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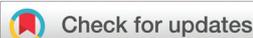CCS CHINESE CHEMICAL SOCIETY 中国化学会

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Pyrazolium-ylide [3 + 2] cycloaddition/oxidative aromatization for the construction of 1*H*-pyrrolo[1,2-*b*]pyrazoles

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Despite their simple 10π aromatic nature and considerable functional potential, the chemistry of 5/5-fused N-heteroaromatic systems remains underdeveloped. Herein, we report a general strategy for accessing 1*H*-pyrrolo[1,2-*b*]pyrazoles, a largely unexplored "orphan" class of heterocycles. The methodology features the generation of pyrazolium ylides followed by [3 + 2] cycloaddition with alkynes under mild conditions, and a subsequent oxidative aromatization step that effectively suppresses undesired ring-opening and excessive addition pathways. The substrate scope demonstrates broad functional-group tolerance and accommodates diverse substitution patterns. Combined experimental and computational studies indicate a stepwise cycloaddition mechanism, the involvement of intrinsically unstable cyclo-adducts, and the presence of competing pathways that render the chemoselectivity highly sensitive to subtle changes in reaction conditions. Finally, downstream derivatization highlights the utility of the 5/5-fused framework as a versatile platform for constructing more structurally complex and/or functionally enriched molecules.
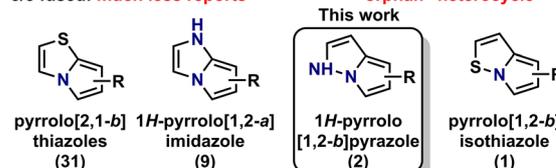
Introduction

Nitrogen-containing heterocycles play an increasingly important role in medicinal chemistry, with 82% of drugs launched between 2013 and 2023 incorporating these structures.[1] Beyond pharmaceuticals, nitrogen-containing heterocycles are also utilized in agrochemicals, metal complexes, advanced materials, and various other applications, leading to the synthesis of numerous valuable compounds.[2] Among these, 10π aromatic heterocycles, such as indole derivatives commonly found in biomolecules, are key components of many pharmaceutical compounds. Notably, numerous 5/6-fused compounds have been synthesized and evaluated for their bioactivities, as well as their potential roles in advanced materials (Scheme 1A).[3] In contrast, research on 5/5-fused N-heterocyclic rings has lagged far behind, despite their potential advantages, such as the possibility that more compact fused rings could enhance affinity for target proteins and that altered substituent orientations and nitrogen atom positions could yield the desired physical properties. For example, pyrrolo[2,1-*b*]thiazole[4] and 1*H*-pyrrolo[1,2-*a*]imidazole,[5] which contain N–C–X (X

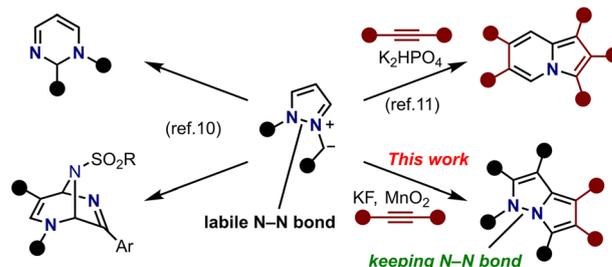**A. Number of journal publications on synthesis** (as of Jan. 2026)

5/6 fused: many reports (selected 2 ≤ N)

| indole (318,996) | indazole (15,247) | benzimidazole (87,765) | indolizine (16,967) |
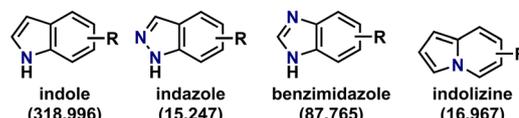
5/5 fused: much less reports   **"orphan" heterocycle**

This work

| pyrrolo[2,1-*b*]thiazoles (31) | 1*H*-pyrrolo[1,2-*a*]imidazole (9) | 1*H*-pyrrolo[1,2-*b*]pyrazole (2) | pyrrolo[1,2-*b*]isothiazole (1) |

B. Reactions on pyrazolium ylides

K$_2$HPO$_4$ (ref.11)

This work   KF, MnO$_2$

labile N–N bond   *keeping N–N bond*   (ref.10)   SO$_2$R   Ar

Scheme 1 Background of this work.

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2228 | *Org. Chem. Front.*, 2026, **13**, 2228–2234

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= N or S) bonds, have been far less investigated, even though they have been reported to exhibit notable biological activities, including anticancer activity.[6] Furthermore, only a few reports on 1*H*-pyrrolo[1,2-*b*]pyrazole and pyrrolo[1,2-*b*]isothiazole, featuring adjacent heteroatoms, have been reported to date, despite their potential for attractive applications similar to those of other 10π heteroaromatic compounds.[7] Thus, no studies have been conducted on their physicochemical properties or biological activities.

The 1,3-dipolar cycloaddition of azomethine ylides is a powerful strategy for the construction of five-membered nitrogen-containing heterocycles, as it enables the formation of two bonds in a single step with excellent atom economy.[8] For 5/6-fused ring systems, the [3 + 2] cycloaddition of pyridinium ylides has been established as an efficient method for accessing indolizines, typically starting from readily available pyridines.[9] In contrast, applying analogous ylide chemistry to pyrazoles—a class of inexpensive and accessible N-heterocycles—presents several intrinsic challenges:

1. Pronounced susceptibility toward N–N bond cleavage. To date, all reported studies involving pyrazole-derived ylides ultimately result in fragmentation of the N–N bond (Scheme 1B).[10]

2. Instability of the resulting intermediates. Even when cycloaddition occurs, the initially formed enamines are inherently unstable, preventing the construction of 5/5-fused ring systems.[11]

Herein, we report a strategy that overcomes these limitations and enables the synthesis of polysubstituted 1*H*-pyrrolo [1,2-*b*]pyrazoles through the cycloaddition of pyrazolium ylides. The protocol involves the generation of pyrazolium ylides under mild conditions, [3 + 2] cycloaddition with alkynes, and a subsequent oxidative aromatization in a single operation that collectively enables the smooth formation of this previously inaccessible 5/5-fused heteroaromatic framework.

Results and discussion

At the outset of this study, the reaction conditions were optimized using pyrazolium salt **1a** as a representative ylide precursor (Table 1). Treatment of **1a** with 1.0 equiv. of dimethyl acetylenedicarboxylate (DMAD, **2a**), 1.2 equiv. of *m*-chloroperoxybenzoic acid (*m*CPBA), and 2.0 equiv. of dipotassium hydrogenphosphate in *N,N*-dimethylformamide (DMF, 0.05 M) at 50 °C afforded only a trace amount of 1*H*-pyrrolo[1,2-*b*]pyrazole **3a** (entry 1). Screening of oxidants showed that the use of manganese(IV) oxide increased the NMR yield of **3a** to 23%, although the mass balance remained poor (entries 2 and 3). Lowering the reaction temperature slightly improved the yield and resulted in the detection of indolizine **4a** in 5% NMR yield (entry 4). Subsequent examination of bases revealed that potassium fluoride provided the highest yield among those tested (entries 5–7). Using 2.0 equiv. of DMAD increased the yield of **3a**, whereas employing a larger excess resulted in no further improvement (entries 8 and 9). The reaction concentration significantly influenced the chemoselectivity: a higher concen-

Table 1 Optimization of reaction conditions[a]
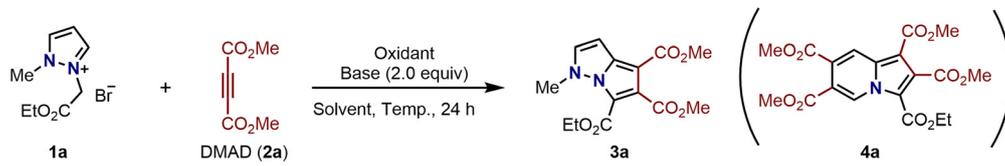
Entry	2a (equiv.)	Oxidant (equiv.)	Base	Solvent (M)	Temp.	Yield[b] of 3a (%)	Yield[b] of 4a (%)
1[c]	1.0	*m*CPBA (1.2)	K$_2$HPO$_4$	DMF (0.05)	50 °C	Trace	ND
2[c]	1.0	H$_2$O$_2$ (1.2)	K$_2$HPO$_4$	DMF (0.05)	50 °C	11	ND
3[c]	1.0	MnO$_2$ (20)	K$_2$HPO$_4$	DMF (0.05)	50 °C	23	ND
4	1.0	MnO$_2$ (20)	K$_2$HPO$_4$	DMF (0.05)	rt	27	5
5	1.0	MnO$_2$ (20)	KF	DMF (0.05)	rt	34	7
6	1.0	MnO$_2$ (20)	NaF	DMF (0.05)	rt	21	1
7	1.0	MnO$_2$ (20)	CsF	DMF (0.05)	rt	3	ND
8	2.0	MnO$_2$ (20)	KF	DMF (0.05)	rt	40	2
9	4.0	MnO$_2$ (20)	KF	DMF (0.05)	rt	35	2
10	2.0	MnO$_2$ (20)	KF	DMF (0.1)	rt	10	27
11	2.0	MnO$_2$ (20)	KF	DMF (0.025)	rt	44	Trace
12	2.0	MnO$_2$ (40)	KF	DMF (0.025)	rt	61 (53)[d]	1
13	2.0	MnO$_2$ (60)	KF	DMF (0.025)	rt	55	Trace
14	2.0	MnO$_2$ (40)	KF	DCM (0.025)	rt	14	Trace
15	2.0	MnO$_2$ (40)	KF	Toluene (0.025)	rt	10	1
16	2.0	MnO$_2$ (40)	KF	DMSO (0.025)	rt	22	14
17[e]	2.0	MnO$_2$ (40)	KF	DMF (0.025)	rt	7	ND

[a] Conditions: unless mentioned otherwise, all reactions were performed with **1a** (0.2 mmol), DMAD, MnO$_2$, base, and solvent under an argon atmosphere at room temperature for 24 h. [b] Determined by ^{1}H NMR using triphenylmethane as an internal standard. [c] The reaction was carried out for 18 h. [d] Isolated yield. [e] Activated MnO$_2$ was used instead of the commercially available reagent.

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*Org. Chem. Front.*, 2026, **13**, 2228–2234 | **2229**

tration led to increased formation of indolizine **4a**, whereas dilution to 0.025 M provided **3a** in higher yield with almost no detectable by-products (entries 9–11). In addition, despite the heterogeneous nature of manganese(IV) oxide, increasing its stoichiometry to 40 equiv. furnished **3a** in 61% yield (entries 12 and 13).

Solvent screening revealed that DMF was the most effective solvent for this transformation (entries 14–16). Finally, the use of manganese(IV) oxide activated according to Attenborough's method resulted in a significantly lower yield (entry 17).[12] Thus, the conditions shown in entry 12 were identified as optimal. It should be noted that this protocol enables scale-up synthesis with only minor modifications (see the SI).

With the optimal conditions for the synthesis of 1*H*-pyrrolo [1,2-*b*]pyrazoles in hand, we next examined the substrate scope (Scheme 2). We began by exploring substituent effects at the 4-position of the pyrazolium salt. Substrates bearing fluoro, bromo, iodo, or methyl substituents underwent smooth transformation to give the corresponding products **3b–3e**, whereas

an electron-donating methoxy substituent resulted in a decreased yield of **3f**. The structure of the brominated product **3c** was unambiguously confirmed by X-ray crystallography, representing the first structural visualization of the 1*H*-pyrrolo [1,2-*b*]pyrazole framework. Furthermore, a variety of 4-aryl pyrazolium salts, irrespective of the electronic nature of the aryl group, were compatible with the reaction to afford heterocycles **3g–3j** in high yields. We then investigated substituent effects at the 1-position of the ylide precursor. Primary alkyl groups such as ethyl and benzyl were well tolerated, whereas a secondary alkyl group (isopropyl) led to diminished reactivity (**3k–3m**). Pyrazolium salts bearing methyl or phenyl substituents at the 5-position also participated in the reaction to deliver **3n** and **3o** in 20–23% yields. In contrast, the use of a 5-iodo pyrazolium salt did not provide the corresponding 1*H*-pyrrolo[1,2-*b*]pyrazole but instead afforded the 4(3*H*)-pyrimidinone derivative **5**, suggesting that a ring-opening/re-cyclization sequence precedes the cycloaddition under the reaction conditions.[13] Next, we examined an electron-withdrawing group (EWG[1]) at
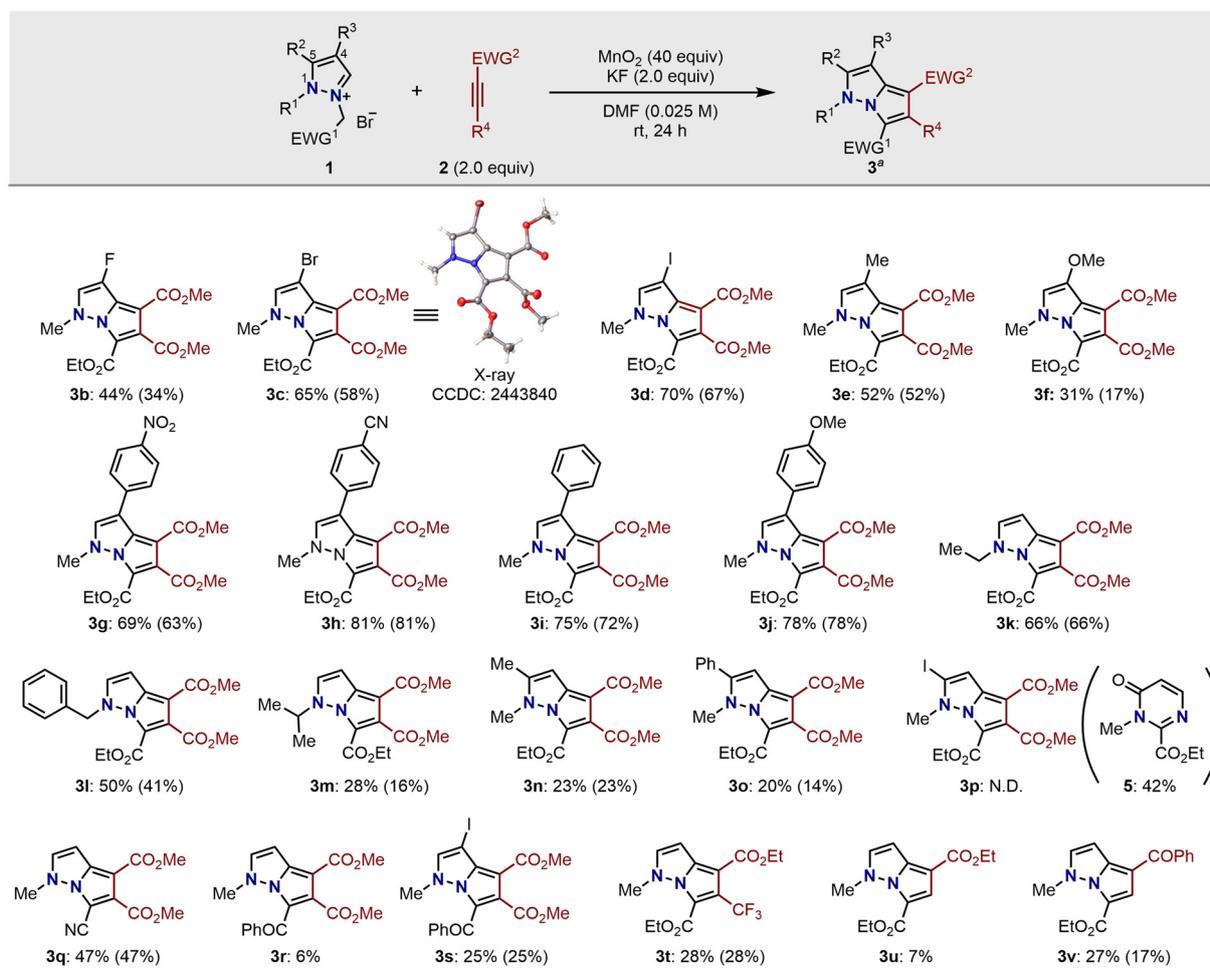
Scheme 2 Scope and limitations of the [3 + 2] cycloaddition of pyrazolium ylides with alkynes. Reaction conditions: pyrazolium salt (0.16–0.21 mmol), alkyne (0.32–0.42 mmol), MnO$_2$ (6.4–8.4 mmol), KF (0.32–0.42 mmol) and DMF (6.4–8.4 mL) at room temperature. [a]The yield was determined by ^{1}H NMR using triphenylmethane as an internal standard. Values in parentheses show isolated yields.

2230 | *Org. Chem. Front.*, 2026, **13**, 2228–2234

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the 2-position. A cyano group was well tolerated, whereas in the case of a ketocarbonyl substituent, the presence of an iodo group at the 4-position proved necessary for the cycloaddition to proceed (**3q–3s**).

Finally, we explored the scope of dipolarophile alkynes. A trifluoromethyl-substituted alkyne underwent cycloaddition to furnish **3t** in 28% yield, whereas more electron-rich alkynes were unreactive. The reaction with ethyl propiolate proceeded sluggishly (**3u**), and benzoyl acetylene was barely tolerated, affording **3v** in low yield. These results suggest that although a relatively low LUMO energy is important, it does not necessarily lead to high yields. The decrease in yield is presumed to arise from the decomposition of the unstable intermediate and/or excess adducts (see the SI).

To elucidate the reaction pathway, we attempted to identify the reaction intermediate. *In situ* ^{1}H NMR analysis of the

mixture obtained after treating **1a** and DMAD (**2a**) with potassium fluoride in DMF for 1.5 h proved highly complex, preventing unambiguous signal assignment. In contrast, FAB-MS analysis of the resulting mixture detected an *m/z* value consistent with the calculated exact mass of the proposed cycloadduct **6a** (Scheme 3). Subsequent treatment of this mixture with manganese(IV) oxide for 24 h resulted in the detection of a trace amount of **3a**. Notably, a similar experimental procedure performed without NMR monitoring also afforded **3a** in 5% NMR yield. These results indicate that cycloadduct **6a** is a highly unstable intermediate in this reaction sequence and that the presence of manganese(IV) oxide is essential for the efficient formation of 1*H*-pyrrolo[1,2-*b*]pyrazoles.

With the aim of gaining insight into the chemoselectivity of the reaction, DFT calculations were performed using pyrazolium ylide **A** as a model compound (Scheme 4). The calculations were carried out at the B3LYP/6-311G(d,p) (SMD, solvent = DMF)//B3LYP/6-31G(d,p) (gas phase) level of theory. The energy barrier for **TS1** for nucleophilic addition to DMAD was calculated to be 8.9 kcal mol^{-1}, which is lower than that of the ring-opening process (**TS4**, 10.0 kcal mol^{-1}). Both transformations are predicted to be irreversible, as the Gibbs free energies of the resulting intermediates are significantly lower than those of the starting species. It should be noted, however, that the ring-opening pathway is intramolecular in nature and thus the energies are not strictly comparable. Given the small energy difference, the calculations suggest that the ring-opening process may be favoured depending on the position and nature of the substituents, consistent with the formation of 4(3*H*)-pyrimidinone **5** observed experimentally (also see
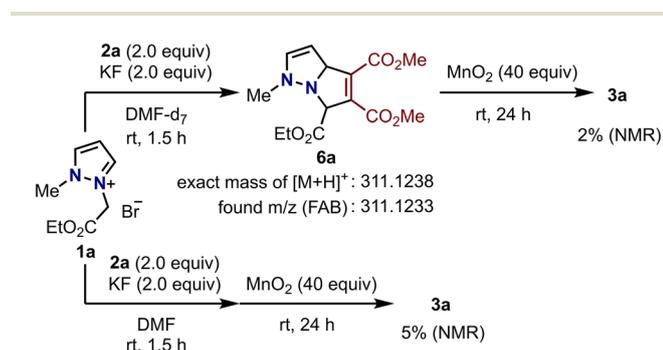
Scheme 3 Elucidation of the reaction pathway.
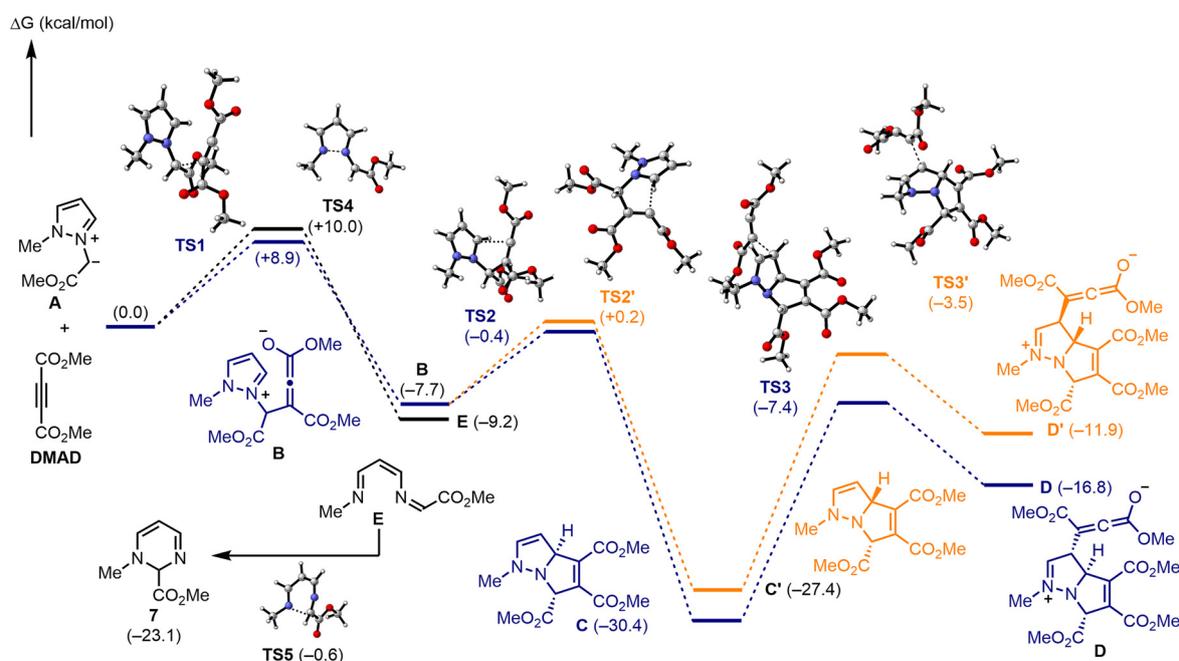
Scheme 4 The reaction profile of ring-opening of the pyrazolium ylide and [3 + 2] cycloaddition. All calculations were conducted at the level of B3LYP/6-311G(d,p) (SMD, solvent = DMF)//B3LYP/6-31G(d,p) (gas phase).

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Org. Chem. Front., 2026, **13**, 2228–2234 | **2231**

Scheme 2). Indeed, the computed pathway toward **7** indicated that the subsequent ring-closure step also proceeds smoothly.

The intramolecular nucleophilic additions of ynolate **B** were associated with activation barriers of 7.3 kcal mol^{-1} and 7.9 kcal mol^{-1}, respectively, suggesting the irreversible formation of the two diastereomeric intermediates **C** and **C′**, which arise from newly generated stereocenters adjacent to the angular hydrogen and methoxycarbonyl substituent. Finally, manganese(IV) oxide-mediated oxidative aromatization of **C** and **C′** furnishes the corresponding 1*H*-pyrrolo[1,2-*b*]pyrazole. The activation energies for **TS3** and **TS3′** for the subsequent nucleophilic additions of DMAD, reported by Derksen,[11] were 23.0 kcal mol^{-1} and 23.9 kcal mol^{-1}, respectively—values that are higher than those of the other steps, yet still compatible with reaction progress under the experimental conditions. These data are consistent with the observation that, at high substrate concentrations, the formation of indolizine **4** becomes competitive with or even predominant over oxidation (also see Table 1, entry 10). Overall, these computational studies indicate that the formation of 1*H*-pyrrolo[1,2-*b*]pyrazole proceeds through a stepwise cycloaddition followed by rapid oxidative aromatization and underscore that precise control of the reaction parameters is required to suppress competing ring-opening pathways and/or undue nucleophilic addition, thereby maintaining high chemoselectivity.

Finally, to demonstrate the synthetic utility of this protocol, several chemical transformations of the 1*H*-pyrrolo[1,2-*b*]pyrazole framework were carried out (Scheme 5). The 3-iodinated

product **3d** smoothly underwent both Sonogashira coupling and the Mizoroki–Heck reaction, affording the corresponding internal alkyne **8** and alkene **9**, respectively. Moreover, the Vilsmeier–Haack reaction of **3a** was feasible, delivering the 3-formylated derivative **10** and thereby highlighting the versatility of this scaffold in C–C bond-forming elaborations. In addition, the *N*-benzylic derivative **3l** was successfully converted into the deprotected 1*H*-pyrrolo[1,2-*b*]pyrazole **11**. Collectively, these transformations demonstrate that a range of cross-coupling reactions and functional-group manipulations can be applied to this framework, enabling access to more structurally complex and functionally enriched molecules.
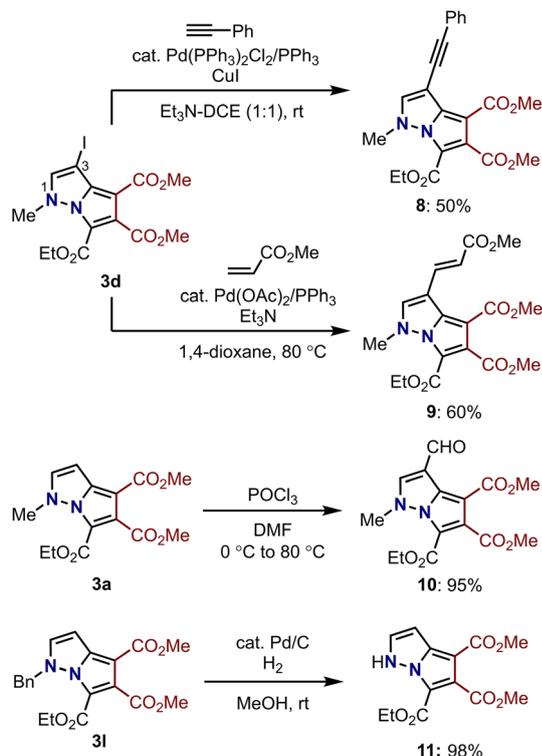
Conclusions

In conclusion, we have developed a synthetic method for accessing previously unexplored 10π-aromatic 1*H*-pyrrolo[1,2-*b*]pyrazoles. The sequence, which comprises pyrazolium ylide generation, cycloaddition with alkynes, and oxidative aromatization, proceeds under conditions that effectively suppress the competing ring-opening and excessive nucleophilic addition pathways, thereby enabling high chemoselectivity. The substrate scope and limitations were examined, revealing that a variety of substitution patterns and functional groups are compatible, although only electron-deficient alkynes proved sufficiently reactive toward the pyrazolium ylide. Experimental and computational investigations shed light on the reaction mechanism, demonstrating that (1) the cycloaddition proceeds in a stepwise manner, (2) the resulting cycloadducts are intrinsically unstable and thus require rapid oxidation for productive conversion, and (3) the activation energies of the competing pathways are comparable, causing the chemoselectivity to be highly sensitive to subtle changes in reaction conditions. Furthermore, derivatization studies highlight the potential of this framework to serve as a versatile platform for constructing more structurally complex and/or functionally enriched molecules. We anticipate that this strategy will stimulate further exploration of the synthesis and functionalization of useful molecules based on this scaffold and will contribute to the broader development of new 5/5-fused heteroaromatic chemistry.

Author contributions

Motohiro Yasui: conceptualization, funding acquisition, investigation, methodology, project administration, writing – original draft, and writing – review & editing. Tatsuya Tsumori: investigation. Masato Morita: investigation. Shigeyuki Yamada: writing – review & editing and supervision. Tsutomu Konno: writing – review & editing and supervision.

Scheme 5 Transformations of 1*H*-pyrrolo[1,2-*b*]pyrazole derivatives.

Conflicts of interest

There are no conflicts to declare.

2232 | *Org. Chem. Front.*, 2026, **13**, 2228–2234

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Data availability

The data supporting this article have been included as part of the supplementary information (SI): detailed synthetic procedures, complete characterization data for all new compounds, X-ray crystallographic data and DFT calculations. See DOI: **https://doi.org/10.1039/d6qo00070c**.

CCDC 2443840 (**3c**) contains the supplementary crystallographic data for this paper.[14]

Acknowledgements

References

1   (*a*) C. M. Marshall, J. G. Federice, C. N. Bell, P. B. Cox and J. T. Njardarson, An Update on the Nitrogen Heterocycle Compositions and Properties of U.S. FDA-Approved Pharmaceuticals (2013–2023), *J. Med. Chem.*, 2024, **67**, 11622–11655; (*b*) L. D. Pennington and D. T. Moustakas, The Necessary Nitrogen Atom: A Versatile High-Impact Design Element for Multiparameter Optimization, *J. Med. Chem.*, 2017, **60**, 3552–3579; (*c*) N. Kerru, L. Gummidi, S. Maddila, K. K. Gangu and S. B. Jonnalagadda, A Review on Recent Advances in Nitrogen-Containing Molecules and Their Biological Applications, *Molecules*, 2020, **25**, 1909; (*d*) M. M. Heravi and V. Zadsirjan, Prescribed Drugs Containing Nitrogen Heterocycles: An Overview, *RSC Adv.*, 2020, **10**, 44247.

2   (*a*) Y. Li, T. Liu and J. Sun, Recent Advances in N-Heterocyclic Small Molecules for Synthesis and Application in Direct Fluorescence Cell Imaging, *Molecules*, 2023, **28**, 733; (*b*) A. Amin, T. Qadir, P. K. Sharma, I. Jeelani and H. Abe, A Review on The Medicinal And Industrial Applications of N-Containing Heterocycles, *Open Med. Chem. J.*, 2022, **16**, e187410452209010; (*c*) M. Zhong and M. Yuan, Recent advances in the use of N-heterocyclic carbene adducts of N, P, C elements as supporting ligands in organometallic chemistry, *RSC Adv.*, 2025, **15**, 15052–15085; (*d*) N. Sidhu, P. Jain, C. Mukherjee, P. S. Pratheep, A. F. Anwar, A. Satheesh, M. Kaur, K. Gairola, D. Mukherjee and B. Moza, Recent advancements in heterocyclic compounds as agrochemicals – A review, *Indian J. Heterocycl. Chem.*, 2025, **35**, 443–450; (*e*) D. Chen, S.-J. Su and Y. Cao, Nitrogen heterocycle-containing materials for highly efficient phosphorescent OLEDs with low operating voltage, *J. Mater. Chem. C*, 2014, **2**, 9565–9578.

3   (*a*) R. S. M. de Moraes, A. B. M. Botelho, G. T. A. Pinto, S. C. Rodrigues, M. T. M. Martins, D. L. A. Soares, C. C. Cruz, A. A. Pinto, F. R. F. Dias, P. D. Fernandes and A. C. Cunha, Chemistry, Applications, and Synthesis Methods of Indole Derivatives: A Comprehensive Review, *Chem. Rec.*, 2025, **25**, e202500121; (*b*) J. S. A. Badaro, B. Godlewski and D. T. Gryko, Advances in the synthesis of indolizines and their π-expanded analogues: update 2016–2024, *Org. Chem. Front.*, 2025, **12**, 2860–2907; (*c*) A. Singampalli, P. Kumar, R. Bandela, S. M. Bellapukonda, S. Nanduri and V. M. Yaddanapudi, Indazole – an emerging privileged scaffold: synthesis and its biological significance, *RSC Med. Chem.*, 2025, **16**, 5196–5221.

4   Recent examples: (*a*) J.-L. Wang, G.-Y. Wu, J.-N. Luo, J.-L. Liu and C.-X. Zhuo, Catalytic Intermolecular Deoxygenative Coupling of Carbonyl Compounds with Alkynes by a Cp*Mo(II)-Catalyst, *J. Am. Chem. Soc.*, 2024, **146**, 5605–5613; (*b*) A. L. Guzman, A. N. Mann and T. R. Hoye, Alkynes to (Free) Carbenes to Polycyclic Cyclopropanes, *J. Am. Chem. Soc.*, 2024, **146**, 28642–28647; (*c*) V. A. Motornov, A. A. Tabolin and S. L. Ioffe, Oxidative [3+2]-annulation of nitroalkenes and azolium ylides in the presence of Cu(II): efficient synthesis of [5,5]-annulated N-fused heterocycles, *New J. Chem.*, 2022, **46**, 4134–4141; (*d*) H. Zhang, M. Wang, X. Wu and C. Zhu, Heterocyclization Reagents for Rapid Assembly of N-Fused Heteroarenes from Alkenes, *Angew. Chem., Int. Ed.*, 2021, **60**, 3714–3719; (*e*) M. Pawliczek, L. K. B. Garve and D. B. Werz, Exploiting amphiphilicity: facile metal free access to thianthrenes and related sulphur heterocycles, *Chem. Commun.*, 2015, **51**, 9165–9168.

5   (*a*) W. Li, H. Wang, Y. Zhang, L. Zhao, P. Guo, H. Cao and X. Liu, Copper-Catalyzed Formal [4 + 1] Annulation toward Diverse Trifunctionalized Indolizines from Pyridinium 1,4-Zwitterionic Thiolates and Diazos, *J. Org. Chem.*, 2023, **88**, 7199–7207; (*b*) A. V. Agafonova and A. F. Khlebnikov, An isoxazole strategy for the synthesis of alkyl 5-amino-4-cyano-1H-pyrrole-2-carboxylates – versatile building blocks for assembling pyrrolo-fused heterocycles, *Org. Biomol. Chem.*, 2021, **19**, 1976–1984; (*c*) M. Kucukdisli and T. Opatz, A Modular Synthesis of Polysubstituted Indolizines, *Eur. J. Org. Chem.*, 2012, 4555–4564; (*d*) C. Ma, H. Ding and Y. Wang, Novel Annulation Reactions of Aryl Methyl Ketenes with Zwitterions Derived from Dimethyl Acetylenedicarboxylate and N-Alkylimidazoles, *Org. Lett.*, 2006, **8**, 3133–3136; (*e*) I. Yavari, M. Sabbaghan and Z. Hossaini, Reaction of Hexachloroacetone with Activated Acetylenes in the Presence of N-Heterocycles. Synthesis of Trichloromethylated Bridgehead N-Heterocycles, *Synlett*, 2006, 2501–2503; (*f*) H. Kojima, K. Yamamoto, Y. Kinoshita and H. Inoue, Synthesis of indolizines and pyrrolo[2,1-*b*] azoles from 2-pyridylmagnesium bromide and 2-lithiated azoles using tris(alkylthio)-cyclopropenyl cations as a three-

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Org. Chem. Front., 2026, **13**, 2228–2234 | **2233**

carbon building block, *J. Heterocycl. Chem.*, 1992, **29**, 1473–1476; (*g*) Y. Matsuda, H. Gotou, K. Katou, H. Matsumoto, M. Yamashita, K. Takahashi, S. Ide, K. Furuno and K. Torisu, A novel 1,6-Cyclization of Imidazolium N-allylides (2): Formation of the Mesomeric Betaine, 7-Iminoimidazo-[1,2-a]pyridiniumide, *Heterocycles*, 1991, **32**, 2217–2224.

6 (*a*) T. Liu, Z. Sui and J. Ji, Thieno[3,2-b] Pyrrole[3,2-d]pyridazinone Derivatives and Their Use as PKM2 Derivatives for the Treatment of Cancer, Obesity and Diabetes Related Disorders, WO2020/167976A1, 2020; (*b*) Y. Shen, M. Zhang, X. Yao and C. Qi, Pyrrole[2,1-b] Thiazolium Compound and Preparation Method and Anti-tumor Application thereof, CN101654459A, 2010; (*c*) N. Suzuki, A. Nakayama, T. Saijiyou, M. Hasegawa and S. Yokohama, 3-Exo-methylenepyrrolo(2,1-b)thiazole derivative, JPH03128385(A), 1991; (*d*) Y.-M. Shen, P.-C. Lv, M.-Z. Zhang, H.-Q. Xiao, L.-P. Deng, H.-L. Zhu and C.-Z. Qi, Synthesis and antiproliferative activity of multisubstituted N-fused heterocycles against the Hep-G2 cancer cell line, *Monatsh. Chem.*, 2011, **142**, 521–528; (*e*) X. Liang, Y. Shen, Z. Duo and C. Qi, Pyrrole [1,2-a] Imidazolium Compound and Preparation Method and Anti-tumor Application Thereof, CN101654455A, 2010.

7 (*a*) C. W. Ong, C. M. Chen, L. H. Wang and J. J. Jan, Efficient Synthesis of Pyrroles from Chemoselective Addition of Primary Amines to 1,6-Dioxo-2,4-dienes, *J. Org. Chem.*, 1998, **63**, 9131–9134; (*b*) T. Solanki, A. Waskele, P. Barfa, A. Kumar and P. Sharma, EcoScale MCR Sustainability to Impart Rapid Access to Pyrrolo[1,2-b]pyrazoles Scaffolds Assisted by Recyclable HClO$_4$·SiO$_2$ Heterogeneous Catalytic System, *Indian J. Chem.*, 2023, **62**, 1218–1222.

8 (*a*) I. Coldham and R. Hufton, Intramolecular Dipolar Cycloaddition Reactions of Azomethine Ylides, *Chem. Rev.*, 2005, **105**, 2765–2809; (*b*) C. Nájera and J. M. Sansano, Azomethine Ylides in Organic Synthesis, *Curr. Org. Chem.*, 2003, **7**, 1105–1150; (*c*) A. V. Gulevskaya and J. I. Nelina-Nemtseva, 1,3-Dipolar cycloaddition reactions of azomethine ylides and alkynes, *Chem. Heterocycl. Compd.*, 2018, **54**, 1084–1107.

9 (*a*) S. Dong, X. Fu and X. Xu, [3+2]-Cycloaddition of Catalytically Generated Pyridinium Ylide: A General Access to Indolizine Derivatives, *Asian J. Org. Chem.*, 2020, **9**, 1133–1143; (*b*) G. Bertuzzi, L. Bernardi and M. Fochi, Nucleophilic Dearomatization of Activated Pyridines, *Catalysts*, 2018, **8**, 632.

10 (*a*) A. N. Koronatov, N. V. Rostovskii, A. F. Khlebnikov and M. S. Novikov, Rh(II)-Catalyzed Ring Expansion of Pyrazoles with Diazocarbonyl Compounds as a Method for the Preparation of 1,2-Dihydropyrimidines, *J. Org. Chem.*, 2018, **83**, 9210–9219; (*b*) J. O. Strelnikova, A. N. Koronatov, N. V. Rostovskii, A. F. Khlebnikov, O. V. Khoroshilova, M. A. Kryukova and M. S. Novikov, Rhodium-Catalyzed Denitrogenative Diazole–Triazole Coupling toward Aza-Bridged Structures and Imidazole-Based Chelating Ligands, *Org. Lett.*, 2021, **23**, 4173–4178; (*c*) L. Li, Y. Ning, H. Chen, Y. Ning, P. Sivaguru, P. Liao, Q. Zhu, Y. Ji, G. de Ruiter and X. Bi, Dearomative Insertion of Fluoroalkyl Carbenes into Azoles Leading to Fluoroalkyl Heterocycles with a Quaternary Center, *Angew. Chem., Int. Ed.*, 2024, **63**, e202313807; (*d*) Q. Chen, X. Liu, F. Guo and Z. Chen, An unexpected rearrangement of pyrazolium halides based on N–N bond cleavage: synthesis of 1,2-dihydropyrimidines, *Chem. Commun.*, 2017, **53**, 6792–6795; (*e*) K. Matsumoto, H. Iida, H. Katsura, T. Machiguchi, H. Uekusa and Y. Ohashi, Unusual formation and X-ray crystal structure of stable anti-Bredt compounds by reaction of 3a,6a-diazapentalenes with dimethyl acetylenedicarboxylate, *J. Chem. Soc., Perkin Trans. 1*, 1996, 2333.

11 R. Tran, D. K. Brownsey, L. O'Sullivan, C. M. J. Brandow, E. S. Chang, W. Zhou, K. V. Patel, E. Gorobets and D. J. Derksen, Leveraging Pyrazolium Ylide Reactivity to Access Indolizine and 1,2-Dihydropyrimidine Derivatives, *Chem. – Eur. J.*, 2024, **30**, e202400421.

12 J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen and T. Walker, 194. A synthesis of vitamin A from cyclohexanone, *J. Chem. Soc.*, 1952, 1094–1111.

13 Our result of DFT calculations shows that the activation energy of ring-opening is lowered. See the SI.

14 CCDC 2443840: Experimental Crystal Structure Determination, 2026, DOI: **10.5517/ccdc.csd.cc2n10k9**.

2234 | *Org. Chem. Front.*, 2026, **13**, 2228–2234

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