

Cite this: *Chem. Sci.*, 2026, 17, 5240

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Expanding the chemical space of peptides via biocompatible tryptophan C7-arylation

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Late-stage functionalization of peptides and amino acids is a powerful strategy for modulating biological activity and enabling targeted molecular imaging, offering a promising route for expanding the chemical space of peptides. Here, we report a Rh-catalyzed, P(III)-directed C7-selective arylation of tryptophan residues using a removable *N*-P^tBu₂ auxiliary. This method exhibits broad substrate scope, excellent regioselectivity, and high functional group tolerance, enabling efficient and modular derivatization of tryptophan-containing amino acids and peptides. The resulting C7-arylated Trp derivatives serve as fluorogenic probes with environment-sensitive, turn-on fluorescence suitable for wash-free imaging of bacterial cells. Moreover, incorporation of these modified residues into antimicrobial peptides significantly enhanced antifungal activity against *Aspergillus fumigatus*, achieving up to 49-fold improvement over the parent peptide. By enabling this biocompatible tryptophan C7-arylation, this work establishes a versatile platform for peptide diversification and therapeutic peptide engineering.

Received 28th October 2025

Accepted 12th January 2026

DOI: 10.1039/d5sc08312e

rsc.li/chemical-science

Introduction

Peptides, as essential scaffolds in biological systems, have garnered increasing attention in therapeutic development and molecular imaging due to their high specificity, biocompatibility, and structural tunability.¹ Chemical modification serves as a powerful strategy to optimize their bioactivity and pharmacokinetic properties, with metal-catalyzed late-stage functionalization emerging as a particularly attractive approach to diversify peptide structures while preserving native function.²

Among proteinogenic amino acids, tryptophan (Trp) presents unique opportunities for selective modification owing to its distinctive reactivity and intrinsic fluorescence.³ In natural products and bioactive peptides, C7-arylated Trp residues often play pivotal roles in structural conformation, molecular recognition, and biological activity, as exemplified by Chloropectin I and AL-471 (specific inhibitors of HIV gp120-CD4 interaction) and TMC-95A-B (HIV therapeutic candidates targeting 20S proteasome inhibition) (Fig. 1A).⁴ The synthesis of these

compounds has attracted significant attention, with the Hoveyda,⁵ Boger,⁶ Zhu,⁷ Danishefsky,⁸ and Hirama⁹ groups achieving total syntheses of cyclic peptides Chloropectin I and TMC-95A-B *via* coupling reactions, where tryptophan C7-arylation served as the key step. While the Hoveyda group successfully constructed the C7-arylated tryptophan motif in Chloropectin I through palladium-mediated Stille coupling in 2003,⁵ this method suffered from limitations including stoichiometric palladium usage and prerequisite preparation of aryl iodides/stannanes, resulting in cumbersome and inefficient syntheses (Fig. 1B). Moreover, these methods face limitations such as poor atom economy, the need for pre-installed leaving groups, and challenges in achieving catalytic processes within complex biomolecular systems. Consequently, the development of more efficient and facile methodologies remains an ongoing pursuit.

Prized for their ability to rapidly generate chemical complexity, C-H activation and functionalization reactions have enabled a paradigm shift in synthetic chemistry. In this context, metal-catalyzed C-H activation has significantly streamlined the syntheses of bioactive complex molecules.¹⁰ While C7-arylation of simple indole substrates has been reported,¹¹ the lack of efficient catalytic strategies for achieving highly regioselective C7-arylation of tryptophan-containing peptides under biocompatible conditions remains a critical bottleneck, severely limiting the development of innovative tryptophan-modified peptide therapeutics. Despite recent advances in Trp functionalization at the C2, C4, and N1 positions,¹² selective arylation at the Trp(C7) position remains particularly challenging due to the inert nature of the C7-H bond, the relatively low reactivity of

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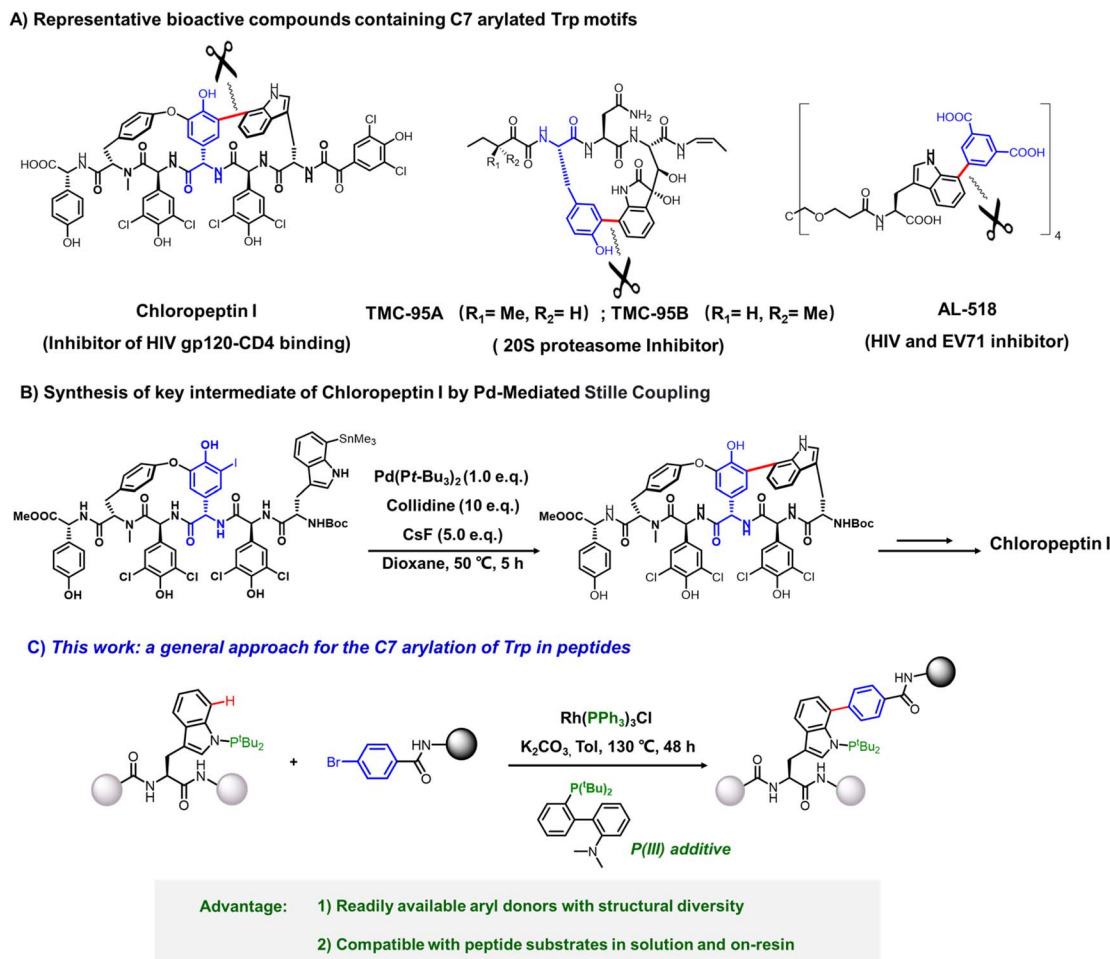


Fig. 1 Late-stage Trp(C7) arylation of peptides via $P^{(III)}$ -directed Rh-catalysis. (A) Representative bioactive compounds containing C7 arylated Trp motifs. (B) Synthesis of key intermediate of Chloropeptin I by Pd-Mediated Stille Coupling. (C) This work: a general approach for the C7 arylation of Trp in peptides.

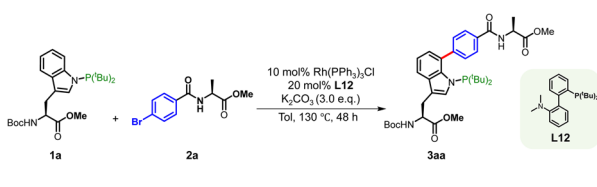
aryl electrophiles compared to C2 or C4 positions, and competing side reactions that complicate site selectivity.¹³

Herein, we report a biocompatible system that overcomes these long-standing limitations and achieves late-stage C7 arylation of Trp residues in both amino acids and peptides (Fig. 1C). In addition to the $P^t\text{Bu}_2$ directing group installed at the Trp(N) to ensure regioselectivity, we employed a Rh catalyst pre-ligated with an intrinsic phosphine ligand in combination with an external P-based small-molecule additive. This design proved crucial for enhancing the catalytic efficiency in peptide substrates. This method utilizes simple and readily available bromoaryl compounds as aryl donors and is compatible with both solution-phase and solid-phase peptide synthesis (SPPS), providing access to structurally diverse Trp-modified peptides. Furthermore, we demonstrate its utility in constructing environmentally sensitive Trp-derived fluorescent probes and in enhancing the bioactivity of antimicrobial peptides through strategic C7 functionalization. This method not only broadens the substrate scope and enhances reaction efficiency but also provides a potentially general solution for achieving selective C7 arylation in complex peptide contexts.

Results and discussion

We initiated our study with BocNH-($N-P^t\text{Bu}_2$)Trp-CO₂Me (**1a**) and aryl bromide-modified alanine derivative **2a**, employing Rh(PPh₃)₃Cl (6 mol%) as the catalyst and K₂CO₃ as the base in toluene at 120 °C for 24 h, which afforded C7-selective adduct **3aa** in ~6% yield (Table S1, entry 1). NMR analysis confirmed that the arylation occurred selectively at the C7 position of the Trp residue (Fig. S1). Screening a series of mono- and bidentate ligands revealed Ligand 12 (**L12**) as optimal, improving the yield to 30% (Tables S1 and S2, entry 9). Subsequent optimization of reaction parameters, including temperature, reaction time, solvent, catalyst and ligand loading, further improved the efficiency, delivering up to 80% yield (Table 1, entry 1, entries 7–13). Increasing the catalyst loading to 15 mol% gave only marginal improvement (Table S1, entry 13). Other catalysts, such as [Rh(cod)Cl]₂ and [Rh(coe)₂Cl]₂, proved much less effective (Table 1, entries 2 and 3), and control experiments confirmed the essential role of rhodium catalysis (Table 1, entry 4). Alteration of the base failed to improve the reaction efficiency (Table 1, entries 5 and 6). The optimized conditions were



Table 1 Optimization of reaction conditions^a


Entry	Variation from the "standard conditions"	Yield of 3aa ^b (%)
1	None	80
2	[Rh(cod)Cl] ₂ instead of Rh(PPh ₃) ₃ Cl	5
3	[Rh(coe) ₂ Cl] ₂ instead of Rh(PPh ₃) ₃ Cl	Trace
4	Without Rh(PPh ₃) ₃ Cl	—
5	Using NaOAc instead of K ₂ CO ₃	10
6	Using ^t BuOLi instead of K ₂ CO ₃	—
7	6 mol% Rh(PPh ₃) ₃ Cl, without L12	12
8	6 mol% Rh(PPh ₃) ₃ Cl, 10 mol% L12	30
9	6 mol% Rh(PPh ₃) ₃ Cl, 20 mol% L12	65
10	24 h	40
11	120 °C	32
12	DME as the solvent	57
13	PhCl as the solvent	73

^a Conditions: **1a** (0.10 mmol), **2a** (0.30 mmol), 20 mol% **L12**, K₂CO₃ (0.3 mmol), 10 mol% catalyst, solvent (1.0 mL), at 130 °C under Ar atmosphere for 48 h. ^b Isolated yields are reported.

thus established as: 10 mol% Rh(PPh₃)₃Cl, 3.0 eq. K₂CO₃, 20 mol% **L12**, with toluene as solvent at 130 °C for 48 h.

Next, we evaluated the substrate scope of the P(III)-directed Trp(C7) arylation (Fig. 2). Using Trp derivative **1a** and simple aryl bromides as model substrates, we found that **L12** could be omitted without loss of efficiency. A wide range of aryl bromides proved suitable, including *ortho*-, *meta*-, and *para*-substituted derivatives, affording products **3ab–3ai** in 72–92% yields. Lipidation is an important modification of peptides and proteins.¹⁴ Notably, a *para*-aliphatic aryl bromide (**2j**) delivered the lipidated product **3aj** in 79% yield, highlighting the utility of this method for site-specific lipid installation in Trp(C7) (Fig. 2, entry **3aj**). Functional handles such as N-heterocycles (methylindole, quinoline), photoreactive groups (benzophenone, 9-fluorenone), and polycyclic aromatics were also well tolerated, giving **3ak–3aw** in 69–90% yields. Importantly, the protocol accommodated fluorescent motifs, with bromo-BODIPY (**2x**) and bromo-tetraphenylethylene (**2y**) furnishing **3ax** and **3ay** in 88% and 87% yields, respectively. To address the potential epimerization issue during the reaction, substrates **1a** and **1a'** were synthesized and subjected to reactions with aryl bromide **2i**. Results showed that crude reaction mixtures of **1a** and **1a'** gave distinct retention times when analyzed by HPLC (Fig. S2), indicating that the stereochemical integrity was retained and no epimerization occurred under the reaction conditions. These results underscore the broad compatibility of the method with structurally diverse and functionalized aryl bromides.

Vendrell and Lavilla *et al.* have shown that direct C2-conjugation of BODIPY to tryptophan affords environmentally sensitive fluorophores suitable for imaging membrane interactions.¹⁵ The C7-BODIPY-conjugated tryptophan derivative **3ax**

exhibited the characteristic absorption at 498 nm and emission at 520 nm of BODIPY fluorophores (Fig. 2 and S3). Notably, **3ax** showed a substantial enhancement in fluorescence emission efficiency under hydrophobic conditions, with a 12-fold increase in emission intensity at 515 nm when the solvent was changed from H₂O/dioxane (95 : 5) to pure dioxane. A second example compound **3ay**, featuring C7-conjugation of tetraphenylethylene (TPE) to tryptophan, introduced a distinct substitution pattern that significantly enhanced the aggregation-induced emission (AIE) effect compared to the parent TPE molecule (Fig. 2). A pronounced fluorescence turn-on was observed even at low water fractions in H₂O/DMSO mixtures, highlighting the sensitivity of conjugate **3ay** to changes in solvent polarity and aggregation state. Collectively, these findings highlight both the synthetic utility of the P(III)-directed Rh-catalyzed Trp(C7) arylation strategy and the potential of site-selective fluorophore installation to create unnatural amino acids with tunable photophysical properties.

The robustness of this arylation method prompted us to explore its application in the site-selective modification of Trp(C7) in short peptides (Fig. 3A). To access the required peptide substrates, we leveraged Fmoc- or Boc-protected N-P(^tBu)₂-Trp as a versatile building block compatible with both liquid-phase and solid-phase peptide synthesis, and subsequently incorporated this residue into target sequences through standard peptide assembly protocols. Notably, in these peptide-based reactions, the presence of ligand **L12** was indispensable for productive arylation. Using aryl bromide-modified alanine **2z** as the arylation reagent, Trp-containing dipeptides **1b–1j** were all converted into the corresponding Trp(C7)-arylated peptide-Ala conjugates in good yields (entries **3bz–3jz**). A broad range of side chains, including protected Tyr, Ser, Lys, Trp, His, Asp, Glu, unprotected Met and Phe were well tolerated in this protocol with no observable methionine oxidation. The position of the Trp(N-P(^tBu)₂) residue in peptides exerted minimal influence, as illustrated by the efficient generation of **3kz–3mz**. We further applied this method in the Trp(C7) modification of tri-, tetra- and pentapeptides with **2z**, affording modified products **3nz–3pz** in 50–63% isolated yields. To further assess whether arylation compromises stereochemical integrity, we used dipeptide **3fz** as a model compound. The arylation reaction mixture of compound **3fz** was subjected to Marfey's reagent (FDLA) derivatization and analyzed by LC-MS. Results showed that the amino-acid configuration is well retained during the reaction, with no detectable epimerization (Fig. S4). We next applied this method to solid-phase peptide synthesis (SPPS) (Fig. 3B and S5). BocNH-(N-P(^tBu)₂)Trp-COOH was synthesized as a building block and incorporated into model hexapeptide **P1** following standard SPPS protocols. Direct on-resin C7-arylation of the resin-supported **P1** was conducted under standard conditions. The resulting peptide product was cleaved and deprotected with 95% TFA, followed by HPLC purification, affording product **P3ai** in 9% overall isolated yield. This result showed that the reaction was feasible on resin, further demonstrating the utility of this method.

Crosslinking amino acids and peptides represents a powerful approach for generating oligomers and expanding their



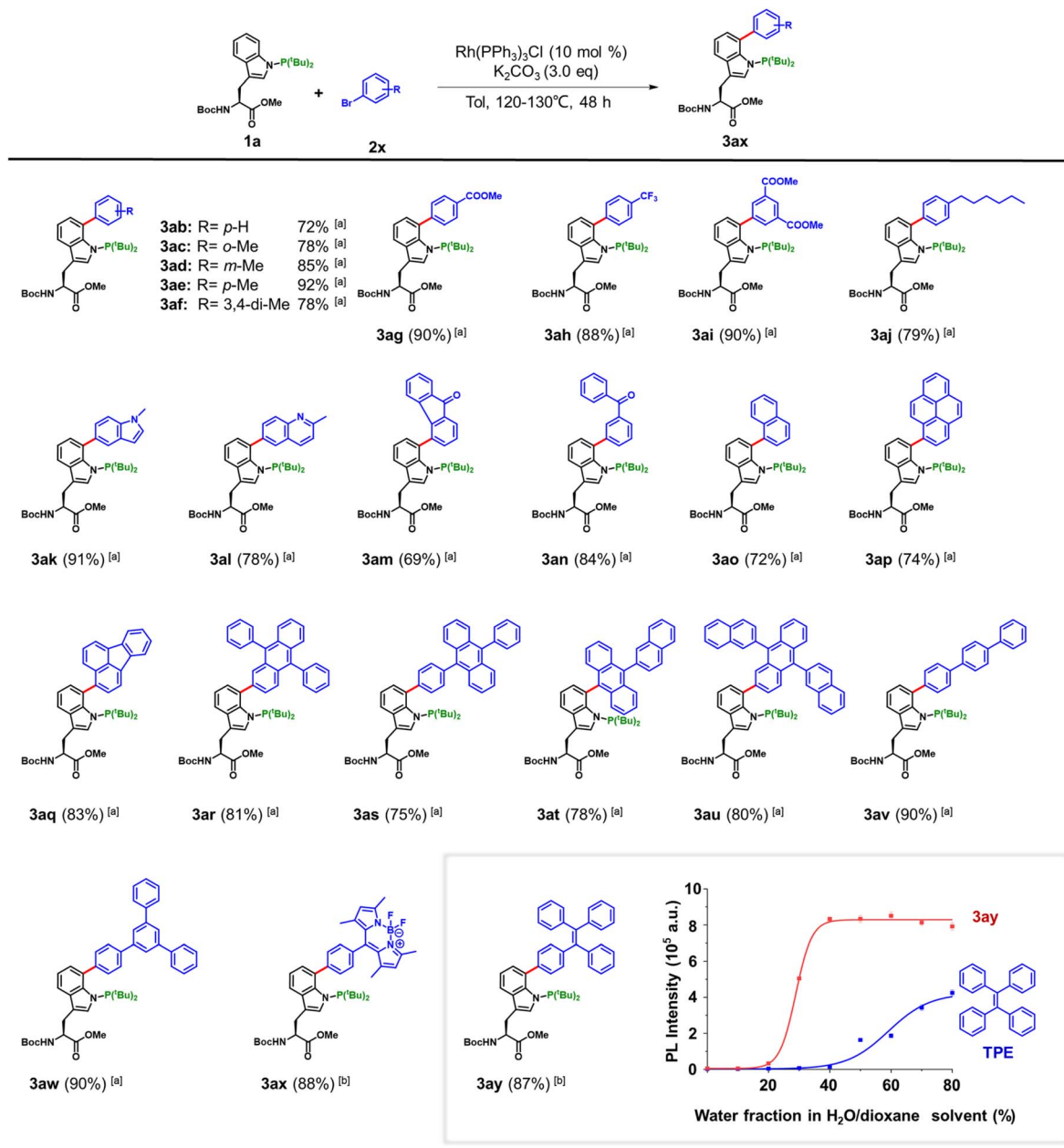


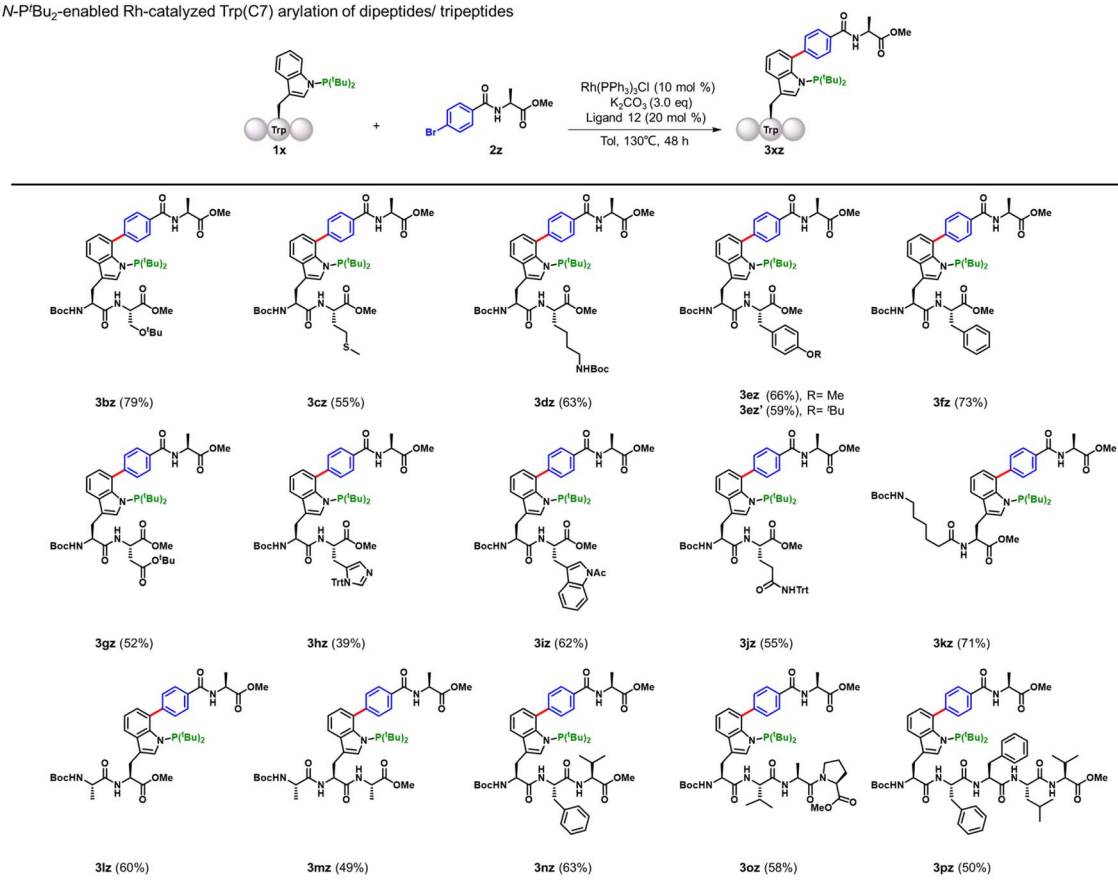
Fig. 2 *N*- $\text{P}(\text{tBu})_2$ -directed Rh-catalyzed Trp(C7)-selective arylation of substrate **1a**. Conditions: [a] **1a** (0.1 mmol), **2x** (0.3 mmol), K_2CO_3 (0.3 mmol), 10 mol% $\text{Rh}(\text{PPh}_3)_3\text{Cl}$, solvent (1.0 mL), at 120 °C under Ar atmosphere for 48 h. [b] 130 °C. Isolated yields are reported. Fluorescent emission spectra of **3ay** and TPE (10 μM) were recorded in $\text{H}_2\text{O}/\text{dioxane}$ mixtures upon excitation at 325 nm.

structural and functional diversity, as exemplified by aryl–aryl crosslinks in dimeric peptide natural products.¹⁶ Inspired by this, we next explored our method for crosslinking of amino acids using di- and tribromoaryl linkers (Fig. 4). Dibromobenzene derivatives **3a–3e** efficiently generated Trp–Trp dimers in good yields (Fig. 4, entries **4aa–4ae**). Other linkers, including dibromo-substituted terphenyl, naphthalene, 1-phenyl-4-(4-phenylphenyl)benzene, fluorescent chrysene derivatives and aliphatic substituted bromoaryl compounds also delivered Trp dimers in moderate to good yields (entries **4af–4aj**). Remarkably, trimerization could be realized with 1,3,5-

tribromobenzene and 1,3,5-tris(4-bromophenyl)benzene, affording the Trp trimers **4ak** and **4al** in 41% and 45% yield, respectively. These findings underscore the broad versatility of this arylation strategy in constructing structurally complex peptide architectures.

To address the challenge of removing the *N*- P^tBu_2 directing group from Trp(C7) arylation products, we established tailored deprotection protocols for both amino acid and peptide substrates (Fig. 5). Treatment with TBAF at 80 °C for 12 hours afforded the deprotected Trp(C7)-arylated amino acids and peptides in good yields, as demonstrated by **5i'** and **5j'** in 66%



A) *N*-P^tBu₂-enabled Rh-catalyzed Trp(C7) arylation of dipeptides/ tripeptides

B) On-resin Trp(C7) arylation of peptides

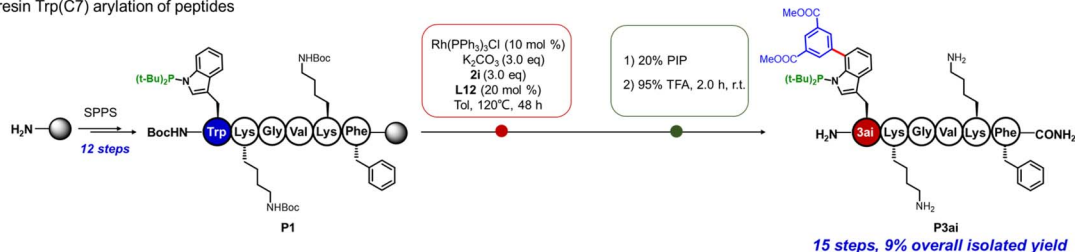


Fig. 3 In solution and on-resin Trp(C7) arylation of peptides. (A) *N*-P^tBu₂-enabled Rh-catalyzed arylation of di-, tri-, tetra- and pentapeptides at the C7 position of Trp residues. Conditions: **1x** (0.1 mmol), **2z** (0.3 mmol), K_2CO_3 (0.3 mmol), 20 mol % **L12**, 10 mol % $\text{Rh}(\text{PPh}_3)_3\text{Cl}$, solvent (1.0 mL), 48 h, at 130 °C under Ar. (B) On-resin Trp(C7) arylation of peptides. Conditions: **P1** (0.1 mmol), **2i** (0.3 mmol), K_2CO_3 (0.3 mmol), 20 mol % **L12**, 10 mol % $\text{Rh}(\text{PPh}_3)_3\text{Cl}$, solvent (3.0 mL), 48 h, at 120 °C under Ar. Isolated yields are reported.

and 71% yields, respectively (Fig. S6). This procedure demonstrated excellent compatibility with common N- and C-terminal protecting groups, including N-terminal triflyl (Tf) groups and C-terminal methyl esters. For Trp(C7)-arylated peptides synthesized *via* SPPS, the *N*-P^tBu₂ protecting group can be removed concomitantly under standard global deprotection conditions by extending the reaction time (Fig. 5 and S7, entry 6c).

With the methodology established, we applied our Trp(C7) arylation platform to synthesize functional Trp derivatives and peptides. Fluorescent amino acids are valuable tools for non-invasive labeling of peptides and proteins.^{3a,b,17} While native Trp **5a** absorbs at 280 nm and emits around 350 nm, modification of its indole chromophore through conjugation with

alkenes, aryl groups, fluorophores and other substituents can significantly enhance its photophysical properties.^{15d,18} Motivated by this, we combined Trp C–H modification strategies, including our C7 arylation, to design derivatives with tailored fluorescence. Compound **5b** was synthesized from TfNH-Trp-CO₂Me (**5a**) *via* Pd-catalyzed C4 olefination (Fig. 6A). Compared to native Trp, the UV-vis absorption spectrum of **5b** was significantly red-shifted with absorption extending to 408 nm (Fig. 6B and S8). Sequential C7 arylation (*N*-P^t(*t*Bu)₂-directed Rh catalysis), C2 arylation, and C4 alkenylation furnished **5d** (Fig. 6A). The additional arylation further red-shifted the absorption edge to 460 nm (Fig. 6B and S8). Compound **5d** exhibited an emission maximum at 500 nm, corresponding to a Stokes shift of 140 nm (Fig. S9). Encouraged by these results,



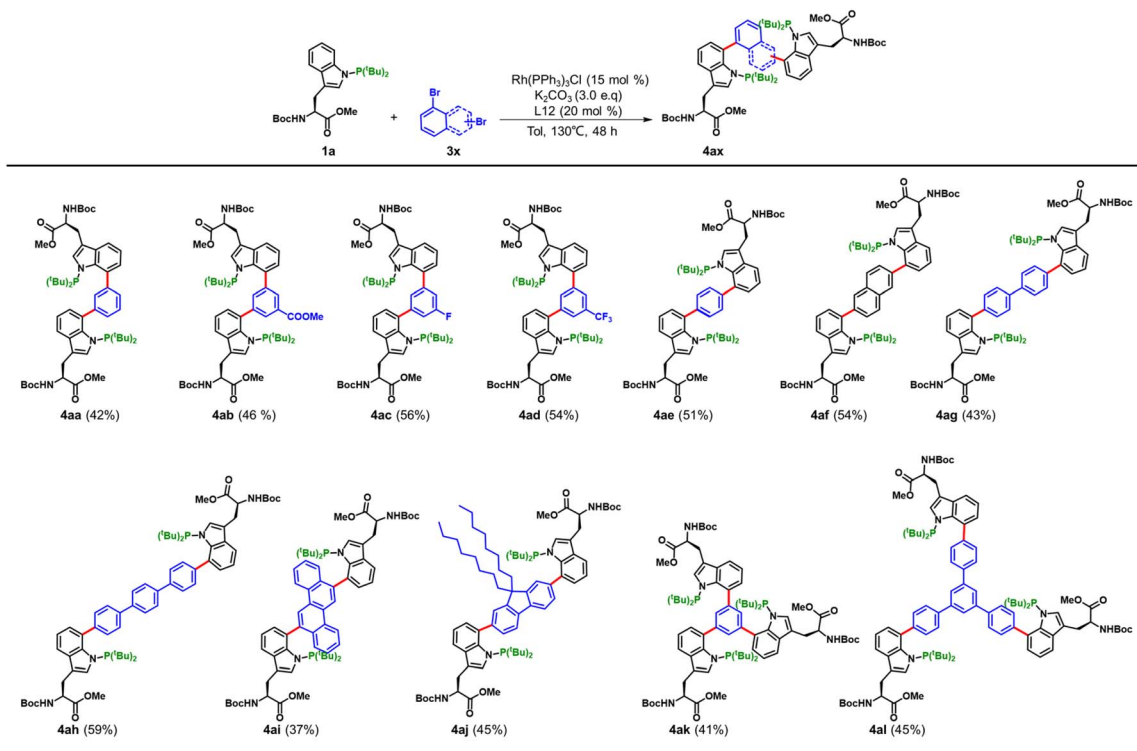


Fig. 4 Crosslinking of Trp *via* C7 arylation. Standard conditions: **1a** (0.6–0.9 mmol), **3x** (0.1 mmol), K_2CO_3 (0.3 mmol), 20 mol% **L12**, 15 mol% $Rh(PPh_3)_3Cl$, solvent (1.0 mL), 48 h, at 130 °C under Ar. Isolated yields are reported.

we synthesized a series of Trp derivatives (**5b–5f**) bearing C2 and C7 arylations in combination with C4 olefination (Fig. S8). All tryptophan derivatives demonstrated excellent stability when stored at room temperature and under daylight (Fig. S10).

Fluorescence studies in H_2O /dioxane mixtures, simulating hydrophobic and hydrophilic microenvironments, revealed pronounced environmental sensitivity of **5b–5f** (Fig. S11). Notably, **5c** exhibited a 296-fold fluorescence enhancement when the solvent was changed from water to 99% dioxane, whereas **5b** increased only 7.8-fold, highlighting the critical role of C7 arylation in modulating environmental responsiveness. Similarly, compound **5d** displayed a 172-fold fluorescence enhancement under the same conditions, underscoring the potential of these derivatives for wash-free imaging applications (Fig. 6C and S11). Comparison across derivatives demonstrates

that the site of modification strongly influences photophysical properties of Trp: C7 arylation consistently imparts enhanced environmental sensitivity and fluorescence turn-on effects, while C2 and C4 modifications primarily tune absorption maxima. This site-specific tuning enables the rational design of unnatural Trp derivatives with distinct and predictable optical behaviors, providing a versatile platform for the development of fluorescent probes and functional peptides.

Next, we employed compound **5d** as a fluorophore for live-cell fluorescence imaging, taking advantage of its 460 nm absorption and strong fluorescence turn-on response in hydrophobic environments. Through SPPS, amino acid **5g** (a derivative of **5d**) was incorporated into the amphiphilic, bacterial membrane-targeting peptide PAF26 to generate the labeled peptide **5h** (Fig. 6D and S12).¹⁹ Compound **5g** displayed

Removal of the N - P^tBu_2 group via global deprotection after SPPS

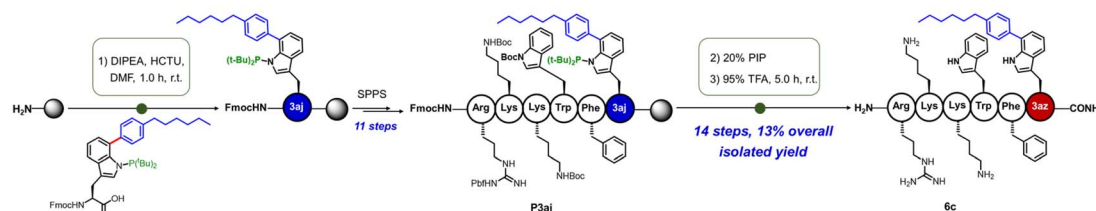


Fig. 5 Deprotection of the $P^{(III)}$ directing group. Removal of the N - P^tBu_2 directing group *via* global deprotection of peptides synthesized from SPPS. TFA cleavage cocktail (TFA/TIPS/ H_2O = 95/2.5/2.5, v/v/v), 5 h, at 30 °C.



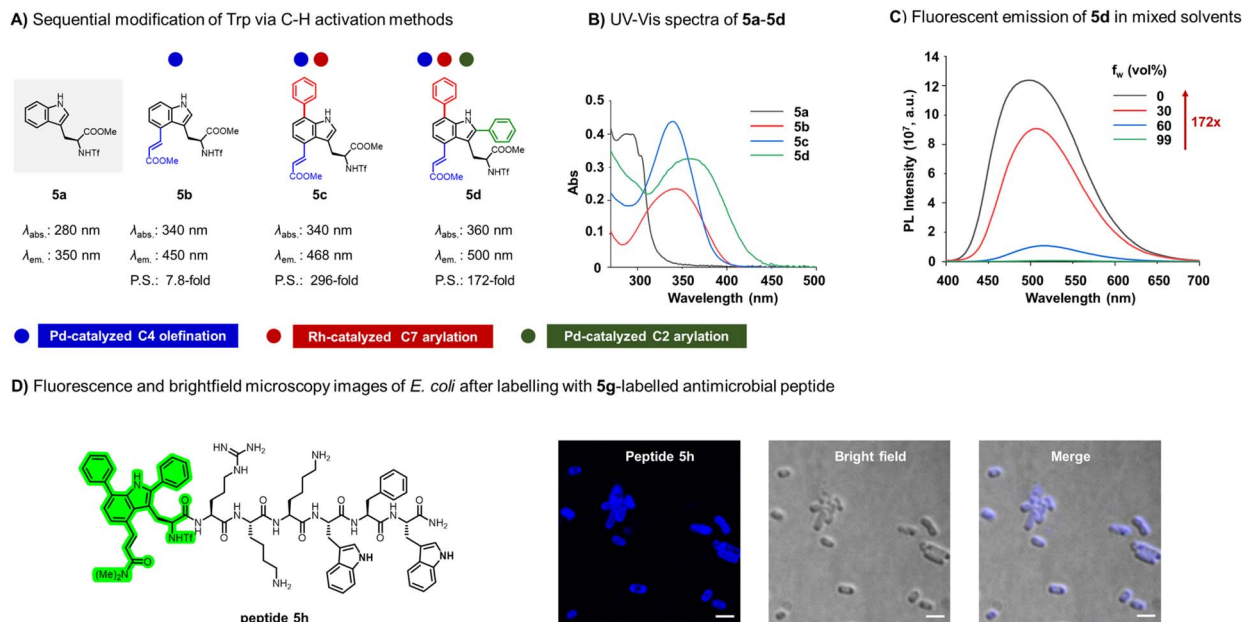


Fig. 6 Synthesis of tryptophan fluorescent molecules by *N*- $P^t\text{Bu}_2$ -enabled Rh-catalyzed arylation of Trp. (A) Sequential modification of Trp via C-H activation methods. (B) UV-vis absorption spectra of **5a–5d** (10 μM) in MeCN. (C) Fluorescence-fold of **5d** were determined in H_2O /dioxane mixtures (0.1: 9.9 to 0: 100, v/v) at a concentration of 5 μM , with excitation at 355 nm. f_w (V%) represents the volumetric fraction of water. (D) Fluorescence and brightfield microscopy images of *E. coli* after labelling with **5g**-labelled antimicrobial peptide (25 mM) (excitation at 488 nm). Scale bar: 2 μm .

excellent chemical stability and was fully compatible with standard SPPS protocols.

To evaluate imaging performance, various concentrations of **5h** were incubated with *E. coli* before analyzed by flow cytometric, and 25 μM was identified as optimal (Fig. S13). Owing to its environment-responsive turn-on behavior, **5h** enabled direct visualization of bacterial cells without the need for washing steps. Real-time, wash-free imaging of *E. coli* cultures was successfully achieved using confocal laser scanning microscopy (CLSM), delivering high signal-to-noise ratios (Fig. 6D). These results demonstrate that the C7-arylated fluorescent Trp derivative can be used to label bacterial-targeting peptides without compromising their function, while also providing a practical platform for wash-free imaging in live cell environments.

Lipidation and arylation have proven to be robust and effective strategy for improving the therapeutic potential of peptide therapeutics.²⁰ We next evaluated the function of various C7-modified Trp derivatives by installing them into the antifungal hexapeptide **PAF26**. Six **PAF26** analogs (**6a–6f**) bearing distinct modified Trp residues were synthesized *via* Rh-catalyzed arylation (Fig. 7 and S14). Growth-inhibition assays against drug-resistant, marine-derived *Aspergillus fumigatus* revealed clear structure-activity relationships. Introduction of *N*- $P^t\text{Bu}_2$ alone (compound **6a**) produced only marginal enhancement relative to **PAF26** ($\text{IC}_{50} = 89.2 \mu\text{M}$ vs. $97.9 \mu\text{M}$). Incorporation of an aryl substituent lacking the alkyl chain (**6b**) or a phenyl-alkyl lipid tail without *N*- $P^t\text{Bu}_2$ (**6c**) afforded moderate improvements ($\text{IC}_{50} = 78.4$ and $73.7 \mu\text{M}$, respectively), indicating that neither organophosphorus substitution nor lipidation alone is sufficient to substantially boost antifungal

activity. In striking contrast, dual modification with both *N*- $P^t\text{Bu}_2$ and a phenyl-alkyl chain (residue **3aj**, compound **6d**) resulted in a dramatic activity increase ($\text{IC}_{50} = 2.0 \mu\text{M}$), representing ~ 49 -fold higher potency than native **PAF26** and ~ 35 -fold stronger inhibition than lipidated analog **6c**. These comparisons demonstrate that lipidation and phosphoramidate substitution act cooperatively to strengthen antifungal activity—consistent with reports that organophosphorus motifs can favorably influence bioactivity.²¹ Together, the SAR trends across these Trp derivatives highlight the utility of C7-selective Trp arylation for the systematic modulation of peptide function, providing a versatile platform for antifungal peptide optimization and bioactive peptide probe development.

Conclusions

In conclusion, we have developed a robust, regioselective Rh(I)-catalyzed C7 arylation of tryptophan *via* a removable *N*- $P^t\text{Bu}_2$ directing group, enabling late-stage modification of amino acids and peptides. This versatile platform accommodates diverse aryl bromides and peptide scaffolds, facilitating the synthesis of structurally and functionally diverse Trp derivatives. The approach supports the design of environmentally responsive fluorophores with large Stokes shifts for wash-free imaging, as well as lipidated peptide analogues with enhanced antifungal activity. A key advance of this study is the identification of electron-rich, sterically hindered $P(\text{III})$ ligands as critical promoters of Rh-catalyzed Trp(C7) arylation in peptide substrates. These ligands likely suppress coordination interference from peptide amide bonds and side chains while



Compound	IC ₅₀ (μM)
PAF26	97.9
6a	89.2
6b	78.4
6c	73.7
6d	2.0
6e	68.0
6f	73.0

Fig. 7 Antimicrobial activities of PAF26 derivatives against *Aspergillus fumigatus*.

facilitating oxidative addition and reductive elimination, thereby enhancing reaction efficiency. The rate-accelerating effect of bulky phosphine ligands has been validated in related Pt/Pd-catalyzed C–H activation systems.²² Collectively, these results highlight the potential of site-selective Trp(C7) functionalization as a powerful strategy to expand the chemical space of peptides, enabling the rational design of functional probes and bioactive peptides with tailored photophysical and biological properties.

Author contributions

H. W. and Z. S. initiated and directed this study. L. W., Y. Z. and Y. S. carried out the design, chemical synthesis and characterization of amino acids and peptides. B. W., Y. X. and T. W. performed antibiotic experiments. All authors participated in the data analysis and manuscript preparation.

Conflicts of interest

There are no conflicts to declare.

Data availability

Supplementary information (SI): data for this article, including experimental procedures, and characterization data of all the substrates and products, are available in the supplementary information of the manuscript. See DOI: <https://doi.org/10.1039/d5sc08312e>.

Acknowledgements

This work is supported by NSF of China (Grant 22325702), National Key R&D Program of China (2025YFA0922700), the Natural Science Foundation of Jiangsu Province (BK20253010, BK20232020 and BG2025036), Fundamental and Interdisciplinary Disciplines Breakthrough Plan of the Ministry of Education of China (JYB2025XDXM507), and Yachen Foundation of Nanjing University.

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