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Topic-'Synthetic Application of Suzuki Reaction and their Biological Importance'

Introduction

The formation of carbon–carbon bonds is central to organic synthesis because it enables the construction of molecular frameworks from simpler building blocks, allowing chemists to assemble complex natural products, pharmaceuticals, and functional materials. Strategic C–C bond-forming reactions control molecular connectivity, stereochemistry, and functionality, and therefore underpin target-oriented synthesis, library generation for medicinal chemistry, and modular construction in materials science. Efficient, selective, and broadly applicable coupling methods shorten synthetic routes, improve overall yields, and reduce waste — all crucial factors in modern research and industrial settings.

Akira Suzuki's development of the Suzuki–Miyaura cross-coupling in 1979 represented a major advance in the toolbox for making C–C bonds. The method, which couples organoboron reagents with organic electrophiles under palladium catalysis, combined high functional-group tolerance with operational simplicity. Recognition of cross-coupling chemistry by the 2010 Nobel Prize in Chemistry (awarded jointly to Richard F. Heck, Ei-ichi Negishi, and Akira Suzuki) highlights the transformative impact of these reactions on synthetic chemistry. The prize underscored how reliable cross-coupling methods revolutionised the way complex molecules are constructed in academia and industry, enabling routes that were previously impractical or impossible.

Earlier cross-coupling methods such as the Kumada, Negishi, and Heck reactions each contributed important capabilities but had limitations that the Suzuki reaction helped to overcome. Kumada couplings (Grignard reagents with halides) and Negishi couplings (organozinc reagents) are powerful but often require strictly anhydrous conditions and can be incompatible with many functional groups. The Heck reaction (palladium-catalysed arylation of alkenes) is invaluable for C–C bond formation to alkenes but addresses a different substrate class and can give issues with regio- and stereoselectivity in some contexts. Suzuki–Miyaura coupling improved upon these methods by using organoboron partners that are less nucleophilic and more tolerant of protic solvents, allowing milder, more chemoselective conditions and broad substrate scope.

synthesized these strands by demonstrating the practical cross-coupling of organoboron reagents with organic electrophiles under palladium catalysis, showing high functional-group tolerance and operational simplicity. Over subsequent decades, iterative advances (new ligands, alternative boron reagents such as MIDA boronates and organotrifluoroborates, and mechanistic studies) expanded the scope to sp2–sp2, sp2–sp3, and increasingly challenging sp3–sp3 couplings.

The award of the 2010 Nobel Prize in Chemistry to Heck, Negishi, and Suzuki recognized the transformative impact of palladium-catalysed cross-coupling on synthetic chemistry. For the research community, the Prize affirmed how these methods changed retrosynthetic planning, enabling routes that reduced step counts, minimized protecting-group manipulations, and opened access to molecules that were previously impractical to make. The Nobel recognition also accelerated industrial adoption and funded further methodological innovation, underscoring cross-coupling as a central pillar of modern organic synthesis.

General Reaction and Mechanism

General Reaction

Mechanism

$$Ar - X + Ar' - B(OH)_2 \xrightarrow[Pd(0)]{Base} Ar - Ar' + By - products$$

Where:

- Ar–X = Aryl halide (X = Cl, Br, I)
- Ar'–$B(OH)_2$ = Aryl boronic acid
- Pd(0) = Palladium catalyst
- Base = K_2CO_3, NaOH, etc.

Mechanism of Suzuki Reaction

Oxidative addition. The catalytic cycle typically begins with oxidative addition of an aryl or vinyl halide (Ar–X) to a low-valent Pd(0) complex to give a Pd(II)–Ar–X species. This step increases the oxidation state of palladium and places the organic fragment on the metal, creating

Anticancer Agents

Many tyrosine kinase inhibitors and targeted therapies contain biaryl or heteroaryl linkages delivered by Suzuki coupling. The method enables late-stage diversification of aryl substituents to tune potency and selectivity.

Antimicrobials & Antivirals

Suzuki-derived scaffolds show antibacterial, antifungal and antiviral activities. The capacity to append heteroaryl fragments is critical for interacting with diverse biological targets.

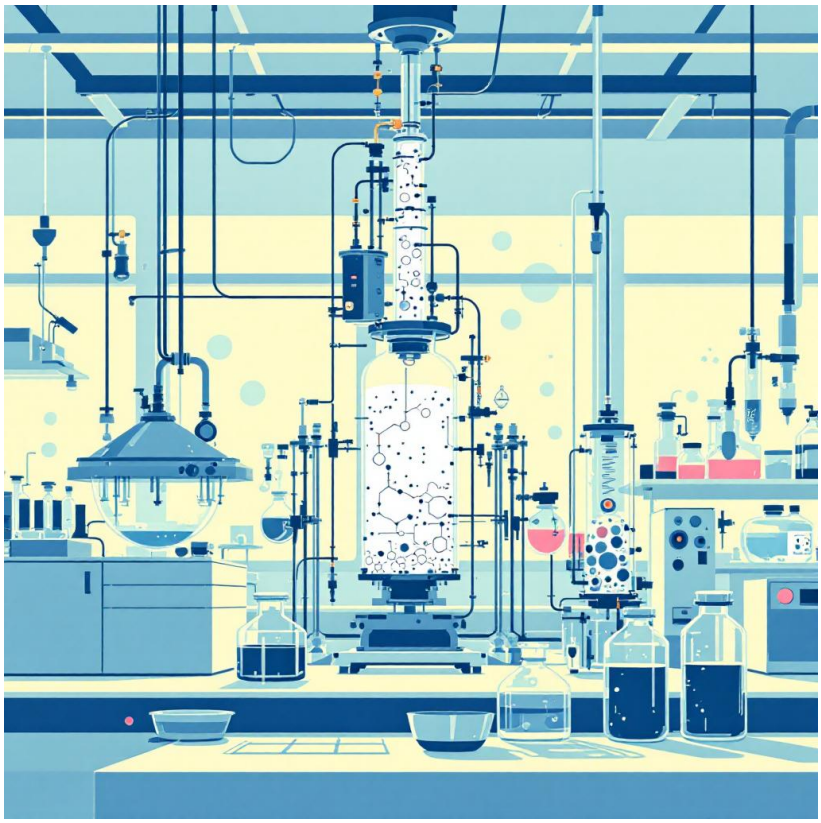
Additional classes include anti-inflammatory agents and enzyme inhibitors (e.g., COX inhibitors), where aryl–aryl connectivity modulates binding geometry and pharmacokinetic properties.

Antimicrobials & Antivirals

Antibacterial agents containing Suzuki-accessible motifs include diverse scaffolds where appended heteroaryls modulate binding to bacterial enzymes or ribosomal components. Examples from literature and discovery programs include substituted biaryl diaryl ether analogues and heteroaryl-linked inhibitors of bacterial topoisomerases and cell-wall enzymes; while specific marketed antibiotics are less commonly purely Suzuki-derived, many lead series in antibacterial discovery rely on cross-coupling to explore heteroaryl substitutions that improve

Recent Advances

Methodological innovations over the last decade have been crucial for addressing the practical



limitations of Suzuki–Miyaura chemistry described previously. By improving catalyst design, reaction media, activation strategies, and process formats, researchers have expanded the reaction's usable substrate space and the range of workable conditions, enabling couplings that were previously low-yielding or impractical at scale. Mechanistic insight — from detailed kinetic studies to computational transition-state analyses — has guided rational ligand and precatalyst design, informed strategies to suppress deleterious side reactions (e.g., protodeboronation or β-hydride elimination), and enabled the translation of bench-scale discoveries into robust manufacturing workflows. These advances have also delivered measurable sustainability and cost benefits: lower catalyst loadings (higher TON/TOF), recyclable heterogeneous systems, and greener solvent choices reduce raw material use, analytical burden for residual metals, and overall process mass intensity (PMI). The past 10–15 years have seen a rapid sequence of developments: early-2010s work on ligand-accelerated palladium systems and NHCs; mid-2010s maturation of nanoparticle and supported Pd technologies and micellar aqueous catalysis; late-2010s–early-2020s scale-out of continuous-flow and packed-bed reactor concepts; and, most recently, integration of computational and machine-learning tools to predict conditions and design catalysts for challenging sp3 couplings and stereospecific variants (representative reviews: Buchwald & co., 2010–2018 ligand developments; Lipshutz, 2011–2020 micellar catalysis; Ley/Plutschack, 2016–

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