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Cyclic (amino)(barrelene)carbene Ru-complexes: synthesis and reactivity in olefin metathesis†

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The synthesis of ruthenium-complexes with cyclic (amino)(barrelene)carbenes (namely CABCs) as ligands is reported. Isolated in moderate to good yields, these new complexes showed impressive thermal stability at 110 °C over several days. Good catalytic performances were demonstrated in various ring-closing metathesis (RCM), macrocyclic–RCM, ring-closing enyne metathesis (RCEYM), cross-metathesis (CM), and ring-opening cross metathesis (ROCM) reactions.

Considered as an eco-friendly process to build carbon–carbon bonds, olefin metathesis[1] represents one of the most efficient synthetic tools in modern organic chemistry.[2] The recent development of well-defined ruthenium complexes containing a cyclic (alkyl)(amino)carbene, namely the CAAC ligand,[3] led to significant breakthroughs in this field by reaching the highest TONs reported so far (up to 2 600 000 in ethenolysis[4] and 68 000 in RCM[5]). It should be noted that this impressive productivity relies on the improved stability of the corresponding Ru–methylidene species toward bimolecular decomposition.[6] While numerous catalysts bearing five-membered CAACs (called CAAC-5) have been intensively developed through the modification of the *N*-aryl fragment and/or the substituents of the quaternary centre (**Ru-1**, Fig. 1A),[7] the structural variation of the heterocyclic backbone has scarcely been investigated. In 2020, Grubbs and co-workers reported a ruthenium complex containing a six-membered CAAC[8] (CAAC-6; **Ru-2**, Fig. 1A) while Tuba and co-workers described a bicyclic CAAC **Ru-3** complex[9] (BiCAAC, Fig. 1A). Unfortunately, these complexes demonstrated lower catalytic performances than the original **Ru-1** type catalysts. Based on these reports, we decided to examine a new type of CAAC-5 ligand, namely cyclic (amino)(barrelene)carbene or CABC, recently reported in 2022.[10]

Readily accessible through an intramolecular [4 + 2] cycloaddition between an alkyne and an anthracene derivative, this ligand features a barrelene skeleton, which provides a unique steric environment.[10] Herein, we report the synthesis of related CABC–ruthenium complexes (**Ru-4**) and their catalytic performances in various olefin metathesis transformations (Fig. 1B).

We initiated our study by preparing ruthenium CABC complexes **Ru-4a–d** from the corresponding iminium salts of **CABC(a–d)**·X bearing isopropyl, adamantyl, phenyl and mesityl *N*-substituents, respectively (Scheme 1, eqn (1)). To our delight, deprotonation of **CABC(a–d)**·X with potassium hexamethyldisilazide (KHMDS) in toluene followed by reaction with the Hoveyda–Grubbs catalyst 1st generation (**HG1**) over 2 to 16 hours afforded the corresponding CABC **Ru-4a–d** in low

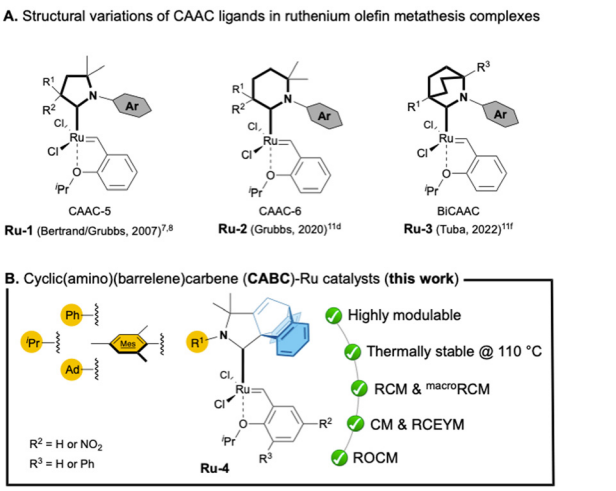

Fig. 1 Structural modifications of CAACs (A) and the development of a new CAAC featuring a barrelene scaffold (B, this work).

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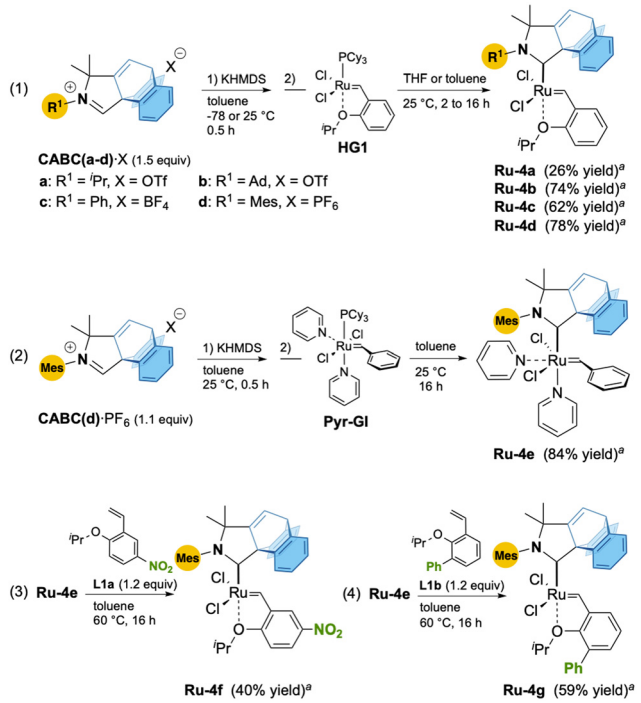


Scheme 1 Synthesis of CABC–ruthenium complexes. [a] Isolated yield.

to good isolated yields (26–78%). Following the same protocol, bis-pyridine **Ru-4e** was isolated in 85% yield from ^{Mes}**CABC (d)**·PF_6 and **Pyr-GI** precursors (Scheme 1, eqn (2)).[11] Finally, the reaction between **Ru-4e** and styrenylether ligands **L1a,b** led to the corresponding nitro-Grela-[12] and Blechert-type[13,14] **Ru-4f** and **Ru-4g** in 40% and 59% yield, respectively (Scheme 1, eqn (3) and (4)).[15]

Suitable crystals of **Ru-4a–d,f** allowed us to perform X-ray diffraction analyses (Fig. 2). Unfortunately, all attempts to obtain suitable crystals for **Ru-4e**,**-4g** were unsuccessful.

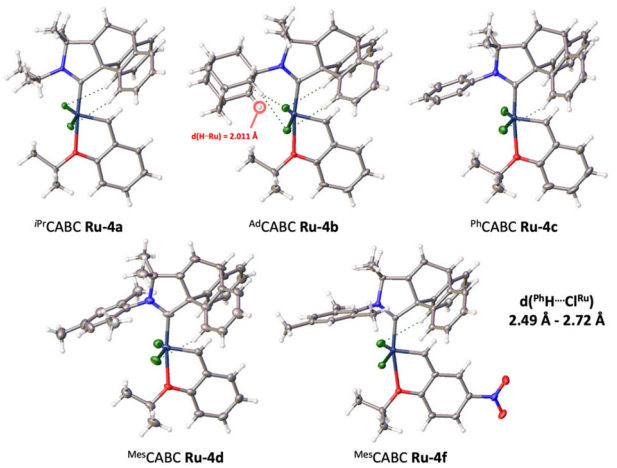


Fig. 2 Solid-state structures of CABC-complexes **Ru-4a–d,-f** from single crystal X-ray diffraction. Displacement ellipsoids are drawn at 30% probability.

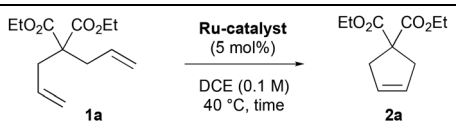
Unexpectedly, the solid-state structures showed that the barrelene fragment is above the styrenylether moiety, in contrast to most of the previously reported CAAC–Ru complexes, for which the *N*-aryl unit is above the styrenylether.[7,16] It is noteworthy that relatively less intramolecular hydrogen bonding interactions were observed between barrelene C^{Ph}–H and Cl^{Ru} atoms (d = 2.49–2.72 Å) across all complexes. It should be noted that for **Ru-4b**, these interactions are also observed in solution as shown by a significant downfield shift of the corresponding proton by ^{1}H NMR spectroscopy with respect to the corresponding iminium salt (see the ESI† for details).

For the adamantyl CABC **Ru-4b**, additional C^{Ad}–H bond interactions lock the chlorine atoms into a constrained configuration, which explains the unusually large Cl–Ru–Cl bond angle ($\measuredangle$ = 154.44°) and the very short intramolecular hydrogen–ruthenium (2.01 Å) distance within the range of classical agostic interactions (≈1.8–2.3 Å). With respect to thermal stability, all complexes are stable to air and moisture as solids. We also studied the stability of ^{Mes}CABC **Ru-4d** at 110 °C in aerated toluene-d_8 solution and observed less than 4% degradation after ten days (see ESI† section 2.2. for further details).

With these results in hand, we next investigated the catalytic performance of all CABC **Ru-4a–g** complexes in the RCM of DEDAM **1a** (Table 1). At 40 °C, poor reactivity was observed with CABC **Ru-4a–d** (1–7% yield, entries 1–4†) after 18 h of reaction at 5 mol% catalyst loading. In comparison, bis-pyridine **Ru-4e** led to 41% yield (entry 5), while the nitro-Grela congener ^{Mes}CABC **Ru-4f** afforded 13% yield (entry 6). In marked contrast, ^{Mes}CABC–Blechert **Ru-4g** afforded higher reactivity, obtaining cyclopentene **2a** in 73% yield (entry 7). Gratifyingly at 110 °C, RCM with **Ru-4g** was completed within 4 hours yielding **2a** in 97% (entry 8) in agreement with the excellent thermal stability of this family of carbene complexes.

Having identified Blechert ^{Mes}CABC **Ru-4g** as the most efficient catalyst, we then investigated its performance in various olefin metathesis transformations under optimised

Table 1 Catalytic performances of CABC **Ru-4a–g** in the RCM of DEDAM **1a**[a]



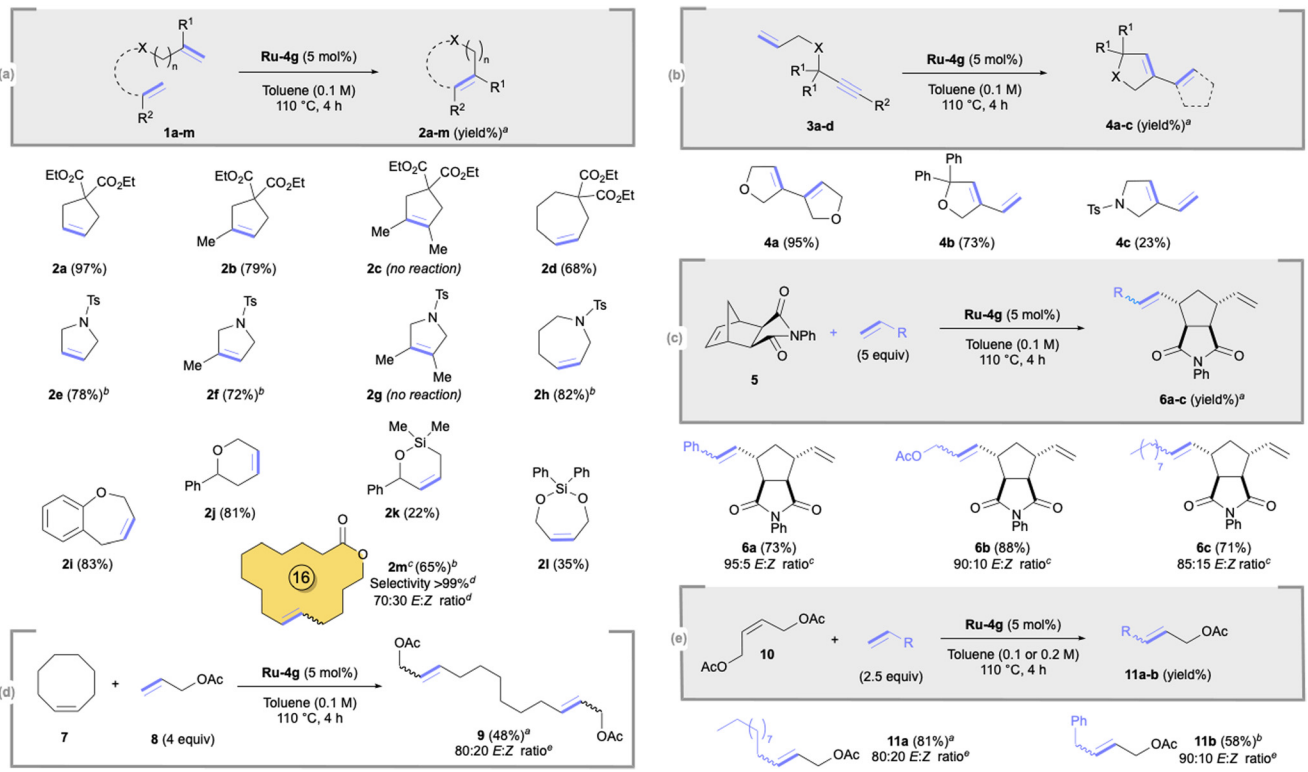
Entry	Catalyst	Time (h)	Conv. (yield)[b](%)
1	**Ru-4a**	18	5 (1)
2	**Ru-4b**	18	3 (2)
3	**Ru-4c**	18	7 (5)
4	**Ru-4d**	18	9 (7)
5	**Ru-4e**	18	45 (41)
6	**Ru-4f**	18	14 (13)
7	**Ru-4g**	18	75 (73)
8[c]	**Ru-4g**	**4**	**99 (97)**

[a] Reaction conditions: DEDAM **1a** (0.17 mmol), catalyst (0.0085 mmol), DCE (1.7 mL), argon. [b] Determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal reference (see the ESI†). [c] Reaction performed in toluene at 110 °C.

conditions (5 mol%, 110 °C; Scheme 2). Di- or tri-substituted cyclopentenes **2a,b,e,f** were formed in good to excellent yields (72–97%). Similar good yields (68–83%) were also observed for seven-membered cycloalkenes **2d,h,i**. However, no reaction occurred for tetrasubstituted cyclopentenes **2c,g** and low 22–35% yields were obtained for silane derivatives **2k,l**. To our delight, **Ru-4g** was also efficient in macroRCM, leading to a valuable odorant[17] 16-membered macrocycle **2m** in 65% yield without any isomerised side product (>99% selectivity).[18] Ring-closing enyne metathesis (RCEYM) was also examined, in which **Ru-4g** demonstrated good activity (73–95%), except for cyclic diene **4c** (23%; Scheme 2b). We next focused on the ring-opening cross-metathesis (ROCM) of *exo*-norbornene **5** and cyclooctene **7** with different cross-olefin partners.

The corresponding *trans*-cyclopentanes **6a,b,c** were formed in good yields (71–88%; Scheme 2c) while acyclic diene **9** was obtained in a moderate 48% yield (Scheme 2d). Lastly, we investigated the catalytic performance of **Ru-4g** in cross-metathesis (CM; Scheme 2e). The reaction between 1-dodecene and *cis*-1,4-diacetoxy-2-butene **8** furnished the corresponding alkene **11a** in 81% yield with an 80 : 20 *E* : *Z* ratio. Nevertheless, a lower 58% yield and a 90 : 10 *E* : *Z* ratio were observed for product **11b** resulting from the CM between homoallyl benzene and allyl acetate **10**.

According to a broadly accepted mechanism (Fig. 3), productive metathesis involves the formation of a transient unsaturated 14e Ru–methylidene ^{syn}**AS** prone to coordinating with incoming alkenes *via* a π-complex intermediate. Subsequent oxidative [2 + 2] cycloaddition results in the formation of a Ru (IV) ruthenacyclobutane which is able to undergo reductive elimination to reform the reactive unsaturated 14e Ru–methylidene ^{anti}**AS** with the elimination of the corresponding product. As shown by Grubbs and others,[1a,19] the configuration of the chlorine atoms around the ruthenium centre is subject to change in order to facilitate this process. Intrigued by the unexpected stability of these complexes and the need for thermal activation (110 °C) with Blechert ^{Mes}CABC **Ru-4g** (see Table 1, entry 8), we performed preliminary DFT studies (density functional theory) at the B3LYP-D3 level of theory. Transient unsaturated 14e-Ru–methylidene intermediates resulting from the Hoveyda–Grubbs **Ru-4a–d** were successfully optimized in the *syn*- and *anti*-configurations (^{syn}**AS-4a–d** and ^{anti}**AS-4a–d** respectively) of the chlorine atoms. In all cases, we found *anti*-configurations to be significantly higher in energy with respect to ^{cis}**AS-4a–d**. This difference is more significant with adamantyl **4b** for which the *anti*-conformer lies significantly above the *syn*-conformer (19.5 kcal mol^{-1}). To better understand these differences, we also considered the steric map profile of these intermediates, which points to a distorted configuration of the chlorine atoms in the *anti*-configuration. Together with the relatively less intramolecular hydrogen bonding interactions observed in the solid state (also more



Scheme 2 Scope of RCM (a), RCEYM (b), ROCM (c and d) and CM (e) catalysed by the Blechert ^{Mes}CABC **Ru-4g** complex. [a] Yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. [b] Isolated yield. [c] Reaction performed at 0.005 M. [d] Determined by GC analysis. [e] *E*/*Z* ratios were monitored by ^{1}H NMR.

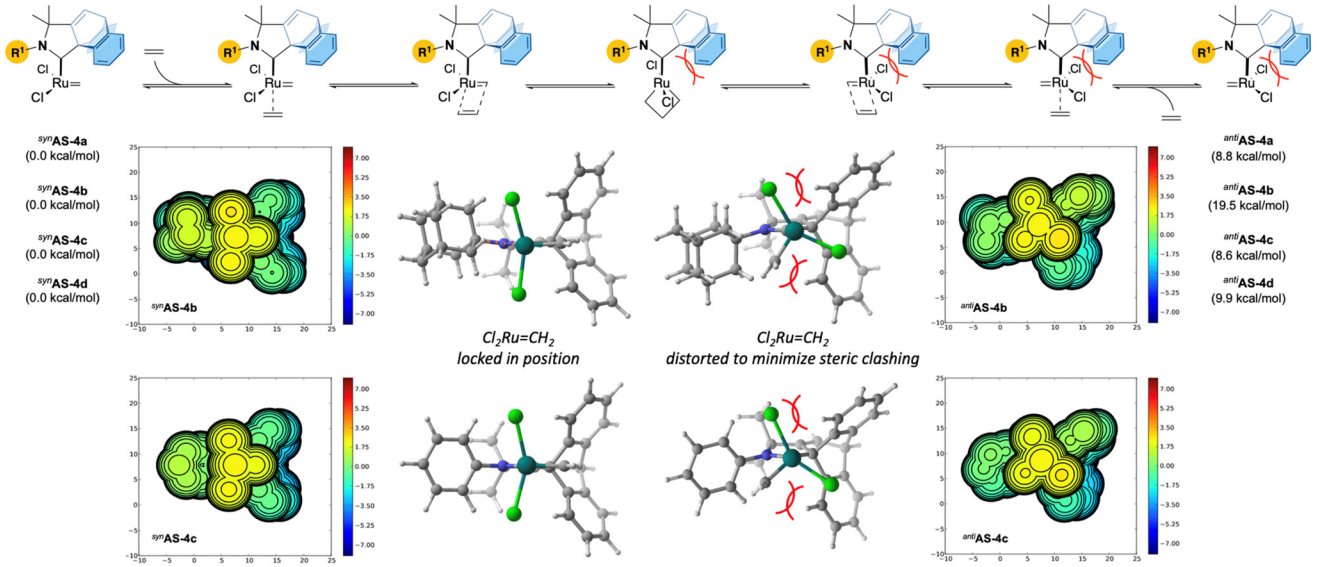


Fig. 3 Preliminary DFT studies (performed at the B3LYP-D3 level of theory) and steric maps highlight the importance of steric crowding during the propagation.

pronounced with adamantyl **4b**), the unusual stability of these complexes points to a mechanical gridlock situation wherein the steric profile of the barrelene clashing with chlorine atoms impairs the metathesis step.

Conclusions

A set of seven new Ru-complexes containing cyclic (amino)(barrelene)carbene (CABC) ligands were synthesized in moderate to good yields and fully characterized. This novel class of complexes demonstrated remarkable thermal stability in solution at 110 °C over 10 days. The Blechert-type ^{Mes}CABC **Ru-4g** was the most efficient, affording good yields in various metathesis reactions (RCM, macroRCM, RCEYM, CM, and ROCM). In addition, DFT calculations provided key insights into the initiation step and the propagating CABC–Ru–methylidene active species, thus explaining why thermal activation is required for this family of olefin metathesis catalysts.

Data availability

All experimental and crystallographic data associated with this work are available in the ESI.†

Author contributions

R. J., G. B. and Ma. M. conceptualized and supervised this work. M. R. S. prepared the CABC precursors. J. T., A. D. V., S. C. R. and J. M. developed the catalytic methodologies. Mo. M. performed the DFT studies and T. R. performed the X-ray diffraction analysis. The manuscript was written by R. J. and Ma. M. and reviewed by all the authors.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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