



Computational comparison of $\text{Rh}_2(\text{esp})_2$ and $\text{Rh}_2(\text{O}_2\text{CH})_4$ as catalysts in a carbenoid reaction

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ABSTRACT

A computational study of $\text{Rh}_2(\text{esp})_2$ -catalysed cyclopropanation of styrene with ethyl bromodiazooacetate is presented. The calculated structures and the energy profile of the reaction show a high level of similarity between $\text{Rh}_2(\text{esp})_2$, a catalyst with sizeable, tethered ligands, and the simplified model catalyst $\text{Rh}_2(\text{O}_2\text{CH})_4$.

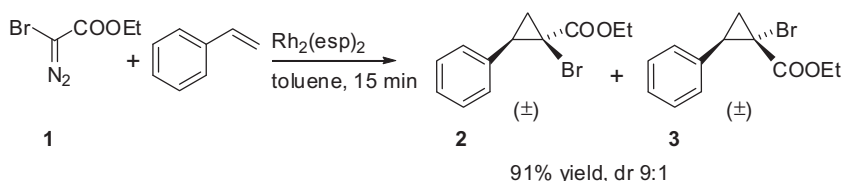
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The use of halodiazoacetates in carbenoid reactions represents a facile method for selective formation of α -halocarbonyl compounds.¹ Rhodium(II)-catalysed decomposition of halodiazoacetates in the presence of electron-rich, sterically unencumbered alkenes gives halocyclopropanes in good to excellent yields, with good diastereoselectivity.^{1b} The catalyst of choice in these cyclopropanation reactions is $\text{Rh}_2(\text{esp})_2$,² a dirhodium complex with tethered carboxylate ligands.³ We recently reported a full computational study⁴ of Rh(II)-catalysed cyclopropanation reactions with ethyl iodo-, bromo- and chlorodiazoacetate at the B3LYP level of theory. The results obtained with the basis sets LANL2DZ, 6-31G* and 6-311G* corresponded well with experimental results. The considerable size of the $\text{Rh}_2(\text{esp})_2$ ligands makes their inclusion in comprehensive computational studies too impractical and time-consuming, so in the interest of computational facility, $\text{Rh}_2(\text{O}_2\text{CH})_4$ was used as a model catalyst. We now present a study of the $\text{Rh}_2(\text{esp})_2$ -catalysed cyclopropanation of styrene with the representative halodiazoacetate, ethyl bromodiazooacetate (**1**) (Scheme 1), at the same level of theory. We explore the properties of $\text{Rh}_2(\text{esp})_2$ compared to those of the model catalyst $\text{Rh}_2(\text{O}_2\text{CH})_4$. This comparison between the two catalysts will show to what degree $\text{Rh}_2(\text{O}_2\text{CH})_4$ may be a reliable model for $\text{Rh}_2(\text{esp})_2$ in computational studies of carbenoid reactions.

Originally designed for C–H amination reactions,³ the robust $\text{Rh}_2(\text{esp})_2$ has gained considerable acclaim in the field of nitrenoid reactions,⁵ and has also been recognised as a good catalyst in certain carbenoid reactions,^{1,6} but $\text{Rh}_2(\text{esp})_2$ has, to the best of our knowledge, not previously been the subject of a computational study.

Computational energy optimisation of $\text{Rh}_2(\text{esp})_2$ showed that the conformation depicted in Figure 1, with the two phenyl rings parallel to each other, and thus with identical top and bottom catalyst faces, is the most stable. The conformation in which one phenyl ring is flipped in the opposite direction is disfavoured by 0.6 kcal/mol. The computationally optimised structure of $\text{Rh}_2(\text{esp})_2$ corresponds very well with the reported X-ray structure³ (Table 1); the calculated values closely mirror those obtained from the X-ray structure, with only very small deviations in the bond lengths and angles.

The structures formed during the $\text{Rh}_2(\text{esp})_2$ -catalysed cyclopropanation of styrene with ethyl bromodiazooacetate (**1**) are shown in Scheme 2. Figure 2 shows the energy profile of the reaction, together with the energy profile of the analogous $\text{Rh}_2(\text{O}_2\text{CH})_4$ -catalysed reaction⁴ for comparison. The initial coordination of **1** to $\text{Rh}_2(\text{esp})_2$ gives complex **4**, with a stabilisation energy of 6.2 kcal/mol. Nitrogen is extruded from this complex in transition state



Scheme 1. $\text{Rh}_2(\text{esp})_2$ -catalysed cyclopropanation of styrene with ethyl bromodiazooacetate (**1**).

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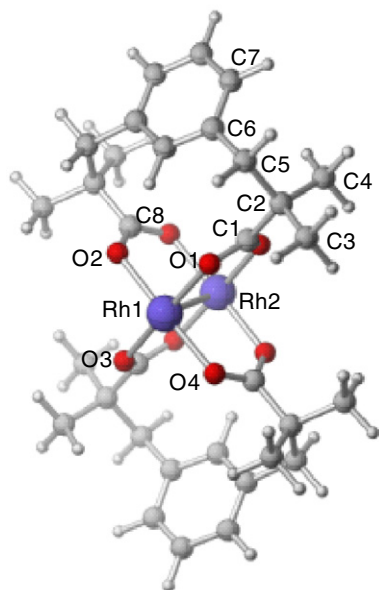


Figure 1. Energy-optimised structure of $\text{Rh}_2(\text{esp})_2$.

Table 1

Calculated values for selected bond lengths and angles compared to the corresponding values from the X-ray structure³ of $\text{Rh}_2(\text{esp})_2$

Bond length/ angle	Calcd value	Value from X-ray structure	Deviation relative to X-ray value (%)
Rh1–Rh2	2.383 Å	2.382 Å	+0.04
Rh1–O1	2.074 Å	2.040 Å	+1.6
Rh1–O2	2.072 Å	2.048 Å	+1.2
Rh1–O3	2.061 Å	2.037 Å	+1.2
Rh1–O4	2.062 Å	2.029 Å	+1.6
O1–C1	1.276 Å	1.271 Å	+0.4
O2–C8	1.276 Å	1.274 Å	+0.2
Rh2–Rh1–O1	88.1°	87.4°	+0.8
Rh2–Rh1–O2	88.2°	87.8°	+0.5
Rh2–Rh1–O3	88.5°	89.0°	–0.6
Rh2–Rh1–O4	88.4°	88.6°	–0.2
C1–C2–C3	107.5°	107.7°	–0.2
C1–C2–C4	110.8°	111.2°	–0.4
C2–C5–C6–C7	–92.8°	–92.9,0°	–0.1

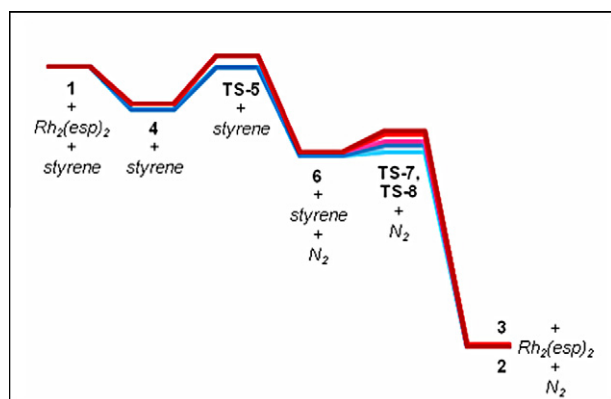


Figure 2. Energy profile for the cyclopropanation of styrene with ethyl bromodiazoacetate (**1**). $\text{Rh}_2(\text{esp})_2$ -catalysed reaction in red coloured lines, $\text{Rh}_2(\text{O}_2\text{CH})_4$ -catalysed reaction in blue.

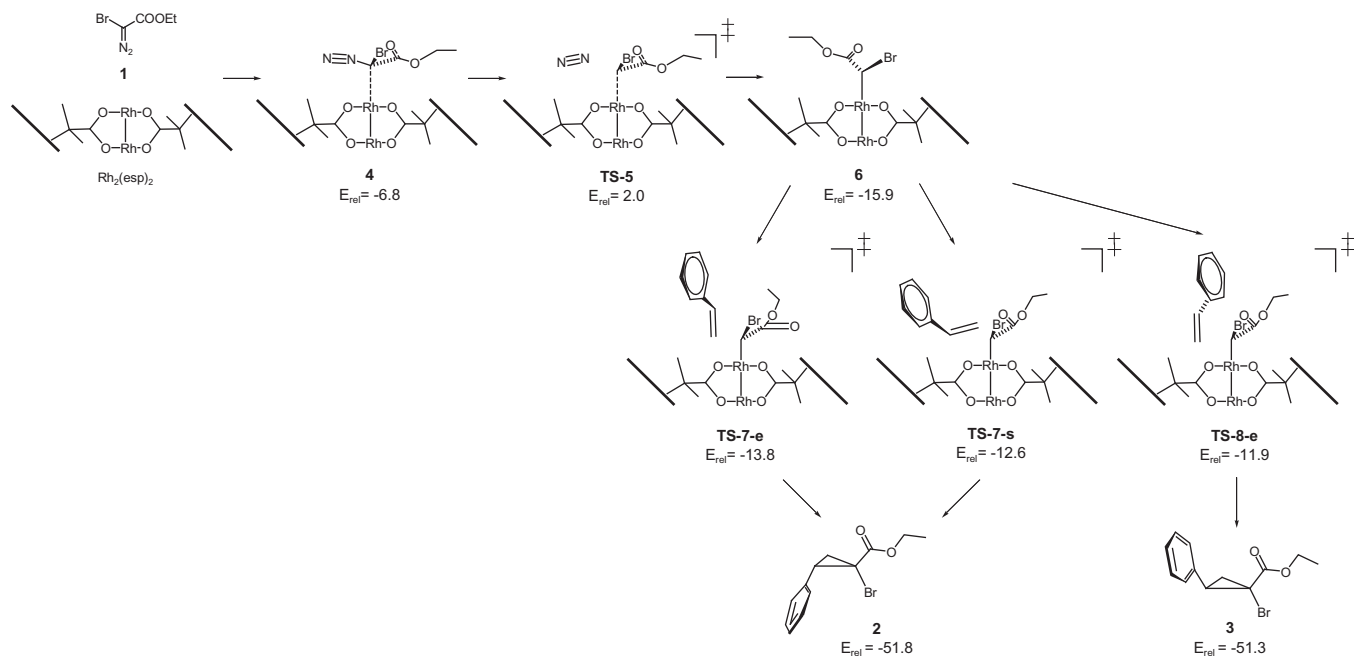
TS-5, which represents a calculated barrier of 8.8 kcal/mol, resulting in carbenoid complex **6**. The carbenoid complex has a relative energy of -15.9 kcal/mol, and is thus 9.0 kcal/mol more stable than

its precursor, complex **4**. Then follows the cyclopropanation step leading to two diastereomeric cyclopropanes, *Z*-substituted cyclopropane **2** and *E*-substituted **3**. Two principally different transition states leading to cyclopropane **2** were found: one with styrene approaching the carbenoid in an end-on manner, the alkene parallel to the Rh–C axis (**TS-7-e**), and one with a side-on approach (**TS-7-s**). The end-on trajectory transition state is the more favoured of the two; **TS-7-e** represents a calculated barrier of 2.0 kcal/mol, while **TS-7-s** represents a barrier of 3.0 kcal/mol. For cyclopropane **3**, only an end-on trajectory transition state could be located, **TS-8-e**, representing a barrier of 4.0 kcal/mol. The transition states are very similar to those in the $\text{Rh}_2(\text{O}_2\text{CH})_4$ -system⁴ in structures and bond orders, as illustrated in Figure 3. The paths from the transition states to the cyclopropanes are strongly downhill; the relative energies of **2** and **3** are -51.8 and -51.3 kcal/mol, respectively.

All structures **4–7** closely mirror those observed with $\text{Rh}_2(\text{O}_2\text{CH})_4$ in the placement of the diazo or carbenoid substituents relative to the oxygen atoms of the carboxylate ligands on the Rh(II) core. The bromine substituent almost eclipses one of the oxygen atoms in structures **4**, **TS-5**, **TS-7-e**, **TS-7-s** and **TS-8-e**, and is close to staggered in the carbenoid complex **6**. The two ligands in $\text{Rh}_2(\text{esp})_2$ are identical, but the favoured orientation of the two phenyl rings means that for each conformation of the carbenoid substituents relative to the ligand oxygen atoms, there are four possible orientations of the substituents relative to the ligands as a whole.

The conformation of **4** shown in Scheme 2 is the most favoured by 0.6 kcal/mol, and this placement of the carbenoid substituents relative to the ligands is the most favoured in structures **6**, **TS-7-e** and **TS-7-s**. With **TS-5** and **TS-8-e**, there is in both cases one other rotamer that is 0.2 kcal/mol lower in energy than the depicted structure, with the carbene-substituents rotated 180° and 90° clockwise relative to the ligands. With such small energy differences, along with a low barrier for rotation of the carbene-moiety relative to the carboxylate ligands,⁸ it is possible that these rotamers are also of importance, along with other low-energy rotamers for all structures. The rotation of the ester group also results in other possible conformations of the transition states. While **TS-7-e** has the carbonyl oxygen pointing away from the incoming styrene, and **TS-7-s** and **TS-8-e** have the carbonyl oxygen pointing towards it, in all three instances there also exist conformers with the ester tilted in the opposite direction, 0.1, 0.7 and 0.4 kcal/mol higher in energy, respectively.

The overall $\text{Rh}_2(\text{esp})_2$ -catalysed cyclopropanation of styrene with ethyl bromodiazoacetate (**1**) is exothermic, as is each step of the reaction. The rate-limiting step is nitrogen extrusion in **TS-5**, with a predicted barrier of 8.8 kcal/mol. We have shown earlier that the barrier for nitrogen extrusion from the analogous complex formed with $\text{Rh}_2(\text{O}_2\text{CH})_4$, of 8.0 kcal/mol, is remarkably low when compared to the barriers with other diazo compounds.⁴ The barrier observed with $\text{Rh}_2(\text{esp})_2$ is only 0.8 kcal/mol higher, and thus also quite low, in line with the high activity and rates observed in laboratory experiments. Another observation that corresponds well with experimental results is the relative stability, compared to the starting materials, of carbenoid **6**. This can be explained by a stabilising π -interaction between the bromine substituent and the carbenoid carbon, as implied by the relatively high C–Br bond order of 1.26. The charge distribution throughout the course of the reaction shows that carbenoid **6**, with an NBO-charge⁹ of +0.13, is an electrophilic carbenoid, and that charge transfer from styrene to the carbenoid precedes charge transfer in the opposite direction in the transition states for cyclopropanation. The barriers for the cyclopropanation step are slightly higher with $\text{Rh}_2(\text{esp})_2$ as the catalyst than with $\text{Rh}_2(\text{O}_2\text{CH})_4$. While **TS-7-e**, **TS-7-s** and **TS-8-e** represent barriers of 2.0, 3.0 and 4.0 kcal/mol, the corresponding barriers in the $\text{Rh}_2(\text{O}_2\text{CH})_4$ -system are 0.7, 1.8 and 2.0 kcal/mol,



Scheme 2. Reaction course for the $\text{Rh}_2(\text{esp})_2$ -catalysed cyclopropanation of styrene with ethyl bromodiazooacetate (**1**). The structure of $\text{Rh}_2(\text{esp})_2$ in the scheme is simplified for clarity. Energies in kcal/mol.

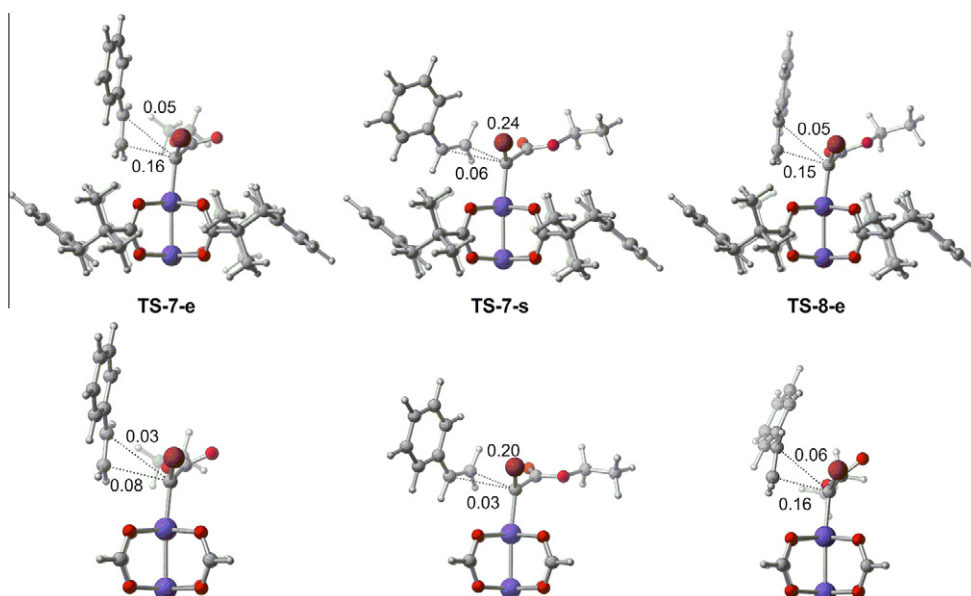


Figure 3. Transition states for the cyclopropanation of styrene with **1**, catalysed by $\text{Rh}_2(\text{esp})_2$ (top) or $\text{Rh}_2(\text{O}_2\text{CH})_4$ (bottom).⁴ The numbers refer to Wiberg bond indices.

respectively.⁴ Another notable difference between the two systems is that while a side-on trajectory transition state leading to cyclopropane **3** was found in the $\text{Rh}_2(\text{O}_2\text{CH})_4$ -system, no such transition state could be found with $\text{Rh}_2(\text{esp})_2$ as the catalyst. Both these observations can be explained based on steric effects of the catalysts. The sterically encumbering ligands of $\text{Rh}_2(\text{esp})_2$ make the approach by styrene slightly less favoured than with the simplified model catalyst $\text{Rh}_2(\text{O}_2\text{CH})_4$ in **TS-7-e**, **TS-7-s** and **TS-8-e**, in which the styrene phenyl ring is pointing up and away from the ligands, but completely prevent a side-on trajectory transition state leading to **3**, where the phenyl ring would need to point down towards the ligands. The absence of this side-on trajectory transition state does

not, however, set the $\text{Rh}_2(\text{esp})_2$ -catalysed reaction apart from the $\text{Rh}_2(\text{O}_2\text{CH})_4$ -catalysed process in a practical sense; the analogous transition state in the $\text{Rh}_2(\text{O}_2\text{CH})_4$ -system is too high in energy to be of importance.

In summary, we have presented a full computational study of the cyclopropanation of styrene with ethyl bromodiazooacetate, catalysed by $\text{Rh}_2(\text{esp})_2$. The computationally optimised structure of $\text{Rh}_2(\text{esp})_2$ is highly similar to the X-ray structure. Our findings include a remarkably low barrier for rate-determining extrusion of nitrogen, and a relatively stable carbenoid that reacts with styrene via transition states that represent barriers of 2.0 kcal/mol or higher. The results from this study closely mirror those obtained

with $\text{Rh}_2(\text{O}_2\text{CH})_4$ as the catalyst. This similarity shows that the simplified $\text{Rh}_2(\text{O}_2\text{CH})_4$ catalyst is a good model for the computationally impractical $\text{Rh}_2(\text{esp})_2$ in this reaction, and also implies that it may be so in other studies of carbenoid reactions as well.

Density functional theory (DFT) was employed to investigate the reaction mechanism, using the B3LYP hybrid functional.¹⁰ The stationary structures of the potential energy surfaces were fully optimised at the B3LYP level of theory using the LANL2DZ basis set for Rh, 6-31G* for C, H, N and O, and 6-311G* for Br. The method and the basis sets are shown to give reliable results for other rhodium(II) carbenoids,¹¹ and are the same as those used in our previous study of the same reaction catalysed by $\text{Rh}_2(\text{O}_2\text{CH})_4$.⁴ Natural bond orbital (NBO) analyses⁹ were performed at the same level of theory. Wiberg bond indices¹² and NBO charges were calculated from NBO theory as implemented in GAUSSIAN 03. Stationary structures were characterised by normal coordinate analysis: no imaginary frequencies for equilibrium structures, and one imaginary frequency for transition structures. The reported energies are the zero-point corrected sum of electronic and thermal energies at 25 °C, scaled according to the literature (0.9806).¹³ All calculations were carried out using the GAUSSIAN 03 programme package.¹⁴

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.07.169.

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