Rearrangement

Ni(NHC) Catalyzed Rearrangement of 1-Acyl-2-vinylcyclopropanes: Tackling a Mechanistic Puzzle by Combined Experimental and Computational Studies

Anna Zens,[a] Florian Bauer,[b] Benedikt Kolb,[a] Fabian Mannchen,[a] Philipp Seubert,[a] Robert Forschner,[a] Kim S. Flaig,[c] Andreas Köhn,*[b] Doris Kunz,*[c] and Sabine Laschat*[a]

Abstract: The Ni(NHC) catalyzed rearrangement of 1-acyl-2-vinylcyclopropanes to the corresponding 4-acyl-cyclopent-1-enes is highly promising for the synthesis of keto-functionalized annelated bi- and tricyclic subunits of natural products. Therefore, we investigated the catalytic activity of Ni(NHC) complexes in the rearrangement of 1-acyl-2-vinylcyclopropanes with different ring sizes and substitution patterns. Surprising effects regarding substrate scope and stereoselectivity of the Ni(NHC) catalyzed vinylcyclopropane-cyclopentene rearrangement were observed. Only vinylcyclopropanes with 1-methyl, 1-phenyl, 1,2-dialkyl or 2-phenyl-substitution at the vinyl moiety could be rearranged successfully. Moreover, an endo-configuration on the cyclopropane ring was required for successful rearrangement. By treatment of the vinylcyclopropanes with Rh catalysts or Lewis acids, the involvement of Lewis acid catalysis could be ruled out. In order to understand these experimental results and to rationalize the reactivity of the Ni(NHC) complexes computational studies were performed, which provided insights into mechanistic details.

Introduction

Cyclopropanes[1a–1f] and particularly vinylcyclopropanes[1g–1n] are highly valuable key building blocks and intermediates for a large variety of organic target compounds due to their high reactivity and propensity for rearrangement.

Since the discovery of the [1,3]-sigmatropic rearrangement of vinylcyclopropanes to cyclopentenes more than 50 years ago,[2] the so-called thermal vinylcyclopropane (VCP) rearrangement has been studied extensively both with regard to mechanistic details and applications in total synthesis of natural products.[3] Whereas the parent hydrocarbons require elevated temperatures to undergo VCP rearrangement, activated, e.g. donor-acceptor-substituted vinylcyclopropanes, can react under much milder conditions, eventually promoted by Lewis acids.[4] Furthermore, transition metal-catalyzed rearrangements have been developed,[5] notably with Pd,[6] Rh,[7] Ni,[8] Mo,[9] Cr,[10] Cu,[11] Fe[12] and more recently Ir[13] complexes. However, in many cases transition metal catalysts need activated substrates, carrying at least two activating groups (EWG and/or EDG), heteroatoms, dienes, ene-ynes or allenes. In contrast, Louie and Tantillo[8d,8e] reported a Ni(NHC) catalyzed VCP rearrangement of unactivated vinylcyclopropanes with alkyl or aryl substituents (e.g. 3 → 4, Scheme 1), as well as some activated alkoxy-substituted substrates. As carbonyl groups are rather useful for further functionalization of the rearrangement product, we wondered whether the substrate scope of Ni-catalyzed VCP-cyclopentene rearrangements in the presence of NHC ligands could be extended to keto functionalized vinylcyclopropanes with different ring sizes and substitution pattern on the alkene moiety. The respective bicycles are important subunits of a variety of biologically active natural product families such as tetramic acid macrolactams,[14–16] e.g. maltophilin (10),[17] or triquinanes, e.g., (-)-hirsutene (7).[18,19] By examining previous work from Hudlicky[17] who described the conversion of bicyclic vinylcyclopropane 1 to the bicyclo[3.3.0]octane 7 in the presence of stoichiometric amounts of Rh complexes, and Louie[8e] (Scheme 1), we were interested in comparing the catalytic activity of Ni(NHC) complexes with Rh complexes in the rearrangement of 1-acyl-2-vinylcyclopropanes 5 to the respective bicycles 6. Ni(NHC) complexes were recently extensively studied in catalytic C–C[20] and C–X[21] bond formations and computational studies provided mechanistic insights.[22] Furthermore, we were also interested in studying whether the steric demand of the NHC ligand is controlling the catalytic activity. Thus, a series of...
different NHCs was investigated. Upon application of the optimized conditions on the rearrangement of vinylcyclopropanes we noticed surprising effects regarding substrate structure (reactivity) and stereoselectivity and thus examined the Ni(NHC) catalyzed rearrangement by quantum chemical methods. The results of this experimental and computational study are discussed below.

**Results and Discussion**

In order to obtain the vinylcyclopropane substrates for the catalytic studies, we relied on our previously reported procedure,[23] which allowed in only two steps a simplified access to 1-acyl-2-vinylcyclopropanes with alkyl or aryl substituents on the alkene moiety via sulfur ylides (Scheme 2).[24] First, the tetrahydrothiophenium salts were synthesized in yields up to 97 % by treating the respective allylic bromide with tetrahydrothiophene.[23] With tetrahydrothiophenium salts in hand the conjugate 1,4-additions to cyclopentenone and cyclohexenone were performed. Deprotonation of the allylsulfonium salts were synthesized in yields up to 97 % by treating the respective allylic bromide with tetrahydrothiophene.[23]

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Thus, initial catalytic experiments were performed with a (80:20) diastereomeric mixture of (E)-6-(prop-1-en-1-yl)bicyclo[3.1.0]hexan-2-one 5b as model substrate using different Rh complexes, following the seminal work of Hudlicky.[3k] Instead of the formation of the desired rearranged bicyclo[3.3.0]octenone 6b, only ring opening reactions to (E)-3-(buta-1,3-dien-1-yl)cyclopentanone 51 and (E)-3-(but-2-en-1-yl)cyclopent-2-en-1-one 13b could be observed[25] (Table S1, Supporting Information). As we surmised that Lewis acid catalysis might be involved in the reaction, compound 5b was also treated with different Lewis acids. But the VCP rearranged product 6b was not detected at all (Table S2, Supporting Information). Therefore, further experiments were performed with 5b using Ni(NHC) complexes, according to Louie[8e] (Table 1).

We examined the Ni-catalyzed conversion of bicyclo[3.1.0]hexanone 5b using 10 mol-% of Ni(iPr)2 generated in situ from 10 mol-% Ni(COD)2, 20 mol-% [14·HCl and 20 mol-% KOtBu in toluene (Table 1). As can be seen from Table 1, no conversion was observed at temperatures between room temperature and 100 °C (entries 1–5). After 3 h at 120 °C, only dienone 13b (13 %) was detected by GC (entry 6). When the catalysis was performed with 10 mol-% Ni(COD)2 and 20 mol-% of ligand 14 at 150 °C under microwave irradiation, the starting material 5b decomposed (entry 7). In a final attempt vinylcyclopropane 5b was treated with 20 mol-% of Ni(COD)2 and 100 mol-% of BF₃·OEt₂ at room temperature. After 45 h, enone 15b was obtained in 77 % yield (entry 8), suggesting a Lewis acid catalysis mechanism for the ring opening pathway.

The failure of vinylcyclopropane-cyclopentene rearrangement of 5b to 6b agrees with results by Louie,[8d,8e] who found that non-activated substrates with vic-disubstituted C=C double bonds were in most cases poorer substrates for the Ni(NHC)-catalyzed VCP rearrangement as compared to those with gem-
Scheme 2. Synthesis of racemic vinylcyclopropanes from sulfur ylides and cyclopentenone or cyclohexenone.

Table 1. Ni-catalyzed VCP-cyclopentene rearrangement of compound 5b

| Entry | Catalyst | Ligand/ additive | T (°C) | t [h] | Product | Yield [%] |
|-------|----------|------------------|--------|-------|---------|-----------|
| 1     | Ni(COD)₂ | 14               | r.t.   | 3     | –       | n.r.      |
| 2     | Ni(COD)₂ | 14               | 40     | 3     | –       | n.r.      |
| 3     | Ni(COD)₂ | 14               | 60     | 3     | –       | n.r.      |
| 4     | Ni(COD)₂ | 14               | 80     | 3     | –       | n.r.      |
| 5     | Ni(COD)₂ | 14               | 100    | 3     | –       | n.r.      |
| 6     | Ni(COD)₂ | 14               | 120    | 3     | 13b     | 77        |
| 7     | Ni(COD)₂ | 14               | 150    | 1     | –       | n.r.      |
| 8     | Ni(COD)₂ | BF₃·OEt₂         | r.t.   | 45    | 15b     | 77        |
| 9     | Ni(COD)₂ | _[e]             | r.t.   | 3     | –       | n.r.      |
| 10    | Ni(COD)₂ | _[e]             | 120    | 3     | –       | n.r.      |

[a] Reaction conditions: 10 mol-% of Ni(COD)₂, 20 mol-% NHC precursor, 20 mol-% KOrBu, toluene, concentration 0.1 mmol mL⁻¹; the catalyst was prepared in situ by equilibration of Ni(COD)₂ with 2 equiv. of ligand precursor and 2 equiv. KOrBu for 30 min at room temperature prior to substrate addition (1 equiv. 5b dr (endo/exo) = 80:20); entry 7: microwave irradiation; entry 8: 20 mol-% Ni(COD)₂ and 100 mol-% of BF₃·OEt₂. [b] Isolated yields. [c] Determined by GC using dodecane as internal standard. [d] Decomposition of starting material. [e] Blank test, Ni(COD)₂ (10 mol-%). n.r. = no reaction.
disubstituted C=C double bonds. Therefore, the Ni-catalyzed VCP rearrangement was studied with isopropenyl-bicyclo[3.1.0]-hexane 5c (Table 2).

Table 2. Ni(NHC) catalyzed VCP-cyclopentene rearrangement of 5c at various temperatures\(^{[a]}\)

| Entry | Catalyst | Ligand | T (°C) | t [h] | Conv. [%]\(^{[b]}\) | Product ratio\(^{[b]}\) |
|-------|----------|--------|--------|------|------------------|------------------|
| 1     | Ni(COD)\(_2\) | 14     | r.t.   | 3    | 0                | –                |
| 2     | Ni(COD)\(_2\) | 14     | 60     | 3    | 21               | 44:56            |
| 3     | Ni(COD)\(_2\) | 14     | 60     | 48   | 79               | 14:86            |
| 4     | Ni(COD)\(_2\) | 14     | 80     | 3    | 44               | 35:65            |
| 5     | Ni(COD)\(_2\) | 14     | 80     | 20   | 86               | 23:77            |
| 6     | Ni(COD)\(_2\) | 14     | 100    | 3    | 52               | 42:58            |
| 7     | Ni(COD)\(_2\) | 14     | 100    | 24   | 100              | 41:59            |
| 8     | Ni(COD)\(_2\) | 14     | 120    | 3    | 81               | 68:32            |
| 9     | Ni(COD)\(_2\) | 14     | 120    | 19   | 100              | 69:31            |
| 10    | Ni(COD)\(_2\) | \(\text{L}^\text{Cl}\) | 120    | 3    | 0                | –                |

\(^{[a]}\) Reaction conditions: 10 mol-% of Ni(COD)\(_2\), 20 mol-% NHC precursor, 2 equiv. KOtBu for 30 min at room temperature prior to substrate addition (1 equiv. 5c dr (endo/exo) = 100:0); reproducibility was verified by several runs. \(^{[b]}\) Determined by GC with dodecane as internal standard.

In order to figure out the temperature dependence of the VCP rearrangement to bicyclic product 6c vs. the isomerization to diene 13c, a series of catalytic reactions with 10 mol-% of Ni(COD)\(_2\) and 20 mol-% of ligand precursor 14-HCl were run in toluene at various temperatures (Table 2).

Aliquots were taken after 1 h, 2 h, 3 h, and 20 h respectively and analyzed by GC using n-dodecane as internal standard. The results in Table 2 clearly indicate that reaction temperatures below 100 °C favored isomerization to 13c (entries 2–5), whereas at 100 °C almost equimolar amounts of bicyclo[3.3.0]octene 6c and diene 13c were formed (entries 6, 7). At 120 °C, VCP rearrangement was preferred resulting in a (69:31) mixture of 6c and 13c after 19 h and complete consumption of the starting material (entry 9).

It should be noted that the Ni-catalyzed reactions of non-activated vinylcyclopropanes studied by Louie were run at room temperature or in some cases at 60 °C\(^{[8d,8e]}\). In our case, the presence of the carbonyl group seems to increase the activation barrier of the reaction. Longer reaction times at moderate temperature changed the product ratio in favor of 13c (entries 2,3, and 4,5) indicating an induction period for the formation of 13c. Ring-opening reactions to 13c which are favored at moderate temperatures can thus be reduced by increasing the reaction temperature to above 100 °C.

Based on these results we studied the influence of a series of NHC ligands 16–25 (Scheme 3) on the catalytic reactions. As described above, ligand precursors 16-HCl–25-HCl were converted in situ to the free NHC ligands 16–25. In order to suppress the formation of the ring-opened product 13c, the reactions were performed at 120 °C (Table 3). When \(N\)-heterocyclic carbene 16, the saturated counterpart of 14, was used, the desired bicycle 6c was exclusively formed and no trace of 13c could be detected (entries 1, 2). Increasing the electron dona-
ing character, but also reducing the steric demand, by using ligand 17 resulted in decreased conversion and selectivity (entries 3, 4). After 3 h 63 % of 6c/13c (72:28) were obtained (entry 3), which changed to 70 % after 16 h (6c/13c = 60:40) (entry 4).

A similar product ratio albeit at complete conversion was detected for the ligand 18 with decreased steric hindrance as compared to 16 (entries 5, 6). Substituting the 5-membered carbene in 18 by a 6-membered carbene in ligand 19 again raised the ratio in favor of 6c (100:0), but at the expense of catalytic activity (34 % conversion after 16 h, entry 8). Next aromatic NHCs with alkyl substituents of different steric bulkiness were tested. While ligands 21 and 23 gave no conversion at all (entries 11, 12, 15, 16), ligands 22 and 20 provided only the diene 13c (entries 9, 10, 13, 14). From the above mentioned results we would have expected that ligand 25 with a non-aromatic imidazolidinylidene unit should outperform 24 with an aromatic NHC moiety. Surprisingly, 24 showed a clear preference for 6c over 13c (90:10) at quantitative conversion after 23 h (entry 18), while 25 was completely inactive even after prolonged reaction times (entry 20).

We then studied the substrate scope using the optimum NHC ligand 16 under the reaction conditions described above (Scheme 4). The substituted vinlycyclopropanes 5a–e were treated as diastereomeric mixtures with 10 mol-% Ni(COD)2, 20 mol-% NHC precursor 16·HCl and 20 mol-% KOTBu in toluene at 120 °C. The phenyl-substituted VCP 5a did not give the desired product 6a, but produced instead the regioisomer 26, which was isolated in 5 % yield. Presumably, compound 26 was formed via VCPR and subsequent C=C-double bond shift to the thermodynamically favored regioisomer 26. In the case of 5b, no conversion of the starting material was observed after 3 h. Vinlycyclopropanes 5c,d with gem-disubstituted C=C double bonds, rearranged successfully to the desired bicyclic products 6c and 6d in yields of 23 and 22 %. According to the 1H-NMR spectra of 6d (See Figure S3, Supporting Information), we assumed that a diastereomeric mixture (dr = 84:16) of the bicyclic product 6d was formed during rearrangement. Surprisingly, the formation of the tricyclic product 6e starting from the diastereomeric mixture of 5e failed. In conclusion, the 1,1-disubstituted alkenes 5c–d gave better yields than the 1,2-disubstituted olefins 5a–b, in accordance with Louie’s reports.[8d,8e]

To examine the influence of the ring size and the alkene geometry of the vinylcyclopropanes on the Ni-catalyzed VCPR, endo- and exo-bicyclo[4.1.0]heptan-2-ones endo-8 and exo-8 with different substitution patterns were treated in parallel experiments with 10 mol-% Ni(COD)2, 20 mol-% 16·HCl and 20 mol-% KOTBu for 19 h at 120 °C (Table 4). To test whether endo/exo-isomerization of the vinlycyclopropanes might take place during the Ni-catalyzed reaction, 1H-NMR experiments with the respective diastereomeric mixtures were performed in [D6]DMSO at room temperature and 120 °C. No isomerization

Scheme 4. Substrate scope of Ni-catalyzed rearrangement with 16 as NHC ligand.
effects could be observed, except for the phenyl-substituted 8a. Upon heating of 8a to 120 °C the diastereomeric ratio shifted from 67:33 to 20:80 in favour of exo-8a (For details see Figure S22, Supporting Information). Therefore, the Ni-catalyzed VCPR was studied with a (20:80) mixture of endo-8a and exo-8a, rather than the pure diastereomers (Table 4, entry 1). However, instead of the desired bicyclic product 9a only the monocyclic by-products (Z)-3-((E)-3-phenylallylidene)cyclohex-1-en-1-ol S2 and 3-(3-phenylpropyl)cyclohexan-1-one S3 (See Scheme S1, Supporting Information) with a side chain at C-3 were isolated. Next, the *vicinal* substituted vinylcyclopropanes endo-8b and exo-8b were treated in separate experiments for 19 h at 120 °C with the optimized Ni-catalyst, which was prepared in situ by equilibration of 10 mol-% Ni(COD)2 with 20 mol-% NHC precursor 16·HCl (Scheme S2, Supporting Information). Therefore, the Ni-catalyzed VCPR could not be achieved. Fortunately, the desired rearranged product 9b could be isolated in 30 % yield (entry 6). When the *exo*- and *endo*-cyclopentene-substituted vinylcyclopropanes endo-8c and exo-8e were subjected to Ni catalysis, no trace of the desired tricyclic product was detected (entry 7,8). Furthermore, the vinylcyclopropanes 8f with an unsubstituted vinyl moiety did not undergo isomerization, independent of the *endo* or *exo* configuration of the vinylcyclopropanes (entries 9,10).

We surmised that the observed difficulties in the Ni-catalyzed VCP rearrangement might be due to the problems associated with the in situ formation of the NHC from the correspondifying imidazolium salts and KOtBu. It should be noted that Trnka[27] has reported on a nucleophilic attack of an alcoholate to the imidazolium salt, in which especially imidazolium salts with saturated backbones were found to be sensitive. The resulting formal NHC-alcohol adduct might prevent the formation of the catalyst systems from the free carbene. Therefore, the deprotonation of the NHC precursor 16·HCl and subsequent Ni-catalyzed VCPR of *gem*-methyl-substituted vinylcyclopropane endo-8c was examined with various non-nucleophilic bis(trimethylsilyl)amide bases (Table 5).

### Table 4. VCPR of bicyclo[4.1.0]heptan-2-ones endo-8 and exo-8.[a]

| Entry | VCP         | Product | Yield |
|-------|-------------|---------|-------|
| 1     | ![Image](FullPaper) | ![Image](FullPaper) | 0% from 8a (dr (endo/exo) = 20 : 80) |
| 2     | ![Image](FullPaper) | ![Image](FullPaper) | 0% from endo-8b |
| 3     | ![Image](FullPaper) | ![Image](FullPaper) | 0% from exo-8b |
| 4     | ![Image](FullPaper) | ![Image](FullPaper) | 38% from endo-8c |
| 5     | ![Image](FullPaper) | ![Image](FullPaper) | 0% from exo-8c |
| 6     | ![Image](FullPaper) | ![Image](FullPaper) | 30% from 8d (dr (endo/exo) = 31 : 69) |
| 7     | ![Image](FullPaper) | ![Image](FullPaper) | 0% from endo-8e |
| 8     | ![Image](FullPaper) | ![Image](FullPaper) | 0% from exo-8e |
| 9     | ![Image](FullPaper) | ![Image](FullPaper) | 0% from endo-8f |
| 10    | ![Image](FullPaper) | ![Image](FullPaper) | 0% from exo-8f |

[a] In addition (Z)-3-((E)-3-phenylallylidene)cyclohex-1-en-1-ol S2 and 3-(3-phenylpropyl)cyclohexan-1-one S3 was formed from 8a in 18 % and 12 % yield (Scheme S1, Supporting Information).

### Table 5. Ni-catalyzed VCP-cyclopentene rearrangement of endo-8c in the presence of various bases at 120 °C.[a]

| Entry | Base      | Yield [%] |
|-------|-----------|-----------|
| 1     | KOtBu     | 38[b]     |
| 2     | LiOtBu    | 23[c]     |
| 3     | KHMDMS    | 27[c]     |
| 4     | NaHMDS    | 18[d]     |
| 5     | LiHMDS    | 23[d]     |

[a] Reaction conditions: Ni(COD)2, 20 mol-% NHC precursor, 20 mol-% base, toluene, concentration 0.1 mmol mL⁻¹; the catalyst was prepared in situ by equilibration of Ni(COD)2 with 2 equiv. of the NHC precursor and 2 equiv. base for 30 min at room temperature prior to substrate addition. [b] Isolated yield. [c] ¹H-NMR yields with mesitylene as internal standard.

The catalyst was prepared in situ by equilibration of 10 mol-% Ni(COD)2, 20 mol-% 16·HCl and 20 mol-% LiOtBu instead of KOtBu, prior to addition of substrate endo-8c. But the change...
of a counterion led to a decreased yield (23 %) of the desired product 9c compared to 38 % for KOtBu (entries 1, 2). When KHMDS was employed as the base the bicyclic product 9c was only formed in 27 % yield (entry 3). The use of NaHMDS or LiHMDS gave even poorer yields (entries 4,5). Consequently, a higher nucleophilic character of the base was even beneficial for this reaction. The results revealed that the in situ formation of the catalytically active species from Ni(COD)_2, 16·HCl and base had a pronounced influence on the VCPR.

In order to minimize potential interactions of the salts formed during the in situ generation of the carbene ligand, and to avoid decomposition of the free carbene, the generated free NHC SiPr (16) was trapped with CO_2 and converted into the corresponding imidazolium carboxylate 16·CO_2 following the method of Naumann. With this CO_2 adduct in hand, subsequent thermal decarboxylation of 16·CO_2 (20 mol-%) by heating at 120 °C in toluene in the presence of Ni(COD)_2 (10 mol-%) and vinylcyclopropane 8c did not give any trace of the desired product 9c. Variations of this method (Scheme S4, see Supporting Information) failed as well. Therefore, the above discussed product 9c was not reactive. For one NHC ligand, the computed free energy of the complex decreases by 1.5 kJ/mol. An exchange of the remaining COD ligand with another NHC ligand further decreases the free energy by 5.1 kJ/mol, thus Ni(NHC)_2 is the most stable complex in the regarded system. Nevertheless, at finite temperatures all three Ni complexes will be present in significant concentrations and we assume, in analogy with the theoretical results of Wang and Tantillo, that the Ni(NHC)(COD) complex (II) acts as the catalytically active species.

We note that the energetics of the above ligand exchange reaction are difficult to compute, and strong variations have been found using different density functionals. E.g. for the B3LYP functional, the Ni(NHC)_2 complex (I) is far more stable than Ni(COD)_2. However, we take confidence in the B2PLYP-corrected results, as test calculations using the high-level PNO-LCCSD(T)-F12 method on a system with a simplified NHC ligand (with N,N-dimethyl substitution) indicate that the strong energy lowering for Ni(NHC)_2 (I) predicted by B3LYP is incorrect (for details see Supporting Information). The B2PLYP computations are in much better agreement with the high-level coupled-cluster computations, although the stability of Ni(NHC)_2 (I) might be slightly underestimated with this functional.

### Computational Investigations

In order to gain more insight into the mechanism of the VCPR rearrangement and to rationalize the puzzling results discussed above regarding substrate scope, quantum chemical calculations on the B3LYP-D3-COSMO/def2-TZVP level (with single point corrections using the double-hybrid functional B2PLYP) were carried out (see Computational details).

In the following, we focus on the Ni-catalyzed VCPR of bicyclo[3.1.0]hexan-2-one endo-5c and the respective bicyclo[4.1.0]heptan-2-one endo-8c. These vinylcyclopropanes, with a geminal methyl group at the alkene moiety, rearranged successfully to the desired bicyclic products 6c and 9c, independent of their ring size, whereas substrates with a vicinal methyl group did not react at all under the same conditions (compare endo-8b/endo-8c: Table 4, entries 2,4; endo-5b/endo-5c: Scheme 4).

The catalyst conformation is generally chosen, such that the rings of the aryl groups are orthogonal to the NHC five membered ring. Other conformations are considered unlikely due to the bulky isopropyl groups, however, the isopropyl groups themselves can rotate freely. To ensure consistency in the calculations the start geometries were always chosen in such a way, that the hydrogens which are not part of the methyl groups face one another, pointing towards the center of mass of the molecule. The conformational space for the substrates endo-5b, endo-5c, endo-8b and endo-8c is limited due to the two aneled rings. From the two possible conformations, only the one for which all the transition structures can be found is considered in the following. For further details on this see the Supporting Information.

### Computational Investigations Regarding the Catalytically Active Species of the VCPR

One central question is which compound acts as the catalytically active species. If the Ni(COD)_2 exchanges one COD ligand for one NHC ligand, the computed free energy of the complex decreases by 1.5 kJ/mol. An exchange of the remaining COD ligand with another NHC ligand further decreases the free energy by 5.1 kJ/mol, thus Ni(NHC)_2 is the most stable complex in the regarded system. Nevertheless, at finite temperatures all three Ni complexes will be present in significant concentrations and we assume, in analogy with the theoretical results of Wang and Tantillo, that the Ni(NHC)(COD) complex (II) acts as the catalytically active species.

The mechanism presented here qualitatively contains the same major transition state structures as were presented by
Scheme 5. Proposed mechanism of the Ni(NHC)-catalyzed rearrangement of 1-acyl-2-vinylcyclopropanes.

Investigation of the Substrate Dependence

Figure 2. shows the computed Gibbs free energies of the proposed reaction paths for substrates endo-5c, endo-8c as well as endo-5b and endo-8b. All energies are given relative to the respective initial intermediate INT1. For all cases, transition structure TS3, corresponding to the isomerization step from INT2 to INT3, has the highest relative energy and we consider this energy as the effective barrier height of the overall reaction from INT1 to INT4. For the substrates with geminal methyl groups the barrier heights are 98.6 kJ/mol (for endo-5c) and 118.3 kJ/mol (for endo-8c), respectively, significantly lower than the values of 153.3 kJ/mol (endo-5b) and 141.2 kJ/mol (endo-8b) found for the substrates with vicinal methyl groups. From these barrier heights, effective rate constants and correspond-
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Figure 2. Relative energies of the proposed catalytic cycle for the four substrates endo-5c and endo-8c as well as endo-5b and endo-8b. Energies were computed at the B3LYP-D3-COSMO/def2-TZVP level, corrected with B2PYLP; see Computational details. For substrate endo-8c the intermediate INT2 is energetically higher than the preceding TS2, which is a consequence of using different methods for computing structures and energies, but is uncritical as it does not affect the total barrier height of the reaction path.

ing half-life estimates for the respective INT1 compounds can be determined. For substrates endo-5c and endo-8c these half-lives lie within the realm of seconds/minutes with approximately 1 s and 440 s respectively, whereas for the substrates endo-5b and endo-8b they are in the realm of days with 5600 h and 140 h. This very likely explains the unsuccessful reaction for the latter substrates in the experiment. It also has to be noted that the overall reactions are expected to be slower than these half-lives suggest, since the rate for the formation of INT1 was not taken into account.

For all investigated substrates, intermediate INT4 has the lowest energy in the catalytic cycle and a subsequent ligand exchange reaction to regenerate INT1 is exergonic. In particular, for substrates endo-5c and endo-8c the exchange is exergonic by −39.0 kJ/mol and −40.4 kJ/mol, respectively, while for the substrates endo-5b and endo-8b values of −60.6 kJ/mol and −52.4 kJ/mol are computed, respectively.

In summary, the proposed mechanism is consistent with the observed reactivities and explains the preference for the geminal substituted vinyl units with the endo-configuration of the cyclopropane ring.

Conclusion

Two series of keto-functionalized vinylcyclopropanes 5, 8 with different substitution patterns at the vinyl unit were synthesized from cyclopentenone or cyclohexenone and sulfur ylides. Compounds 5, 8 were submitted to the catalytic vinylcyclopropane-cyclopentene (VCP) rearrangement using Ni(NHC) complexes to obtain the bicyclo[3.3.0]octenone 6 and bicyclo[4.3.0]none 9 respectively. A temperature dependent screening of different Ni(NHC) complexes revealed that the VCP rearrangement is favoured over the competing ring opening towards 3-(2-methylprop-1-en-1-yl)cyclopent-2-en-1-one 13c at temperatures ≥ 120 °C. With regard to the type of NHC ligand, combinations of the aliphatic NHC cores with peripheral bulky aryl units or aromatic NHC units with peripheral bulky alkyl units were found to be beneficial for the VCP rearrangement. Thus, the ligand 1,3-bis(2,6-diisopropylphenyl)-imidazolinium chloride (16·HCl) provided the best compromise between conversion and reactivity. Screening of the substrate scope revealed that vinylcyclopropanes with geminal-disubstituted vinyl units were better suited than vinylcyclopropanes with vicinal-disubstituted vinyl unit, which is in good agreement with the results obtained by Louie and Tantillo[8d,8e] for unfunctionalized vinylcyclopropanes. Moreover, the relative configuration of the cyclopropane unit played an important role for the reactivity, i.e. the endo-configured vinylcyclopropanes underwent the VCP rearrangement in contrast to their exo-configured counterparts. Quantum chemical calculations of the reaction pathways showed lower energies for the relevant intermediates and transition states of the geminal-disubstituted substrates, exemplary for the endo-vinylcyclopropanes, supporting their high reactivity. Thus, the combined efforts of computational and experimental studies unraveled the puzzling reactivity issues, substrate scope and stereoselectivity of the Ni(NHC)-catalyzed rearrangement of 1-acyl-2-vinylcyclopropanes and delivered a tool for further exploration in the synthesis of complex bicyclic target compounds.

Computational Details

The calculations were carried out with the TURBOMOLE V7.2.1 program package.[32] Resulting structures were visualized with Avogadro 1.2.0.[133] Molecular geometries were optimized using density functional theory (DFT) in conjunction with the B3LYP functional[29] including dispersion effects through Grimme’s D3 correction[34a] with Becke–Johnson damping.[34b] Numerical in-
tegration was carried out on an m3 grid and density fitting (multipole accelerated resolution of the identity) \cite{35} was enabled to speed up the integral evaluation. For all calculations the def2-TZVP basis set \cite{36} was used. Solvent effects were accounted for with the conductor-like screening model (COSMO) \cite{37} using a dielectric constant of \( \varepsilon = 2.07 \) to mimic the polarity of toluene at 120 °C. Finite temperature effects were accounted for using the RRHO (rigid rotor harmonic oscillator) approximation assuming a temperature of 120 °C, in accordance with the usual experimental conditions. Vibrational frequencies were scaled by a factor of 1.0043. \cite{38} The Gibbs free energies computed at the B3LYP-D3-COSMO level were corrected by additional single point calculations with the double hybrid functional B2PLYP-D3. \cite{39} The corrected energies were obtained as \( G = G(B3LYP-D3-COSMO) - E(B3LYP-D3) + E(B2PLYP-D3) \), where \( E \) refers to purely electronic energies. Starting guess structures for transition state searches were obtained with the wellfounding program \cite{39} of TURBOMOLE and an in-house version thereof. All transition structures were verified to possess only a single mode with imaginary frequency. IRC (internal reaction coordinate) calculations starting from the transition structures yielded no relevant new intermediate structures on a low level of theory (BP86-D3/def2-SVP). \cite{36,40} The PNO-LCCSD(T)-F12 \cite{41} calculations were done with the quantum chemistry package MOLPRO V2019.2. \cite{42}

Supporting Information (see footnote on the first page of this article): Description of procedures for substrates 5 and 6, full Characterization of new Compounds, \(^1\)H- and \(^13\)C-NMR Spectra of all.
