

Mechanistic Snapshots of Rhodium-Catalyzed Acylnitrene Transfer Reactions

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Catalytic C–N bond formation stands as a crucial and highly sought-after process in the realms of synthetic, medicinal, and materials chemistry, offering a pathway to valuable nitrogen-containing compounds. While the Buchwald–Hartwig coupling method has emerged as a practical approach for furnishing valuable amine products,^{1,2} catalytic C–H amination is also considered as an attractive strategy, obviating the demand for pre-functionalized substrates and directly converting hydrocarbon precursors into the desired amine products.^{3,4} “Transition-metal-catalysis platforms have been devised to facilitate hydrocarbon aminations through metal–nitrenoid transfer routes, employing nitrene precursors, most notably organic azides,” said Professor Sukbok Chang, from the Institute for Basic Science and Korea Advanced Institute of Science and Technology (IBS and KAIST, Daejeon, South Korea). He further noted: “While integrating *N*-acylamino groups into hydrocarbons is another significant transformation to produce various amido compounds, direct C–H amidation through acylnitrenoid transfer with organic acyl azides poses challenges. This is mainly due to the high temperature requirement and to the unstable nature of acyl azides, which tend to decompose to the corresponding isocyanates by the Curtius-type rearrangement.”

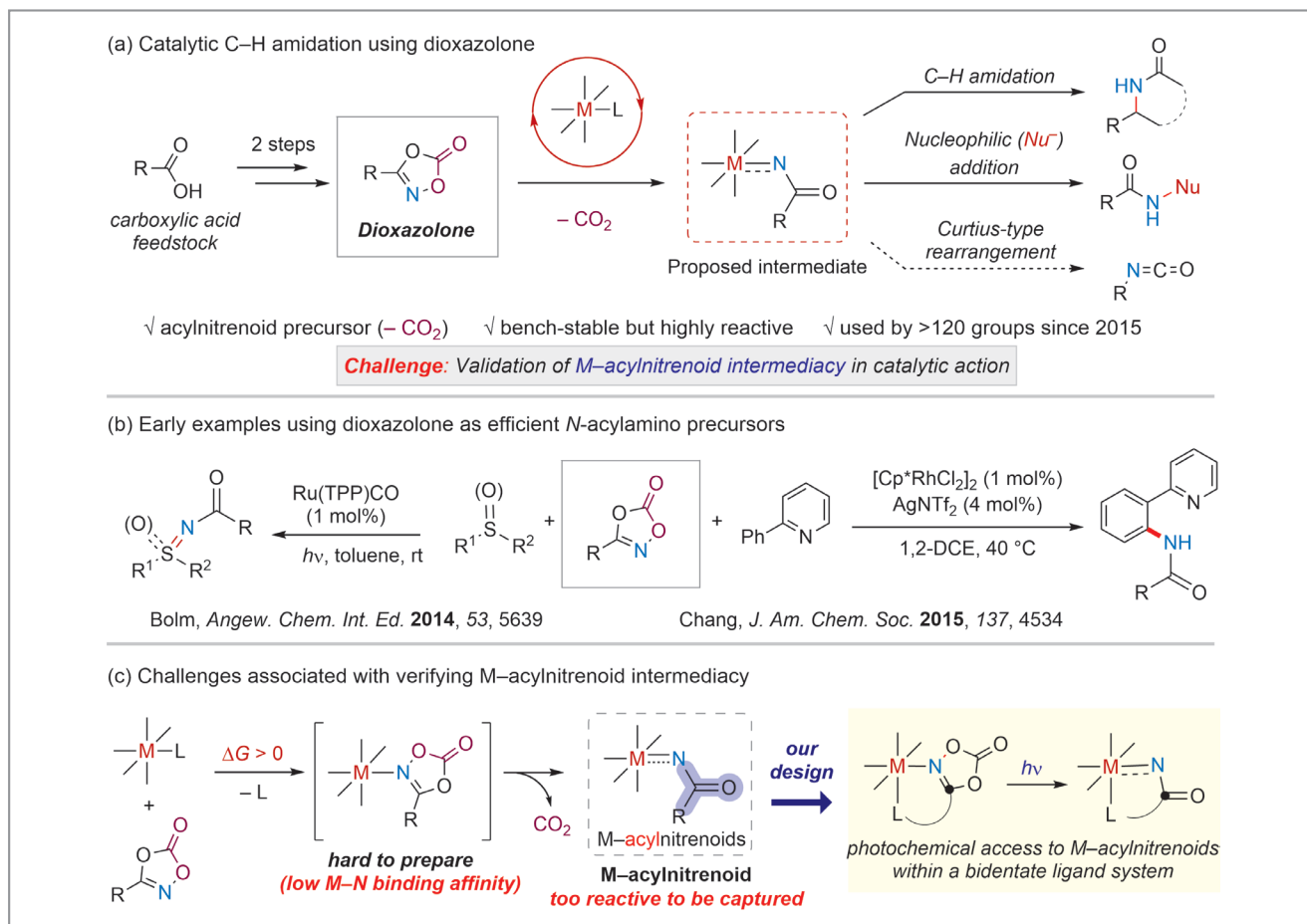
Professor Chang’s group stands at the forefront of research aiming to identify alternative pathways for the challenging C–H amidation. “Recently, instead of using acyl azides as the nitrene precursors, the broader synthetic organic community has shifted its focus to 1,4,2-dioxazol-5-ones (dioxazolones), which have shown promise as user-friendly and highly reactive *N*-acylamino sources (Scheme 1a). Dioxazolones can be easily derived from readily available carboxylic acid feedstocks, and their transformation to acylnitrenoids results in the emission of CO₂ as a sole byproduct,” Professor Chang explained. He continued: “Since Bolm’s efforts with sulfur imidation through ruthenium photocatalysis,⁵ and also with our studies on C–H amidation using half-sandwich group *d*⁶ transition metal catalysts,⁶ dioxazolones have now become popular *N*-acylamino precursors, as more than 120 research groups utilized this strategy from 2015 to 2022 (Scheme 1b).^{7,8}” Based on distinct advantages over conventional acyl azides, dioxazolones exhibited remarkable benefits in terms of substrate scope, reactivity, and selectivity. Prof. Chang’s and

other groups exemplified these advantages by utilizing group 9 transition-metal catalysts to leverage the reactivity of anticipated metal–acylnitrenoid species, leading to the creation of value-added products like lactams,⁹ arylamines,⁶ and hydrazides.¹⁰

In this regard, Professor Chang explained that the transition-metal–acylnitrenoid species has long been postulated as a key intermediate in catalytic C–H amidation processes, yet has remained uncharacterized due to associated challenges (Scheme 1c). “Since our first discovery in catalytic C–H amidation using dioxazolones as the nitrene precursors in 2015, observing the metal–acylnitrenoid intermediacy has been on our bucket list,” said Prof. Chang. He continued, explaining the key challenges: “However, due to their high reactivity, characterizing these metal–acylnitrenoid species has proven exceedingly difficult. Most representatively, the inherent susceptibility of metal–acylnitrenoids to undergo the Curtius-type rearrangement makes the situation more challenging. Furthermore, the low binding affinity of dioxazolones to transition-metal centers introduces another inherent complication, hindering the preparation of the necessary metal-bound dioxazolone adducts and thereby adding complexity to the exploration of the nitrenoid formation and transfer mechanisms.”

Professor Chang went on by explaining that in some cases, transition-metal–nitrenoid intermediates were characterized through the utilization of azides and transition-metal complexes. In previous studies, researchers often designed bulky ligands to protect the metal–nitrenoid structure from reacting with other substrates (Betley,¹¹ Munz^{12,13}). Beyond ligand design strategies, Powers,^{14,15} Schneider^{16,17} and others utilized photo- or thermal-induced crystallographic approaches, wherein the structure of the metal–nitrenoid could be captured in the crystalline matrix from single crystals of the metal–azide complex upon irradiation or thermal perturbation. “However, the literature precedents all utilized azides to obtain structures of alkyl, aryl, and sulfonyl nitrenes, and still, elucidating the structure of metal–acylnitrenoids using dioxazolones remains a challenge,” Prof. Chang commented.

Professor Chang’s group has now solved this long-standing challenge of characterizing transition-metal–acylnitrenoid species, which resulted in this paper in *Science*.¹⁸ The first



Scheme 1 Dioxazolones as an efficient amidation source: scope, reactivity, and challenges

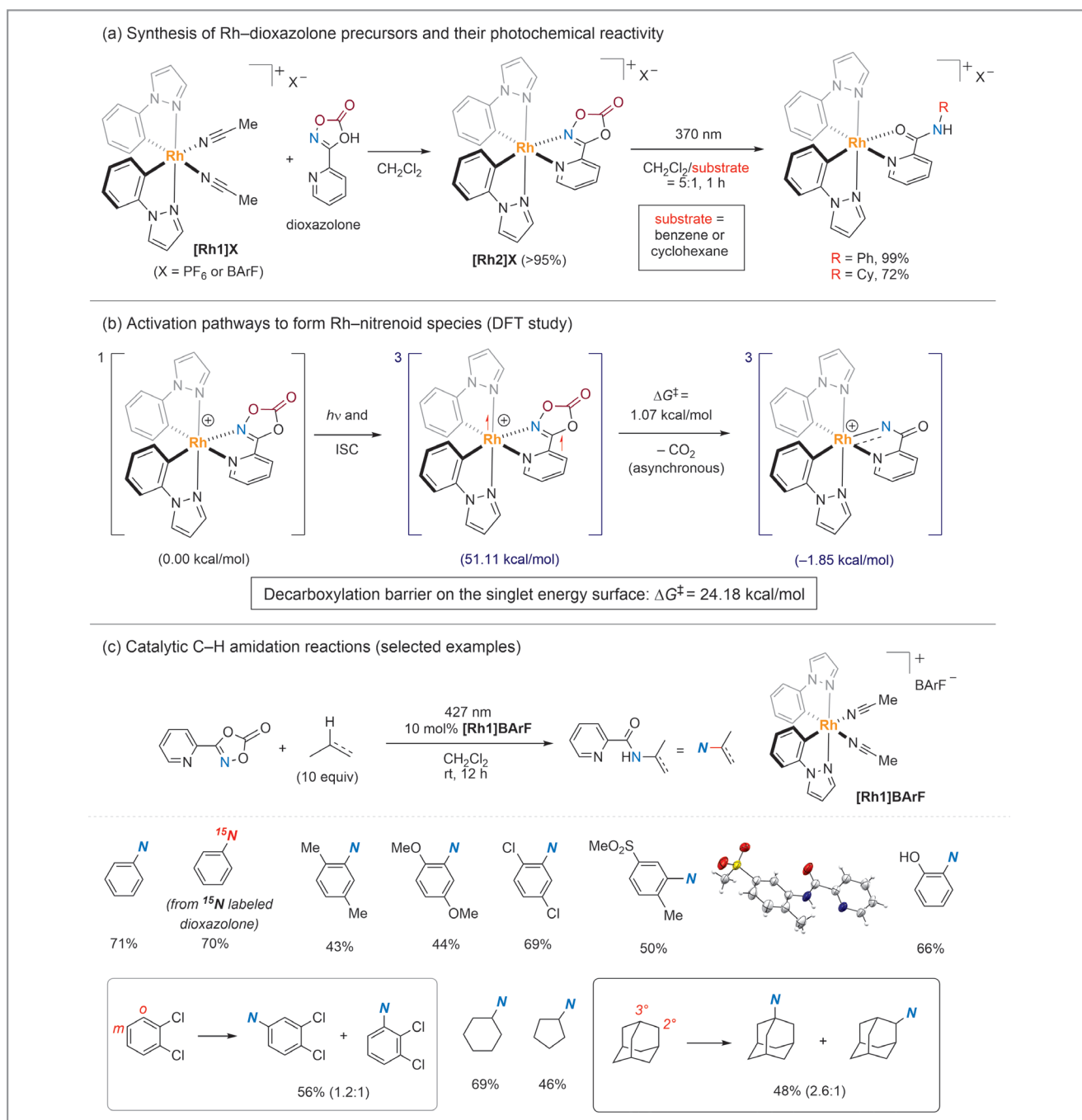
author, Hoimin Jung, explained: “To solve this challenge, we strategically designed a photosensitizable octahedral rhodium complex that coordinates with a bidentate dioxazolone to serve as an *N*-acylamino precursor.” He continued: “We developed a photocatalytic hydrocarbon amidation reaction with a pyridinyl dioxazolone by using an octahedral rhodium catalyst inspired by the Meggers-type photocatalyst.¹⁹ We successfully isolated the rhodium-bound dioxazolone adduct, and further photochemical studies showed that this new platform exhibits photocatalytic nitrene transfer reactivity toward both C(sp²)-H and C(sp³)-H amidations (Schemes 2a and 2c). Combined experimental and computational studies indicated that photochemical activation of the Rh–dioxazolone adduct could induce the formation of Rh–acylnitrenoid species via metal-to-ligand charge transfer (MLCT) activation of the dioxazolone (Scheme 2b). Also, mechanistic probe experiments and computational studies supported the involvement of singlet Rh–acylnitrene species responsible for nitrenoid transfer.”

Interestingly, the newly prepared rhodium–dioxazolone complex also showed photochemical reactivity in the solid reaction phase. The co-corresponding author Dongwook Kim emphasized: “With the single crystal of Rh–dioxazolone complexes in hand, we investigated the subsequent photoinduced decarboxylation step using an X-ray photocrystallography experiment in the Pohang Accelerator Laboratory (Korea).” He continued: “It was possible to capture the highly reactive species using the synchrotron facility, as the measurements could be finished within a few minutes. When using a Rh–dioxazolone crystal with a bulky tetrakis{3,5-bis(trifluoromethyl)phenyl}borate (BArF) anion, we finally captured and resolved a glimpse of the Rh–acylnitrenoid formation at 100 K upon 370 nm irradiation. After 30 min of irradiation, we found ~33% conversion of the starting rhodium–dioxazolone complex, where the Rh–N bond length contracted significantly from 2.153(2) Å to 2.02(2) Å upon the formation of the Rh–acylnitrenoid species. Remarkably, upon structure analysis, we

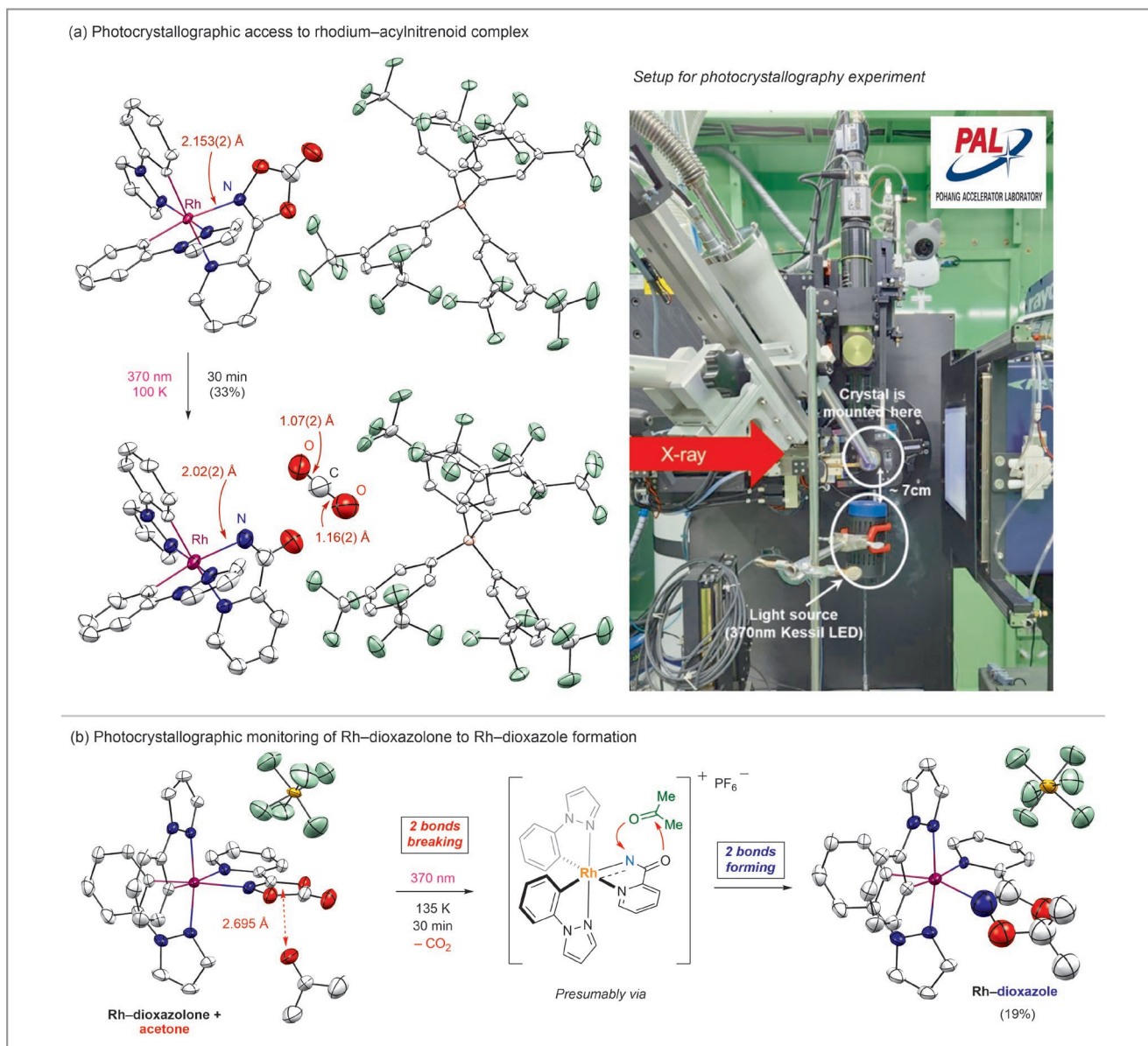
observed the extruded CO_2 molecule naturally (without geometrical restraints), which resides between the bulky BARF anion and the Rh–acylnitrenoid fragment (Scheme 3a)."

However, observing the rhodium–acylnitrenoid structure itself may not be sufficient to fully understand its catalytic

reactivity. Hence, the authors designed another photo-crystallography experiment that could directly support the reactivity nature of the sought-after rhodium–acylnitrenoid complex (Scheme 3b). First author Dr. Jung said, "By switching the counter anion to a smaller PF_6 anion, we prepared a



Scheme 2 Synthesis of rhodium–dioxazolone coordination complexes and their photochemical reactivity



Scheme 3 Photocrystallographic access to rhodium–acylnitrenoid species and crystallographic reaction monitoring

co-crystal of Rh–dioxazolone with one acetone molecule in the crystalline matrix, where the acetone was found very close to the dioxazolone moiety (2.695 Å).” Dr. Kim continued by explaining: “When subjecting this acetone co-crystal to the X-ray photocrystallographic analysis, we were able to observe significant residual electron densities, indicating the formation of the corresponding Rh–dioxazole molecule as the photoproduct, wherein acetone is incorporated into the *in situ* generated Rh–acylnitrenoid in the solid state. For this experiment, a slightly higher temperature of 135 K was op-

timal to induce the change, and 19% of Rh–dioxazole structure was observed after 30 minutes irradiation with the 370 nm light source.” Professor Chang further highlighted: “With this series of X-ray photocrystallographic analyses, we captured the complete mechanistic snapshot of acylnitrene transfer, which includes the two-bond-breaking decarboxylation and two-bond-associating dioxazole formation. In addition to the structural characterization of the Rh–acylnitrenoid intermediate, we also found experimental evidence on the electrophilic nature of such intermediates.”

Professor Chang concluded: “We have solved the long-standing challenge of identifying metal–acylnitrenoid intermediacy in the catalytic C–H amidation process. Our study represents a significant breakthrough in catalytic hydrocarbon amidation, offering new insights into the mechanism of this crucial reaction and presenting a strategic avenue for characterizing metal–acylnitrenoid intermediates and their electrophilic nature. The isolation and characterization of the Rh–acylnitrene complex serve as a long-sought-after key mechanistic motif, furnishing vital new perspectives for the design of more efficient and selective catalytic systems.”

Matt's favorite

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About the authors



Dr. H. Jung

Hoimin Jung earned his B.Sc. in chemistry from Korea Advanced Institute of Science and Technology (KAIST, South Korea) in 2018 as a KAIST presidential fellow (KPF). He participated in internship programs with Prof. Mu-Hyun Baik (KAIST), and also visited Prof. Tehshik P. Yoon's group (UW-Madison, USA) as an undergraduate researcher. He then pursued a Ph.D. in chemistry at KAIST under the supervision of Prof. Sukbok

Chang. In 2023, he received his Ph.D. and now he is a postdoctoral researcher at the Institute for Basic Science (IBS), South Korea. His research interest is focused on the development of C–H amination reactions using transition-metal catalysis and photoredox catalysis, as well as mechanistic understanding by both computational and experimental methods.



Dr. D. Kim

Dongwook Kim received his Ph.D. in chemistry at Ulsan National Institute of Science and Technology (UNIST, South Korea) in 2018 under the supervision of Prof. Myoung Soo Lah. During his Ph.D. research, he focused on the structure-based fundamental study of metal–organic frameworks with various guests and network analysis related to molecular building units, complexes and cages. In 2018, he joined the Center for Catalytic Hydrocarbon Functionalizations (CCHF), Institute for Basic Science

(South Korea), and now he has been promoted to a senior research fellow at the same research center. He is interested in the structural investigation of intermediates of organic, organometallic, and inorganic compounds and their analytical evaluation using single-crystal X-ray diffraction.



Prof. S. Chang

Sukbok Chang is a Director at the Institute for Basic Science (IBS, South Korea) and also a Distinguished Professor of Chemistry at KAIST (South Korea). He earned his Ph.D. in organic chemistry in 1996, at Harvard University (USA) under the guidance of Professor Eric N. Jacobsen. After one and half years of postdoctoral experience with Professor Robert H. Grubbs at Caltech (USA), he joined Ewha Womans University in Seoul, Korea,

as an Assistant Professor in 1998 and then moved to KAIST in 2002. Since 2012 he has been leading the Center for Catalytic Hydrocarbon Functionalizations at IBS as a Director. His recent awards and distinctions include the Korea Best Scientist and Engineer Award (2019) and Samsung Ho-Am Prize (2022). Also, he has been recognized as a highly cited researcher by Clarivate Analytics from 2015 to 2022. His research interests are in the development, understanding, and synthetic applications of transition-metal catalysis.