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Unlocking catalytic potential: a rhodium(II)-based coordination polymer for efficient carbene transfer reactions with donor/acceptor diazoalkanes[†]

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Herein, we report the use of a molecular-defined rhodium(II) coordination polymer (Rh-CP) as a heterogeneous, recyclable catalyst in carbene transfer reactions. We showcase the application of this heterogeneous catalyst in a range of carbene transfer reactions and conclude with the functionalization of natural products and drug molecules.

Rhodium(II) carboxylate paddlewheel complexes feature two rhodium centers, a rhodium–rhodium single bond and four bridging carboxylate ligands. They represent a privileged class of catalysts, primarily due to each rhodium center having a free coordination site, central for facilitating for example carbene or nitrene transfer reactions (Scheme 1A).^{1–4} While the development of homogeneous rhodium paddlewheel catalysts has received significant attention,^{3,4} the use of their heterogeneous counterparts has been much less explored.^{5–8} Previous efforts primarily focused on the immobilization of homogeneous catalysts on a surface or polymer.⁵ The catalytic activity of this material, however, is achieved through a single-molecule catalyst grafted onto the heterogeneous support (Scheme 1B). Studies on the application of heterogeneous rhodium-based carbene transfer catalysts, where the catalytically active site is an integral part of the heterogeneous material, however, received only little attention (Scheme 1C).^{6–8} Studies on such heterogeneous catalysts are in high demand as these would allow facile catalyst recovery from the reaction mixture and may result in enhanced catalyst lifetime, which—given the low abundance and high price of rhodium—would have a significant impact on the environmental footprint of rhodium-catalyzed reactions.⁴

Building on our interest in metal-catalyzed carbene transfer reactions using,⁹ we considered that a Rh(II)-based coordination polymer (Rh-CP) could serve as a viable starting point to access a heterogeneous, molecular-defined rhodium catalyst with a repetitive paddlewheel structure (Scheme 1D). Such Rh-CP would differentiate from other approaches, where molecular-defined rhodium catalysts are heterogenized by immobilization to surfaces.⁵ We got intrigued by a previous report by Buntkowsky and co-workers, who described a straightforward synthesis of such a Rh(II)-based coordination polymer by a ligand exchange reaction of $\text{Rh}_2(\text{OAc})_4$ (Scheme 1C).⁶ A related report by Furukawa *et al.* reports on the formation of octahedral clusters using benzene-1,3-dicarboxylic acid.⁷ Very much to our surprise, only limited applications in catalysis were described, which focus on the reaction of ethyl diazoacetate.⁶

We commenced our studies by performing a ligand exchange reaction between $\text{Rh}_2(\text{OAc})_4$ and terephthalic acid (H_2BDC) to obtain the Rh-CP as a green powder in excellent yield (Fig. 1A, 97%). The Rh-CP was authenticated to the literature⁶ by PXRD analysis (see Fig. S1, ESI[†]), TGA analysis (Fig. S2 and S3, ESI[†]) ATR-IR (Fig. S4, ESI[†]), and diffuse reflectance spectra (Fig. 1B). Importantly, diffuse reflectance spectra in an Ulbricht sphere (Fig. 1B) indicate the persistence of the paddlewheel structure within the Rh-CP. This structural motif is crucial for the catalytic properties.¹⁰

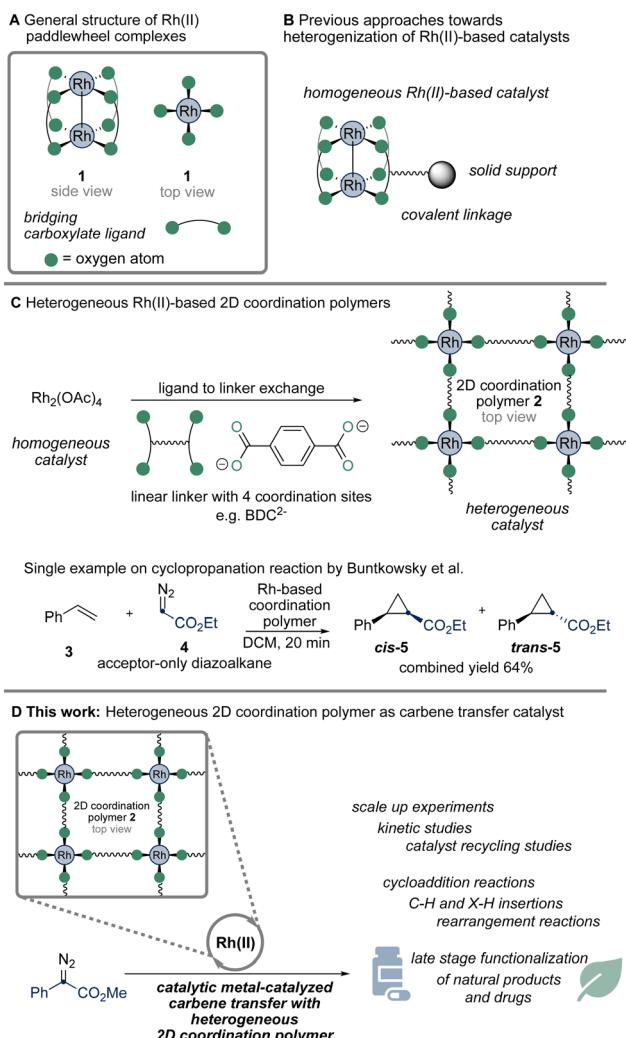
¹H NMR measurements were carried out to determine the degree of ligand exchange. For this purpose, Rh-CP was digested in a mixture of DMSO-d_6 and D_2SO_4 , whereby the integrals of the BDC linker and acetate gave a ratio of about 82 to 3 corresponding to a molar BDC:OAc ratio of 20:1 (Fig. S7 and S8, ESI[†]). Scanning electron microscopy (SEM) shows our Rh-CP as comparatively small agglomerates, which are characterized by a lamellar morphology at higher magnification (Fig. S5 and S6, ESI[†]). EDX elemental mapping indicates a homogeneous dispersion of rhodium throughout the synthesized Rh-CP, confirming a consistent elemental distribution within the compound (Fig. 1C).

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Scheme 1 Rh(II) paddlewheel complexes and Rh(II)-CP in carbene transfer reactions.

To evaluate the catalytic efficiency and stability in catalysis of the Rh-CP and to probe differences to homogeneous, achiral rhodium(II) catalysts, we investigated the model reaction of donor/acceptor diazoalkane **6** with styrene **3** to give cyclopropane **7** (Scheme 3). In a first step, we performed the reaction on 10 mmol scale of diazoalkane **6** (1.9 g) employing 0.5 mg Rh-CP (23.1% Rh-content) to evaluate stability and activity of Rh-CP. Complete consumption of the diazoalkane was observed and the desired cyclopropane was isolated in 92% yield (2.31 g) in high diastereoselectivity. The diastereoselectivity was comparable to achiral, homogeneous Rh(II) catalysts, which is suggestive that the coordination polymer backbone has little influence on the geometry of transition state in this cyclopropanation reaction. A further reduction of the Rh-CP catalyst loading to 0.236 mg gave the desired cyclopropane **7** in slightly reduced yield of 91% (2.29 g).

Recycling studies further showed that the first five cycles gave a relatively constant yield of >86% of cyclopropane **7**, while the amount of recovered Rh-CP constantly decreased to 60%. This reduction might be attributed to mechanical forces

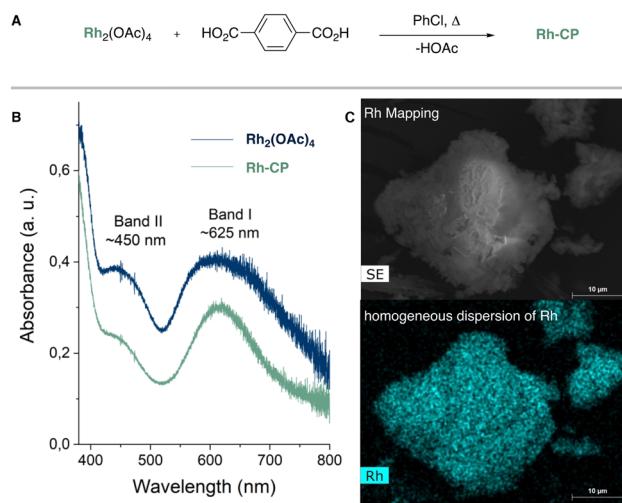
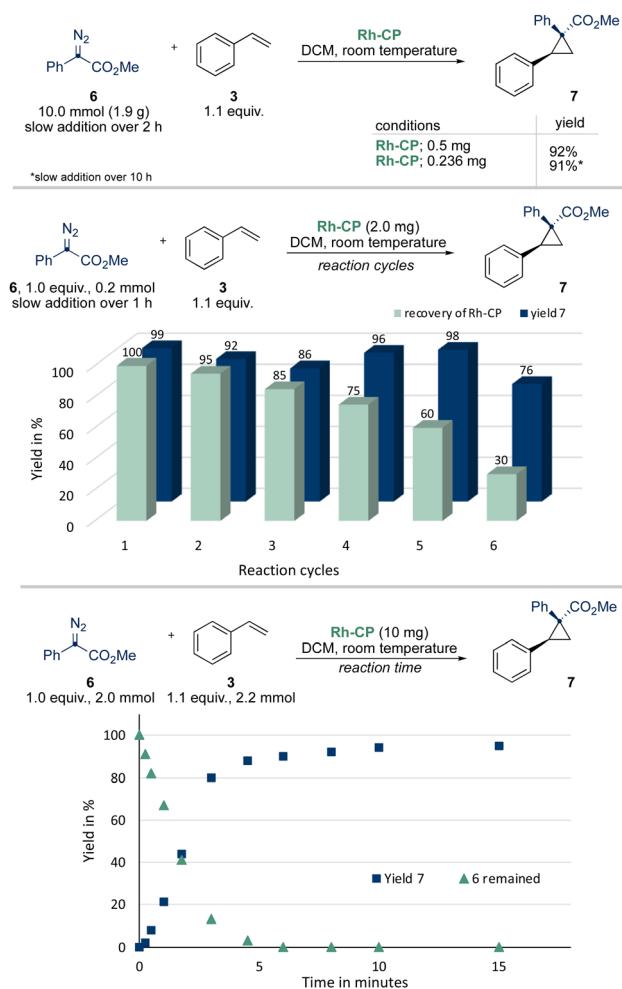


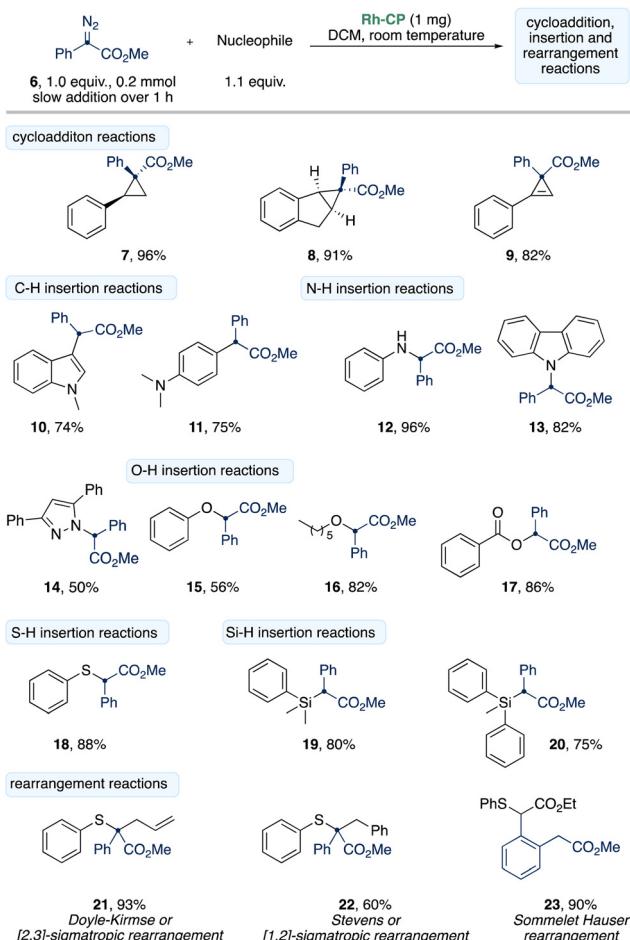
Fig. 1 (A) Synthesis of Rh-CP. (B) Optical Kubelka–Munk spectra of $\text{Rh}_2(\text{OAc})_4$ and Rh-CP obtained from diffuse reflectance spectra. (C) EDX Rh mapping of Rh-CP.



Scheme 2 Studies on Rh-CP catalyzed cyclopropanation of styrene.

on the Rh-CP catalyst during stirring the reaction mixture that results reduction of particle sizes and reduced catalyst recovery.





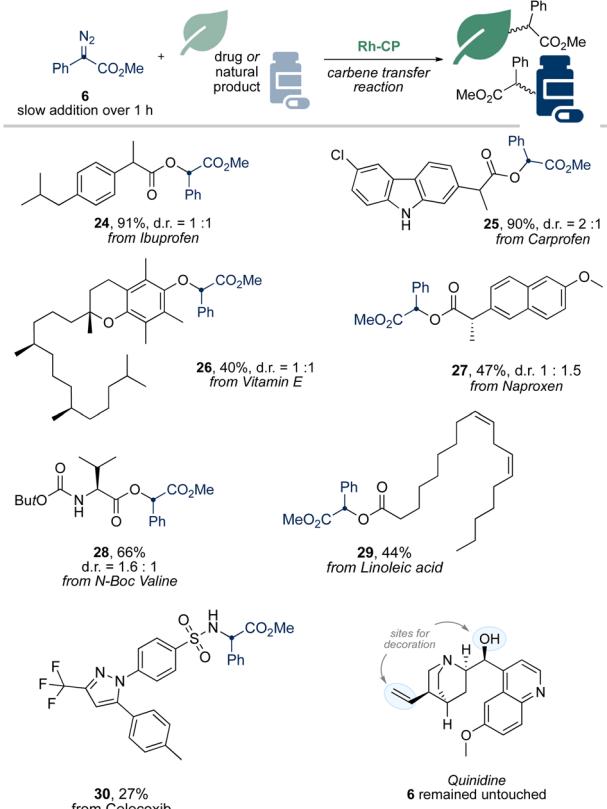
Scheme 3 Scope of different nucleophiles in Rh-CP catalyzed reactions.

The increase of product yield in the fourth and fifth catalytic cycle might result from this particle size reduction that would also result in an increased catalytically active surface of the heterogeneous catalyst. Notably, the amount of recovered Rh-CP significantly decreased after the fifth cycle (30%) resulting in a reduced yield of 76% of the desired cyclopropane. After the sixth cycle only traces of Rh-CP were recovered, and no further reactions were performed.¹¹ Kinetic studies of the Rh-CP were investigated next. Using 10 mg of Rh-CP a rapid and linear consumption of diazoalkane 6 was observed. The reaction rate only slowed down after a consumption of >90% of diazoalkane 6 (Scheme 2 and Table S1, ESI†).

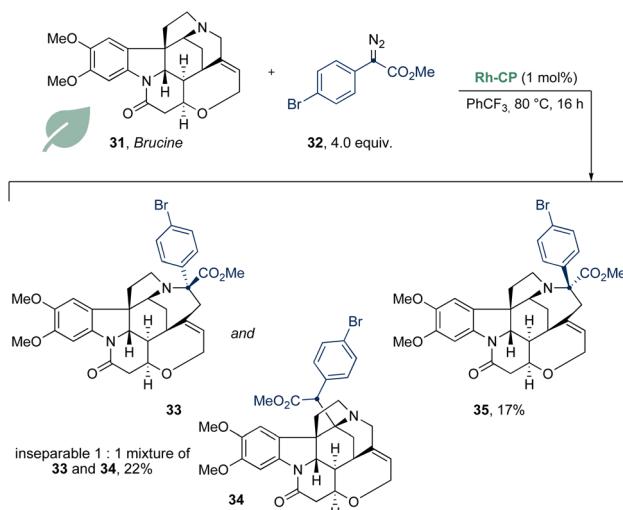
In a next step, we investigated the applicability of the Rh-CP in the reaction of donor/acceptor diazoalkane 6 in carbene transfer reactions (Scheme 3). Only a minor excess of the corresponding nucleophile was used to emphasize the high efficiency of the Rh-CP. To our delight, the Rh-CP is compatible with a broad range of different substrates and performs excellent in cyclopropanation reactions (7–9). N-Methyl indole gave the product of C3-functionalization 10 in 74% yield and N,N-dimethyl aniline reacted smoothly in *para*-C–H functionalization to give 11 75% yield.

X–H reactions (X = N, O, S, Si) gave the desired reaction products (12–20) in up to 96%. Yet, a longer reaction time of up

A Functionalization of simple natural products and drugs



B Functionalization of Brucine



Scheme 4 Scope of natural products and drugs in Rh-CP catalyzed carbene transfer reactions.

to 24 h was required to achieve the full conversion of diazoalkane 6. This observation could be explained by a potential catalyst poisoning as the desorption of products or reagents might be energetically disfavored. We further examined rearrangement reactions of sulfur ylides and were able to isolate the products of Doyle–Kirmse (21), Stevens rearrangement (22) and Sommelet–Hauser (23) rearrangement reactions in up to 93% yield (Scheme 3).

To further underline the applicability of Rh-CP, we studied more complex natural products and drugs in the reaction with donor/acceptor diazoalkanes (Scheme 4). Simple drug molecules such as Ibuprofen, Naproxen or Carprofen gave the desired O–H functionalization products (24, 25, 27) in high yield. Notably, only the O–H functionalization product of Carprofen was observed, while the free N–H function remained untouched.

We further explored natural products; vitamin E reacted in an O–H functionalization reaction to give the desired O–H functionalization product **26** in moderate yield. Derivatives of amino acids (28) and celecoxib (30) underwent X–H functionalization with Rh-CP catalyst. Quinidine, however, remained unreactive and no reaction was observed with the diazoalkane **6** staying untouched, which is indicative of catalyst poisoning (Scheme 4A).

In a last step, we studied the functionalization of brucine **31** in Rh-CP catalyzed reaction with diazoalkane **32**. Under similar reaction conditions as reported by Beckwith and co-workers,¹² we were able to obtain three different reaction products (33–35) in a total yield of 39% using 4 equivalents of diazoalkane **32** (Scheme 4B).¹³

In summary, we described here the application of a Rh(II)-based coordination polymer as a heterogeneous catalyst in carbene transfer reactions. Based on the IR and UV-Vis data, we were able to prove that the paddlewheel structure of the Rh₂(OAc)₄ precursor is also present in the synthesized Rh-based coordination polymer. Moreover, detailed studies on catalyst recycling and catalyst efficiency were performed. We were able to demonstrate the broad applicability ranging from X–H and C–H functionalization reactions towards rearrangement reactions and the functionalization of natural products and drugs.

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Data availability

The data supporting this article have been included as part of the ESI.†

Conflicts of interest

There are no conflicts to declare.

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