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Cite this: DOI: 10.1039/c8cc08911f

Dioxygen activation with stable N-heterocyclic carbenes†

Jinghua Tang,‡[ab] Xuejiao J. Gao, ‡[c] Huarong Tang*[b] and Xiaoming Zeng *[ab]

Received 8th November 2018,
Accepted 10th January 2019

DOI: 10.1039/c8cc08911f

rsc.li/chemcomm

Dioxygen activation with both cyclic (amino)(alkyl)carbenes and di(amino)carbenes at ambient temperature is described. Theoretical studies suggest that electron rearrangement from the doubly filled σ orbital of carbene carbon to its vacant p orbital through the π* antibonding orbital of $^3O_2$ can be considered for $C_{carbene}$–O bond formation.

Dioxygen is essential for life. Its reaction plays a crucial role in various fundamental biological processes and industrial chemistry. Dioxygen activation in nature is mainly achieved by metalloenzyme complexes.[1,2] Artificial chemical mimics using electronically and coordinatively unsaturated transition metal complexes have been widely adopted, and readily proved their usefulness as reactants in applications throughout academia and the chemical industry.[3–5] Although main-group elements possess different electronic properties as compared to transition metals, these organic motifs show appealing reactivities like transition metal complexes in the activation of small molecules such as H_2, NH_3, C_2H_4 and CO_2.[6–9] In contrast, the interaction of ground-state molecular dioxygen ($^3O_2$) with main-group compounds has rarely been explored, although it is well known that many organic structural motifs are sensitive to an air atmosphere. Striking results recently highlighted N-heterocyclic carbene (NHC)-stabilized disilicon **II**,[10] diphosphorus **III**[11] and silylenes **I**[12] showing unique reactivity in the activation of $^3O_2$, as well as using siloxysilylene **IV**[13–16] and frustrated Lewis pair **V**[17] (Fig. 1). To our knowledge, there are no reports of reactions of $^3O_2$ with stable, and readily available NHCs, and the relevant reactivity remains largely unknown,[18–20] despite the fact that a thermal reaction with a prototypic persistent carbene has been observed by irradiation of phenylchlorodiazirine under an argon atmosphere containing $^3O_2$ at low temperature (35 K).[21]

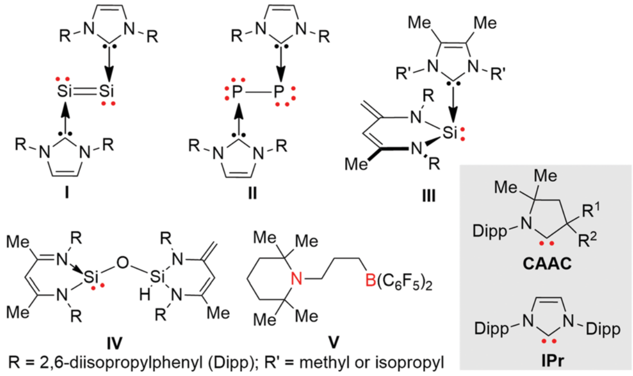

Fig. 1 Selected examples of activation of molecular dioxygen with main-group element compounds.

Stable NHCs possess a lone pair of valence electrons and an accessible vacant p orbital, which endow them with unique reactivity in reactions with small molecules serving as good σ-electron-donors and π-electron-acceptors.[22–25] Remarkable achievements include the activation of hydrogen and ammonia using cyclic (amino)(alkyl)carbenes (CAACs)[26,27] and *N*,*N*′-diamidocarbenes.[28] In contrast to the treatment with excited dioxygen ($^1O_2$), the reaction between $^3O_2$ and singlet carbene suffers from a formidable spin-forbidden obstacle. Mechanistic exploration for interpreting plausible pathways in the reaction would be theoretically appealing. Herein, we report that dioxygen activation was enabled by stable, singlet and readily available cyclic mono(amino)carbenes (CAACs)[29] and 1,3-bis(2,6-diisopropylphenyl)-1,3-dihydro-2*H*-imidazol-2-ylidene (IPr) at ambient temperature, forming the related lactam and cyclic urea derivatives through a formal oxygenation (Fig. 1).

By bubbling dioxygen (99.999% purity) in a tetrahydrofuran (THF) solution containing CAACs (**1** with 1-(2,6-diisopropylphenyl)-3,3,5,5-tetramethylpyrrolidine-2-ylidene (^{Me}CAAC), **2** with

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[a] *Frontier Institute of Science and Technology, Xi'an Jiaotong University, Xi'an 710054, China. E-mail: zengxiaoming@scu.edu.cn*
[b] *College of Chemistry and School of International Studies, Sichuan University, Chengdu 610064, China. E-mail: tanghuarong@scu.edu.cn*
[c] *College of Chemistry and Chemical Engineering, Jiangxi Normal University, Nanchang 330022, China*

† Electronic supplementary information (ESI) available. CCDC 1539794. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8cc08911f

‡ J. Tang and X. J. Gao contributed equally.

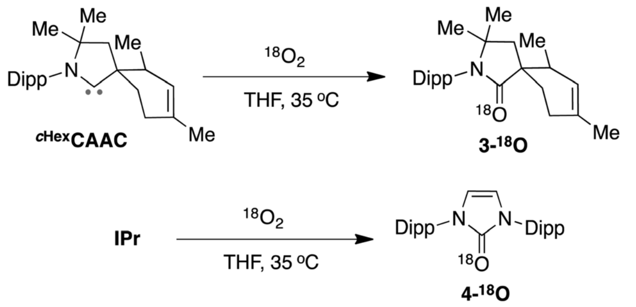
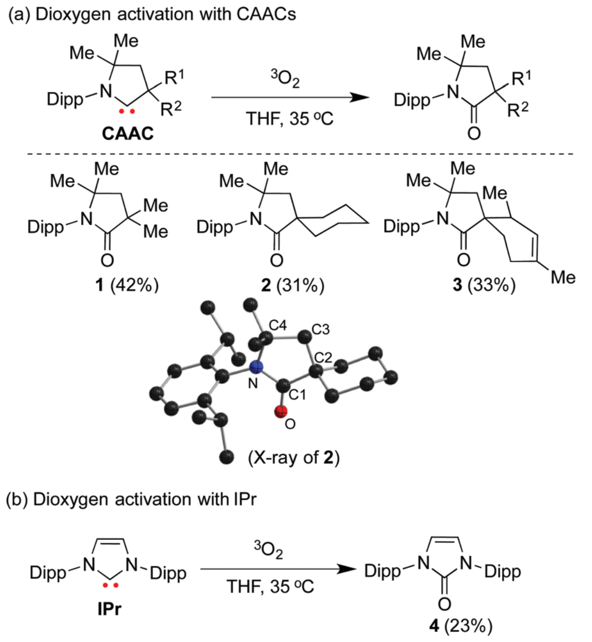


Fig. 2 The reactions between stable and readily available N-heterocyclic carbenes with molecular dioxygen.

2-(2,6-diisopropylphenyl)-3,3-dimethyl-2-azaspiro[4,5]decan-1-ylidene (^{Cy}CAAC), and **3** with 2-(2,6-diisopropylphenyl)-3,3,6,8-tetramethyl-2-azaspiro[4,5]dec-7-ene-1-ylidene (^{cHex}CAAC)[30]), the lactams of **1**, **2**, and **3** were formed in 20–45% yields at 35 °C (Fig. 2a). Their compositions were corroborated by carbon nuclear magnetic resonance (^{13}C NMR) singlet resonances with the appearance of characteristic chemical signals at 179.5 ppm (**1**), 179.1 ppm (**2**), and 177.1 ppm (**3**) for the corresponding carbon signals of the C=O moieties. These were shifted dramatically upfield by $\Delta\delta$ of 124–143 ppm compared with that of free carbenes. The characteristic absorption bands in the infrared spectra for the C=O groups were observed at 1677, 1676, and 1675 cm^{-1}, respectively. The molecular structure of lactam **2** was confirmed by crystallographic analysis (Fig. 2b). The pyrrole ring in **2** adopts a slightly twisted conformation (twist angle τ = 14.2°) with an out-of-plane C2–C3–C4 fragment on the five-membered ring backbone.

Inspired by these results, we then turned our attention to examining the possibility of the activation of $^3O_2$ with cyclic di(amino)carbene. We were delighted to find that oxygenation using stable, commercially available IPr proceeded smoothly by bubbling $^3O_2$ into a THF solution, resulting in the formation of cyclic urea **4** in 34% isolated yield (Fig. 2). It showed a characteristic absorption band for the C=O group at 1676 cm^{-1} in the infrared spectrum and the related carbon signals at 152.1 ppm in the ^{13}C NMR spectrum. When saturated 1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene (SIPr) was, instead, conducted by bubbling $^3O_2$ into THF, the related carbene-oxo adduct was not detected by *in situ* NMR and GC-MS analyses (see ESI†).

To confirm that the oxygen moiety on the lactam and cyclic urea derivatives was produced from molecular dioxygen, ^{18}O labeling experiments were performed by vigorously stirring a THF solution containing free carbenes of ^{cHex}CAAC or IPr under an atmosphere of $^{18}O_2$ (>99% purity). The corresponding products were isolated and characterized by a high-resolution mass spectrometer, showing major peaks at 370.2988 and 407.2921 *m*/*z*, which are consistent with the molecular weights of **3-^{18}O** and **4-^{18}O**, respectively (Scheme 1). This suggests that the ^{18}O of molecular dioxygen was introduced into the scaffolds of the free carbenes (^{cHex}CAAC and IPr).



Scheme 1 ^{18}O-Labelling experiments.

To gain mechanistic insight into the bonding model involving dioxygen activation with singlet NHCs and plot the energy profiles of the possible pathways, we performed density functional theory (DFT) calculations by choosing the reaction of ^{cHex}CAAC with $^3O_2$ as a model. As shown in Fig. 3a and b, ^{cHex}CAAC initially employs its lone pair to interact with the frontier orbitals of $^3O_2$, forming an intermediate ^{3}**Int1** through the transition state ^{3}**TS1** by overcoming the activation energy barrier of 21.9 kcal mol^{-1}. Subsequently, an intersystem crossing (ISC) process can be considered with an exothermicity of 2.5 kcal mol^{-1} to give the intermediate ^{1}**Int1**. Such an ISC process is rationalized by a potential energy surface across S0 and T1 (please see ESI† for details). Without the ISC pathway, the following cleavage of the oxygen–oxygen bond by the reaction with another molecule of ^{cHex}CAAC is proved to be thermodynamically unfavorable in the formation of the lactam because of the high activation barrier (68.9 kcal mol^{-1}). Compared with a continuous reaction with another molecular ^{cHex}CAAC, the homo-interaction with ^{1}**Int1** itself overcomes a relatively low reaction energy (21.9 *versus* 27.9 kcal mol^{-1}) in the formation of the related lactam product combined with a release of $^1O_2$. On the other hand, the reaction of ^{cHex}CAAC with excited state dioxygen ($^1O_2$) allows the straightforward formation of ^{1}**Int1** by overcoming a low activation energy of 5.7 kcal mol^{-1}.

Fig. 4a shows the geometric structure of ^{3}**Ts1**. For clarity, the schematic orbital interactions between the two singly occupied molecular orbitals (SOMO), *i.e.* the π_{2p_z}* and π_{2p_y}* orbitals of $^3O_2$, the empty 2p$_z$ and the doubly occupied sp^2 orbitals of carbene carbon of ^{cHex}CAAC are shown in Fig. 4b. The π_{2p_z}* and π_{2p_y}* orbitals of $^3O_2$ are vertically arranged, as well as the empty 2p$_z$ and doubly occupied sp^2 orbitals of the carbene carbon of ^{cHex}CAAC. The π_{2p_z}* and π_{2p_y}* orbitals of $^3O_2$ overlap with the

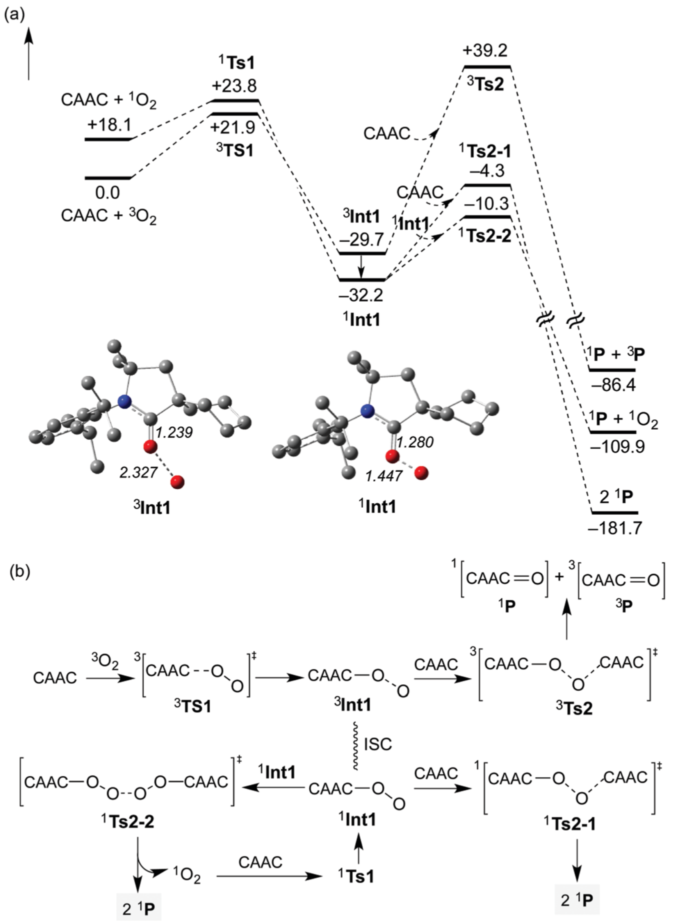


Fig. 3 Relative energy profiles for possible pathways of the reaction of $^3O_2$ with ^{cHex}CAAC (represented by CAAC), and selected frontier molecular orbitals for transition states of ^{3}**TS1**. (a) Energy profiles for the oxygenation of ^{cHex}CAAC. Bond distances (Å) are given in the structure drawings. (b) Possible pathways for the oxygenation of ^{cHex}CAAC.

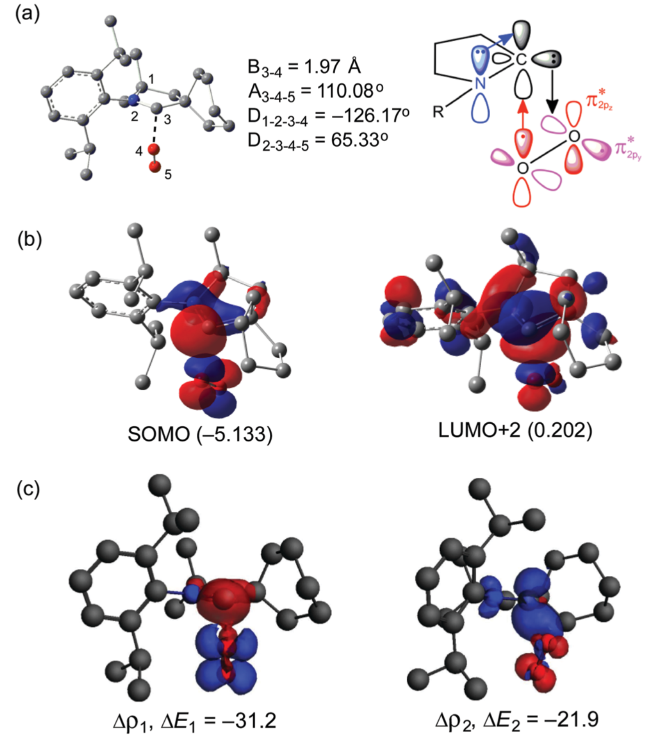


Fig. 4 (a) The geometric structure of ^{3}**Ts1** with key bond lengths, angles and dihedrals that are labelled. The schematic orbital interactions between $^3O_2$ and ^{cHex}CAAC. (b) Calculated ^{cHex}CAAC–$^3O_2$ interaction frontier molecular orbitals, SOMO and LUMO+2, of ^{3}**TS1**. Computed energies (in parentheses) are given in electronvolt. (c) Plot of deformation densities ($\Delta\rho_1$ and $\Delta\rho_2$) of the orbital interaction between ^{cHex}CAAC and $^3O_2$ in ^{3}**TS1** with the corresponding interaction energies (ΔE (kcal mol^{-1})).

$2p_z$ and sp^2 orbitals of carbene carbon, respectively, which corresponds to the interactions illustrated by the SOMO and LUMO+2 of ^{3}**Ts1** (Fig. 4c).

The nature of the electronic interaction between ^{cHex}CAAC and $^3O_2$ was further analysed by extended transition state analysis combined with natural orbitals for chemical valence (ETS-NOCV).[31] Fig. 4b shows that the differential densities corresponding to the interactions contribute the most to the bonding between $^3O_2$ and ^{cHex}CAAC in ^{3}**Ts1**. It was found that the charge flows from the red to the blue area. This can be ascribed to electron density transfer from the doubly occupied σ orbital of ^{cHex}CAAC to one of the π* antibonding orbitals of $^3O_2$ and back donation from the π* antibonding orbitals of $^3O_2$ to the unoccupied p orbital of ^{cHex}CAAC, respectively. The former is the dominating interaction, having the interaction energy of −31.2 kcal mol^{-1}. The results of these theoretical studies indicate that electron rearrangement from the σ orbital of the carbene centre into one of the π* antibonding orbitals of $^3O_2$ essentially contributes to the formation of the lactam σ bond in ^{3}**Int1**. The electron density may then flow into the unoccupied p orbital of the carbene carbon, contributing to the formation of the lactam π bond.

In conclusion, we developed an oxygenation reaction by the activation of molecular dioxygen with stable, readily available NHCs. The strong nucleophilicity and electrophilicity of these singlet carbenes possessing electron-donating and electron-accepting frontier orbitals endow them with the unique ability to break the oxygen–oxygen bonds at ambient temperature.[32–34] This finding explains why such stable NHCs are sensitive to air in organic media and provides an entry to form pyrrolidinones and imidazolones by the use of molecular dioxygen as a "green" oxidant. It demonstrates that NHCs are able to serve as mimics of complexes toward the activation of molecular dioxygen, just as a transition metal function.[6]

Support for this work by NSFC (No. 21202128 and 21572175), the State Key Laboratory of Elemento-organic Chemistry (Nankai University), the Beijing National Laboratory for Molecular Sciences and the SCU is gratefully acknowledged. We thank Prof. Xingfa Gao (JXNU) for the help in calculations and Prof. Gernot Frenking (PUM) for valuable suggestions.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 B. J. Wallar and J. D. Lipscomb, *Chem. Rev.*, 1996, **96**, 2625–2657.
2 W. Nam, *Acc. Chem. Res.*, 2007, **40**, 465–634.
3 M. Costas, M. P. Mehn, M. P. Jensen and L. Que Jr., *Chem. Rev.*, 2004, **104**, 939–986.
4 C. E. MacBeth, A. P. Golombek, V. G. Young Jr, C. Yang, K. Kuczera, M. P. Hendrich and A. S. Borovik, *Science*, 2000, **289**, 938–941.
5 M. T. Kieber-Emmons and C. G. Riordan, *Acc. Chem. Res.*, 2007, **40**, 618–625.
6 P. P. Power, *Nature*, 2010, **463**, 171–177.
7 D. Martin, M. Soleilhavoup and G. Bertrand, *Chem. Sci.*, 2011, **2**, 389–399.
8 D. W. Stephan and G. Erker, *Angew. Chem., Int. Ed.*, 2015, **54**, 6400–6441.
9 S. K. Mandal and H. W. Roesky, *Acc. Chem. Res.*, 2012, **45**, 298–307.
10 Y. Wang, M. Chen, Y. Xie, P. Wei, H. F. Schaefer III, P. V. R. Schleyer and G. H. Robinson, *Nat. Chem.*, 2015, **7**, 509–513.
11 Y. Wang, Y. Xie, P. Wei, H. F. Schaefer III, P. V. R. Schleyer and G. H. Robinson, *J. Am. Chem. Soc.*, 2013, **135**, 19139–19142.
12 Y. Xiong, S. Yao, R. Müller, M. Kaupp and M. Driess, *Nat. Chem.*, 2010, **2**, 577–580.
13 S. Yao, Y. Xiong, M. Brym and M. Driess, *J. Am. Chem. Soc.*, 2007, **129**, 7268–7269.
14 H. Bornemann and W. Sander, *J. Am. Chem. Soc.*, 2000, **122**, 6727–6734.
15 H. Cui, J. Zhang, Y. Tao and C. Cui, *Inorg. Chem.*, 2016, **55**, 46–50.
16 R. Rodriguez, D. Gau, T. Troadec, N. Saffon-Merceron, V. Branchadell, A. Baceiredo and T. A. Kato, *Angew. Chem., Int. Ed.*, 2013, **52**, 8980–8983.
17 T. Wang, G. Kehr, L. Liu, S. Grimme, C. G. Daniliuc and G. Erker, *J. Am. Chem. Soc.*, 2016, **138**, 4302–4305.
18 A. Igau, H. Grützmacher, A. Baceiredo and G. Bertrand, *J. Am. Chem. Soc.*, 1988, **110**, 6463–6466.
19 A. J. Arduengo, R. L. Harlow and M. Kline, *J. Am. Chem. Soc.*, 1991, **113**, 361–363.
20 Y. Wang and G. H. Robinson, *Inorg. Chem.*, 2014, **53**, 11815–11832.
21 G. A. Ganzer, R. S. Sheridan and M. T. H. Liu, *J. Am. Chem. Soc.*, 1986, **108**, 1517–1520.
22 A. J. Arduengo and G. Bertrand, *Chem. Rev.*, 2009, **109**, 3209–3210.
23 M. N. Hopkinson, C. Richter, M. Schedler and F. Glorius, *Nature*, 2014, **510**, 485–496.
24 M. Soleilhavoup and G. Bertrand, *Acc. Chem. Res.*, 2015, **48**, 256–266.
25 J. P. Moerdyk, D. Schilter and C. W. Bielawski, *Acc. Chem. Res.*, 2016, **49**, 1458–1468.
26 G. D. Frey, V. Lavallo, B. Donnadieu, W. W. Schoeller and G. Bertrand, *Science*, 2007, **316**, 439–441.
27 M. Melaimi, R. Jazzar, M. Soleilhavoup and G. Bertrand, *Angew. Chem., Int. Ed.*, 2017, **56**, 10046–10068.
28 T. W. Hudnall, J. P. Moerdyk and C. W. Bielawski, *Chem. Commun.*, 2010, **46**, 4288–4290.
29 V. Lavallo, Y. Canac, C. Präsang, B. Donnadieu and G. Bertrand, *Angew. Chem., Int. Ed.*, 2005, **44**, 5705–5709.
30 X. Zeng, G. D. Frey, R. Kinjo, B. Donnadieu and G. Bertrand, *J. Am. Chem. Soc.*, 2009, **131**, 8690–8696.
31 S. Grimme, S. Ehrilich and L. Goerigk, *J. Comput. Chem.*, 2001, **32**, 1456–1465.
32 D. Martin, N. Lassauque, B. Donnadieu and G. Bertrand, *Angew. Chem., Int. Ed.*, 2012, **51**, 6172–6175.
33 A. Fürstner, M. Alcarazo, H. Krause and C. W. Lehmann, *J. Am. Chem. Soc.*, 2007, **129**, 12676–12677.
34 B. Rao, H. Tang, X. Zeng, L. Liu, M. Melaimi and G. Bertrand, *Angew. Chem., Int. Ed.*, 2015, **54**, 14915–14919.