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A Heterogeneous Iridium Single Atom Site Catalyst for Highly Regioselective Carbenoid O-H Bond Insertion

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Abstract

Transition metal-catalyzed carbenoid insertion of hydroxyl groups represents a robust and versatile method to forge C-O bonds. Achieving site-selective functionalization of alcohols using this transformation has undoubted synthetic value, but remains challenging. Here we report a strategy exploitng an engineered heterogeneous iridium single atom (Ir-SA) catalyst for selective carbenoid O-H insertion, thus providing opportunities in merging material science and catalysis for organic transformations. This catalytic protocol delivers excellent selectivities (up to 99:1) for functionalization of aliphatic over phenolic O-H bonds, even in cases where the analogous homogeneous catalyst, Ir(ttp)COCl, provided modest preferences. DFT calculations suggest that the site-selectivity derives from the lower oxidation state of iridium metal center in the heterogeneous catalyst and its impact on the absorption energies of catalytic species. These results comprise an example of a heterogeneous single atom catalyst providing superior site-selectivity and provide a complementary strategy to address challenges in catalysis for organic synthesis.

Introduction

Transition metal-catalyzed carbenoid insertion reactions have emerged as a powerful route in the

construction of carbon-carbon and carbon-heteroatom bonds.(*1-8*) This elegant methodology most commonly employs diazo reagents to access the crucial metal carbene species, which participate in a wide range of reactivity modes.(*9-15*) For example, these metal carbene intermediates engage in dipolar cycloaddition reactions to rapidly construct biologically important heterocycles and macrocyclic molecules,(*16, 17*) react with carbon-carbon π-bonds to form highly substituted cyclopropanes,(*7, 18*) and have been employed in transition metal-catalyzed construction of stereogenic quaternary carbons.(*20*) Moreover, direct functionalization of carbon-hydrogen and heteroatom-hydrogen bonds via carbenoid insertion has gained much attention over the last decades.(*2, 3, 21-24*) The combination of a diverse set of transition metals and ligands are often the key to controlling the range of reactivity afforded by these intermediates and to leveraging their potential in the syntheses of pharmaceuticals and natural products.

Along with these advances, enantioselective carbenoid insertion of O-H bonds (*4*) has also been well-established. In contrast, only a few methods to realize site-selective O-H insertion among various hydroxyl groups have been reported.(*25-26*) This challenge plausibly arises from the reactivity of electron-withdrawing group typically present in the carbene intermediates, which further enhances the high electrophilicity of these species and renders control of site-selective insertion of nucleophilic hydroxyl group difficult.(*3*) Notably, a selective O-H insertion of glycosides has been reported by Tang and co-workers; however, density functional theory (DFT) calculations suggest that the site- and stereo-selectivity are induced by the axial substituent adjacent to the reactive O-H moiety.(*26*) Encouraged by the high synthetic values of carbenoid insertion, we sought to explore single-atom site (SAs) catalysts to promote and control these reactions with the goal of assessing this catalytic system as an opportunity to address the aforementioned challenging of selectivity.

SAs catalysts have emerged as a class of materials and been gained significant attention in catalysis applications. Chemical modulations of the SAs support is often essential in order to achieving high catalytic reactivity.(*27-34*) Notably, in comparison to traditional heterogeneous catalysts based on metal clusters and nanoparticles, this unique class of SAs catalysts features atomically dispersed metal atoms immobilized on the supports.(*35-38*) Benefiting from the maximum atom-utilization efficiency and fully exposed active sites, SAs catalysts exhibit excellent catalytic performance in a spectrum of organic transformations, as recently reported by our group and others.(*39-45*) The well-defined structure and coordination environment of the transition metal, in SAs catalysts, can lead to alternative modes of catalytic activity and provide opportunities to achieve chemo- and regioselective reactions. Moreover, in some case, these features enable the identification of active sites and, as result, the study of catalytic mechanism at the atomic level. (*41, 46-56*).

The vast majority of effort in this area has focused on the identification of potential SAs catalyst to exhibit better reactivity than the corresponding transition metal nanoparticle- or cluster-based catalysts (29,*36*). In contrast, studies aimed at discerning the selectivity differences between SAs and analogous homogeneous catalysts are rare (*57*). In this respect, we were encouraged to evaluate

the potential of SAs materials as a platform for the development of heterogenized homogeneous catalyst with the potential to access distinct selectivity in organic transformation. More specifically, in this communication we describe the development of a designed iridium SAs heterogeneous catalyst and compare its performance with its analogous homogeneous catalyst in carbenoid O-H insertions. Our SAs catalyst delivered excellent selectivities for carbenoid insertion into aliphatic O-H bonds, and the origin of this site-selectivity was investigated by kinetic studies and DFT calculations.

Results

Synthesis and characterization of Ir-SA

The fabrication process for the Ir-SA catalyst is schematically presented in Fig. 1a. Zeolite imidazolate frameworks-8 (ZIF-8) was dispersed uniformly in methanol solution that was introduced into a solution containing iridium (IV) chloride and the monomer, poly(cyclotriphospazene-co-4,4'-sulfonyldiphenol) (PZS). Subsequently, trimethylamine (TEA) initiated polymerization of the poly(cyclotriphospazene-co-4,4'-sulfonyldiphenol) and iridium (IV) precursors on the surface of ZIF-8 produced the ZIF-8/Ir@PZS composites. As depicted in Supplementary Fig. 1, the ZIF-8/Ir@PZS structure with a polyhedral morphology was obtained. Finally, the Ir-SA catalyst was supported on heteroatoms-doped carbon by pyrolysis of ZIF-8/Ir@PZS at 950 °C under an argon atmosphere.

The sharp contrast between the edge and the center in transmission electron microscopy (TEM) and high angle annular dark field scanning TEM (HAADF-STEM) images of this Ir-SA catalyst provided direct insight into the hollow interior (Fig. 1b, 1c and Supplementary Fig. 2) and support for the fact that the morphology of Ir-SA catalyst remains uniformly hollow. As observed in HAADF-STEM image, no obvious metallic Ir nanoparticles were formed during the synthesis of the supported Ir-SA catalyst. Consistent with the results of HAADF-STEM, the powder X-ray diffraction (PXRD) pattern of Ir-SA catalyst showed one broad peak located at about 25°, consistent with the graphitic carbon, and no detectable metallic Ir nanoparticles signals (Supplementary Fig. 3). The Ir content of the Ir-SA catalyst was found to be 2.20 wt% using inductively coupled plasma optical emission spectrometry (ICP-OES). The energy-dispersive spectroscopy (EDS) images of Ir-SA catalyst established that Ir, N, P, S and C elements were evenly displayed throughout the hollow layer (Fig. 1d). Moreover, aberration-corrected HAADF-STEM (AC HAADF-STEM) analysis revealed the dispersion state of Ir species at the atomic scale. As illustrated in Fig. 1e-f, some individual bright dots, labelled with yellow circles, were clearly distinguished from the heteroatoms-doped carbon support without any agglomeration, consistent with the existence of single Ir atoms in the Ir-SA catalyst. The atomic dispersion of Ir species in Ir-SA catalyst was confirmed by the analysis of intensity profiles (Fig. 1g). In addition, Brunauer-Emmett-Teller (BET) surface area (604.0 $m^2 \cdot g^{-1}$) and pore size distribution (~0.5 nm) of the Ir-SA catalyst were calculated (Supplementary Fig. 13), indicating that heterogeneous Ir-SA possesses a porous structure with a

large surface area that provides access to the Ir single-atom active sites.

To further establish the chemical state of C, N, P and S elements in Ir-SA catalyst, X-ray photoelectron spectroscopy (XPS) analysis was performed. As shown in Supplementary Fig. 4, four peaks at the binding energy of 284.8 eV (C=C), 288.1 eV (C-N), 285.7 eV (C-P) and 284.6 eV (C-S) for the C $1s$ spectrum were fitted. The N $1s$ spectrum displays four peaks located at 398.6 eV, 400.6 eV, 401.2 eV and 403.8 eV, attributed to pyridinic N, pyrrolic N, graphitic N and pyridinic N^+-O^-, respectively (Supplementary Fig. 5). The presence of two peaks at the binding energy of 132.5 eV and 133.8 eV in the P $2p$ spectrum indicate the existence of P-C and P-O respectively (Supplementary Fig. 6). As shown in the XPS spectrum of S $2p$ spectrum, three peaks at 168.4 eV, 165.4 eV and 163.9 eV, associated with $2p3/2$, $2p1/2$ splitting of the S$2p$ spin orbital (-C-S-C-) and oxidized S $2p3/2$, respectively, were simulated (Supplementary Fig. 7). Taken together, these results are most consistent with the conclusion that N, P and S species were doped into the hollow carbon substrate.

Atomic structure analysis of Ir-SA

X-ray absorption fine structure (XAFS) measurements were carried out to examine the atomic dispersion and geometric configuration of Ir-SA catalyst. As shown in Fig. 2a, only one intensity maximum peak located at approximately 1.6 Å was examined in Fourier transform (FT) extended X-ray absorption fine structure (EXAFS) curve for Ir-SA. This signal was attributed to the contribution of Ir-N coordination. Comparison with the Ir powder which displayed a main peak at approximately 2.5 Å assigned to Ir-Ir bond, found that this metallic interaction was not present in the synthesized Ir SAs, consistent with the existence of single Ir atoms. Further, wavelet transform (WT) analysis, a powerful tool for discriminating the backscattering atoms with high resolution in both k and R space, was performed to investigate the atomic dispersion of Ir. For Ir powder, one intensity maximum was detected at about 8.3 Å^{-1}, owing to Ir-Ir coordination (Fig. 2b). The WT plots of Ir-SA exhibited only one intensity maximum at 4.0 Å^{-1}, without any other signals similar to those in the WT plots of Ir powder (Fig. 2b). The above results further support the conclusion that the catalyst is primarily composed of single Ir atoms. The white-line peak, located between those of Ir and IrO$_2$ in the Ir L$_3$-edge X-ray absorption near-edge structure (XANES) curve (Fig. 2c) of Ir-SA catalyst suggests that the Ir single atoms in Ir-SA carry an average oxidation state. As shown in Supplementary Figure 15, a more reliable quantitative analysis on the valence state was established from the integrated area of the white line. The resulting average oxidation state of Ir in Ir-SA is approximately 2.1, which is lower than the previously reported formal oxidation state of the Ir(III) homogeneous catalyst (*58, 59*). A least-squares EXAFS fitting was carried out to obtain quantitative structural parameters of the Ir atoms in the Ir-SA catalyst. The EXAFS fitting parameters were listed in Supplementary Table 1 and the fitting curves were depicted in Fig. 2d and Supplementary Figures 8-12. The main peak of the Ir-SA at approximate 1.6 Å originates from the first shell of Ir-SA-N scattering. Together with further analysis (Supplementary Figures 14-16 and Tables 2-3) and DFT modelling (Supplementary Figures 17 and 39), the optimized geometric configuration of Ir-SA

catalyst (inset of Fig. 2d) was determined to possess a Ir single atom anchored to the heteroatoms-doped carbon support through four-fold coordinated by N atoms.

Reaction scope and selectivity

Armed with the composition and structure of synthesized heterogeneous Ir-SA catalyst, this material was studied as catalysts for a reaction typically associated with homogeneous transition metal catalysis. At the outset of the investigation, heterogeneous Ir-SA catalyzed carbenoid insertion of alcohol **2a** with diazo ester **1a** was examined (Fig. 3A). The Ir-SA with only1 mol% catalyst loading exhibited excellent reactivity affording **3aa** in 90% yield. Next, the scope of both the diazo reagents and the coupling nucleophilic partners in the Ir-SA catalyzed carbenoid insertion was examined. Notably, various electronically different substituents at the aryl groups of diazo (**1b-1d**) were well tolerated, affording the corresponding O-H insertion products (**3ba-3da**) in good to excellent yields. Alcohols bearing aryl moieties and aliphatic substituents such as cyclohexyl, trifluoromethyl, chloro or silyl ether functional groups were also amenable (**3ab-3aj**), demonstrating the synthetic potential of this heterogenous catalytic system. In addition, carbenoid insertion reactions into N-H bond of aniline and C-H bond of 4-methylindole, respectively, were also tested and generated **3ak** and **3al** in excellent yields.

Given both structural and electronic similarity between our engineered Ir-SA catalyst and porphyrin-based homogeneous complex Ir(ttp)COCl, a direct comparison of the selectivity in O-H carbenoid insertion reactions catalyzed by these two catalysts was sought (Fig. 3B). In this context, carbenoid insertion of 4-(hydroxymethyl)phenol **2m**, bearing phenolic $C(sp^2)$- and aliphatic $C(sp^3)$-OH, with diazo **1a** was chosen as the model reaction (Supplementary Fig. 21). Interestingly, homogeneous Ir(ttp)COCl gave an unselective mixture (~50 : 50) of both mono- and bis-insertion products (**3am** and **3am"** respectively), whereas heterogeneous Ir-SA provided extraordinary selectivity (99%) towards mono-insertion of $C(sp^3)$-OH. Similarly, other substrates bearing two hydroxyl group (**2n-2r**) also showed high selectivities (up to 99%) towards either the benzylic or less hindered hydroxyl group. In addition, the heterogeneous Ir-SA catalyzed carbenoid insertion of **2s,** bearing N-H and O-H functional groups, was gave the product with excellent selectivity (99%) in favor of the insertion into N-H moiety.

In order to evaluate the potential of this catalyst platform for reuse, the structure of the catalyst that was re-isolated after the reaction was complete was analyzed by TEM, HAADF-STEM and x-ray absorption spectroscopy (EXAFS and XANES). The electron-microscopy experiments showed isolated iridium atoms (bright points) and no obvious nanoparticles aggregation was detected, suggesting that the atomic dispersion of Ir species was still preserved after the catalytic reaction (Supplementary Fig. 19). Moreover, the L_3-edge k^3-weighted Fourier transform (FT) spectra of the used Ir-SA and fresh Ir-SA showed a single major peak in the EXAFS spectra at ~1.80 Å and ~1.60 Å, respectively (Supplementary Fig. 20 and Table 4). No Ir-Ir signals were observed in either the freshly prepared Ir-SA or used Ir-SA catalysts. These observations further support the conclusion that the atomic dispersion of the iridium is maintained during the catalytic reaction. Finally, the Ir

L$_3$-edge XANES curve suggests that average oxidation state of the iridium atoms in the used Ir-SA catalyst is only higher than that of the unused Ir-SA catalyst (Supplementary Fig. 20b).

Taken together, these observations suggest that the Ir-SA catalyst maintains its structure and can be recovered and reused. In the event, recycled catalyst lost some activity (from 99% to 67% conversion over 16 h). Given that the TEM and XAFS studies suggest that the iridium atoms in the reused catalyst retain nearly identical structure to the fresh catalyst, a hot filtration test was performed to examine whether leaching of the single atom catalyst led to the observed decrease in activity (Supplementary Fig. 18). After conducting catalysis with both model substrates **1a** and **2m** over 1 hour, the Ir-SA catalyst was removed by filtration. The resulting clear filtrate was stirred further for 11 hours, yielding (from 1% to 10%) the double insertion adduct **3am"** without formation of additional **3am** (Supplementary Fig. 18). These results are consistent with the leaching of small amount iridium, which catalyzed the unselective reaction. Moreover, inductively coupled plasma (ICP) analysis of fresh Ir-SA and used Ir-SA showed a small decrease in iridium content from 2.20 wt% to 2.01 wt%, further supported that leaching of iridium from the catalyst is limited. Nevertheless, the high selectivity of the reaction observed prior to filtration supports the hypothesis that the majority of the reaction occurred at the single atom sites of the heterogeneous Ir-SA catalyst.

Mechanistic studies

DFT calculations, assessing both reaction energies and activation barriers, were performed in order to gain insight into the origin of selectivity difference between heterogeneous Ir-SA and homogenous Ir(ttp)COCl. A series of elementary steps including formation of iridium carbene (C=Ir) intermediate (more details in Supplementary Fig. 40 and Fig. 41) and subsequent O-H insertion have been taken into account. In order to simplify the DFT analysis, Ir-porphyrin, which has little difference (0.07 eV) on the adsorption energy of carbene (C$_6$H$_5$CCOOCH$_3$) compared to Ir(ttp)COCl, was chosen for these studies (Supplementary Fig. 33 and Table 5). At the outset of calculation, both concerted and stepwise paths for the carbenoid O-H insertion reaction were examined. The concerted mechanism showed lower activation barriers for both the homogeneous and heterogeneous catalyst systems (Supplementary Fig. 36). Next, the free energy landscape for the reaction catalyzed by the heterogeneous Ir-SA catalyst, which is comprised of decomposition of diazo **1a** to form C=Ir carbene intermediate followed by selective O-H insertion, was examined (Fig. 4a, more details in Supplementary Fig. 34). Notably, the difference in the activations barriers for the insertion of C(sp^3)O-H (0.21 eV) and C(sp^2)O-H (0.65 eV) into C=Ir intermediate is consistent with the selective formation of 3**am** over 3**am'**. Moreover, the second insertion into C(sp^2)O-H of **3am** was calculated to be proceeded through a transition state with even higher energy (0.74 eV) thus impeding the production of **3am"** (Supplementary Fig. 34). With respect to homogeneous reaction catalyzed by Ir-porphyrin (Fig. 4b, more details in Supplementary Fig. 35), a lower activation barrier for C(sp^3)O-H insertion (1.28 eV) compared with C(sp^2)O-H insertion (1.62 eV) was found, suggesting that **3am** is initially formed. However, an even lower activation barrier for the subsequent C(sp^2)O-H insertion of **3am** (1.01 eV) was calculated in this homogeneous system,

consistent with the formation of an unselective mixture of mono-insertion **3am** and bis-insertion **3am"** (Supplementary Fig. 35).

The microscopic origin of aforementioned distinct activation barriers in homogenous and heterogeneous systems was examined. Although both catalysts possess planar four-coordinate structure, the chemical potential of iridium carbene intermediate is expected to be influenced by the oxidation states of catalytically active metal center (Supplementary Fig. 15). Analysis of projected density of states (PDOS) of Ir-SA and Ir(ttp)COCl showed that the increased cationic charge character of the Ir in Ir(ttp)COCl results in a stronger bonding and adsorption energies of the carbene fragment, $C_6H_5CCOOCH_3$, to Ir(ttp)COCl (-1.35 eV) compared to Ir-SA (-0.37 eV) (Supplementary Fig. 37). Correlation of the activation barriers with the adsorption energies of $C_6H_5CCOOCH_3$ as a descriptor, established the activity and selectivity trend (Supplementary Fig. 38). Thus, the rate-determining step is expected to be the metal carbene formation for Ir-SA rather than the first $C(sp^2)O-H$. Experimentally, an absence of dependence on alcohol concentration (Supplementary Fig. 24-27) and a dependence of the reaction on diazo concentration (Supplementary Fig. 28-31) strongly supports turnover limiting formation of the iridium carbene intermediate (*60*). Combined with these observations, the activity and selectivity analysis suggest that the ideal binding energy (E_{ad} = -0.55 eV) requires an Ir oxidation state between that of Ir-SA and Ir(ttp)COCl. Therefore, the loss of selectivity that results from generation of bis-insertion **3am"** likely arises due to the further strengthening the binding energies (E_{ad} < -1.04 eV) found in the higher oxidation states of metal carbene in the homogenous catalyst (Supplementary Fig. 38).

Conclusions

In summary, we have elaborated a two-step pyrolysis protocol for the synthesis of an iridium single atom catalyst supported by nitrogen, phosphorus and sulfur co-doped hollow carbon polyhedron. With this catalyst in hand, carbene insertion of methyl phenyl diazoacetate with various alcohols, aniline and *N*-protected indole was examined. High compatibility with a range of functional groups was observed in these Ir-SA-catalyzed reactions. Moreover, the heterogeneous Ir-SA catalyst displayed a significant improvement in turnover number (TON = 1456) compared to its homogeneous counterpart (TON = 462). The Ir-SA heterogeneous catalyst provided excellent control of selectivities (up to 99%) favoring $C(sp^3)$-OH carbene insertion over reaction with phenolic O-H bonds. On the basis of DFT calculation and experimental studies, the origin of the improved selectivity observed with the Ir-SA catalyst is posited to be correlated to the absorption energy of the metal carbene intermediate which results in the modulation of the activation barrier for the insertion reactions. Finally, given the potential for structural diversity in single atom site catalysts, this work highlights the opportunity to develop selective transformations through merging of material science with application in organic synthesis.

Methods

Catalyst Preparation. A solution of $Zn(NO_3)_2 \cdot 6H_2O$ (5.58 g) in 150 mL of methanol was added to

a solution of 2-methylimidazole (6.16 g) in 150 mL methanol. After stirring at room temperature for 24 h, the obtained ZIF-8 precipitates were collected by centrifugation and dried in vacuum at 80 °C. Subsequently, the obtained ZIF-8 (600 mg) powder was dispersed in 100 mL methanol and to which was added a methanol solution of iridium (IV) chloride (1 mg/mL, 7.08 mL). To this iridium-containing solution was added a mixture of 4,4′-sulfonyldiphenol (800 mg) and phosphonitrilic chloride trimer (375 mg) in 250 mL methanol.   After vigorous stirring for 15 min, 3 mL triethylamine was added. The resulted mixture was stirred for 15 h, the as-obtained ZIF-8/Ir@PZS precipitates were separated by centrifugation and dried in vacuum at 80 °C. The as-obtained ZIF-8/Ir@PZS was placed in quartz boat and then maintained at 950 °C for 3 h in a tube furnace with a heating rate of 5 °C min^{-1} under a flow of argon atmosphere. After allowing to cool to room temperature, the as-prepared sample of Ir-SA was collected and used without further treatment.

XAFS data analysis details. The acquired EXAFS data was processed according to the standard procedure using the ATHENA module implemented in the IIRFFIT software packages. The EXAFS spectra were collected by subtracting the post-edge background from the overall absorption and then normalizing with respect to the edge-jump step. Then, χ(k) data of Ir L$_3$-edge were Fourier transformed to real (R) space using a hanning windows (dk=1.0 Å^{-1}) to separate the EXAFS contributions from different coordination shells. To obtain the quantitative structural parameters around central atoms (*61*), we performed least-squares curve parameter fitting by using the ARTEMIS module of IIRFFIT software packages. The following EXAFS equation (1) was used:

$$\chi(k)=\sum_j \frac{N_j S_o^2 F_j(k)}{k R_j^2}\exp[-2k^2\sigma_j^2]\exp[\frac{-2R_j}{\lambda(k)}]\sin[2kR_j+\phi_j(k)] \tag{1}$$

In equation (1), S_o^2: the amplitude reduction factor; $F_j(k)$: the effective curved-wave backscattering amplitude; N_j: the number of neighbors in the jth atomic shell; R_j: the distance between the X-ray absorbing central atom and the atoms in the jth atomic shell (backscatterer); λ: the mean free path in Å; σ_j: the Debye-Waller parameter of the jth atomic shell (variation of distances around the average R_j); $\phi_j(k)$: the phase shift (including the phase shift for each shell and the total central atom phase shift). The functions $F_j(k)$, λ and $\phi_j(k)$ were calculated with the ab initio code FEFF8.2. (*62*)

General procedure for selective O-H carbenoid insertion. In a glovebox, diazo ester **1X** (0.10 mmol, 2.0 equiv.) and alcohol **2Y** (0.05 mmol, 1.0 equiv.) were added sequentially to a suspension of Ir-SA (0.50 mol%) in 1,2-dichloroethane (0.50 mL) in a two-dram vial. The reaction vial was sealed and stirred at 60 ºC for 20 hours. After cooling to room temperature, the volatiles were removed by rotary evaporator and the obtained crude mixture was purified by silica gel flash chromatography using petroleum ether and EtOAc as eluents. The molar ratio of products was determined by ^{1}H-NMR spectroscopy.

Computational methods. DFT calculations were conducted using the Vienna Ab initio Simulation Package (VASP) with the revised Perdew-Burke-Ernzerhof (rPBE) *(63)* performing the generalized

gradient approximation (GGA). A 8×8 single-layer graphene with 15 Å vacuum space was built to describe the model of Ir-SA, where the Ir atom was stabilized by 4 N atoms and the surface was also doped by S and P atoms (Supplementary Fig. 32a). A Monkhorst-Pack k-point 2×2×1 was used in all the calculations on Ir-SA. The reaction over Ir(ttp)COCl catalyst was calculated in a large supercell with the lattice of $20×20×20$ Å^3 to avoid the interactions in the periodic calculations, where A Monkhorst-Pack k-point 1×1×1 was used (Supplementary Fig. 32b). Ir-Porphyrin (Supplementary Fig. 33a) was employed in DFT studies of the catalytic reaction using Ir(ttp)COCl (Supplementary Fig. 33b) due to the large computational costs. The calculated adsorption energy of carbene ($C_6H_5CCOOCH_3$) to these two structures displayed only a small difference (0.07 eV), which supports the reliability of the model constructed using Ir-Porphyrin (Supplementary Table 5). A 400 eV cut-off energy was set for the plane-wave basis set. Structure optimizations were performed with the convergence force of 0.05 eV·Å^{-1}, and all the transition states were obtained using the climbing image nudged elastic band (CI-NEB) method *(64)* with the convergence force smaller than 0.1 eV·Å^{-1}.

Free energy corrections. The free energy corrections were conducted in this work to simulate the reaction condition at 333 K. Standard free energy corrections were performed by the equation:

$$\Delta G = \Delta E_{DFT} + \Delta E_{ZPE} + \Delta E_U - T\Delta S \tag{2}$$

where ΔE_{DFT} refers to the electronic energy from DFT calculations. ΔE_{ZPE}, ΔE_U and ΔS are the correction of zero-point energy, inner energy, and entropy, respectively. Only vibrational motion was considered for adsorbates on the surface of catalysts, while translational, rotational, and vibrational motions were all considered for gas molecules. The detail of the correction, including adsorbates, transition states and gas molecules, is displayed in Supplementary Table 6.

Data availability

Data relating to the characterization data of materials (TEM, STEM, XANES, EXAFS, XPS, XRD), general methods, experimental procedures, mechanistic studies, mass spectrometry and NMR spectra, DFT computational studies are available in the Supplementary Information.

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Author contributions

J. Z., S. J. and P. G. performed most of the experiments and analyzed the experimental data, co-wrote the paper. C. G. performed computational studies and analyzed the computational data and co-wrote the paper. H. L. and J. D. helped to collect and analyze the XAFS data. J. Z., D. W., Y. L. and F. D. T. designed and guided the research, and co-wrote the paper. All the authors discussed the results and contributed to the writing the manuscript.

Competing interests

The authors declare no competing interests.

Figure legends/captions

Figure 1 | Synthesis and structural characterizations. a, Illustration of fabrication process of Ir-SA catalyst. **b,** TEM image of Ir-SA catalyst. Scale bar, 300 nm. **c,** HAADF-STEM image of Ir-SA catalyst. Scale bar, 300 nm. **d,** The HAADF-STEM image and element maps (Ir: cyan, C: red, N: green, P: orange, S: yellow). **e,** AC HAADF-STEM image of Ir-SA catalyst, scale bar: 5 nm. **f,** The enlarged AC HAADF-STEM image of Ir-SA catalyst. Scale bar: 1nm. **g,** Intensity profiles of Ir-SA catalyst obtained in dotted rectangle region in **e.**

Figure 2 | Atomic structural analysis of the Ir-SA catalyst. a, Ir L_3-edge k^3-weighted Fourier transform (FT) spectra of the Ir-SA, Ir powder and IrO_2 samples, respectively. **b,** Wavelet transform (WT) of the Ir-SA and Ir powder samples, respectively. **c,** Ir L_3-edge XANES spectra of the Ir-SA, Ir powder and IrO_2 samples, respectively. **d,** the corresponding EXAFS R space fitting curves; Inset: Schematic model of Ir-SA, Ir (purple), C (grey), N (blue), S (yellow) and P (green).

Figure 3 | Performance of Ir-SA catalyzed O-H carbenoid insertion. a, Scope of alcohols and diazo esters. Reaction conditions: **1X** (0.075 mmol), **2Y** (0.05 mmol), **Ir-SA** (1 mol%), 1,2-DCE as solvent (0.50 mL, concentration = 0.10 M) under nitrogen conditions, 60 ºC, 20 hr. **b,** Comparisons of selectivities in carbenoid insertion using **Ir-SA** (0.50 mol%) and **Ir(ttp)COCl** (0.50 mol%) respectively; Reaction conditions: **1a** (0.10 mmol), **2Y** (0.05 mmol), **Ir-SA** (0.50 mol%) or **Ir(ttp)COCl** (0.50 mol%), 1,2-DCE as solvent (0.50 mL, concentration = 0.10 M) under nitrogen conditions, 60 ºC, 20 hr.

Figure 4 | Mechanistic studies by DFT calculations. a, Free energy diagram for the selective O-H bond insertion over heterogeneous Ir-SA catalyst. The red and blue line shows the competitive insertion of $C(sp^2)$O-H and $C(sp^3)$O-H bond respectively; **b,** Free energy diagram for the selective

O-H insertion over homogeneous Ir(ttp)COCl catalyst. The red and blue line shows the competitive insertion of $C(sp^2)$O-H and $C(sp^3)$O-H respectively. All the energies were corrected to free energy at 333 K. Details of optimized structures see Supplementary Information.