Activating catalysts with mechanical force

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Homogeneously catalysed reactions can be ‘switched on’ by activating latent catalysts. Usually, activation is brought about by heat or an external chemical agent. However, activation of homogeneous catalysts with a mechanical trigger has not been demonstrated. Here, we introduce a general method to activate latent catalysts by mechanically breaking bonds between a metal and one of its ligands. We have found that silver(i) complexes of polymer-functionalized N-heterocyclic carbenes, which are latent organocatalysts, catalyse a transesterification reaction when exposed to ultrasound in solution. Furthermore, ultrasonic activation of a ruthenium bincarbene complex with appended polymer chains results in catalysis of olefin metathesis reactions. In each case, the catalytic activity results from ligand dissociation, brought about by transfer of mechanical forces from the polymeric substituents to the coordination bond. Mechanochemical catalyst activation has potential applications in transduction and amplification of mechanical signals, and mechanically initiated polymerizations hold promise as a novel repair mechanism in self-healing materials.

Activation of latent homogeneous catalysts is usually achieved by thermally1–4 or chemically5 induced dissociation of a ligand to give the catalytically active species from a coordinatively saturated metal complex. Latent complexes are useful as precursors because they suspend catalytic activity by keeping the complex in a less active but more stable state, which can be turned on by the appropriate trigger at the desired time. Dissociating ligands with mechanical force is an attractive alternative method to activate homogeneous catalysts because it provides a fundamentally different stimulus to control chemical reactivity6. In order to transfer macroscopic mechanical forces to a metal complex in solution, functionalization with long chains is required7, because shear forces induce bond scission in polymers but not in small molecules8. Using this principle, we have designed latent catalysts that combine a metal with polymer-functionalized ligands, resulting in a long chain with a single coordination complex in the centre. In these latent catalysts, selective scission of a coordination bond, which is weak compared with the covalent bonds in the polymer, results in either a catalytically active ligand or a catalytically active metal site (Fig. 1a).

One of the most efficient ways to apply mechanical forces in solution is by making use of ultrasound9. On sonication, strong shear forces arise around collapsing cavitation bubbles. Under the influence of these forces, polymers of sufficient length are stretched, and eventually break midchain owing to accumulation of stress. Ultrasonic chain scission of polymers is site-specific for cleavage of weak peroxide10, azo11 and coordination12 bonds. Silver(i) complexes with polymer-functionalized N-heterocyclic carbene (NHC) ligands break exceptionally rapidly when exposed to ultrasound. Sonication of solutions containing complexes with less than 10 kDa polymeric substituents results in quantitative conversion of the carbene complexes to imidazolium salts within 10 minutes13.

NHCs have recently gained popularity as versatile organocatalysts for a wide range of chemical transformations14. The free carbenes are usually obtained in situ from imidazolium salts by deprotonation with base14. Silver(i) complexes of NHCs have been used as catalysts that can be activated thermally4. Therefore, the polymer-functionalized silver complexes are excellent candidates to serve as precursors for the mechanochemical activation of organocatalysts.

In order to investigate mechanochemical activation of silver–NHC complexes for catalysis of transesterification15, a mixture of benzyl alcohol (3) and vinyl acetate (4) containing 3 mM of the complex 1a (molecular weight of ligands 5.0 kDa) was sonicated for 60 minutes at 6 ± 2 °C, using a sonication probe (Fig. 1b,c). Sonication resulted in the formation of benzyl acetate (5) with turnover number (TON, defined as the number of substrate molecules converted per molecule of 1a) exceeding 800 (65% conversion). Without sonication, there was less than 3% conversion at the same temperature, and thermal activation of a 0.6 mM solution of 1a required heating to 95 °C to obtain 28% conversion in 45 minutes.

In order to confirm the mechanochemical nature of the catalyst activation, additional control experiments were performed at 0.6 mM latent catalyst concentration with 1a, the higher-molecular-weight complex 1b (molecular weight of ligands 22 kDa) and the low-molecular-weight silver–carbene complex 2. With these complexes, conversion after 10 minutes was 2.9%, 1% and 10% for 2, 1a and 1b, respectively (full time–conversion plots are shown in Supplementary Fig. S22). Sonication of benzyl alcohol and vinyl acetate in the absence of catalyst did not yield benzyl acetate.

The generality of the dissociation-induced activation of latent catalysts was further demonstrated with ruthenium–alkylidene complexes, which are well-defined catalysts for the formation of carbon–carbon double bonds via olefin metathesis reactions, including ring-closing metathesis (RCM) and ring-opening metathesis polymerization (ROMP)16. Latent ruthenium–alkylidene metathesis catalysts have been obtained by increasing the binding strength between the ligands and the ruthenium5. In particular, biscomplexation with NHC ligands has proved to be a successful method for restraining the catalytic activity of metathesis catalysts at room temperature17. The active state of these complexes was obtained by thermal dissociation of one of the ligands at elevated temperatures. We designed a latent catalyst that can be activated by mechanical force, based on the reported low activity of bis[N-(alkyl)-N′-(2,6-diisopropylphenyl)carbene]–Ru complexes. In order to transfer macroscopic mechanical forces to the metal–ligand coordination bond, polymer-functionalized ligands were used, prepared by endcapping living polytetrahydrofuran with the...
Mechanochemical activation of a catalytic ring-closing metathesis (RCM) reaction. \( \textbf{a} \), RCM reaction of DEDAM (9) (0.1 M in toluene-\( d_8 \)) at 20 °C using 6a, 6b and 7 as catalysts. Conversion was determined with \( ^1 \text{H}-\text{NMR} \) spectroscopy. \( \textbf{b} \), Time–conversion plots of sonication-induced RCM of 9. Error bars are based on standard errors in duplicate runs.

At room temperature, the complexes 6a–c are completely inactive for the ring-closing metathesis of diethyl diallylmalonate (DEDAM, 9), a benchmark substrate for this reaction. Reactions at elevated temperatures showed that thermal activation required temperatures of at least 80 °C to obtain 94% conversion within 1 hour. For mechanochemically activated ring-closing metathesis, a 0.1 M DEDAM solution in toluene-\( d_8 \) was sonicated in the presence of 1 mM of 6a at 20 °C (Fig. 2a). RCM of the substrate to diethyl cyclopent-3-ene-1,1,1-tricarboxylate (10) was followed using \( ^1 \text{H}-\text{NMR} \) spectroscopy. After two 1-hour periods of sonication, interrupted for 30 minutes, conversion was 14%. In the presence of the complex 6b under the same experimental conditions, conversion was 36% (Fig. 2b). On sonication, the peak of the alkylidene proton at \( \delta \) 19.20 ppm in the \( ^1 \text{H}-\text{NMR} \) spectrum decreased slowly to approximately 50% of its original intensity after 2 hours. During interruption of sonication, conversion did not increase with either of the catalysts, indicating that the active species generated during sonication has a limited lifetime, although irreversible loss of alkylidene signal indicates that dissociated ligand does not rebind to regenerate the latent catalyst. The significantly higher conversion obtained using the complex 6b with the higher-molecular-weight polymer as latent catalyst supports a mechanical rather than a thermal mechanism of catalyst activation. This hypothesis was further confirmed by sonication of a solution of DEDAM in the

**Figure 1** Concept, catalysts used and reactions of mechanical catalyst activation. \( \textbf{a} \), Cartoon depicting the ultrasound-induced mechnanochemical scission of a metal complex with polymeric ligands, resulting in the activation of a catalyst. In (i), the active ligand catalyses transesterification and in (ii) the metal centre catalyses polymerization. \( \textbf{b} \), Polymeric silver–N-heterocyclic carbene (NHC) complexes \( \text{1a, 1b} \) and ruthenium–NHC complexes \( \text{6a–c} \) used in the present study, with corresponding non-polymeric analogues \( \text{2 and 7} \). \( \textbf{c} \), Ultrasound-induced transesterification between benzyl alcohol (3) and vinyl acetate (4) catalysed by the polymeric silver–NHC complexes \( \text{1a and 1b} \). Sonication was performed in a water-cooled glass vessel under an inert argon atmosphere. Ultrasound was applied using a 13 mm probe at a frequency of 20 kHz, at 30% of the maximum amplitude of 125 μm. The internal temperature of the sonication vessel during sonication was 6 ± 2 °C. pTHF, polytetrahydrofuran.
The presence of the low-molecular-weight complex 7 at 20 °C. After sonication for 2.5 hours, no product signal was observed in the NMR spectrum, indicating a conversion lower than 1% and showing that polymeric substituents are necessary for activation of the catalyst.

A dissociative mechanism of mechanochemical activation was anticipated based on the proposed mechanism of ruthenium–alkylidene metathesis (Fig. 3), and was confirmed in experiments in which a 1 mM solution of the complex 6b in toluene-d₈ was sonicated in the presence of a 10-fold molar excess of tricyclohexylphosphine (PCy₃, 11). ¹H- and ³¹P-NMR spectra showed the appearance of new signals at positions in agreement with the formation of the ruthenium–phosphine complex 12 (Fig. 4a,b). During sonication for 120 minutes, 50% of 6b was converted to 12, in excellent agreement with the expected mechanism.
agreement with the amount of alkylidene signal lost in the sonication experiment without added phosphine. This suggests that these numbers correspond to the actual extent of dissociation. When the 50% conversion to 12 is used as a measure of the fraction of catalyst activated over the course of 2 hours, the number of substrate molecules that each active catalyst species converts to ring-closed form is estimated to be 80.

When a sonication experiment was performed in a solution of 6b containing 100 equivalents of DEDAM in addition to a 10-fold excess of tricyclohexylphosphine, no ring-closed product was detected with 1H-NMR spectroscopy. However, 1H- and 31P-NMR spectra showed the formation of a new species, the chemical shifts detected with 1H-NMR spectroscopy. However, 1H- and 31P-NMR spectra showed the formation of a new species, the chemical shifts determined by 1H-NMR spectroscopy. Thus, under these conditions, DEDAM does react with activated catalyst after initial dissociation of an NHC ligand, but coordination of the phosphine slows down further catalytic cycles to such an extent that formation of product is not observed (Fig. 3)\(^\text{20}\).

For applications in self-healing polymeric materials, it is important to develop efficient mechanochemically activated polymerization reactions. Ruthenium–alkylidenes with NHC ligands are known to be highly efficient initiators for the ROMP of cyclic olefins\(^\text{15}\). Because high molecular weights make activation more efficient, the catalyst 6c, with an increased molecular weight compared with 6a and 6b, was used to study the mechanochemically initiated ROMP of cyclooctene (Fig. 5a). A toluene-\(d_8\) solution containing 0.5 M of cyclooctene (14) and 1 mM of 6c (a cyclooctene:6c ratio of 500:1) was sonicated at 20 °C for two 1-hour periods, interrupted by 30 minutes without sonication. 1H-NMR spectroscopy was used to determine conversion to the product, polyoctenamer (15). After 2 hours, a conversion of 90% ± 5% was reached, corresponding to a substrate turnover number of 450 (Fig. 5b). Size-exclusion chromatography (SEC) analysis of the sonicated reaction mixture after chromatographic removal of the polar catalyst showed a peak corresponding to polyoctenamer with a number-average molecular weight \(M_n\) of 40 kDa based on polystyrene standards and polydispersity index \(M_w/M_n\) of 1.6. The relatively high value of the polydispersity index reflects the continuous but relatively slow initiation during sonication\(^\text{17}\). No conversion was observed when the low-molecular-weight catalyst 7 was used under identical experimental conditions, and a low conversion (2% after 2 hours) was observed when the solution containing 6c was not sonicated. As with the RCM, conversion did not increase while sonication was interrupted. An experiment in which sonication was interrupted after 10 minutes clearly showed ROMP activity when sonication was resumed after 40 minutes, but conversion stopped after 80 minutes (total sonication time 50 minutes) at a lower value (26%) than after continuous sonication for 60 minutes (84%) (see Supplementary Fig. S20). NMR spectra suggested that the lower conversion is due to decomposition of catalyst, because the alkylidene signal continued to decrease during the resting interval.

In conclusion, we have shown that mechanochemical scission of a metal–ligand bond may be used to release the innate catalytic activity of either the ligand or the metal. Limitations of the current process lie in the irreversibility of activation and in the lack of control over the mechanochemical forces, as well as in the limited breaking rate that can be achieved with the use of ultrasound. It is expected that the application of forces on latent catalyst complexes embedded in a crosslinked network will be much less subject to these limitations. The present findings therefore bode well for the development of materials in which mechanochemical activation of latent catalysts is used for autonomous healing\(^\text{12}\) based on polymerization or crosslinking of reactive monomers.

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**References**


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Author contributions

R.P.S. conceived the sonochemical catalyst activation experiment and directed the research. A.P. and S.K. performed the experiments. All of the authors participated in writing the paper.

Additional information

Supplementary information and chemical compound information accompany this paper at http://npg.nature.com/reprintsandpermissions/. Correspondence and requests for materials should be addressed to R.P.S.