting from N–C=N to N=C=N. These simulations therefore show that the NHC release occurs readily, without fracturing the polymer backbone. Thus, compounding mechanophore activation within the PMA network can provide strain relief by releasing stored length.

To empirically verify the mechanical reactivity of the NHC-CDI, we prepared mechanophore **3** and the control NHC-CDI **4**, both of which can be easily synthesized by the condensation of corresponding isocyanates followed by reaction with the desired NHC (Figure 3a). Mechanophore **3** was subsequently incorporated into a PMA network as a crosslinking unit through free-radical polymerization initiated by azobisisobutyronitrile (AIBN). After polymerization, unreacted monomer was washed away by a mixture of $CH_2Cl_2$ and $CD_3Cl$ multiple times until it could no longer be detected by $^1H$ NMR spectroscopy. During the washing step, no unreacted mechanophore was observed, and the mechanophore percentage within the PMA network was calculated to be 5.8 mol% based on the feed ratio and the recovered amounts of reactants. To confirm the stability of the NHC-CDI adduct under the polymerization conditions, the control NHC-CDI **4** was subjected to the same polymerization conditions as **3** (Figure 3b). From the $^1H$ NMR spectrum of the reaction mixture, no obvious side products were observed, and >90% of **4** remained after the polymerization as determined using an internal standard (Supporting Information, Figure S3).

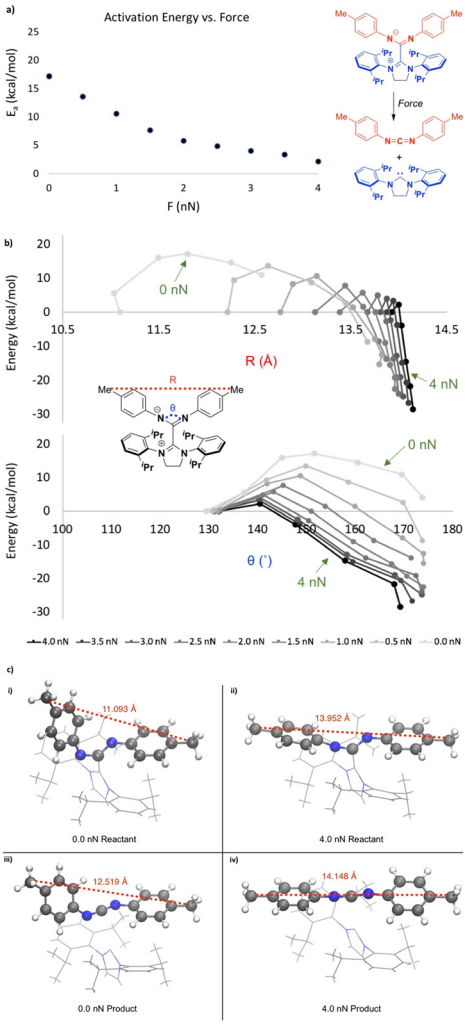


***Figure 2.*** Quantum chemical calculations were employed at the B3LYP level of theory with the LANL2DZ basis set. For each calculation, a tensile force was applied to the terminal carbons in the model to simulate experimental conditions. a) Simulated activation energies ($E_a$) plotted as a function of applied tensile force. b) Reaction paths for mechanophore activation at various magnitudes of applied force. The reaction coordinates chosen are the R distance (top) which represents total elongation of the mechanophore and the $\theta$ angle (bottom) which represents the bond flexing that occurs as the mechanophore is activated. These graphs represent the alterations that are made to reaction potential energy surfaces in the presence of force. c) Geometries for the NHC-CDI mechanophore before and after activation in the ground state (no applied force) and with 4 nN of force applied.

With the desired polymeric material in hand, we then chose phenyl isothiocyanate (PITC) as the trapping agent for the NHC released via flex-activation under uniaxial compression (Figure 4a). Since PITC is a liquid and more electrophilic than the diaryl- carbodiimide,[57] it was expected to react with the NHC faster than the carbodiimide within the polymer backbone and consequently suppress the recombination of released NHC with the carbodiimide. Moreover, literature reports as well as our model experiments indicated high yield in the formation of the NHC-PITC adduct (Section II in the Supporting Information).[58,59] After trapping the NHC, excess PITC was easily removed by reacting

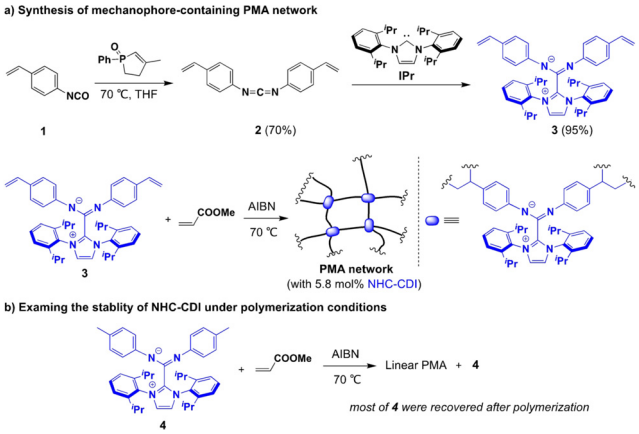


***Figure 3.*** a) Synthesis of the mechanophore-containing PMA network from isocyanate **1** in three steps. b) Using control NHC-CDI **4** to confirm the stability of NHC-CDI under polymerization conditions.

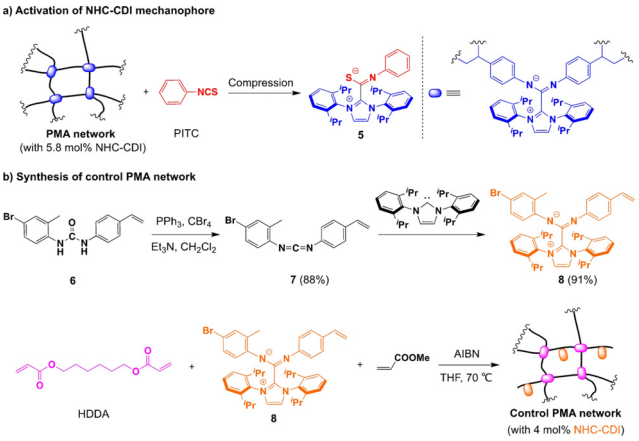


***Figure 4.*** a) Activation of NHC-CDI mechanophore **3** by compression, using PITC as the trapping agent. b) Synthesis of the control PMA network with monofunctional NHC-CDI **8** to confirm the mechanical activation of NHC-CDI mechanophore.

with solid-supported nucleophiles such as polymer-bound benzylamine, avoiding impediments to characterization and quantification of the NHC-PITC adduct by LC-MS. Upon uniaxial compression at 740 MPa for 10 min, 0.41 % of NHC-CDI in the PMA network was activated, as determined by LC-MS using 9-methylanthracene as an internal standard (see Section V of the SI for details). To exclude the possibility that the activation resulted from thermal or other effects during compression, we also prepared a control PMA network that contained 1,6-hexanediol diacrylate (HDDA) as the cross-linker and monofunctional NHC-CDI **8** as the comonomer (Figure 4b). NHC-CDI **8** was synthesized from the urea derivative **6** in two steps. Because **8** only has a single styrenic double bond, the NHC-CDI moieties within the control network are pendent groups on the polymer chains and are not subject to the same mechanical load. In addition, introducing a Br group to the adduct assisted our analysis of side products by its isotopic mass pattern. Under identical compression conditions and using the same trapping agent, the control PMA network only had an activation percentage of 0.03 % and no other obvious side products were observed in the LC-MS spectra. This indicates that activation of the NHC-CDI mechanophore is mainly induced by mechanical force.

We next performed a series of compression experiments at different pressures to evaluate the influence of applied mechanical load on the mechanophore activation. As depicted in Figure 5, no activation was observed without compression of the sample, whereas detectable amounts of trapped NHC were observed once 74 MPa was applied. Additionally, the activation percentage became higher as the applied pressure increased. These results give additional support to the mechanochemical origins of the NHC-CDI activation.

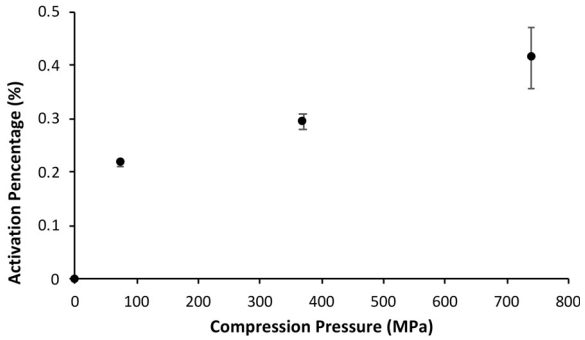


***Figure 5.*** Plot of mechanophore activation percentage versus compression pressure (0, 74, 370, 740 MPa). Pressure was applied for 10 min in each experiment. Error bars represent standard deviations of results from 3 or 6 individual experiments.

In our previous report using a PMA network as the scaffold to achieve the flex-activation of oxanorbornadiene,[28] only one compression could be applied to the material due to its macroscopic failure after compression. However, adding liquid PITC to the NHC-CDI containing PMA network appeared to plasticize and improve the durability of the material. After each compression, the flattened disc-like sample was folded and compressed again, without obvious signs of cracking or other macroscopic failure. A monotonic rise in activation percentage was observed with increasing number of compressions until reaching a plateau of activation (1.06 %) after three compression-activation cycles (Figure 6). The plateau of the activation may be attributed to the heterogeneity of the local forces exerted on NHC-CDI mechanophores within the randomly cross-linked PMA, which concentrates force in a few polymer segments.[60,61]

We next investigated a related NHC structure in addition to the 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) of our original design. Specifically, we prepared materials from the saturated analogue, 1,3-bis(2,6-diisopropylphenyl)I-midazolidin-2-ylidene (SIPr). As shown in Figure 7a, SIPr-CDI mechanophore **9** was synthesized and incorporated into the PMA network through the same pathway as for IPr-CDI mechanophore **3**. However, the molar percentage of **9** within the network was limited to 3.4 mol %, owing to its low solubility in methyl acrylate. An analogue of **9**, similar to IPr-

  

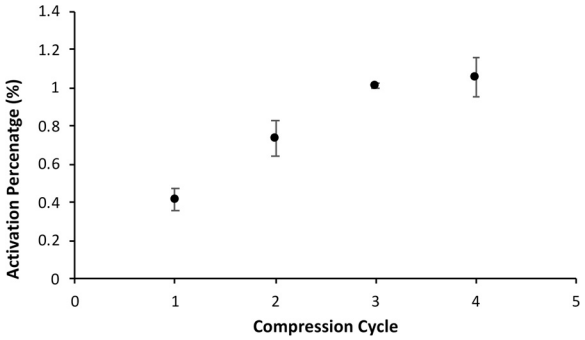


***Figure 6.*** Plot of mechanophore activation percentage versus compression cycle. Experiments were conducted by compressing the sample at 740 MPa for 10 min in each compression cycle and folding each sample between compression cycles. Error bars represent standard deviations of results from 3 or 6 individual experiments.

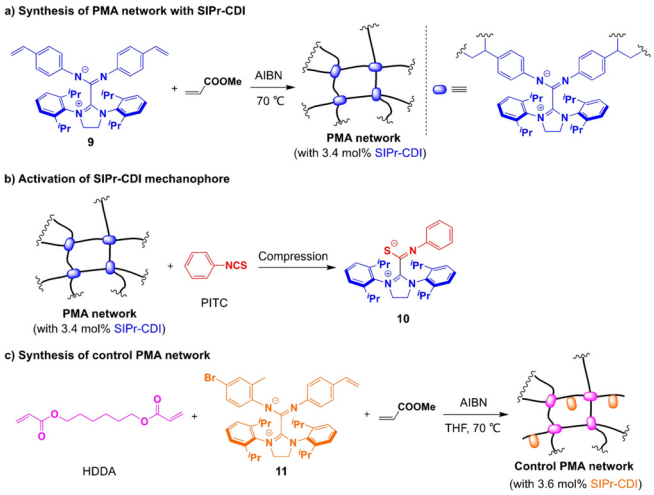


***Figure 7.*** a) Synthesis of the PMA network containing SIPr-CDI **9**. b) Activation of SIPr-CDI mechanophore **9** by compression, using PITC as the trapping agent. c) Synthesis of the control PMA network with monofunctional SIPr-CDI **11** to confirm the mechanical activation of SIPr-CDI mechanophore.

CDI **4**, was also prepared to confirm the stability of SIPr-CDI compounds under the polymerization conditions. According to the $^1$H NMR analysis, $>90\,\%$ of the control specimen was recovered after polymerization, and no side products were detected (Supporting Information, Figure S4).

After compression of the material containing SIPr-CDI **9** at 740 MPa for 10 min, 0.46 % mechanophore activation was calculated from LC-MS results (Figure 7b). Importantly, the control network that was made from the copolymerization of control SIPr-CDI **11** and methyl acrylate only gave 0.003 % activation under the same compression conditions (Figure 7c), which again indicates the mechanically triggered activation of SIPr-CDI mechanophore.

In summary, we have demonstrated a new type of flex-activated mechanophore that features a modular NHC-CDI adduct capable of releasing small molecule NHCs under mechanical load. Quantum chemical calculations were employed to examine how the mechanophore responses to mechanical force. Mechanical activation of NHC-CDI mechanophores showed a positive correlation with the compression pressure as well as increases in the activation percentage over multiple compression-activation cycles. We anticipate that NHC-CDI mechanophores may have diverse applications in advanced functional materials capable of self-healing, self-strengthening and self-reporting initiated by mechanical force. Furthermore, the nucleophilicity and Lewis basicity for various NHCs are well-studied,[62,63] which could enable further research to investigate the relationship between physical organic properties and force-modified potential energy surfaces of systematically varied NHC-CDI mechanophores.

## Acknowledgements

We gratefully acknowledge financial support from the Army Research Office (Grant No. W911NF-15-1-0139 and W911NF-17-1-0595), National Science Foundation (DMR-1452726 to A.J.B., CHE-1551994 to P.M.Z.), and Camille and Henry Dreyfus Foundation. AJB gratefully acknowledges support from the Yamamoto Family and the Office of the Vice Chancellor for Research and Graduate Education at the University of Wisconsin-Madison with funding from the Wisconsin Alumni Research Foundation. NMR and mass spectroscopy facilities are supported by the National Science Foundation (CHE-1048642), National Institutes of Health (1S10 OD020022-1), and a generous gift from the Paul J. and Margaret M. Bender. We also express our gratitude to Prof. Jeremiah Johnson (MIT) and Prof. Stephen Craig (Duke University) for invaluable discussions, encouragement, and breakthroughs in NHC-CDI chemistry and mechanochemical analyses.

## Conflict of interest

The authors declare no conflict of interest.

**Keywords:** mechanochemistry · mechanophores · mechanoresponsive polymers · *N*-heterocyclic carbene · *N*-heterocyclic carbene–carbodiimide

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Manuscript received: January 13, 2021
Revised manuscript received: March 25, 2021
Accepted manuscript online: April 7, 2021
Version of record online: May 7, 2021

  