Academic Program [Oral B] | 14. Organic Chemistry -Aromatic, Heterocyclic, and Heteroatom Compounds-：Oral B

Tue. Mar 19, 2024 3:55 PM - 5:15 PM JST | Tue. Mar 19, 2024 6:55 AM - 8:15 AM UTC E1142(1142, Bldg. 11 [4F])

[E1142-2vn] 14. Organic Chemistry -Aromatic, Heterocyclic, and Heteroatom Compounds-

Chair: Shintaro Takahashi, Takayuki Iwata

English
3:55 PM - 4:15 PM JST | 6:55 AM - 7:15 AM UTC
[E1142-2vn-01]

Development of A Novel 5-5 Fused Heteroaromatic Ring Building Block

○Ryuya Miyazaki[1], Fumito Takada[1], Takunari Kikuchi[1], Yuya Oguro[2], Makoto Kamata[2], Takahumi Yukawa[2], Kei Muto[1], Junichiro Yamaguchi[1] (1. Waseda University, 2. Takeda Pharmaceutical Company)

English
4:15 PM - 4:35 PM JST | 7:15 AM - 7:35 AM UTC
[E1142-2vn-02]

Synthesis and Coordination Behavior of Hexakispyrazolylethane with High Stability

○Yuta Takemasa[1], Kyoko Nozaki[1] (1. School of Engineering, The University of Tokyo)

English
4:35 PM - 4:55 PM JST | 7:35 AM - 7:55 AM UTC
[E1142-2vn-03]

Ring Expansion of Heterocycles via Insertion of a Zinc Carbenoid to Nitrogen-Heteroatom bonds

○Masato Tsuda[1], Taiki Morita[1,2], Hiroyuki Nakamura[1,2] (1. Tokyo Institute of Technology, School of Life Science and Technology, 2. Tokyo Institute of Technology, Laboratory for Chemistry and Life Science)

English
4:55 PM - 5:15 PM JST | 7:55 AM - 8:15 AM UTC
[E1142-2vn-04]

Photoredox Catalysis for the Synthesis of Polycyclic Indole Derivatives via Arylcarboxylation of Unactivated Alkenes with the CO_2 radical Anion

○Suvankar Debbarma[1,2], Saeesh R Mangaonkar[1,2], Hiroki Hayashi[1,2], Wataru Kanna[3], Satoshi Maeda[1,2,3], Tsuyoshi Mita[1,2] (1. WPI-ICReDD, Hokkaido Univ., 2. JST-ERATO, 3. Fac. of Sci., Hokkaido Univ.)

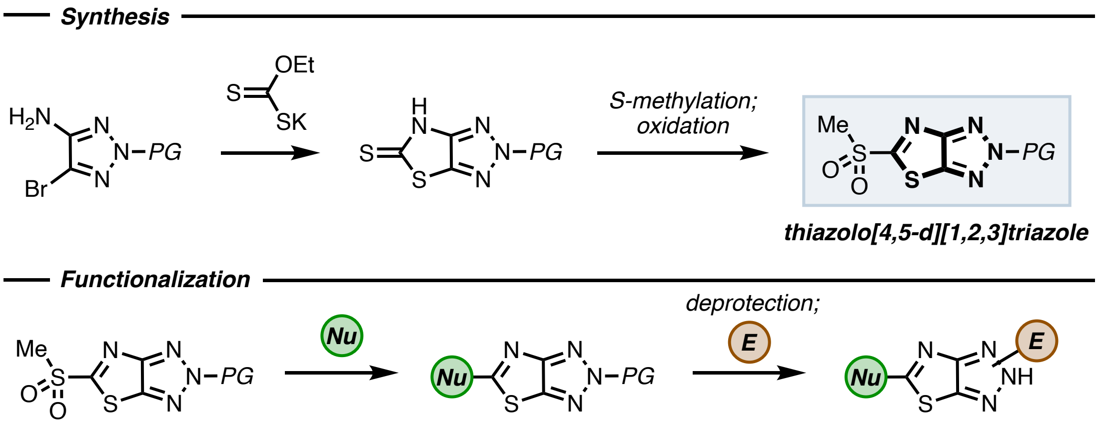
Development of A Novel 5-5 Fused Heteroaromatic Ring Building Block

([1]*Graduate School of Advanced Science and Engineering, Waseda University*, [2]*Takeda Pharmaceutical Company*, [3]*Institute for Advanced Study, Waseda University*)
○Ryuya Miyazaki,[1] Fumito Takada,[1] Takunari Kikuchi,[1] Yuya Oguro,[2] Makoto Kamata,[2] Takahumi Yukawa,[2] Kei Muto,[3] Junichiro Yamaguchi[1]

Keywords: Heteroaromatic Ring; 5-5 Fused Aromatic Ring; Building Block; Thiazole; Triazole

Heteroaromatic rings are privileged structures frequently found in pharmaceuticals. Adopting heteroatoms in an aromatic ring would not only affect physical/chemical properties such as water solubility and polarity, but also control non-covalent interactions with a protein of interest such as hydrogen bonding. To find a better molecular scaffold, many pharmaceutical companies have developed novel heteroaromatic ring systems including bicyclic ring to replace the aromatic moiety of a certain lead compound (scaffold hopping).[1]

Herein, we have successfully synthesized thiazolo[4,5-*d*][1,2,3]triazoles as an unprecedented 5-5 fused heteroaromatic building block. This skeleton was constructed from aminobromo-1,2,3-triazoles and potassium ethylxantates, affording a desired thiazolotriazole with a methyl sulfone on the thiazole ring.[2] Toward the use of this heteroarene as a building block, we established various functionalization on the thiazole ring by using the methyl sulfone as a leaving group. It was also found that the functionalization of the triazole ring was possible.



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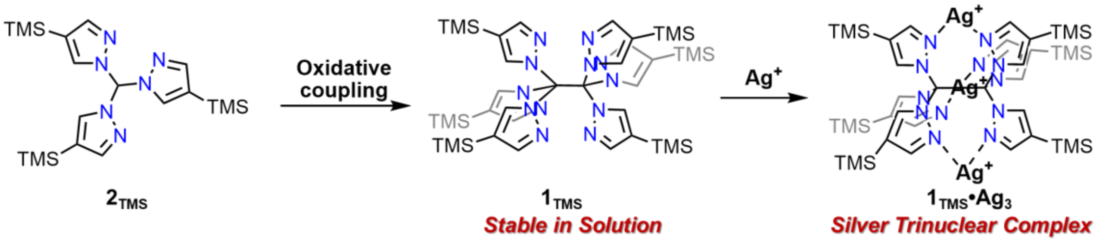
Synthesis and Coordination Behavior of Hexakispyrazolylethane with High Stability

([1]*Graduate School of Engineering, The University of Tokyo*) ○Yuta Takemasa,[1] Kyoko Nozaki[1]

Keywords: *Pyrazole, Hexaarylethane, Trityl radical, Ag complex, Polynuclear complex*

Hexaphenylethane (**HPE**) is one of the most attractive compounds with riddles many researchers have tried to solve for a long time.[1] It is known that there is an equilibrium between hexaphenylethane (α,α-dimer) and trityl radical, which dimerizes to form another isomer, thermally stable quinoidal dimer (α,*p*-dimer). To isolate the labile hexaphenylethane structure, there have been reported two strategies. As one approach, the introduction of sterically bulky substituents was successfully applied to stabilization of the α,α-dimer structure by London dispersion interactions.[2,3] Another strategy is bridging: Phenyl groups of each triarylmethyl unit were covalently connected. We envisaged a novel approach to isolate non-bridged hexaarylethane by introducing heterocycles. Herein, we report the synthesis and isolation of hexakis(4-trimethylsilylpyrazol-1-yl)ethane ($\mathbf{1}_{\mathbf{TMS}}$) which shows much higher stability compared with other non-bridged hexaarylethanes.

$\mathbf{1}_{\mathbf{TMS}}$ was synthesized by the oxidative dimerization of tris(4-trimethylsilylpyrazol-1-yl)methane ($\mathbf{2}_{\mathbf{TMS}}$). Single-crystal X-ray structural analysis of 1_{TMS} showed that the ethane C–C bond (1.623(4) Å) is shorter than that in hexaphenylethane (1.67(3) Å).[3] In solution, 1_{TMS} existed as a single species, contrastive that conventional hexaphenylethanes can keep the central C–C bond only by the aid of additional bridges between the two triarylmethyl units. Theoretical calculations indicated that the stabilization of the central carbon radical is much less significant in case of pyrazolyl compared to phenyl, due to lack of delocalization. Furthermore, introduction of pyrazole groups allowed additional bridging between the two triarylmethyl moieties through metal coordination to the adjacent N atoms: 1_{TMS} exhibited unique coordination to three Ag atoms affording a hexaarylethane analog bearing three N–Ag–N bridges ($\mathbf{1}_{\mathbf{TMS}}\mathbf{\bullet Ag_3}$). In the crystal structure of $\mathbf{1}_{\mathbf{TMS}}\mathbf{\bullet Ag_3}$, the ethane C–C bond (1.73(2) Å) was elongated from 1_{TMS} by coordination.



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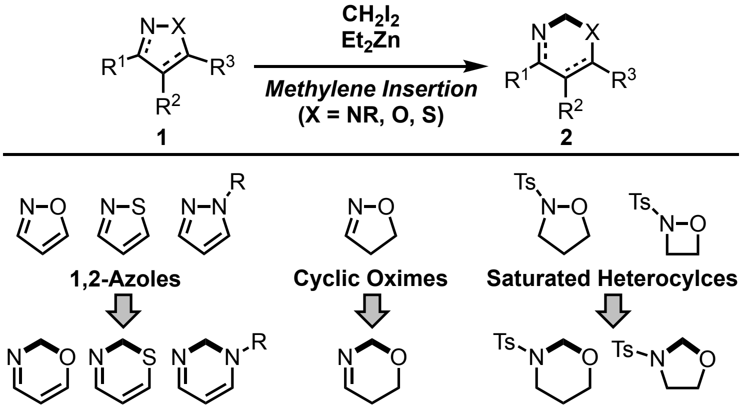
Ring Expansion of Heterocycles via Insertion of a Zinc Carbenoid to Nitrogen-Heteroatom Bonds

(*[1]School of Life Science and Technology, Tokyo Institute of Technology, [2]Laboratory for Chemistry and Life Science, Tokyo Institute of Technology*) ○Masato Tsuda,[1] Taiki Morita,[1, 2] Hiroyuki Nakamura[1, 2]

Keywords: 1,2-Azoles, Zinc-Carbenoid, Insertion, Ring Expansion

Recently, the skeletal transformation of heterocycles has attracted much attention because it allows us to construct scaffolds that are not readily accessible by other means. Current methods for ring-expansion via insertion into nitrogen-heteroatom bonds of 1,2-azoles rely on highly reactive species such as free carbenes1) or transitional metal carbenoids.2) Another approach is rearrangement of azolium ylides which could be prepared from azolium salts,3) but it requires multi-step from 1,2-azoles.

We previously found that a zinc carbenoid inserted into nitrogen-oxygen bond of an isoxazole derivative.4) Herein, we report the ring expansion of a wide variety of heterocycles **1** which have nitrogen-heteroatom (X = NR, O, S) bonds to produce corresponding methylene inserted products **2**. The developed reaction employing a zinc carbenoid could be applicable not only to 1,2-azoles, but also to cyclic oximes and saturated heterocycles. Furthermore, we performed DFT calculations to elucidate the reaction mechanisms, clarifying the distinct reaction paths among different types of rings.5)



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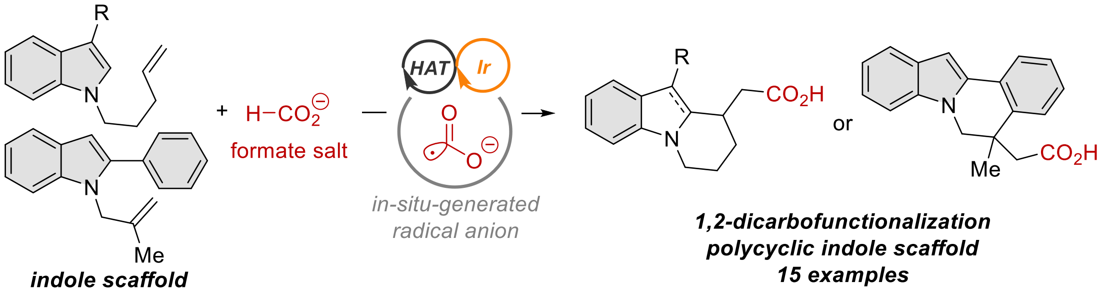
Photoredox Catalysis for the Synthesis of Polycyclic Indole Derivatives via Arylcarboxylation of Unactivated Alkenes with the CO_2 Radical Anion

([1]*WPI-ICReDD, Hokkaido Univ.*, [2]*JST-ERATO*, [3]*Fac. of Sci., Hokkaido Univ.*) ○Suvankar Debbarma,[1,2] Saeesh R. Mangaonkar,[1,2] Hiroki Hayashi,[1,2] Wataru Kanna,[3] Satoshi Maeda,[1,2,3] Tsuyoshi Mita[1,2]

Keywords: Photoredox; Metalloformates; Alkene; Arylcarboxylation; Polycyclic Indole

The arylcarboxylation of alkenes has proven to be a promising method for introducing two consecutive C–C bonds in a single transformation, providing a diverse range of substituted carboxylic acids.[1] However, the photocatalyzed carboxylation of unactivated alkenes with CO_2 presents a significant challenge, primarily attributed to the high reduction potentials of both starting materials.

Metalloformates (HCO_2M) are stand out as a renewable ore of carbon dioxide radical anion ($CO_2^{\bullet -}$), which has been utilized as a potential C1 source of valuable synthetic carboxyl intermediate.[2] Leveraging the reactive nucleophilic radical character of $CO_2^{\bullet -}$ in contemporary organic chemistry,[3] we have developed an effective and robust photochemical method for the arylcarboxylation of unactivated alkenes (reduction potential: −3.2 V). This 1,2-dicarbofunctionalization of alkenes using the indole core and CO_2 radical anion (from HCO_2K) under visible light mediated photoredox-HAT conditions, employing *fac*-[Ir(dFppy)$_3$] as photoredox catalyst and DABCO as hydrogen atom transfer (HAT) source, delivers a diverse array of polycyclic indole derivatives. Indoles bearing an alkene at an appropriate position undergo a dearomative 6-*exo-trig* radical cyclization via the arylcarboxylation pathway. *N*-Allyl substituted 2-phenylindoles and 1*H*-benzo[*g*]indole have been proven to be effective substrates for this arylcarboxylation.



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