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Bis[cyclic (alkyl)(amino)carbene] isomers: Stable *trans*-bis(CAAC) *versus* facile olefin formation for *cis*-bis(CAAC)†

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Isomeric bis(aldiminium) salts with a 1,4-cyclohexylene framework were synthesized. The first isolable bis(CAAC) was prepared from the *trans*-stereoisomer and its ditopic ligand competency was proven by conversion to iridium(I) and rhodium(I) complexes. Upon deprotonation, the *cis*-isomer yielded an electron rich olefin *via* a classic, proton-catalyzed pathway. The C═C bond formation from the desired *cis*-bis(CAAC) was shown to be thermodynamically very favorable and to involve a small activation barrier. Compounds that can be described as insertion products of the *cis*-bis(CAAC) into the E–H bonds of NH_3, CH_3CN and H_2O were also identified.

First reported in 2005,[1] cyclic (alkyl)(amino)carbenes (CAACs) have been rapidly incorporated into the main-group and organometallic ligand toolkit. Their exceptional σ-donating and π-accepting abilities led to the isolation of a flurry of compounds of fundamental and applied interest.[2] Prominent examples include homoleptic late transition metal compounds in low oxidation states,[3] main-group and organoradical spin carriers,[4] elements in unusual oxidation states,[5] and high-performing transition metal catalysts.[6] The growing library of accessible CAACs is facilitating steric and electronic profile tuning of their complexes for tailored applications.[7–9] Along with the much used five-membered Me_2CAAC,[1] CyCAACs,[1] and AdCAAC,[10] other examples include CAACs incorporating imine or phosphine pendant arms,[11] six-membered CAAC-6,[12] and bicyclic BiCAACs[13] (Chart 1). The steady expansion of the CAAC library was facilitated by the straightforward access to the respective aldiminium-salt precursors starting from ubiquitous building blocks, *via* an elegant protonation-cyclization-hydroiminiumation sequence reported by Bertrand.[14]

Despite the growing library of CAAC ligands and the tremendous success of bis(NHC)[15] (NHC = *N*-heterocyclic carbene) and bisphosphine analogs,[16] no bis(CAAC) has been reported to date. We reasoned that this notable absence could be remedied in few synthetic steps, by formally derivatizing CyCAAC,[1] which was shown to be a competent ligand. The cyclohexyl scaffold could be used to build two desirable bis(CAAC)s: A bidentate *cis*-stereoisomer and a ditopic *trans*-stereoisomer (Chart 1). Our investigations targeting these derivatives will be reported herein.

Aldiminium precursors **3a** and **4a** were obtained in gram quantities *via* standard CAAC-building protocols,[14] adapted to accommodate the second CAAC moiety (Scheme 1). A commercially available isomeric mixture of cyclohexane-1,4-dimethanols was converted to cyclohexyl-1,4-dicarboxaldehydes and, following condensation with $DippNH_2$ (Dipp = 2,6-diisopropylphenyl), pure *trans*-diimine **1a** could be isolated in 29% overall yield. Double deprotonation of this precursor with *n*-butyllithium followed by reaction of the resulting aza-allyl anion with 3-bromo-2-methylpropene generated *cis*- and *trans*-**2a**, which were isolated as a mixture.

Layering benzene solutions of this mixture with acetonitrile resulted in selective crystallization of *trans*-**2a** as large colorless blocks in 10% yield. This compound was then subjected to the hydroiminiumation procedure, leading to dialdiminium tetrafluoroborate salt **3a**. *cis*-Dialdiminium tetrafluoroborate **4a** was more conveniently obtained by carrying on the hydroiminiumation

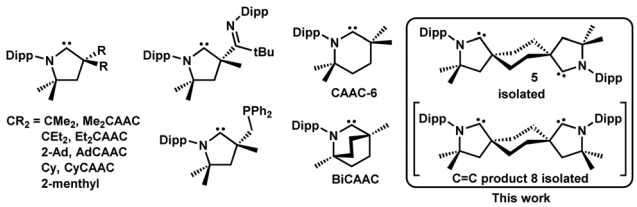

Chart 1 Selected examples of CAACs.

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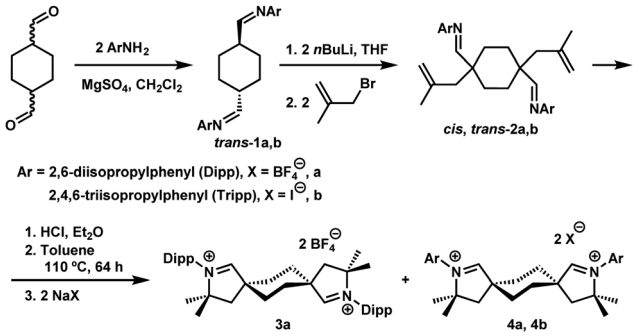
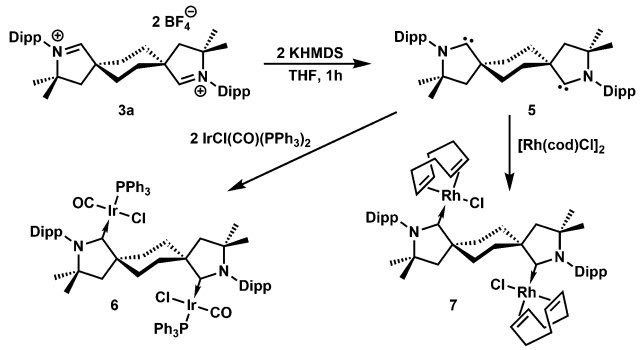


Scheme 1 Succession of reactions leading to the synthesis of bis(CAAC) precursors **3a** and **4a**,**b**.



Scheme 2 Synthesis of free dicarbene **5** and its metal complexes **6** and **7**.

reaction with a mixture of *cis*- and *trans*-**2a.** Extraction of the product mixture with $CHCl_3$ and recrystallization by layering CH_2Cl_2 solutions with hexanes yielded **4a** in 67% yield. The configuration of the aldiminium fragments was readily assessed by ^{1}H NMR, based on coupling patterns for the cyclohexylene linker protons (in CD_2Cl_2, **3a** exhibits two doublet resonances at 1.93 and 2.65 ppm and **4a** features a pair of multiplets at 2.20 and 2.52 ppm), and confirmed by single-crystal X-ray diffraction (Fig. 1).

Addition of two equivalents of potassium hexamethyldisilazide (KHMDS) to *trans*-aldiminium salt **3a** in THF produced the expected dicarbene **5** (Scheme 2 and Fig. 2), displaying a characteristic ^{13}C NMR resonance corresponding to the carbenic carbons at 315.2 ppm in C_6D_6. Under an inert atmosphere, **5** could be handled at room-temperature and no decomposition was observed by ^{1}H NMR after storing the solid at −40 °C for a month. The ditopic nature of **5** was probed *via* reaction with $IrCl(CO)(PPh_3)_2$ or $[Rh(cod)Cl]_2$ in benzene, which yielded complexes **6** (Fig. 3) and **7** (Fig. S67, ESI†), respectively, as yellow, crystalline precipitates. The four ligands in **6** adopt a square planar coordination geometry at iridium, with PPh_3 *trans* to the carbene, as previously observed in analogous $IrCl(CO)(NHC)(PPh_3)$ complexes.[17] The spectral signature of **6** ($\delta_{carbene}$ 255 ppm, δ_{CO} 174 ppm, δ_P 22 ppm, ν_{CO} 1950 cm^{-1}) is also similar to that of $IrCl(CO)(NHC)(PPh_3)$ ($\delta_{carbene}$ 178 ppm, δ_{CO} 171 ppm, δ_P 25 ppm, ν_{CO} 1945 cm^{-1}).[17]

Addition of two equivalents of Et_3N, iPr_2NEt, LiHMDS, LDA, MeLi or Me_3SiCH_2Li to a suspension **4a** in THF of led to intractable mixtures. When lithium-2,2,6,6-tetramethylpiperidide (LiTMP) was employed, an elimination reaction took place, regenerating *cis*-**2a.** A similar behavior was reported by Bertrand for CAAC-6.[12] Immediately upon addition of two equivalents of KHMDS to **4a** at −78 °C, (Fig. S55 and S56, ESI†), a singlet resonance was detected at

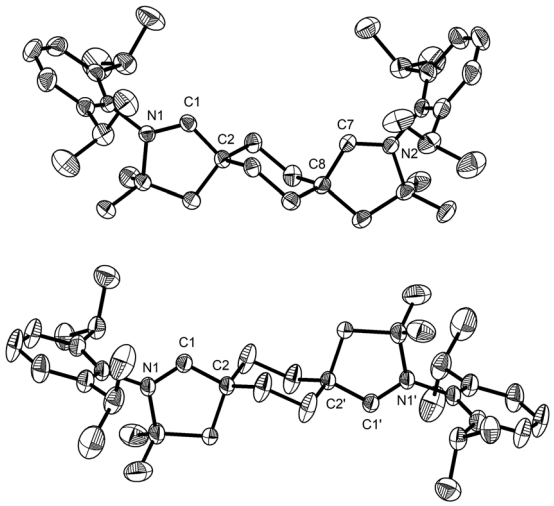


Fig. 1 Solid-state structures of the dications in **3a** (top) and **4a** (bottom) with 50% probability ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths [Å] and angles [°]: **3a**: C1–N1 1.272(4), C1–C2 1.491(4); N1–C1–C2 114.7(2); **4a**: C1–N1 1.275(2), C1–C2 1.482(3); N1–C1–C2 114.76(17).

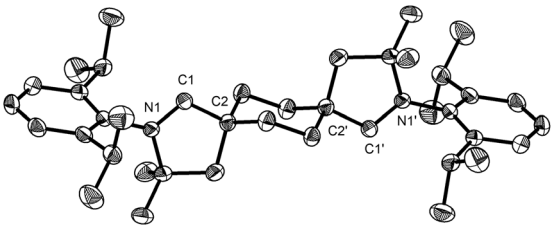


Fig. 2 Solid-state structure of **5** with 50% probability thermal ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths [Å] and angles [°]: N1–C1 1.3065(16), C1–C2 1.5232(17); N1–C1–C2 105.92(10).

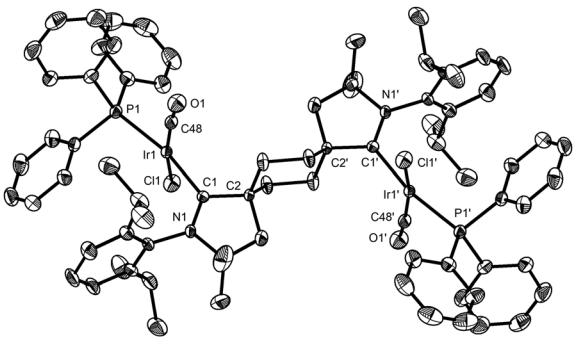
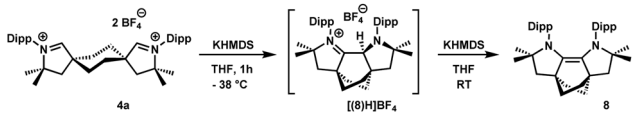


Fig. 3 Solid-state structure of **6** with 50% probability thermal ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths [Å] and angles [°]: Ir1–C1 2.035(3), Ir1–P1 2.3111(8), O1–C48 1.100(3), C1–Ir1–P1 168.68(7), C48–Ir1–Cl1 168.69(9), N1–C1–C2 109.3(2).



Scheme 3 Synthesis of **8** *via* [(**8**)H]BF_4.

318.0 ppm by ^{13}C NMR, suggesting the formation of a CAAC. It rapidly disappeared upon warming to −38 °C with concurrent emergence of a new set of resonances suggestive of a less symmetric compound. In the ^{1}H NMR spectrum, a singlet at 5.08 ppm, within the range observed for protonated NHC-CAAC dimers (4.90–5.32 ppm in CD_3CN;[18] 4.58, 4.72 ppm in $CDCl_3$),[19] was assigned to the protonated olefin intermediate [(**8**)*H*]BF_4 (Scheme 3). Ultimately, warming up the mixture to room temperature led to the formation of a higher-symmetry compound, confirmed *via* X-ray crystallography to be olefin **8** (Fig. S68, ESI†); whole-molecule disorder precluded a detailed discussion of bonding parameters. Similar electron-rich olefins were recently reported by Sarkar.[20] Solutions of **8** in toluene were stable up to 110 °C and the solid could be handled in air. The substantial steric crowding in **8** forces the nitrogen atoms to become pyramidalized (sum of nitrogen bond angles 351.4(4)°). Furthermore, two methyl groups within the Dipp fragments are forced into close proximity to the opposing aryl ring, giving rise to a strongly shielded ^{1}H NMR resonance at −0.02 ppm.

DFT studies showed that, upon single deprotonation of **4a** to a free mono-CAAC, the cyclohexane backbone readily changes conformation from chair to twist boat ($\Delta G^{\ddagger}_{\text{c-tb}}$ = 24 kJ mol^{-1}, Fig. S72, ESI†). A second conformational change from twist boat to boat, accompanied by the formation of a C–C bond to give [**8**(H)]$^+$, is similarly facile ($\Delta G^{\ddagger}_{\text{tb-b}}$ = 12 kJ mol^{-1}). The two-step transformation is overall exergonic (ΔG = −72 kJ mol^{-1}) and expected to take place rapidly even at −38 °C due to the associated small energy barriers. The calculated ^{1}H NMR chemical shifts of [**8**(H)]$^+$ are in good agreement with the experimental values, with a characteristic singlet at 5.91 ppm *vs.* 5.08 ppm observed experimentally for the protonated olefin. A hypothetical *cis*-bis(CAAC) resulting from double deprotonation of **4a** gave a potential energy surface similar to single deprotonation, with greater energy barriers for conformational changes of the cylochexane ring ($\Delta G^{\ddagger}_{\text{c-tb}}$ = 52 and $\Delta G^{\ddagger}_{\text{tb-b}}$ = 40 kJ mol^{-1}, Fig. S73, ESI†). This likely stems from the increased repulsion associated with two carbon atoms with lone pairs. The formation of **8** from the *cis*-bis(CAAC) is overall highly exergonic (ΔG = −262 kJ mol^{-1}) as a C═C double bond is formed between the two carbenic carbon atoms.

The calculations support the intermediacy of [**8**(H)]BF_4 en route from **4a** to **8**. Furthermore, even though double deprotonation of **4a** could take place prior to conformational changes, the energy barriers associated with the cyclohexane ring flip are minor. This suggests that the *cis*-bis(CAAC) species obtained *via* double deprotonation of **4a** is not isolable under any conditions. While these results might initially seem surprising, they become less so upon comparison with data calculated for the dimerization of Me_2CAAC, which show ΔG_{dimer} = −75 and −99 kJ mol^{-1} for *cis* and *trans* product geometries, respectively. Thus, dimerization of two CAACs is always thermodynamically favored but generally kinetically blocked by very high activation barriers ($\Delta G^{\ddagger}_{cis}$ = 189 and $\Delta G^{\ddagger}_{trans}$ = 188 kJ mol^{-1}) that arise in large part from the entropic penalty of dimerization ($-T\Delta S$ = 81 kJ mol^{-1}). No such penalty exists when the two CAAC moieties are part of the same molecule, which supports the facile formation of **8**.

Cyclic voltammetry of **8** in THF revealed two reversible redox waves ($E_{1/2}$ = −0.32 and 0.49 *vs.* Fc/Fc$^+$, Fig. S59, ESI†), corresponding to the oxidation of **8** to its radical cation and further to the dication, respectively. Both oxidations are anodically-shifted in comparison to the values reported by Sarkar,[20] potentially due to the inductive effect of the *N*-aryl substituent in **8** leading to a less electron rich system. The C_2-symmetric radical cation was isolated as purple tetrafluoroborate salt **9** following the oxidation of **8** with [Ph_3C][BF_4]. It was characterized by EPR (Fig. S60, ESI†) and its structure was confirmed by X-ray crystallography (Fig. 4).

Attempting to destabilize the electron rich olefin **8** in favor of a free *cis*-bis(CAAC), the Dipp substituents in **4a** were replaced with Tripp (2,4,6-triisopropylphenyl) (Scheme 1). However, deprotonation of **4b** also led to C═C bond formation and this chemistry will not be detailed here. We then turned our attention to complex formation directly from **4a**, by employing metal reagents featuring Brønsted-basic ligands (Scheme 4). The reaction of NHC salt precursors with Cu_2O or Ag_2O to yield the corresponding metal complexes has been extensively explored.[21] Extrapolation of this method to CAACs is less common,[22] arguably due to the weaker acidity of aldiminium-CAAC salts. Heating an acetonitrile solution of **4a** with Cu_2O over several days in an NMR tube resulted in crystallization of colorless blocks that were identified as ether **12** by single-crystal X-ray diffraction (Fig. S71, ESI†). The structure is reminiscent of the $(Me_2CAACH)_2O$ ether obtained as a side-product while preparing $(Me_2CAAC)_2Ge$.[23] Refluxing **4a** and $Fe(HMDS)_2$ in acetonitrile led to crystallization of **11** (Fig. S65, ESI†). The presence of $(Me_3Si)_2NH$ in the NMR of the product mixture suggests that deprotonation may indeed take place. However, scaling up the reaction led to the isolation of **10** instead (Fig. S70, ESI†). The origin of the nitrogen atom is presumably $(Me_3Si)_2NH$, a byproduct from the reaction of $Fe(HMDS)_2$

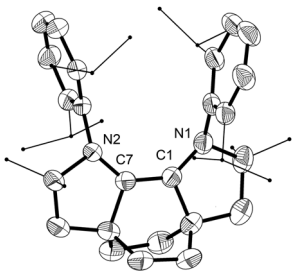
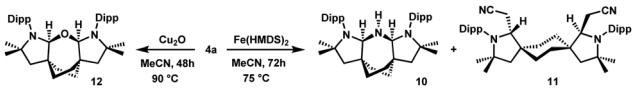


Fig. 4 Solid-state structure of the cation in **9** with 50% thermal ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths (Å) and angles (°): C1–C7 1.409(3), C1–N1 1.357(3), C7–N2 1.360(3).



Scheme 4 Reactivity of **4a** towards transition metal complexes with Brønsted-basic ligands.

and **4a**. Attempted complex formation using $Ca(HMDS)_2$, $Mg(SiTMS_3)_2$, $Pd(OAc)_2$, or $[PtMe_2(\mu\text{-}SMe_2)]_2$ gave intractable mixtures.

In conclusion, two isomeric CAAC-aldiiminium salts **3a** and **4a**, derived from the same parent aldehydes, were synthesized on multi-gram scale. *trans*-Stereoisomer **3a** was doubly deprotonated to yield the first isolable bis(CAAC) **5**, which proved to easily form dinuclear metal complexes, as exemplified by iridium complex **6** and rhodium complex **7**. Upon double deprotonation with KHMDS, *cis*-stereoisomer **4a** formed the electron-rich olefin **8**. Experimental and computational studies suggest the process follows the classic Lewis-acid catalyzed NHC dimerization pathway. DFT calculations showed that the intramolecular C═C bond formation in a free *cis*-bis(CAAC) derived from **4a** is highly exergonic (-262 kJ mol^{-1} *vs.* -75 kJ mol^{-1} for *cis*-dimerization of Me_2CAAC) and involves, for entropic reasons, a small activation barrier that can be lowered even more by proton catalysis. Reaction of **4a** with metal complexes featuring Brønsted-basic ligands led to the identification of **10**, **11**, and **12**, which can be described as insertion products of a bis(CAAC) into the N–H, C–H and O–H bonds of NH_3, CH_3CN and H_2O, respectively. Whether their formation involves a free CAAC intermediate that has been observed at low-temperature by NMR, as described for mono(CAAC)s,[24] or the transient formation of metal complexes, remains to be investigated. 17 years after the first report of a CAAC ligand, our study adds the first bis(CAAC) ligand to the organometallic toolkit.

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Conflicts of interest

There are no conflicts to declare.

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