Steric Modulation of CAACs Controls Orientation and Ethenolysis Performance

Katrina H. Jensen,[2,*] and Brian W. Michel[1,**]

[1]Department of Chemistry and Biochemistry, University of Denver, Denver, CO, 80210, United States

[2]Department of Chemistry, Black Hills State University, Spearfish, SD, 57799, United States

*Correspondence: Katrina.Jensen@bhsu.edu
**Correspondence: Brian.Michel@du.edu

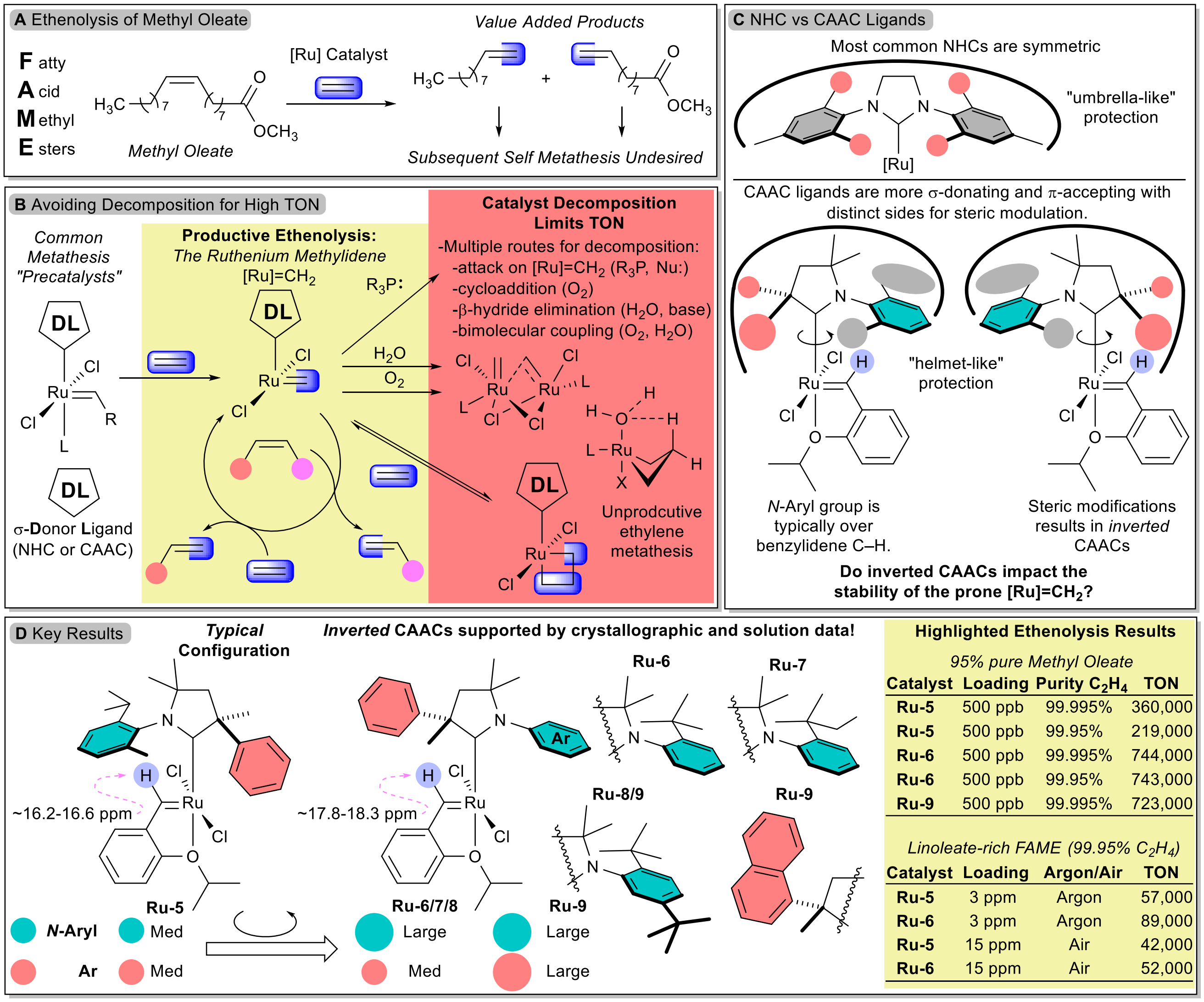
SUMMARY

In this issue of *Chem Catalysis*, Sytniczuk, Kajetanowicz, and Grela report sterically tuned Cyclic(Alkyl)(Amino)Carbene (CAAC) ligands to protect the requisite Ru-methylidene ($[Ru]=CH_2$) intermediate present during ethenolysis of renewable fatty acid methyl esters (FAME). Surprising structural characteristics of the Ru-CAAC complexes resulted in TON up to 740,000 and sub-ppm catalyst loadings.

Ethenolysis of fatty acid methyl esters (FAME) is a promising route for the production of commodity chemicals featuring terminal alkenes from renewal resources, an alternative to the long-standing reliance on petroleum-based sources. Ethenolysis occurs when an internal alkene undergoes cross metathesis with ethylene. For example, Ru-catalyzed ethenolysis of methyl oleate forms 1-decene and methyl 9-decenoate (Figure 1A). Recent approaches suggest these renewable carbon feedstocks can be further broken down via double bond isomerization, followed by further ethenolysis; this repeating sequence eventually leads to fundamental building blocks such as propene.[1,2] To achieve industrially relevant olefin metathesis processes that compete with fossil fuel sources to produce such building blocks, advancements in the ethenolysis process are critical. Achieving a high turn-over number (TON), the theoretical number of substrate molecules converted to product by a single molecule of catalyst, is a key metric towards a viable process. Identifying new ligands that impart high performance and elucidating the key structural features responsible for improving catalyst characteristics will be a central component of achieving this noble goal.

In Ru-catalyzed olefin metathesis the role of the ligands has been and continues to be critical to advancements in the field. The replacement of phosphine ligands with stronger σ-donor *N*-heterocycle carbene (NHC) ligands has directly led to many discoveries with applications in organic synthesis, polymer chemistry, chemical biology, and various industrial applications. One specific benefit of eliminating phosphine ligands has been to avoid phosphine-based decomposition of the key Ru-methylidene ($[Ru]=CH_2$) intermediate (Figure 1B). Despite advances in ligand modulation, a number of pathways have been identified that result in catalyst decomposition from the $[Ru]=CH_2$ and metallocyclobutane species.[3,4] In ethenolysis, protection of these requisite catalytic intermediates that are particularly prone to decomposition remains a challenge to achieving high TONs. Cyclic(Alkyl)(Amino)Carbene (CAAC) ligands have emerged to provide a number of advantages for avoiding decomposition pathways.[5,6] Compared to NHCs, CAACs modulate the electronics of the Ru-center due to their increased σ-donor ability and increased π-backbonding.[7] Additionally, the quaternary carbon provides a more proximal location for steric environment modifications than NHCs (Figure 1C).

In this issue of *Chem Catalysis* Sytniczuk, Kajetanowicz, and Grela have explored the effects of increasing the steric environment imposed by the aryl group of the CAAC leading to high TON for ethenolysis.[8] The authors took a systematic approach starting from known complexes and increasing the size of groups off of the *N*-aryl moiety. Although improved performance is often targeted by synthetic chemists aiming to improve transition metal catalyzed systems, unguided ligand synthesis is a laborious and time-consuming process; if not done purposefully and if the results are not observed by "prepared minds," this significant effort can go unrewarded.



Highlighted Ethenolysis Results

95% pure Methyl Oleate

Catalyst	Loading	Purity C_2H_4	TON
Ru-5	500 ppb	99.995%	360,000
Ru-5	500 ppb	99.95%	219,000
Ru-6	500 ppb	99.995%	744,000
Ru-6	500 ppb	99.95%	743,000
Ru-9	500 ppb	99.995%	723,000

Linoleate-rich FAME (99.95% C_2H_4)

Catalyst	Loading	Argon/Air	TON
Ru-5	3 ppm	Argon	57,000
Ru-6	3 ppm	Argon	89,000
Ru-5	15 ppm	Air	42,000
Ru-6	15 ppm	Air	52,000

Figure 1. Steric modulation of CAAC ligands and influence on FAME ethenolysis.
(A) Ethenolysis of methyl oleate – a major component of FAME.
(B) Summary of mechanistic considerations for ethenolysis reactions and potential routes of decomposition to be avoided for high turnover.
(C) Comparison of the steric protection provided by NHC and CAAC ligands and rotational isomer considerations.
(D) Modifications to the CAAC ligand framework that result in *inverted* configuration and key ethenolysis results under challenge conditions.

The authors synthesized the requisite CAAC precursors as BF_4 salts which were converted to the Grubbs-Bertrand-type complexes bearing a chelating isopropoxy benzylidene (aka Hoveyda-type). Upon characterization two critical and interesting observations were made suggesting an *inverted* orientation of the CAAC relative to the other ligands.

First, the solved crystal structures reported in the present manuscript show that complexes containing some of the sterically more encumbered aryl units have the aryl and alkyl units switched, or *inverted* as compared to the *typical* configuration with the aryl group over the benzylidene ligand and the geminal substituted carbon groups proximal to the chloride ligands (Figure 1D). A notable exception to the *typical* configuration was reported by Mauduit and coworkers, who found both orientations, *vida infra*.[9]

This observation in the solid state is interesting, but ultimately of little relevance in the absence of impacting chemistry occurring in solution. However, a second critical observation supporting *inverted* conformation was made during analysis of the ^{1}H NMR spectra; the authors noted a significant downfield shift in the benzylidene H resonance (i.e. [Ru]=C***H***Ar). As previously noted by Mauduit and coworkers, the shift from

~16-17 ppm range to ~18 ppm can rationally be attributed to the loss of shielding from the aryl ring of the CAAC and taken as evidence of an *inverted* configuration (Figure 1D).[9]

Although seldom discussed in the main text of manuscripts, it is not uncommon to see multiple resonances for the [Ru]=C***H***Ar in CAAC complexes owing to the asymmetric nature of the ligands and diastereomeric rotational conformations.[10] Further there is limited discussion of the possible effects of these rotational isomers on the reaction coordinate. A notable exception, published by Mauduit and coworkers contemporaneously to the submission of this manuscript, describes steric modulation in an effort to influence stereoselectivity using resolved CAAC complexes as catalysts for enantioselective ring-opening cross-metathesis.[9] In that work the *N*-aryl groups were diethylphenyl (DEP) and the modifications were logically focused about the asymmetric quaternary carbon. Their spectroscopic data suggested that most of their complexes preferred the *typical* configuration with the benzylidene proximal to the *N*-aryl group by ~1.1-0.3 kcal/mol. Interestingly, computational results suggest that the main catalytic pathway may initiate from the *inverted* rotational isomer (termed *anti* in their manuscript), which subsequently provides the major stereoisomer of product via a propagating species with the *typical* configuration (termed *syn*). The proposed Curtin-Hammett mechanism may be of significant consequence for Ru-based olefin metathesis. Certainly, the ability to control rotational isomers of Ru-CAAC complexes and catalytic intermediates could impact a number of metathesis applications.

In the context of ethenolysis, an important question remains as to whether the CAAC ligand conformation influences stability of the prone [Ru]=CH_2 intermediate and if this might have beneficial effects for catalyst stability. Sytniczuk, Kajetanowicz, and Grela tackle this question by evaluating catalysts for ethenolysis of prepared methyl oleate (95% pure), a major component of FAME, with ethylene of varying grades. Interestingly, the catalysts bearing a larger *N*-aryl group (**Ru-6**, **Ru-7**, **Ru-8**, and **Ru-9**) and *inverted* orientation gave higher TONs than the reference catalysts (**Ru-4** and **Ru-5**). By going to catalyst loadings as low as 500 ppb, very high TONs over 700,000 were observed! Although conversion is lower, these experiments challenge catalysts to convert as many units of substrate as possible. Notably, selectivity for the desired products remained high, and in some cases improved at low catalyst loadings.

Additional experiments were conducted to further challenge the catalysts. First, parent compounds **Ru-4** and **Ru-5**, were compared to **Ru-6** at low catalyst loadings with both grade 4.5 ethylene (99.9995%) and grade 3.5 ethylene (99.995%), where impurities in the ethylene gas could decompose the prone [Ru]=CH_2 intermediate. While **Ru-4** and **Ru-5** both showed decreased TON with the lower grade ethylene, no reduction in performance was observed for **Ru-6**.

Another set of experiments were conducted challenging **Ru-5** and **Ru-6** using less pure substrate, grade 3.5 ethylene, set up under air or protective argon atmosphere. The reactions set up under air with methyl oleate showed minimal decrease in performance as compared to the protective argon atmosphere. However, the use of linoleate rich FAME (73% methyl oleate, 20% linoleate) significantly reduced the performance of both catalysts, although **Ru-6** still demonstrates significantly higher TON than **Ru-5**. These results are particularly interesting as linoleates are more prone to oxidation due to the presence of weak doubly allylic C-H’s (BDE ~75 kcal/mol).

Empirically it is clear that the increased steric bulk results in more robust catalysis under conditions likely to increase the attractiveness of such processes on an industrial scale. Almost certainly this arises from decreased decomposition of the prone [Ru]=CH_2 intermediate, although the origin of this effect remains to be fully elucidated. Does rapid self-metathesis of ethylene sample both configurations for the [Ru]=CH_2 species or is the *inverted* orientation preferred in this unobserved intermediate? What are the underlying features that block decomposition and which pathways are being inhibited? Could the absence of benzylic hydrogens on the *N*-aryl moieties provide an alternative explanation for enhanced stability?

The exciting performance improvements achieved with CAAC ligands in recent years has stimulated the olefin metathesis community. The work described in this issue of *Chem Catalysis* by Grela and coworkers, along with additional reports described above from others, provides further inspiration. Future synthetic and mechanistic investigations may reveal valuable insight for additional ligand modifications. We find it inspiring that synergy exists within this still vibrant field by researchers who are forging significant new modifications to an increasingly important ligand architecture while targeting disparate applications (green reaction conditions, asymmetric catalysis, and renewable feedstocks). It should be expected for these results to find impact in other applications of olefin metathesis including polymerization chemistry, chemical biology, and sensing applications.

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Declaration of Interests

The authors declare no competing interests.

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