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Nickelacyclobutanes: Versatile Reactivity and Role as Catalytic Intermediates

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Metallacyclobutanes are intermediates in several catalytic cycles such as olefin metathesis and cyclopropanation. Furthermore, nickel is attracting attention as a versatile, earth-abundant metal in developing new homogeneous catalytic transformations. In this context, the current literature on nickelacyclobutanes and their role in catalysis is reviewed. First, catalytic reactions involving a (putative) nickelacyclobutane intermediate are discussed, including cyclopropanations and various transformations of methylenecyclopropane. Second, studies of the stoichiometric reactivity of nickelacyclobutanes relying on their direct observation or even isolation are detailed. In particular, the relationship between the structure of nickelacyclobutanes and their reactivity is highlighted. Finally, future prospects for the development of new catalytic transformations relying on nickelacyclobutane intermediates are briefly outlined.

1. Introduction

Catalysis is an essential tool for the development of more environmentally friendly chemical processes. Our ability to discover new catalytic reactions and improve existing ones relies on a solid understanding of the underlying reaction mechanism and catalytic intermediates.[1] While the nature and reactivity of such intermediates can often be inferred indirectly from kinetic studies and the analysis of product distributions, their transient nature renders direct observation very challenging. Often, the design of relatively stable analogues of unstable intermediates (model compounds) helps understand their structure and reactivity and provides experimental support for the feasibility of putative mechanistic pathways.[2]

Metallacyclobutanes, i.e. saturated four-membered ring compounds containing one metal atom, constitute a versatile class of catalytic intermediates (Scheme 1). They can be formed via three predominant routes: 1) oxidative addition of a cyclopropane ring; 2) [2 + 2] cycloaddition of a metal carbene and an olefin, and 3) transmetalation of a bimetallic prop-1,3-diyl derivative onto a metal dihalide fragment.[3] Metallacyclobutanes can react in different ways, including a) reductive elimination to form cyclopropanes; b) cycloreversion yielding an olefin and a metal carbene; c) β-hydride elimination/reductive elimination yielding olefins and d) insertion, where the introduction of an unsaturated substrate enlarges the ring.[4–8] This multi-faceted reactivity makes metallacyclobutanes key reactive intermediates for catalytic organic transformations such as cyclopropanation and olefin metathesis, but predicting and controlling their reactivity in new systems remains challenging.

Olefin metathesis is perhaps the most prominent reaction involving metallacyclobutanes as intermediates.[9] Its development has been mainly based on second-row transition metals molybdenum and ruthenium, but earth abundant first-row transition metals[10–14] and in particular iron[15–17] have recently been attracting interest. Interestingly, early work by Grubbs and Miyashita showed that nickel can mediate ring-closing metathesis amongst other reactions, presumably *via* carbene and nickelacyclobutane intermediates. Nickelacyclobutanes have also been proposed in catalytic cyclopropanation mechanisms, as well as in several skeletal expansion reactions relying on the ring-opening of cyclopropane derivatives. This versatile reactivity suggests a broader and yet unexploited potential of nickelacyclobutane chemistry for the development of new catalytic reactions.[18,19]

This review provides an overview of the current literature on nickelacyclobutanes, including the most recent developments. First, the different catalytic cycles for which nickelacyclobutanes have been proposed as intermediates are presented. Second, examples in which nickelacyclobutanes have been directly observed and/or isolated are covered with a focus on reactivity. Finally, future prospects in the field are briefly outlined.

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2. Nickelacyclobutanes as intermediates in catalytic processes

This section describes selected catalytic processes where a nickelacyclobutane intermediate has been proposed. We discuss cyclopropanation reactions, olefin metathesis reactions and processes involving the activation of C–C single bonds in strained cyclopropane rings.

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2.1. Nickelacyclobutanes as intermediates for cyclopropanations

Kanai described the first methodology for the cyclopropanation of electron-deficient olefins with gem-dihalides using a nickel-based catalyst ($Ni(PPh_3)_4$) in the presence of zinc and a Lewis acid ($ZnBr_2$).[20] The reaction doesn't work in the absence of nickel or when electron rich olefins are used as substrates. Based on these results, the authors proposed a mechanism starting by the coordination of the olefin to the Ni(0) which proceeds easily with electron-deficient olefins (Scheme 2).[21] The gem-dihalide is then oxidatively added to the Ni center, and the halide ligands are reductively cleaved by Zn. The latter process forms a Ni-methylene bond which undergoes [2 + 2] cycloaddition with the coordinated olefin to form a nickelacyclobutane complex as the key intermediate before the reductive elimination process liberating the cyclopropane product.

More recently, Duong et al. reported an efficient methodology for the cyclopropanation of electron-deficient olefins bearing ketones, esters, or amide substituents.[22] The reaction conditions include $NiCl_2$, CH_2I_2 as gem-dihalide, and Et_2Zn as the reducing agent for the formation of the nickel carbene. The methodologies of Kanai and Duong experimentally demonstrate that both Ni(0) and Ni(II) can be efficient precatalysts for this process. The group of Liu compared the energy of the cyclopropanation reaction pathways catalyzed by Ni(0) and Ni(II) species using DFT calculations. The simplified model used for this study was the cyclopropanation reaction between ethylene and a CH_2 moiety derived from diazomethane, using the precatalysts: $NiCl_2(PH_3)_2$, $NiCl_2$, $Ni(PH_3)_4$ and $Ni(PH_3)_2$. The authors concluded that despite the accessibility to metallacyclobutane intermediates from both oxidation states, the Ni(0) center offered more favored reaction pathways from both kinetic and the thermodynamic viewpoints.[23]

The group of Chen extended the use of nickel to the catalytic cyclopropanation of non-activated olefins.[24] Their methodology used tetramethylammonium triflate activated by n-BuLi as the methylene source and $(PPh_3)_2NiBr_2$ as the catalyst. The authors studied the mechanism in detail, proposing that the resting state of the process is a Ni(0) species coordinated to the alkene substrate (Scheme 3).[25] After the reversible complexation of the ammonium ylide, where the Ni(0) reacts as a Lewis acid, a nickel carbene is formed by extruding NMe_3 during the rate-determining step. The carbene then reacts intramolecularly with the coordinated alkene to form the nickelacyclobutane intermediate, which rapidly undergoes reductive elimination to form the cyclopropane. The main byproduct of the reaction is ethylene gas formed by carbene dimerization in a parallel catalytic cycle involving a Ni(0) – phosphine species.

Finally, related nickelacyclobutane intermediates have been invoked in mechanistic proposals for cyclopropanation reactions in which the nickel-carbene species is formed by the activation of highly strained cycles as bicyclo[1.1.0]butanes[26] or [1.1.1]propellane.[27]

María L. G. Sansores-Paredes obtained her BSc. in Chemistry in 2013 from the Autonomous University of Yucatan (UADY) in Mexico. In 2017, she graduated from the interdisciplinary Erasmus Mundus master SERP-Chem. She was granted a multiple master's degree in chemistry and, material science and engineering by the Université Paris-Saclay, the Adam Mickiewicz University in Poznan, and the University of Genoa. Currently, she is completing her PhD at Utrecht University. Her research focuses on the study of the metal-ligand cooperativity of nickel complexes bearing olefin diphosphine ligands under the supervision of Dr. Marc-Etienne Moret.

Pablo Marcelo Pérez García received his BSc and MSc degrees from the University of Geneva in 2006. After working for some years in several universities in his home country Bolivia, he moved to Lausanne to work with Prof. Xile Hu at EPFL on the development of well-defined cross-coupling nickel catalysts, where he received his PhD degree in 2015. From 2018 on, he is a postdoctoral researcher at Utrecht University with Dr. Marc-Etienne Moret. His current main research is focused on the fundamental understanding of the reaction steps of nickel catalyzed chemical processes.

Marc-Etienne Moret obtained an MSc degree in chemistry from the Ecole Polytechnique Fédérale de Lausanne (EPFL) in 2005, and a PhD degree from the Eidgenössische Technische Hochschule Zürich (ETHZ) with Prof. P. Chen in 2009. After a postdoctoral stay at the California Institute of Technology (Caltech) in the group of Prof. J. C. Peters (2010-2012), he started his independent career at Utrecht University (UU) where he is currently associate professor. His research interests revolve around ligand design for small-molecule activation and catalysis using earth-abundant elements.

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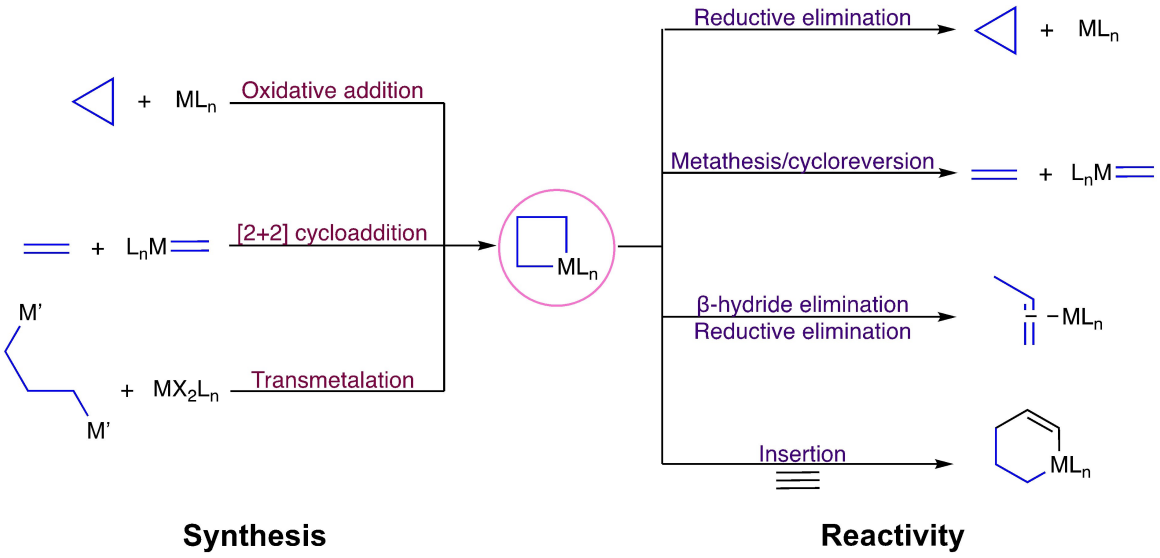
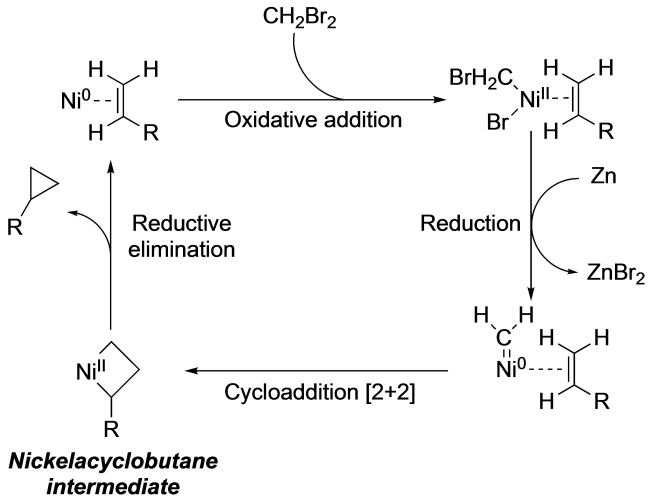
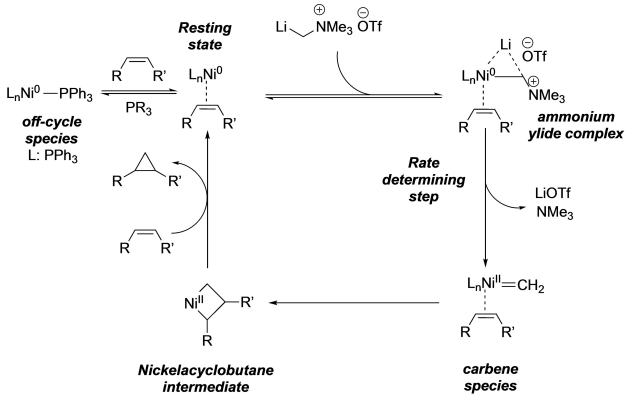


Scheme 1. Synthesis and common reactivity of metallacyclobutanes.



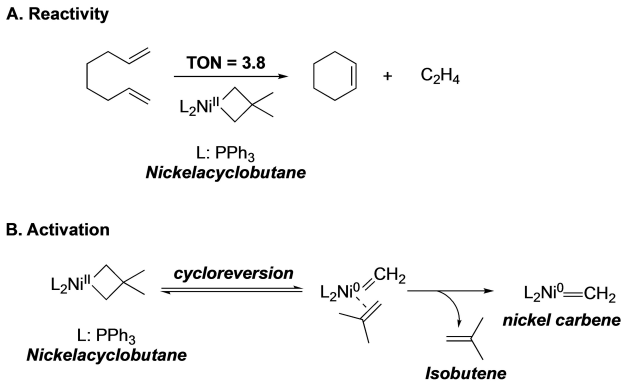
Scheme 2. Catalytic cycle for the cyclopropanation of electron-deficient olefins with Ni(0) complexes ($Ni(PPh_3)_4$). R: CO_2CH_3, CN, $COCH_3$, CHO.



Scheme 3. Catalytic cycle for the cyclopropanation of non-activated olefins with Ni(0) complexes.

2.2. Nickelacyclobutanes as intermediates for olefin metathesis

During the metathesis reaction, the metallacyclobutane intermediate undergoes cycloreversion instead of reductive elimination, leading to an alkene and a metal carbene complex. Miyashita et al. studied in detail the stoichiometric reactions of a nickelacyclobutane complex bearing two PPh_3 anchoring ligands (vide infra section 3.2).[28] This complex has served as a precatalyst for the ring-closing metathesis of 1,7-octadiene with a modest turnover number of 3.8. The process can be rationalized by the activation of the metallacycle by cycloreversion, generating isobutene and the nickel carbene complex, which should be the active catalyst for the metathesis process (Scheme 4).



Scheme 4. Ring-closing metathesis catalyzed by a nickelacyclobutane.

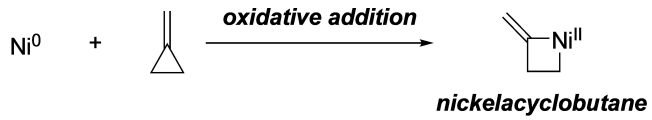
2.3. Nickelacyclobutanes as intermediates for reactions involving the cleavage of C–C single bonds

The activation of saturated and unsaturated three-membered rings by oxidative addition to a transition metal center is facilitated by strain-release. These entities are therefore attractive starting materials for catalytic synthetic methodologies.[29] Among them, methylenecyclopropane (MCP) is a stable and highly strained molecule largely used as a building block in organic synthesis.[30] Nickel(0) catalysts activate this molecule by oxidative addition to form a nickelacyclobutane intermediate (Scheme 5). Controlling the reactivity of this intermediate allows for selective catalytic transformations driven by strain-release.

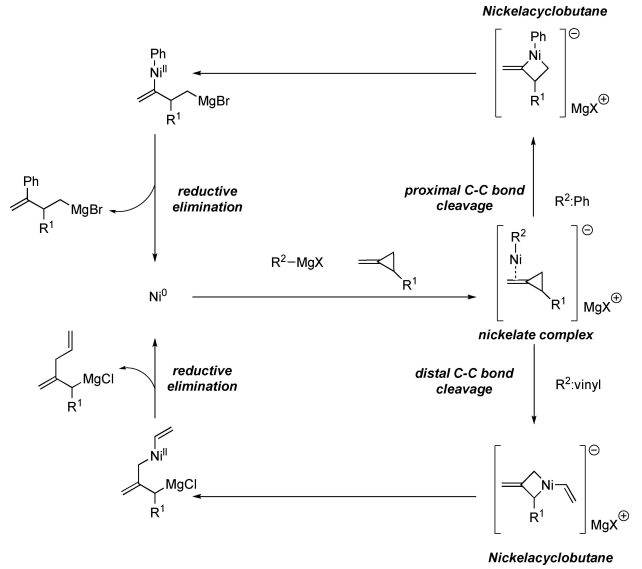
The diverse reactions involving nickelacyclobutane intermediates derived from MCP include cyclodimerisations,[31] the synthesis of silylated allylic alcohols,[32] and the synthesis of unusual Grignard reagents.[33] In the last category, the group of Kambe reported the use of methylenecyclopropane synthons for the generation of new allylic carbomagnesium products. In this process, nickel chloride ($NiCl_2$) catalyzes the selective cleavage of either the proximal or the distal carbon-carbon bond of the methylenecyclopropane motif upon reaction with Grignard reagents (Scheme 6). The chemical nature of the Grignard reagent determines the regioselectivity of the process. Deuterium labeling experiments provided evidence that the activation of the MCP motif proceeds via direct oxidative addition instead of a sequential migratory insertion of the C=C bond and β-carbon elimination. Therefore, the inferred reaction mechanism starts with an *in-situ* formed Ni(0) complex, which reacts with a Grignard molecule and the MCP to yield a nickelate complex. In the reaction with an aryl Grignard reagent, the proximal C–C bond of the MCP ring is oxidatively added to the Ni center, while the distal C–C bond is activated for vinyl Grignard reagents. In both scenarios, the formed nickelacyclobutane intermediate is opened by Ni-to-Mg transmetallation, and the resulting acyclic complex undergoes reductive elimination to generate the final organomagnesium compound.

The activation of MCP by a nickel center can also be used to prepare polycyclic products via highly atom-efficient cycloadditions.[34] For example, Zhang et al. reported a nickel-catalyzed ($Ni(cod)_2$, PPh_3) intramolecular cycloaddition of aryl alkynes with MCPs to generate cyclopenta[α]idene derivatives.[35] The proposed mechanism starts with the oxidative addition of the MCP via the proximal C–C bond to form a nickelacyclobutane intermediate. Then, intramolecular insertion of the alkyne bond generates a nickelacyclohexane intermediate (Scheme 7). Reductive elimination from the latter species is generally difficult,[36] but the authors propose that the presence of a larger conjugated system facilitates the reaction. Related synthetic methodologies for the synthesis of bigger cyclic entities via [3 + 2 + 2] cycloadditions[37] or [3 + 2] cycloaddition reactions of cyclopropyl ketones and alkynes have also been rationalized by mechanisms involving nickelacyclobutane intermediates.[38]

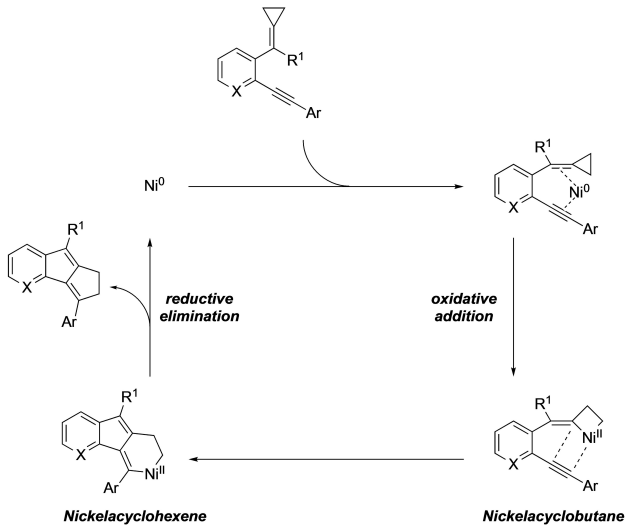
Rearrangements of vinylcyclopropanes to cyclopentenes have been reported by the group of Sonoda[39] and proposed to proceed *via* a nickelacyclobutane intermediate. Namely, the catalytic isomerization of 1-siloxy-1-vinylcyclopropanes to 1-siloxycyclopentenes using a Ni(0) catalyst formed *in situ* by reduction of $(Ph_3P)_2NiCl_2$ with Zn was studied. The proposed rationale for the process starts with coordination of the C=C double bond to the Ni center, followed by oxidative addition of the cyclopropane to form the nickelacyclobutane intermediate. The latter then rearranges into a π-allylnickel complex before



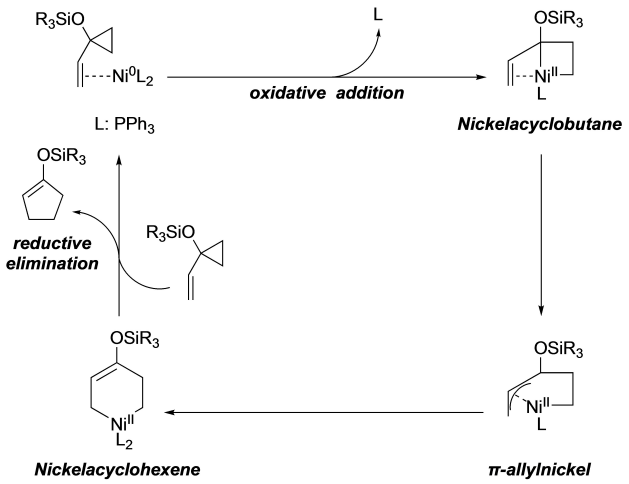
Scheme 5. Activation of methylenecyclopropane by a Ni(0) center.



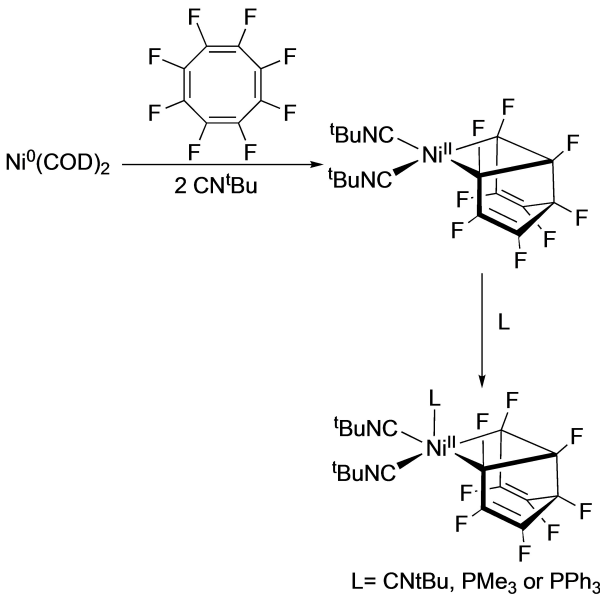
Scheme 6. Proposed mechanism for the nickel catalyzed carbomagnesation of methylenecyclopropanes using $NiCl_2$ as precatalyst.



Scheme 7. Intramolecular cycloaddition via a nickelcyclobutane intermediate formed by activation of a MCP motif by a Ni(0) center ($Ni(cod)_2$, PPh_3).



Scheme 8. Rationale for the isomerization of vinylclopropanes to cyclopentenes.



Scheme 9. Synthesis of a fluorinated nickelacyclobutane from octafluorooctatraene.

forming a nickelacyclohexene (Scheme 8). The group of Louie also studied experimentally and computationally the isomerization of unactivated vinylcyclopropanes to cyclopentenes using an NHC ligand and Ni(0) system.[40,41] They refined the mechanism proposed by Sonoda, excluding diradical mechanisms and confirming the role of the nickelacyclobutane intermediate.

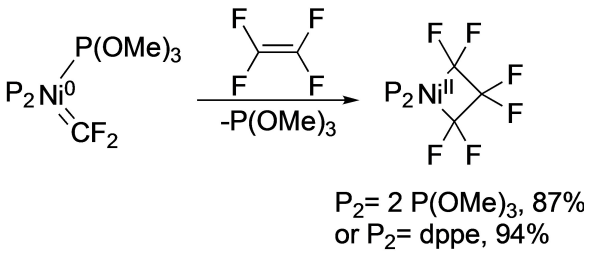
3. Synthesis and stoichiometric reactivity of nickelacyclobutanes

The examples above illustrate the pivotal role of nickelacyclobutane intermediates in a variety of nickel-catalyzed transformations. Valuable insight into the properties of this versatile class of intermediates – and how to control their reactivity – has been gained from targeted stoichiometric studies. Systems are sought in which a nickelacyclobutane is stable enough to be characterized and sometimes even isolated, creating an opportunity to closely inspect its reactivity patterns. The first crystallographically authenticated fluorinated nickelacyclobutanes bore multiple fluorine substituents, which also have a strong influence on reactivity. Therefore, we treat fluorinated and non-fluorinated nickelacyclobutanes in separate subsections.

3.1. Fluorinated nickelacyclobutanes

The first isolated perfluorinated nickelacyclobutane was reported in 1986 by Hughes and coworkers as part of a study on the reactivity of $Ni(COD)_2$ and octafluorocyclooctatetraene in the presence of different exogenous ligands: using two equivalents of tert-butylisocyanide yielded a nickelacyclobutane (Scheme 9). The nickelacyclobutane is resistant to reductive elimination, and additional exogenous ligands form stable pentacoordinated structures. Fortunately, the molecular structure of pentacoordinated nickelacyclobutane with PMe_3 ligand could be determined by X-ray crystallography, providing the first structural characterization of a nickelacyclobutane (Figure 1). The C–C bond lengths are consistent with the sp^3 character. Ni–C bond lengths are comparable with reported Ni–C(sp^3) (~1.9 Å), Ni–C(sp^2) bonds being generally shorter (~1.8 Å).[42] Additionally, a compressed C–Ni–C angle (73°) was observed.[43]

In 2015, Baker and coworkers reported a study on the reactivity of nickel difluorocarbenes, aiming towards catalytic applications in the metal-mediated metathesis or polymerization of perfluoroalkenes.[44] Treating a nickel difluorocarbene (stabilized by either $P(OMe)_3$ or a chelate dppe ligand) with tetrafluoroethylene yielded perfluorinated nickelacyclobutanes via cycloaddition with high yields (Scheme 10). This constituted the first instance of an isolated nickelacyclobutane synthesized from a nickel carbene and an olefin. In addition, the molecular structure of (dppe) perfluoro nickelacyclobutane was determined by X-ray crystallography, showing that the environment around nickel is approximately planar and the C–Ni–C angle is compressed, as previously reported by Hughes (Figure 1).



Scheme 10. Synthesis of perfluorinated nickelacyclobutanes by [2 + 2] cycloaddition. dppe: 1,2-Bis(diphenylphosphino)ethane.

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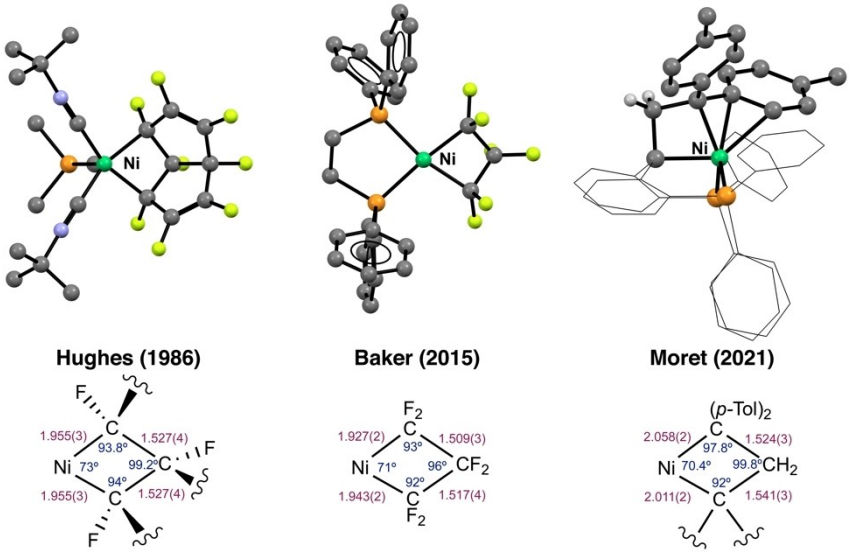
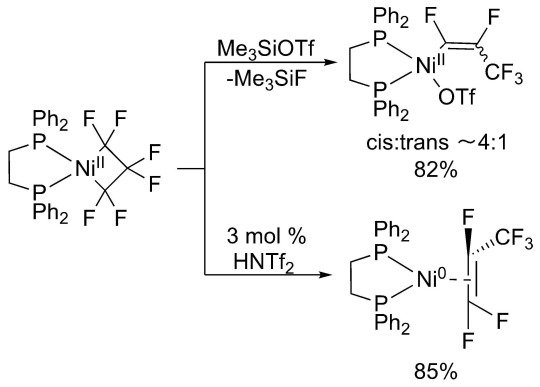
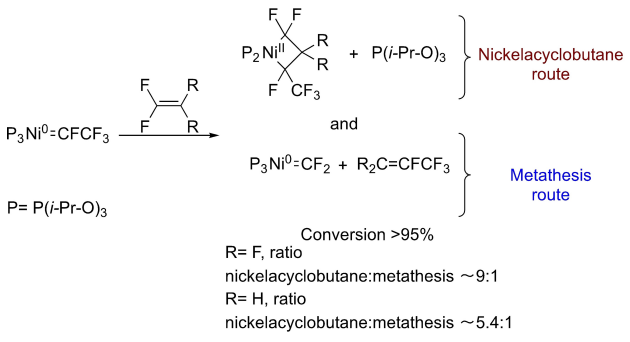


Figure 1. Ball and stick representation of the molecular structures of nickelacyclobutanes as determined by X-ray crystallography. For clarity, solvent molecules and most H atoms are omitted, and some substituents are represented as wireframe.

The reactivity of the dppe-supported perfluoro- nickelacyclobutane was investigated (Scheme 11). Fluoride abstraction with Me_3SiOTf yielded a triflate vinyl Ni(II) complex with a cis: trans ratio of approximately 4:1. Furthermore, catalytic amounts of $HNTf_2$ resulted in isomerization of the four-membered ring yielding a hexafluoropropylene nickel complex in 85% yield.[44]



Scheme 11. Explored reactivity of perfluorinated nickelacyclobutane.



Scheme 12. Reactivity of $P_3Ni{=}CFCF_3$ towards trifluoroethene and 1,1-difluoroethylene.

Further studies from the Baker group uncovered remarkable reactivity pathways. In 2018, they reported the reaction of nickel fluorocarbenes with fluoroalkenes to yield olefin metathesis products without a nickelacyclobutane intermediate. Olefin metathesis is generally thought to involve the formation of a metallacyclobutane intermediate by the [2+2] cycloaddition of a metal carbene and an olefin which then undergoes cycloreversion to yield a new alkene and metal carbene (Chauvin mechanism).[45] Surprisingly, reactions of the tetracoordinated nickel carbenes $P_3Ni{=}CFCF_3$ with different fluoroethylenes (trifluoroethene and 1,1-difluoroethylene) yielded both metathesis products and nickelacyclobutane complexes via distinct pathways (Scheme 12). Different product distributions were obtained for the two different olefins, indicating a sensitivity of the system to olefin substituents. Remarkably, over time the product ratio is maintained even in the presence of an excess of phosphine coligand, suggesting two independent pathways. In addition, the reaction of $P_3Ni{=}CFCF_3$ with 1,1,2-trifluoroethylene yielded metathesis products but the nickelacyclobutane was not observed; instead, two complexes resulting from the decomposition of the nickelacyclobutane intermediates were identified (Scheme 13). The cycloaddition with 1,1,2-trifluoroethylene can lead to two regioisomeric nickelacyclobutanes: the major nickelacyclobutane (route A) undergoes 2,1-fluoride migration resulting in ring contraction to form E/Z isomers of a Ni(0) olefin complex. The minor nickelacyclobutane (route B) undergoes C–F activation to form fluoronickel alkenyl E/Z isomers.[46]

Replacing the phosphine ligands of the nickel fluorocarbene $P_3Ni{=}CFCF_3$ by $P(OMe)_3$ or the tripod $[MeC(CH_2PPh_2)_3]$ significantly influenced the product ratio: interestingly, the reaction with the tripod complex only led to the nickelacyclobutane product.

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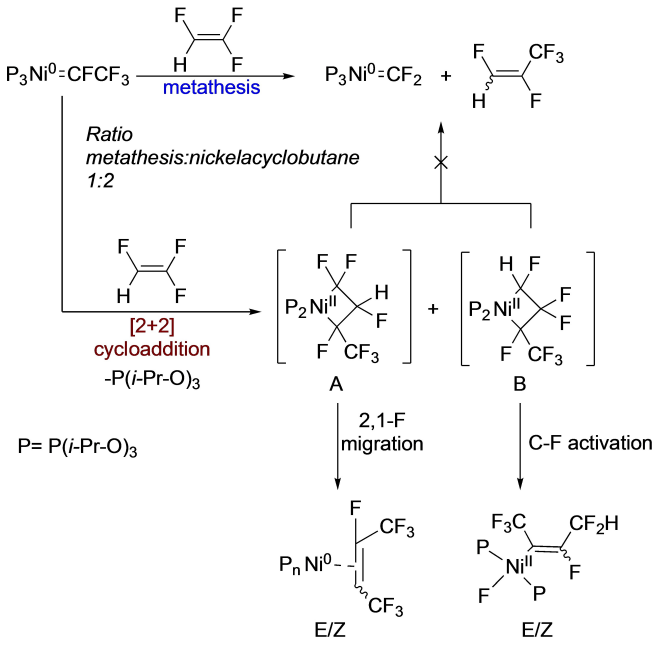
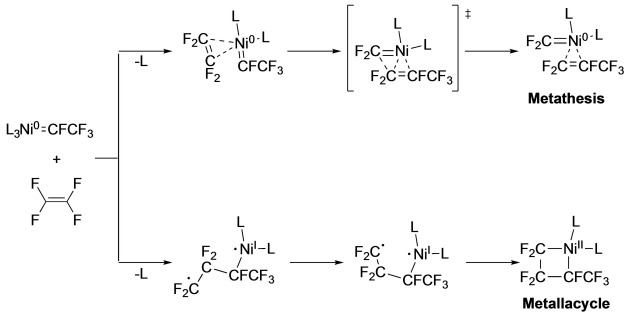
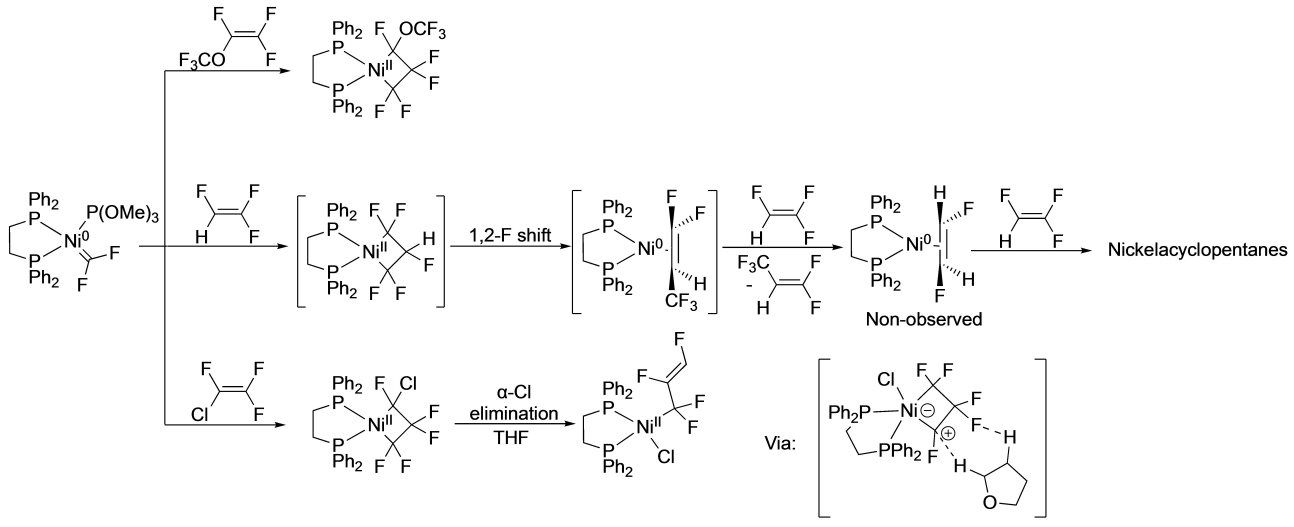


Scheme 13. Reactivity of $P_3Ni{=}CFCF_3$ towards 1,1,2-trifluoroethylene.



Scheme 14. Proposed reaction mechanism for metathesis and metallacycle formation of $L_3Ni{=}CFCF_3$ and tetrafluoroethylene.



Scheme 15. $(dppe)(POMe)_3Ni{=}CF_2$ reactivity towards different fluoroalkenes.

DFT calculations on the reaction mechanism identified two independent pathways (Scheme 14): whereas the nickelacyclobutane is formed via an open-shell singlet diradical intermediate, the metathesis reaction proceeds via a strained bicyclic intermediate.

In 2021, further investigations into the reactivity of nickel fluorocarbenes supported by the chelating diphosphine dppe was reported (Scheme 15). First, reaction of $(dppe)(POMe)_3Ni{=}CF_2$ with perfluoro(methyl vinyl ether) yielded a perfluorinated nickelacyclobutane. In contrast, reaction with trifluoroethylene yielded pentafluoropropene and fluorinated nickelacyclopentane complexes without an observed intermediate species. The proposed mechanism proceeds via a nickelacyclobutane intermediate that subsequently undergoes 1,2-fluoride shift coupled to a ring contraction to a nickelacyclopropane type intermediate. This complex can undergo ligand exchange with another molecule of trifluoroethylene to yield $(dppe)Ni(HFC{=}CF_2)$. From here, the formation of the observed nickelacyclopentanes can be explained by oxidative coupling of 2 molecules of trifluoroethylene. No metathesis products were observed. Finally, reaction with chlorotrifluoroethylene gave insight into the effects of heavier halogen substitution. The first step of the reaction yields a nickelacyclobutane with the Cl substituent in α-position. This complex further reacts yielding a Nickel(II) alkyl/chloride complex. The formation of this unusual complex is proposed to follow an intricate mechanism: α-Cl elimination results in a α-carbenium ion that subsequently reacts with a hydrogen source to yield the product. When rigorously dried THF was used as solvent, 2,3-dihydrofuran was detected, indicating THF as the H source. This was verified by conducting experiments in acetonitrile and benzene, in which no other product than the nickelacyclobutane was observed.[47]

3.2. Non-fluorinated nickelacyclobutanes

Nickelacyclobutanes devoid of additional stabilizing ligands have been studied by mass spectrometry and matrix isolation techniques.

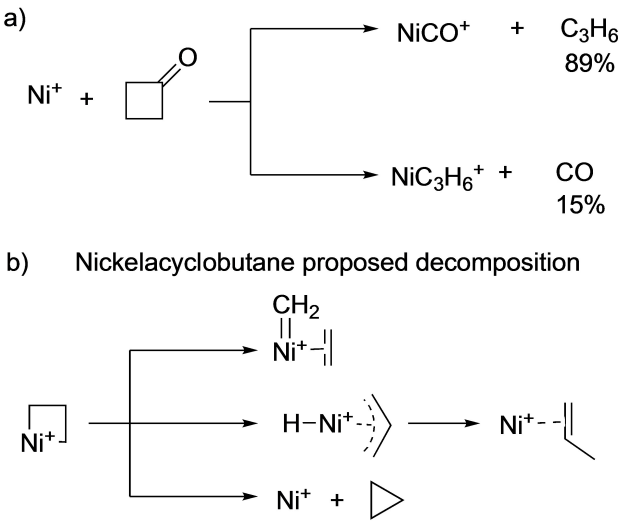
Freiser and coworkers used Fourier transform mass spectrometry to study the the reaction of Ni+ ions with cyclobutanone.[48] While the major ionic product was $Ni(CO)^+$ generated by CO abstraction, a minor product with formula $[NiC_3H_6]^+$ was observed (Scheme 16a). Subsequent reaction with MeCN cleanly yielded $[Ni(NCMe)]^+$, presumably with loss of propene. The authors proposed that the reaction proceeds via the formation of an unstable nickelacyclobutane ion by decarboxylation. The nickelacyclobutane intermediate then decomposes via a β-hydride elimination pathway to yield $[Ni(propene)]^+$ (Scheme 16b).

Gas phase reactions of the nickel cation with cyclopropane have yielded products that could be related to decomposition of nickelacyclobutanes.[49,50] In 1983, Beauchamp and coworkers studied ion beam reactions of Ni^+ towards cyclopropane (Scheme 17), identifying nickel carbene ions and ethylene as the main products. Similar results were obtained in 1990 by Armentrout and Fisher using guided ion beam mass spectrometry. While the nickelacyclobutane intermediate was not directly identified, the reaction products strongly suggest its initial formation followed by [2 + 2] cycloreversion.

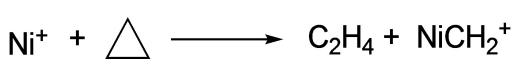
In 1988, Margrave and coworkers studied the generation of a non-ligated nickelacyclobutane from nickel atoms and cyclopropane using matrix-isolation FTIR spectroscopy and studied its photofragmentation (Scheme 18).[51] Condensation of nickel with cyclopropane in an argon matrix led to the formation of the nickelacyclobutane via C–C oxidative addition. Under radiation with $\lambda \geq 500$ nm, the formed nickelacyclobutane underwent metathesis to yield a methylenenickel (ethylene) complex. Subsequent irradiation with UV light led to the formation of a vinylnickel methyl species that released methane upon extended photolysis. The assignment of vibrational spectra was supported by reactions with perdeuterated cyclopropane.

A few years before these studies on "naked" nickelacyclobutanes, Grubbs and Miyashita pioneered the investigation of ligand-stabilized analogues. In 1978, they studied the decomposition products of several nickelacycles, which suggested the transient formation of nickel carbene complexes.[52] A key experiment was the decomposition of a triphenylphosphine-supported nickelacyclohexane bearing deuterium at the α-positions in presence of propene (Scheme 19). The formation of several C4 products resulting from transfer of a CD_2 unit to propene suggested the transient formation of a Ni=CD_2 intermediate. The latter subsequently undergoes cycloaddition with propylene, forming two different nickelacyclobutanes that decompose along several pathways: metathesis, reductive elimination, and β-hydride transfer.

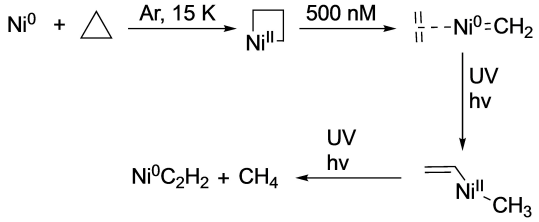
In a subsequent report, the same authors disclosed the synthesis and isolation of two tetracoordinated nickelacyclobutanes (Scheme 20) featuring either triphenylphosphine or the bidentate ligand dppe. The decomposition of dineopentyl nickel(II) complexes via metal insertion into the gamma C–H



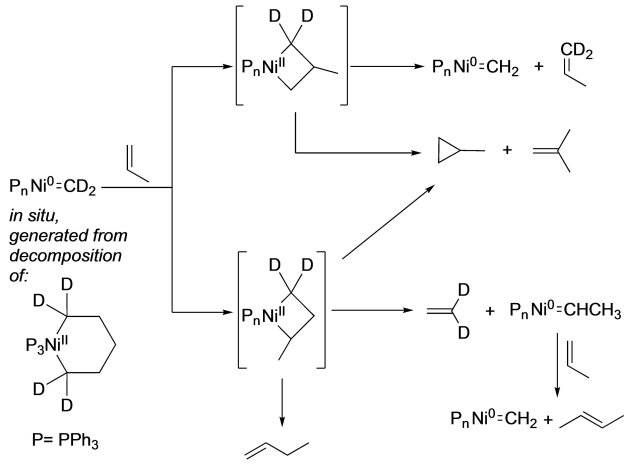
Scheme 16. Gas phase studies of the reactivity with nickel with cyclobutanone.



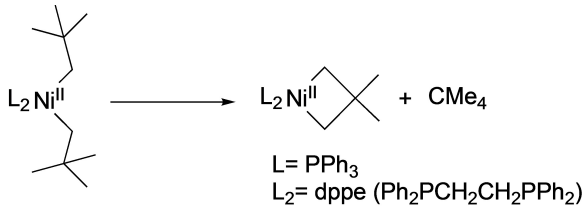
Scheme 17. Ion beam Ni+ reaction with cyclopropane.



Scheme 18. Formation and photochemical decomposition of nickelacyclobutane using matrix-isolation FTIR spectroscopy.



Scheme 19. Proposed formation of phosphine-supported nickelacyclobutanes by [2 + 2] cycloaddition and their decomposition pathways.



Scheme 20. Synthesis of nickelacyclobutanes via gamma C–H insertion.

bond produced the nickelacyclobutanes, which are stable at −20 °C.[28,53]

They analyzed the organic products of a number of reactions of the bis-triphenylphosphine nickelacyclobutane complex (Scheme 21), providing detailed insights into its reactivity. First, open neopentane derivatives were obtained by protolysis (HCl) or oxidation with Br_2. Other oxidants (O_2 or Ce^{IV}) induced reductive elimination of a cyclopropane derivative. The other reported reactions all generate C4 (and some C2 or C1) products that can be traced back to a [2 + 2] fragmentation of the nickelacyclobutane to form a nickel carbene intermediate. First, pyrolysis in the presence of H_2 generates, amongst others, methane and 2-methylpropane. Supporting the involvement of a Ni=CH_2 intermediate, reaction with D_2 produced methane-d_2 and 2-methylpropane-d_2. Second, thermal decomposition at high temperature produced amounts of 2-methylpropene, the direct product of [2 + 2] fragmentation. Third, reaction with CO resulted in formation of 2-methylpropene and a ketene dimer, the latter presumably resulting from the interception of the Ni=CH_2 intermediate by CO. Confirming this interpretation, the intermediate ketene complex was later isolated from a reaction with CO (3 atm) at −50 °C by Miyashita.[54] In addition, performing the reaction in presence of H_2 and CO led to the detection of ethanol, which the authors explained by the hydrogenation of the Ni-ketene intermediate.[53] Finally, the presence of a Ni=CH_2 intermediate was additionally supported by reaction with cyclohexene, which afforded 8% of the cyclopropanation product norcorane.

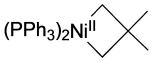
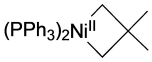
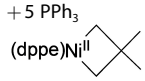
The formation of various hydrocarbons by thermal decomposition of the nickelacyclobutane shed light on the available pathways (Scheme 22). 1,1-dimethylcyclopropane is explained by reductive elimination from the nickelacyclobutane. The other products can be rationalized on the basis of a reversible [2 + 2] cycloreversion to generate a Ni=CH_2 fragment coordinated to 2-methylpropene. Decoordination of the olefin would lead to the observed 2-methylpropene, and subsequent homocoupling of the methylene carbene yields ethylene. In addition, rotation around the Ni-olefin axis followed by [2 + 2] cycloaddition would form a new nickelacyclobutane bearing the methyl groups in α position. As this isomer now possesses protons in the β position, β-hydride elimination can take place to yield a 3-methyl-1-butene.

Interestingly, the ratio between the different products depends on the concentration of the PPh_3 ligand (Table 1). In particular, a 5-fold excess of PPh_3 in toluene promotes C–C bond cleavage, almost doubling the yield of ethylene and 2-methylpropene. This suggests that a pentacoordinated nickelacyclobutane intermediate could favor metathesis-like [2 + 2] cycloreversion.[28]

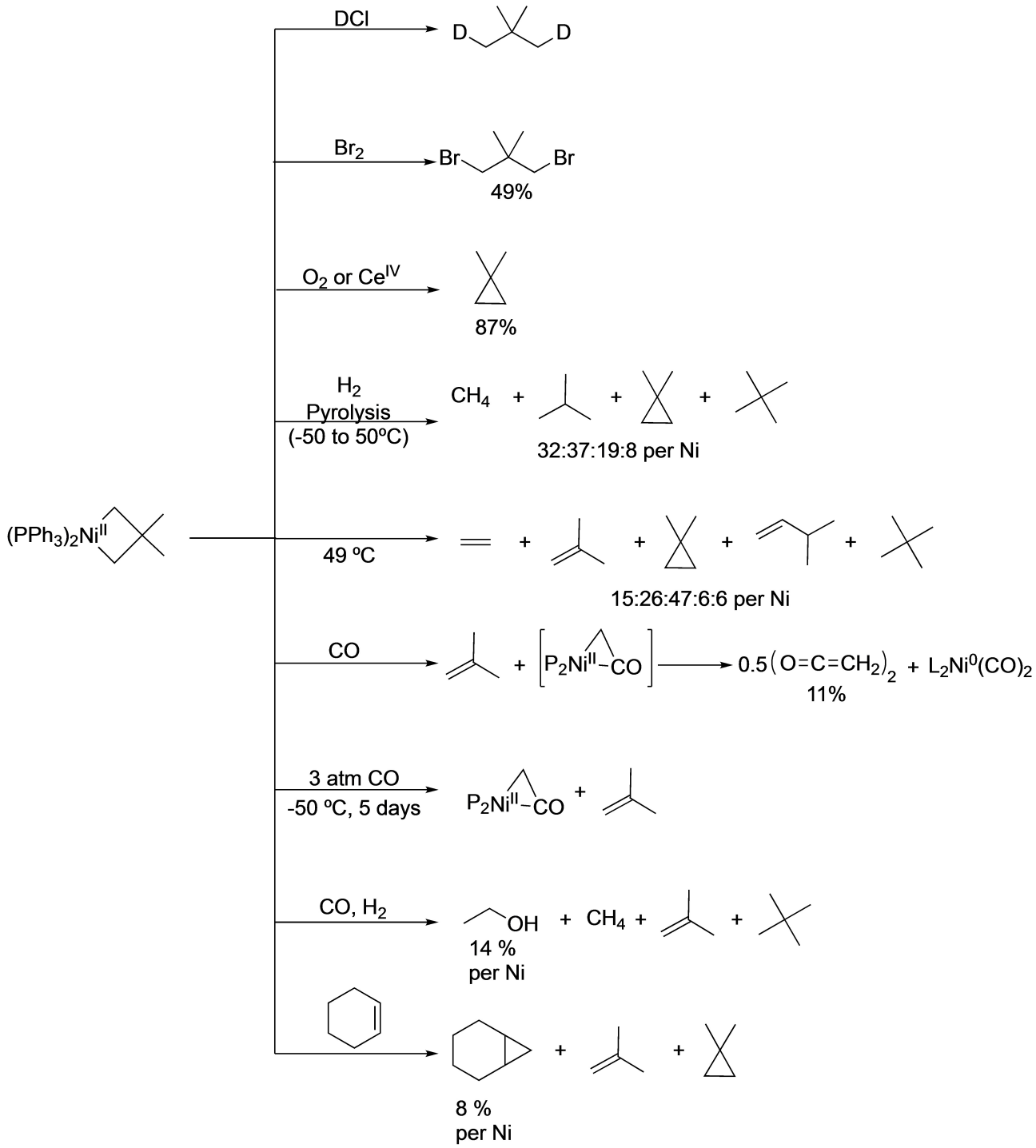
Indirect evidence for the transient formation of a nickelacyclobutane by oxidative addition of a cyclopropane ring was obtained by Binger and coworkers in 1983, who investigated the reaction of (Bpy)Ni complexes (Bpy = 2,2′-bipyridine) with methylenecyclopropane at different temperatures (Scheme 23). They detected diverse products including small quantities of nickelacyclohexanes. These products were rationalized by the formation of an undetected nickelacyclobutane intermediate by oxidative addition of the cyclopropane ring, followed by insertion of a second equivalent of olefin into a Ni–C bond.[55]

In 1986, Neidlein, Wilke, and coworkers synthesized the first examples of nickelacyclobutabenzenes. The addition of cyclopropabenzene to different nickel(0) precursors led to the corresponding nickelacyclobutabenzene via oxidative addition (Scheme 24). The nickelacyclobutabenzenes bearing P(*n*Bu)$_3$ and PPh_3 were stable at room temperature. The identity of these compounds was further established by follow-up reactions: protolysis of the P(*n*Bu)$_3$ complex with HCl led to the quantitative formation of toluene, and exposure to CO_2 at −78 °C induced ring expansion to form a six-membered carboxylate ring.[56]

Table 1. Decomposition reactions of metallacyclobutane complexes.[a]

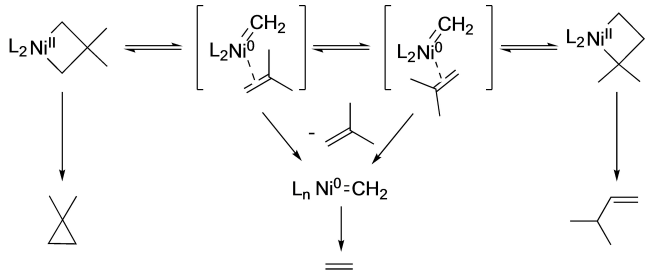
Complex	Temperature [°C]	Time [h]	Products[b] [mol%]				
			C_2H_4				CMe_4
	24	15	15	26	47	6	6
 +5 PPh_3	24	15	28	52	11	7	3
	60	5	14	27	51	3	5

[a] Decomposition reactions were carried out in toluene solution. [b] Product gases in and over the solution were analyzed by GLC and identified by GC/MS and NMR spectroscopy.

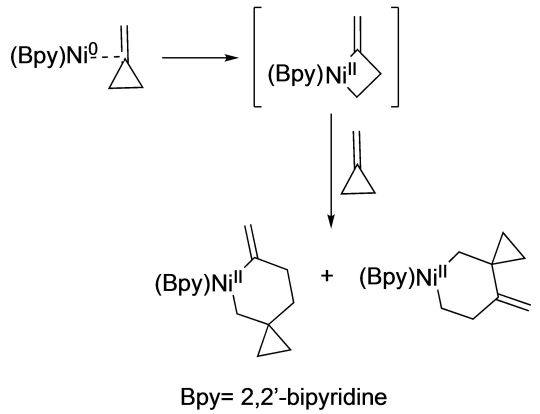


Scheme 21. Reactivity of a bis-triphenylphosphine nickelacyclobutane towards several substrates.

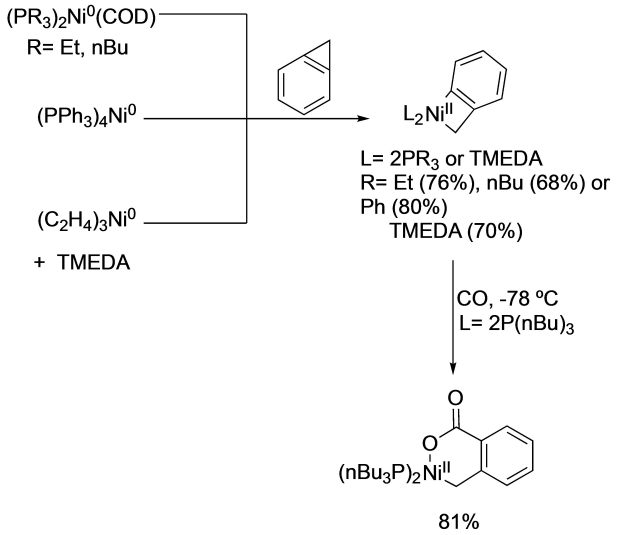
This work was then further expanded to the new precursor 7,7-bis(trimethylsilyl)cyclopropabenzene to study the influence of bulky substituents in the framework of the nickelacycle. The cyclopropabenzene was allowed to react with $Ni(C_2H_4)_3$ and chelating diamine ligands in 1:1 proportion (Scheme 25). The resulting nickelacyclobutabenzenes are stable at room temperature and more stable than their counterparts without bulky substituents. Ligand substitution on the TMEDA derivative afforded the corresponding phosphine complexes in high yields. The molecular structure of the TMEDA derivative was obtained by X-ray crystallography and is the first molecular structure of a nickelacyclobutabenzene derivative (Figure 2). The structure around nickel is planar, and the Csp^2–Csp^2 bond of the benzene ring is still short (1.38(1) Å). The ring angles are similar to nickelacyclobutane structures (Figure 1), presenting the characteristic compressed C–Ni–C angle (71.7°).[57]



Scheme 22. Proposed pathways for the interconversion of nickelacyclobutane to different hydrocarbons.

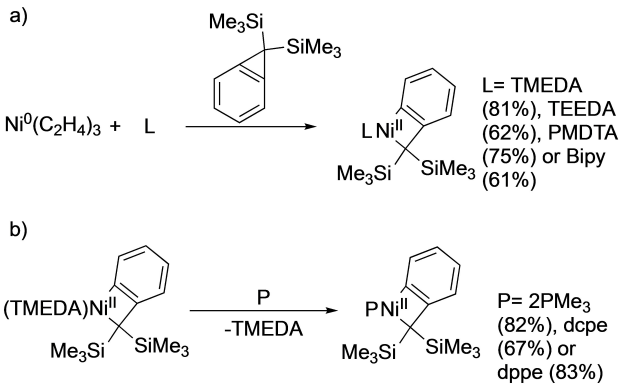


Scheme 23. Proposed reactivity of methylenecyclopropane via nickelacyclobutane intermediate.



Scheme 24. Synthesis and reactivity of nickelacyclobutabenzenes. TMEDA: tetramethylethylenediamine.

Hillhouse reported the synthesis of three novel tetracoordinated nickelacyclobutanes from alkyl nickel(I) complexes via an oxidation/deprotonation sequence (Scheme 26 a,b). Interestingly, the nickelacyclobutane containing a silicon atom in beta position was resistant to reductive elimination even at higher temperatures (140 °C). In contrast, the carbon based nickelacyclobutanes underwent quantitative reductive elimination at



Scheme 25. Synthesis and reactivity of nickelacyclobutanobenzenes derived from 7,7-Bis(trimethylsilyl)cyclopropabenzene. TMEDA: *N,N,N′,N′*-tetramethylethylenediamine; TEEDA: *N,N,N′,N′*-tetraethylethylenediamine, PMDTA: *N,N,N′,N″N‴*-pentamethyldiethylenetriamine; Bipy: 2,2′-bipyridine; dcpe: 1,2-bis(dicyclohexylphosphino)ethane; dppe: 1,2-bis(diphenylphosphino)ethane.

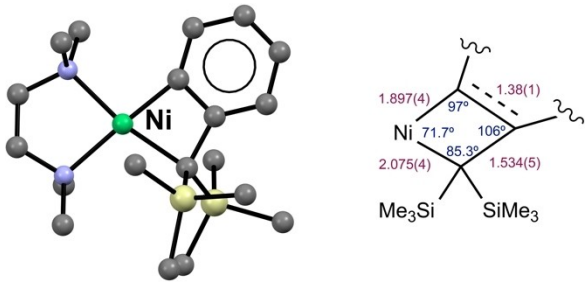
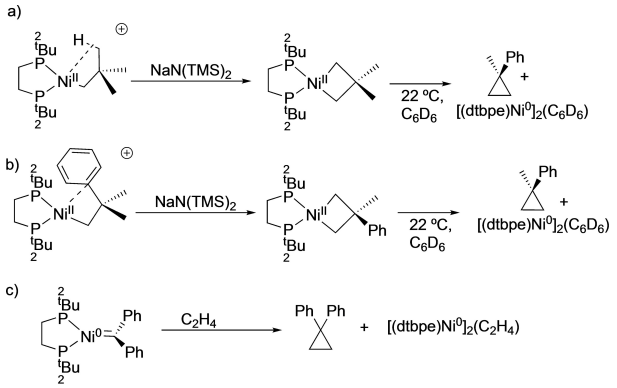


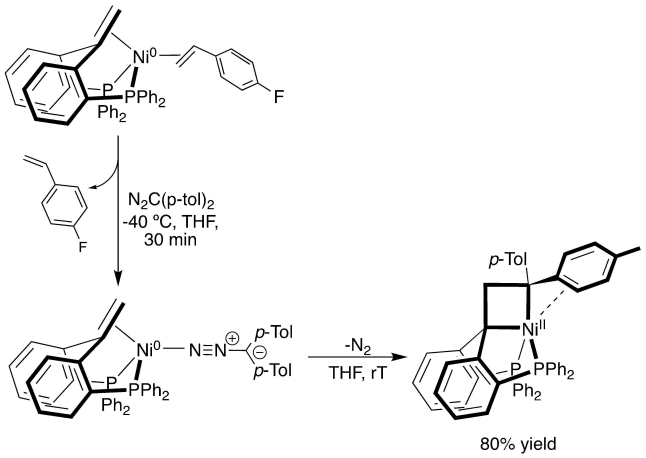
Figure 2. Molecular structure of nickelacyclobutanobenzene. For clarity, solvent molecules and most H atoms are omitted.



Scheme 26. Synthesis of nickelacyclobutanes via C–H gamma activation.

room temperature to yield cyclopropanes and Ni(0) complexes.[58] In contemporary work, Hillhouse reported the synthesis of a nickel carbene based on the same dtbpe ligand that reacted with ethylene to yield cyclopropane. There, no nickelacyclobutane intermediate was detected, but its existence is consistent with the observed reactivity (Scheme 26, c).[42]

We recently reported on the synthesis and reactivity of a nickelacyclobutane incorporated in a pincer framework (Scheme 27).[59] Treating a PC═CP nickel(0) complex with bis(p-tolyl)diazomethane afforded a pentacoordinated nickelacyclo-



Scheme 27. Synthesis of pentacoordinated nickelacyclobutane.

butane. DFT calculations supported a nickel carbene pathway involving a [2 + 2] cycloaddition step to form the metallacycle. The molecular structure of the pentacoordinated nickelacyclobutane was determined by X-ray crystallography (Figure 1). Metrics are similar to those reported for fluorinated nickelacyclobutanes and feature the usual compressed C–Ni–C angle (70.4°). The coordination environment can be described as a trigonal pyramid comprising the phosphines and the carbon atoms of the metallacycle. The coordination sphere is completed with pi donation from one double bond of the p-tolyl groups substituents.

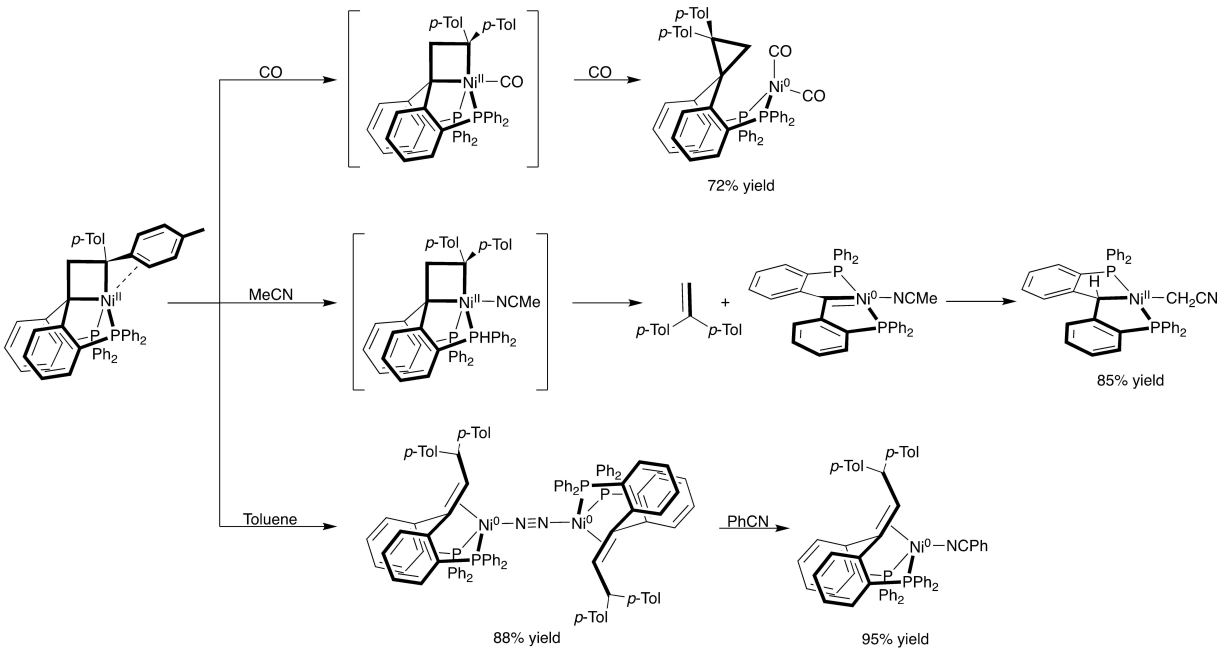
The weak π-interaction with one of the p-tolyl substituents was readily displaced by exogeneous ligands, yielding nickelacyclobutanes with trigonal bipyramidal geometry (Scheme 28). Exposure to the π-accepting ligand CO (1 atm) favored the cyclopropanation pathway: initial coordination of one CO molecule (evidenced by IR and NMR) is followed by reductive elimination to form a cyclopropane ring in a new Ni(0) complex bearing two CO ligands. In contrast, dissolving the nickelacyclobutane in acetonitrile results in a metathesis-like [2 + 2] cycloreversion to form 1,1-diphenylethylene and a new complex resulting from trapping the $PC_{carbene}P$ Ni complex with MeCN via C–H activation. When dissolved in a less coordinating solvent such as toluene, the nickelacyclobutane decomposes to form a new olefin nickel complex. The latter transformation could have suggested a β-hydride elimination/reductive elimination sequence, but a crossover experiment featuring equal amounts of nickelacyclobutane and d^2-nickelacyclobutane supported a complex intermolecular pathway.

4. Conclusions and outlook

The rich chemistry of nickelacyclobutanes and their pivotal role in several Ni-catalyzed transformations creates both challenges and opportunities.

Rationales involving nickelacyclobutane intermediates have been proposed for several efficient synthetic methodologies including cyclopropanations, cycloadditions, and rearrangements. In these catalytic cycles, the nickelacyclobutane is usually formed either by [2 + 2] cycloaddition of an olefin and a nickel-carbene intermediate or by oxidative addition of a cyclopropane derivative. The various reactivity pathways available to nickelacyclobutanes (reductive elimination, insertions, transmetallation) determine the final organic product of the reaction.

In parallel with the development of the abovementioned catalytic reactions, significant progress has been made in the



Scheme 28. Reactivity of pentacoordinated nickelacyclobutane.

observation, characterization, and isolation of nickelacyclobutanes. Non-fluorinated nickelacyclobutanes have been shown to decompose in three main ways: beta hydride/reductive elimination to form a nickel olefin complex, olefin/metathesis, forming an olefin and a nickel carbene and cyclopropanation. Pioneering studies in the gas phase and argon matrix provided evidence for the existence of non-ligated neutral and cationic nickelacyclobutanes that both predominantly decay via [2+2] cycloreversion. Some ligated nickelacyclobutanes showed to be stable enough to be isolated, allowing for a detailed study of their rich reactivity. In particular, several studies showed the impact of the coordination number of the nickelacyclobutane on the product distributions.

Also noteworthy are recent developments in the chemistry of perfluorinated nickelacyclobutanes, which exhibit a markedly different reactivity. Radical pathways were inferred in their formation, and their reactivity is dominated by fluorine shift rearrangements. Remarkably, the formation of perfluorinated nickelacyclobutanes does not follow the Chauvin mechanism; instead, radical processes are involved.

Looking forward, the versatile reactivity of nickelacyclobutanes offers many opportunities for the development of novel catalytic reactions. In particular, the observation of both [2+2] cyclo-additions and -reversions in stoichiometric reactions as well as one catalytic example suggest Ni-catalyzed olefin metathesis as a target of choice. The nucleophilic reactivity observed for isolated Ni carbenes[42b,60] and the fact that certain nickelacyclobutanes are stable enough to be isolated and structurally characterized support the potential feasibility of this reaction. A growing understanding of the dependence of the reactivity of nickelacyclobutanes on their structure will likely allow for better control of their divergent pathways. The design of ligands enforcing specific coordination numbers and geometries will likely be a key aspect to unlock new, selective transformations relying on nickelacyclobutane intermediates.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Keywords: homogeneous catalysis · cyclopropanation · metallacycles · metathesis · nickelacyclobutane

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