Chemical
Science

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: A. C. Shaikh, K. Kaur, P. SINGH, R. D. Thombare, A. K. P. and M. V. Mane, *Chem. Sci.*, 2026, DOI: 10.1039/D6SC03994D.

ROYAL SOCIETY
OF CHEMISTRY

rsc.li/chemical-science

View Article Online
DOI: 10.1039/D6SC03994D

ARTICLE

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Stereoselective Dearomative Formal [3+2] cycloaddition of Indole with Allenols: Access to Structurally Diverse Cyclopenta[b]indoles

Kavneet Kaur,[a$] Puja Singh, [a$] Rahul D. Thombare,[a] Adithya K. P.,[b] Manoj V. Mane,[b] and Aslam C. Shaikh,[a*]

Dearomative cycloaddition reactions of indoles offer a powerful strategy for rapidly increasing molecular complexity, yet intermolecular variants that proceed with high regio- and diastereocontrol remain uncommon. Herein, we report an iron(III) chloride–mediated dearomative formal [3+2] cycloaddition of indoles with arylsulfonyl allenols, providing direct access to densely functionalized cyclopenta[b]indoles with excellent diastereoselectivity. The reaction proceeds under mild Lewis acidic conditions without the use of precious metal catalysts and displays broad substrate scope, tolerating diverse substitution patterns on the indole core and allenols, including electron-rich, electron-deficient, sterically hindered, and fused systems, affording the desired tricyclic scaffold in moderate to excellent yields. The synthetic utility of this protocol is demonstrated through late-stage functionalization of pharmaceutically relevant indole-containing molecules, Double Cascade Dearomative Cycloaddition, gram-scale synthesis, and downstream product diversification. Mechanistic studies, including DFT energy calculation and isotopic labeling experiments, support an ionic, non-radical pathway involving Lewis acid activation of the allenol to generate a transient electrophilic intermediate, followed by a dearomative cyclization. This operationally simple and sustainable method enables rapid construction of structurally complex, nonplanar

[a] *Department of Chemistry, Indian Institute of Technology Ropar, Rupnagar, Punjab 140001, India.*
[b] *Centre of Nano and Material Sciences, Jain (Deemed-to-be-University), Bangalore 562112 Karnataka, India.*

[$] *Both authors equally contributed to this work.*

Supplementary Information available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/D6SC02994D

cyclopenta[b]indole frameworks of potential relevance in medicinal chemistry.Introduction

Dearomative functionalization of heteroarenes[1,2,3] represents a powerful strategy to "escape from flatland" by generating saturated or partially saturated frameworks. The enhanced sp³ character and conformational rigidity improve the potential for specific interactions with biological targets, thus increasing their significance in medicinal chemistry (**Figure 1A**).[4] In this context, Cascade Intermolecular Dearomative Cycloaddition (CIDC) reactions are widely employed to create polycyclic frameworks that are both complex and non-planar.[5,6] Owing to their potent biological activities, widespread occurrence in natural products, and significant pharmaceutical relevance, indoline alkaloids have attracted sustained interest, making the dearomatization of indoles a longstanding and important topic in synthetic chemistry.[7,8,9,10,11] Particularly, cycloadditions such as formal [3+2],[12,13,14,15] [2+2],[16,17,18,19] [5+2][20], and [4+2][21,22,23] processes can transform the indole core into complex ring systems in a single step, which mostly rely on peripheral editing of indoles.[24, 25] However, controlling regioselectivity, enabling intermolecular reactivity, and avoiding competitive pathways remain challenging, especially when using electron-rich heteroarenes. Achieving these transformations generally requires either specialized activation modes or reagents capable of reversing typical reactivity trends.[26] Consequently, the development of efficient, general, and stereoselective dearomative transformations of indoles remains a central objective in synthetic chemistry.

On the other hand, prenyl units are privileged structural motifs widely embedded in natural products and biologically active small molecules, where they play a decisive role in enhancing molecular complexity, conformational rigidity, and functional diversity.[27, 28] In complex molecular frameworks, prenyl substituents frequently act as latent synthetic handles, enabling further structural elaboration through cyclization, oxidation, rearrangement, or skeletal reorganization, thereby facilitating rapid access to higher-order architectures.[29,30] Moreover, prenylation is often correlated with increased lipophilicity, membrane affinity, and enhanced biological activity, particularly in indole-derived and heteroaromatic systems.[31, 32] Despite these advantages, strategies for the direct incorporation of prenyl units during dearomative cycloaddition processes, especially under intermolecular conditions, are limited (**Figure 1A**).[33, 34, 35] This emphasizes the synthetic potential of combining dearomatization of indoles along with the installation of a prenyl unit in one step.

Building on our continued efforts and interest in advancing sulfonyl allene reactivity,[36,37] where allenes are useful synthetic precursors in organic chemistry, as they facilitate a variety of synthetic transformations.[38, 39] We realize that the strong electron-withdrawing sulfonyl group polarizes the cumulene framework, rendering sulfonyl allenes highly reactive toward nucleophilic attack and cycloaddition processes and therefore acts as an electrophile (**Figure 1B**).[40, 41] Moreover, activating cumulated double bonds with Brønsted or Lewis acids allows for nucleophilic attacks, leading to the formation of new C−C or C−heteroatom bonds, either intermolecularly or intramolecularly.[42, 43] We hypothesized that sulfone-substituted allenes could serve as effective coupling partners due to their ability to modulate the intrinsic polarity of the allene framework. Herein, we developed an iron-mediated dearomative formal [3+2] cycloaddition between indoles and sulfone allenols. This intermolecular cascade process induces peripheral dearomatization of the indole nucleus and provides direct access to structurally diverse, nonplanar tricyclic cyclopenta[b]indole frameworks. Notably, the cyclopenta[b]indole core is present in a range of natural products that exhibit diverse biological activities (**Figure 1C**).[44, 45, 46] Further, the resulting formal [3+2] cycloadduct incorporates both sulfone and isoprene structural motifs, leading to a pronounced increase in molecular complexity in a single step. The transformation proceeds under mild conditions, displays broad substrate compatibility, high stereoselectivity, and can be readily performed on a gram scale along with late-stage functionalization and product diversification. Moreover, stereoselectivity and the possible transition state for the formation of the desired product were predicted through DFT studies.

View Article Online
DOI: 10.1039/D6SC03994D

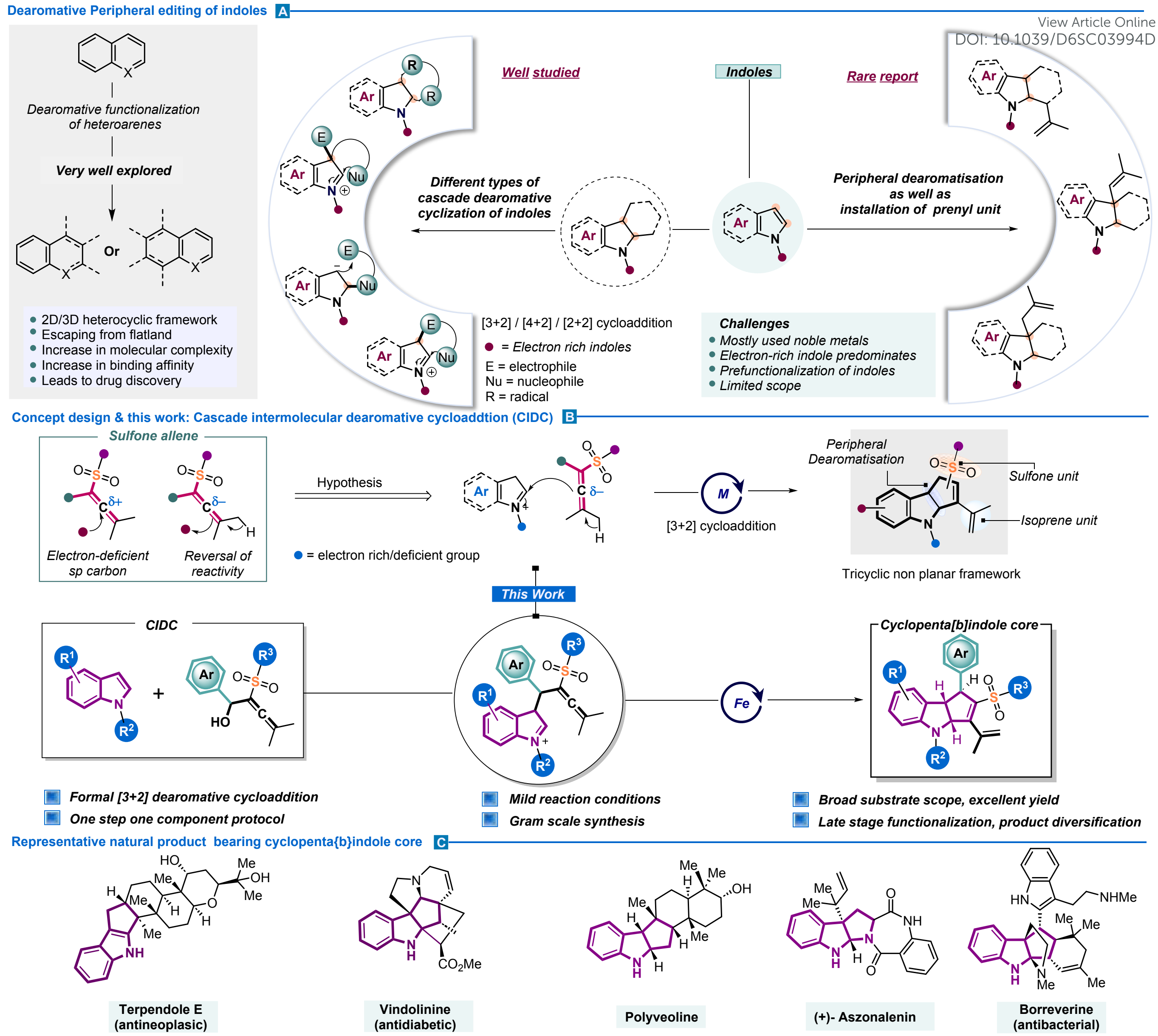
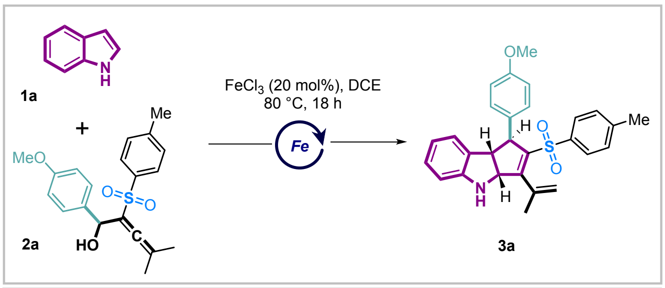


Figure 1: A, Dearomative peripheral editing of Indoles. B, Concept design & this work: Cascade Intermolecular Dearomative Cycloaddition (CIDC). C, Representative natural products bearing cyclopenta[b]indole core.

Results and discussion

Reaction Development: To evaluate the feasibility of the proposed formal [3+2] cycloaddition reaction, we chose *N*-H indole (**1a**) and sulfonyl allenol (**2a**) as model substrates. The details of our findings are summarized in Table 1 and SI. Gratifyingly, after extensive screening of various reaction parameters, we discovered a suitable condition of the formal [3+2] cycloaddition reaction to afford tricyclic non-planar scaffold **3a**. In the presence of 20 mol% $FeCl_3$, a mixture of **1a** (1.3 equiv.) and **2a** (1.0 equiv.) in dichloroethane (DCE) at 80 °C for 18 h smoothly undergoes cycloaddition for the formation of **3a** in excellent yield with more than 99:1 diastereoselectivity (88%, Table 1, entry 1). Attempts to further optimize the reaction, a varied panel of Lewis acids and Brønsted acids were screened, a drop in the yield of **3a** was noted, whereas only p-TsOH.H_2O afforded a comparable yield of **3a** in 72% (entries 2-6). In search of an alternative iron catalyst, we examined $Fe(acac)_3$ and $Fe(OTf)_3$, but this resulted in reduced yield of cycloaddition adduct **3a** (entries 7-8). After screening several reaction media, it was revealed that DCE remained the most ideal solvent for the formal [3+2] cycloaddition reaction (entries 9-12). Furthermore, to see the impact of the inclusion of acid and base additives to standard reaction conditions, we tested AcOH and K_2CO_3; however, a diminished formation of the desired product **3a** was noted (entries 13-14). Lowering the reaction temperature leads to a reduction in the yield of the desired product **3a** (entries 15-16). Following this, the influence of reaction time was analyzed, showing that maximum transformation occurs within 18 hours (entry 17). Finally, halving the reduction in $FeCl_3$ concentration from 20 mol% to 10 mol% resulted in a significant drop in the yield of **3a** to 72%, whereas no conversion occurred in the absence of $FeCl_3$, indicating the critical role of $FeCl_3$ in achieving optimal yield (entries 18-19).

Table 1: Optimization of Reaction Conditions[a,b]

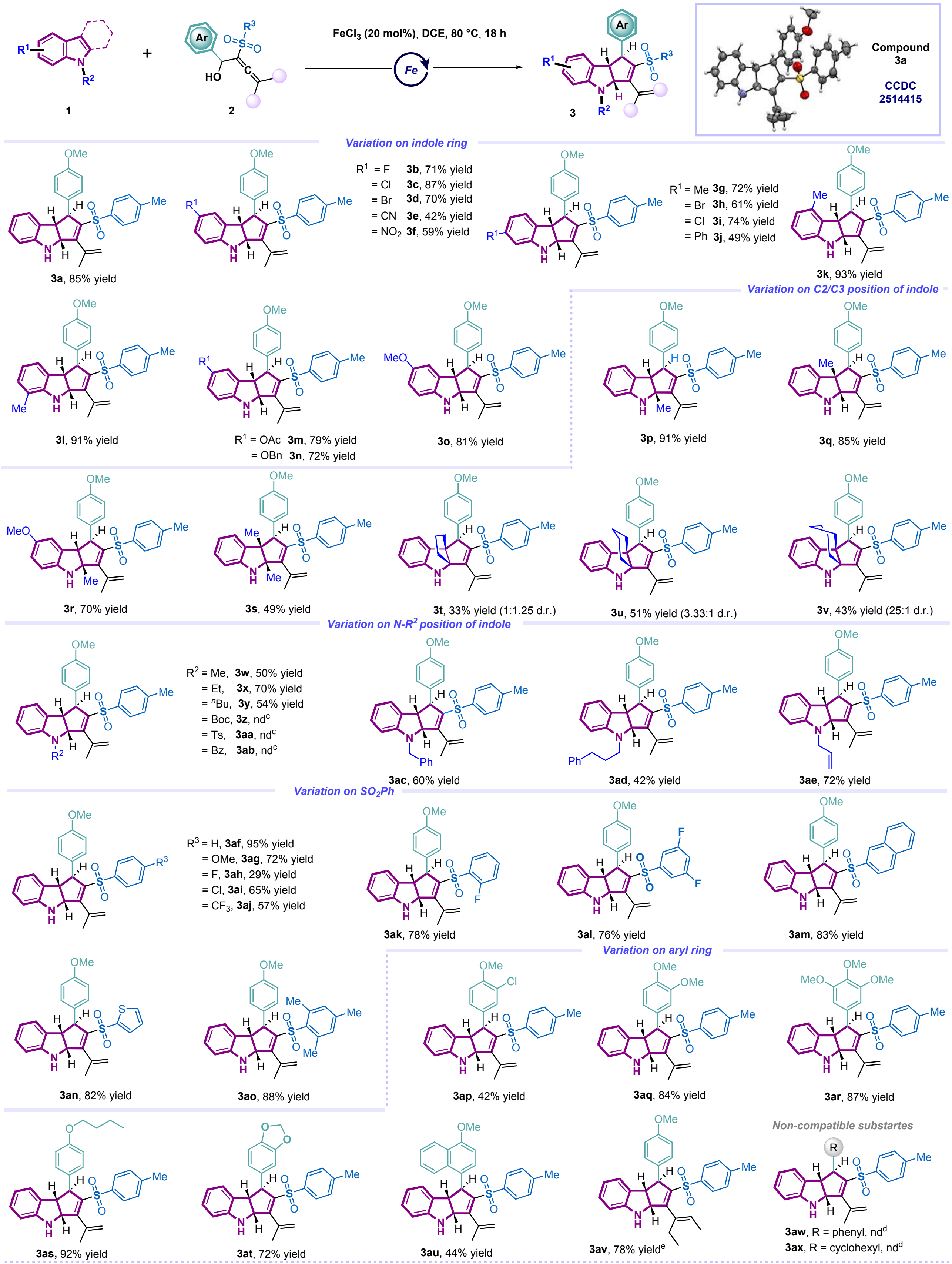


Entry	*Deviation from standard conditions*	*Yield of 3a* [b]	*d.r*
1.	None	88[a]	>99:1
2.	p-TsOH.H_2O instead of $FeCl_3$	72	>99:1
3.	TfOH instead of $FeCl_3$	<5	--
4.	$Sc(OTf)_3$ instead of $FeCl_3$	58	>99:1
5.	$ZnCl_2$ instead of $FeCl_3$	50	>99:1
6.	$AlCl_3$ instead of $FeCl_3$	n.d.	--
7.	$Fe(acac)_3$ instead of $FeCl_3$	65	>99:1
8.	$Fe(OTf)_3$ instead of $FeCl_3$	45	>99:1
9.	DMSO instead of 1,2-DCE	Traces	--
10.	CH_3CN instead of 1,2-DCE	50	>99:1
11.	THF instead of 1,2-DCE	<5	--
12.	Toluene instead of 1,2-DCE	70	>99:1
13.	AcOH as an additive	55	>99:1
14.	K_2CO_3 as an additive	20	>99:1
15.	25 °C instead of 80 °C	n.d.	--
16.	50 °C instead of 80 °C	55	>99:1
17.	12 h instead of 18 h	60	>99:1
18.	10 mol% of $FeCl_3$ employed	72	>99:1
19.	Without $FeCl_3$	n.d.	--

Reaction conditions: a, **1a** (0.056 mmol, 1.3 equiv), **2a** (0.05 mmol, 1.0 equiv), 20 mol% $FeCl_3$, DCE (0.5 ml), 80 °C, 18 h. b, NMR yields are given with 2,4,6-trimethoxy benzene as internal standard. nd = not detected. d.r = diastereomeric ratio. Single diastereomer observed in all the cases.

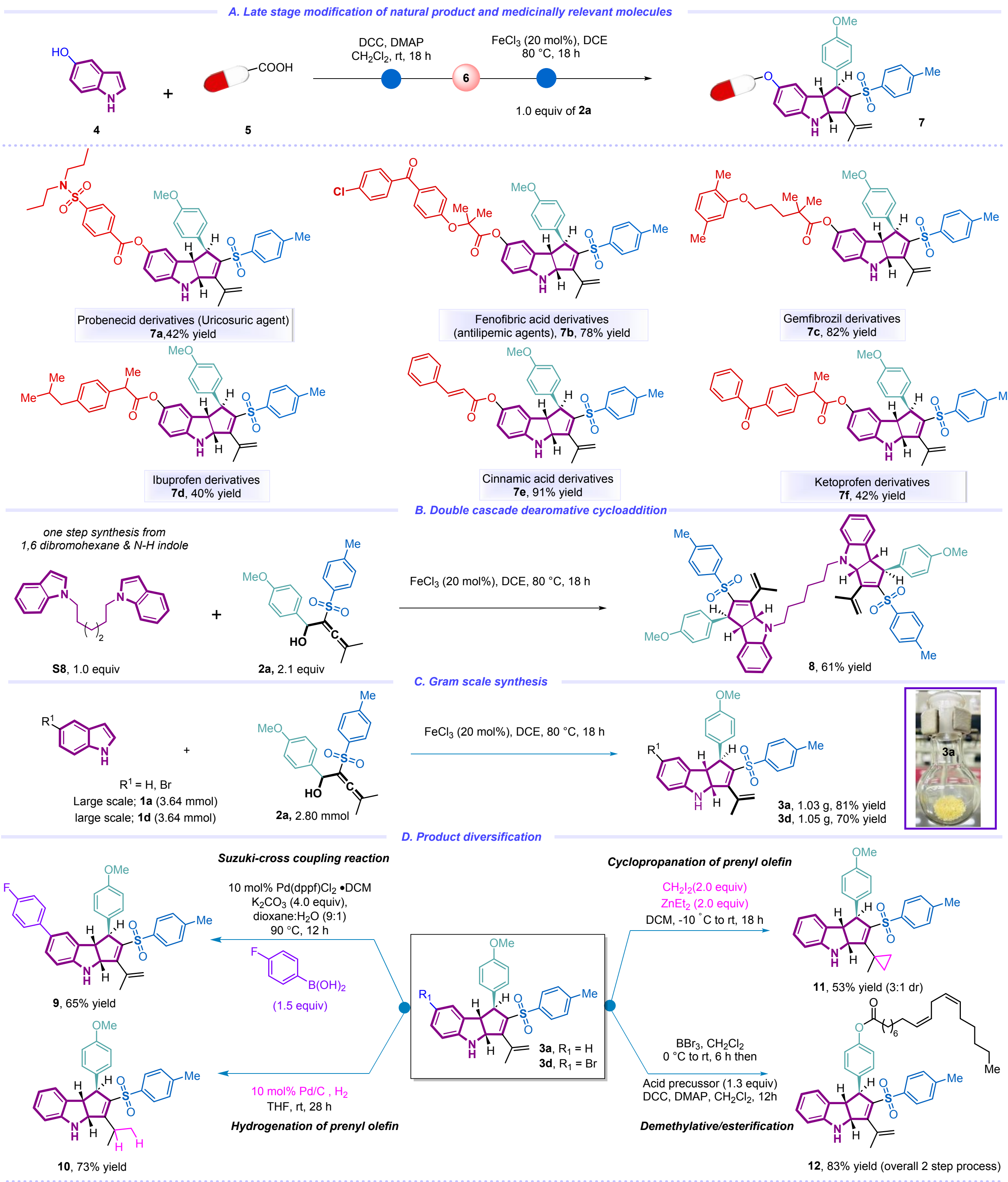
The reaction's generality was demonstrated through a broad substrate scope evaluation that included variations at the indole ring and the sulfonyl allenol fragment of template substrates (**Scheme 1**). The applicability of this method was initially assessed using various indole derivatives. To our surprise, variations on the indole ring with electron-donating (Me, OMe and OBn), weakly electron-donating (OAc), and halo substituents (F, Cl and Br) at different positions were well tolerated to afford the desired [3+2] cycloaddition product in good to excellent yield (**3a**-**3o**, up to 93% yield. It is worth noting that the reaction was compatible with halogen atoms in the indole ring, opening the door for further functionalization of the tricyclic scaffold. However, as expected, strong electron-withdrawing groups (CN and NO_2) on indole offered moderate conversion with 42% and 59% yield, respectively. In the next stages, we achieved a significant transformation of C2 and C3-substituted indoles **(2p**, **2q**, and **2r**). This variation not only resulted in impressive yields but also markedly increased three-dimensional complexity, showcasing the remarkable potential of our approach (**3p**-**3r**, 70-91% yields). Moreover, sterically hindered fused indoles (**2s**, **2t**, **2u**, and **2v**) were converted to the target dearomative cyclopenta[b]indole derivatives, albeit in moderate yield (up to 51%). However, the desired product formed non-separable diastereomers for **3t** and **3u** in ratios of 1.25:1 and 3.33:1, respectively. This strategy has demonstrated noteworthy effectiveness with several N-

View Article Online
DOI: 10.1039/D6SC03994D



View Article Online
DOI: 10.1039/D5SC07994D

Scheme 1. Substrate scope. a, Indole **1** (1.3 equiv.), Aryl sulfonyl allenol **2** (1.0 equiv.), 20 mol% $FeCl_3$, DCE (0.1 M, 3.0 ml), 80 °C, 18 h. b, Isolated yields are given. c, Indole fully recovered. d, starting material recovered completely. e, reaction performed for 24 h. Single diastereomer observed and isolated in most cases...



Scheme 2. A, Late-stage modification of natural products and medicinally relevant molecules. B, Double cascade dearomative formal [3+2] cycloaddition. C, Gram scale reaction. D, Product diversification.

View Article Online
DOI: 10.1039/D5SC03994D

substituted indoles, specifically compounds **3w**, **3x**, **3y**, **3ac**, and **3ad** obtained in moderate to good yield (42-70%). However, it falls short when applied to bulkier N-protected electron-withdrawing groups such as boc (**3z**), tosyl (**3aa**), and benzoyl (**3ab**). This distinction highlights the strategy's potential while also pointing out the challenges it faces with electron-deficient substituents. Also, reactive functionality such as an allyl group on *N*-substitution works well to furnish the desired product **3ae** with a yield of 72%.

Next, we focused our attention on the scope of sulfonyl moiety, which revealed that ortho, meta, and para-substituted aryl sulfonyl groups with various functional groups such as −Me, −OMe, −F, −Cl, −CF$_3$ substituents were well tolerated to deliver the desired product with appreciable yields (**3af**-**3al**, up to 95%), increasing the synthetic utility of this method. Along with this, naphthyl, heteroaryl, and the sterically crowded mesityl group demonstrated effective participation in the established reaction protocol (**3am**-**3ao**, 82-88 % yield). This finding highlights their potential significance within the framework of our research. In subsequent investigations, we evaluated the effect of substituent on the aryl units attached to aryl sulfonyl allenols (**2**), substrates with strong electron donation, either monomethoxy, dimethoxy, or trimethoxy substituent, only undergo dearoamative formal [3+2] cycloaddition with indoles, yielding the desired products **3ap**-**3au** in commendable yields of up to 92%. Replacing the dimethyl unit on allenols with a diethyl unit lengthens the reaction time for smooth conversion, delivering the corresponding product **3av** in a yield of 78%. Furthermore, phenyl and cyclohexyl substituted allenol didn’t let to the formation of desired product (**3aw**-**3ax**).

The FeCl$_3$-mediated formal [3+2] cycloaddition protocol showcases its significant potential for the late-stage functionalization of complex, pharmaceutically relevant molecules (**Scheme 2A**). [47, 48] By efficiently targeting a diverse array of drug-derived indoles, including probenecid (**6a**), fenofibric acid (**6b**), gemfibrozil (**6c**), ibuprofen (**6d**), cinnamic acid (**6e**), and ketoprofen derivatives (**6f**), this innovative approach facilitates the generation of valuable dearomative cyclopenta[b]indole derivatives **7a**-**7f** in moderate to excellent yield (40-91%). More interestingly, the substrate holding two indole units (**S8**) undergoes effective double cascade dearomative cycloaddition to furnish the corresponding product **8** in 61% yield (**Scheme 2B**).[49] This result highlights the strategic application of this protocol, which not only enhances synthetic utility but also contributes to the advancement of drug development in a highly effective manner through the rapid generation of molecular complexity in a single step. Additionally, we were able to scale up the formal [3+2] cycloaddition reaction (**2a**; 2.8 mmol scale), delivering the tricyclic cyclopenta[b]indole adducts **3a** and **3d** in 81% and 70% yield, respectively (**Scheme 2C**). This indicates the robustness, scalability, and operational practicality of this methodology. To effectively demonstrate the synthetic utility of our method, we undertook product diversification of the cyclopenta[b]indole derivative (**3a** and **3d**) through cross-coupling reactions and modification of the isoprenyl unit (**Scheme 2D**). The bromo group of **3d** successfully engaged for Suzuki coupling with 4-fluorophenylboronic acid, leading to the corresponding cross-coupled product **9** in an acceptable yield of 65%. Alternatively, the isoprenyl unit of substrate **3a** is being hydrogenated with Pd/C conditions into the corresponding analogue **10** in 73% yield. Also, Simmons-Smith cyclopropanation reaction[50] has been successfully carried out on **3a** to generate the strained cyclopropyl-embedded product **11** in 53% yield with a 3:1(d.r.). Collectively, these results highlight the wide applicability, functional-group tolerance, and robustness of the developed transformation. Furthermore, the methoxy group bearing an electron-rich aryl fragment of cyclopenta[b]indole derivative (**3a)** has been demethylated in the presence of BBr$_3$ and transformed into another ester analog **12** by using Linoleic Acid as a coupling partner.

Mechanistic Studies

Next, we proceeded to conduct control experiments to gain deeper insights into the underlying mechanism (**Figure 2A**). When the reaction was carried out in a deuterated solvent, deuterium was incorporated only at the N–H position of the product, with no labeling observed elsewhere (**Figure 2A-i**). In addition, using an N–D–labeled indole under the standard conditions led to retention of the N–D bond in the final product (**Figure 2A-ii**); both experiments support a stepwise mechanistic pathway. To validate the possible intermediacy of paraquinone methide species, the reaction of **2a** without indole leads to the formation of a mixture of five-membered oxy-cyclization dihydro-furan[51] and alpha-beta unsaturated ketone, which indicates the existence of possible paraquinone methide species (**Figure 2A-iii**).[52, 53] Further, a reaction in the presence of a TEMPO radical, a slight lowering of desired product formation was noted, which suggested that the reaction follows an ionic pathway. With these control experiments and based on existing literature,[54] we proposed a mechanistic cycle, as illustrated in **Figure 2B**. The first step involves the coordination of FeCl$_3$ to the hydroxy group of aryl sulfonyl allenol, which yields the possible intermediate **IN1**.[55] Subsequently, intermediate **IN1** transforms to transient para-quinone type of species **IN2** by losing FeCl$_3$[OH].[56] Next, indole **1a** immediately reacts with species **IN2** to generate another intermediate **IN3**, driven by nucleophilic attack from the C-3 position of the indole moiety. [57, 58] Instantly, the desired cyclopenta[b]indole core intermediate **IN4** is formed through nucleophilic attack on the C2-position of indole by the sp-carbon of allene.[59, 60] Furthermore, the abstraction of the methyl proton by FeCl$_3$[OH], expelling H$_2$O along with FeCl$_3$, thus completes the catalytic cycle, which indicates greener, sustainable, and economical approach for the construction of desired Cyclopenta[b] indole derivatives.[61]

View Article Online
DOI: 10.1039/D6SC03994D

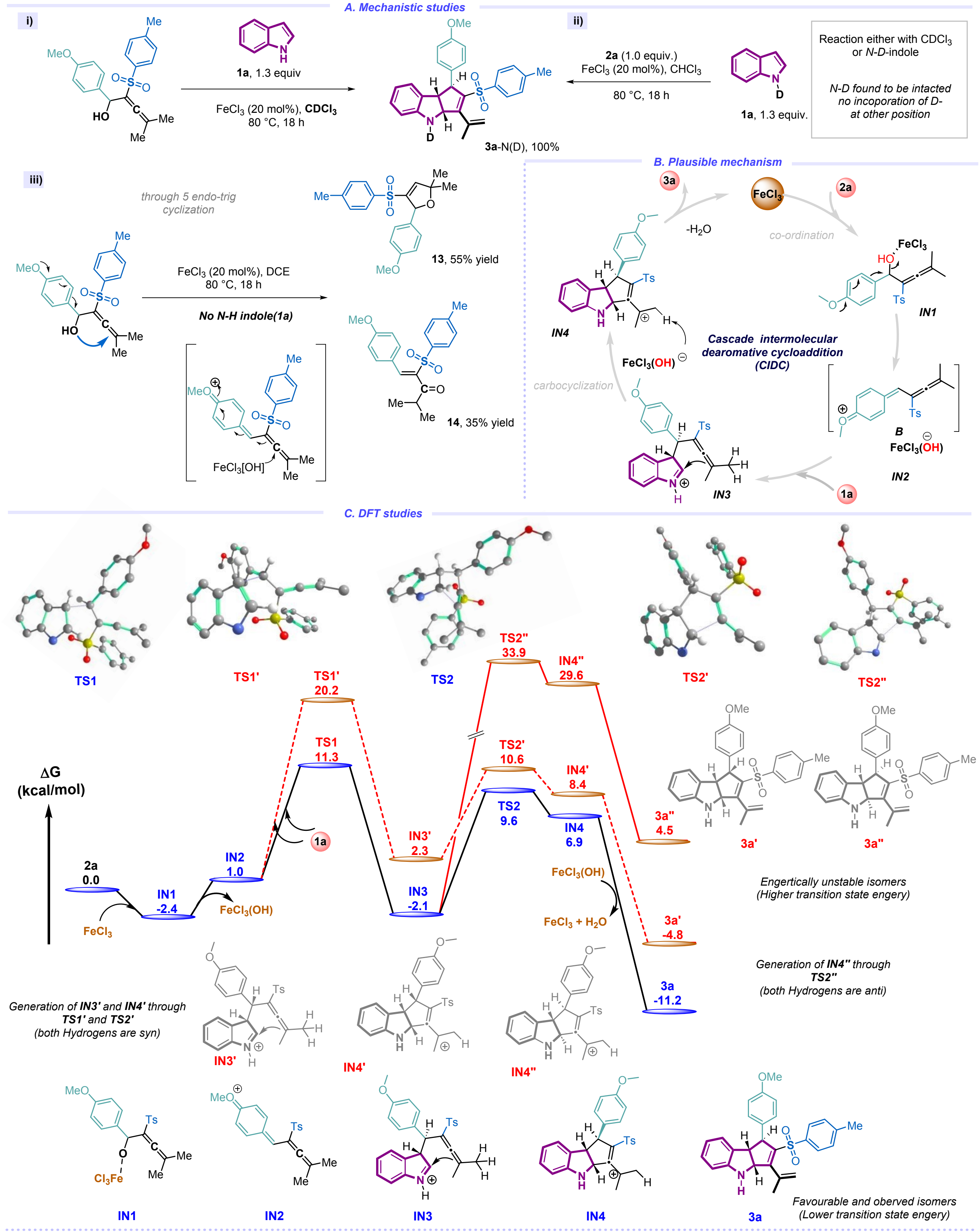


Figure 2. **Mechanistic insight and DFT studies**. A, Mechanistic investigation: i) Reaction with deuterated solvent; ii) Reaction with *N*-D indoles under standard conditions; iii) Reaction without N-H indole. B, Proposed mechanistic cycle. C, DFT analysis: Free energy profile for the formation of 3a. The values are at the M06(SMD)/SDD/def2-TZVP/BP86-D3(BJ)/SDD/def2-SVP level of theory. Non-essential hydrogen atoms are omitted for clarity.

View Article Online
DOI: 10.1039/D6SC03994D

Computational Studies

To gain deeper insight into the reaction mechanism and the formation of an exclusive stereoselective single isomer, quantum chemical calculations using density functional theory (DFT) were performed, guided by control experiments and previous literature (**Figure 2C**).[62, 63] Efforts to identify a transition state for a concerted reaction were unsuccessful; however, energy surfaces for different stepwise processes were discovered. At first, $FeCl_3$ aids in the coordination of sulfonyl allenol, resulting in the formation of the Fe-coordinated intermediate, **IN1**, through an exergonic process with an energy change of -2.4 kcal/mol. Immediately, the loosely bound adduct **IN1** dissociates to generate $FeCl_3(OH)$, which then forms the intermediate **IN2** with energy up by 3.4 kcal/mol. Next, the addition of indole can occur in two distinct orientations to **IN2**, which leads to the formation of various diastereomers. In one orientation, both hydrogen atoms are positioned above the plane, while in another, one hydrogen atom is above the plane and the other is below. Formation of expected product **3a** could occur by construction of the C–C bond at C3 of indole **1a**, yielding the stable intermediate **IN3** via transition state **TS1**, which has an energy barrier of 13.7 kcal/mol. From intermediate **IN3**, cyclization occurs to form another C–C bond, resulting in the production of two different diastereomers. The observed product is achieved via transition state **TS2**, in which back side attack of the allene pi-electron, which has an energy barrier of 11.7 kcal/mol from **IN3**, leads to the formation of possible cationic intermediate **IN4**. The subsequent abstraction of a proton from **IN4** by $FeCl_3(OH)$ produces the stable final product **3a** with an exergonic by 11.2 kcal/mol with the elimination of $FeCl_3$ and water. Moreover, intermediate **IN3** can also yield another isomeric product **3a''**, through **IN4''**, via transition states **TS2''**, in which the possible attack of frontside attack of the allene pi-electron at the C-2 position of indole. This opposite orientation leads to the highest energy barrier of 33.9 kcal/mol via **TS2''**, which could transform to unfavourable isomeric product **3a''** (4.5 kcal/mol) via the intermediary of **IN4''**. Alternatively, if both hydrogen atoms are positioned above the plane, indole addition leads to the formation of the alternative intermediate **IN3'** through transition state **TS1'**, which presents a higher energy barrier of 22.6 kcal/mol. Moreover, transition state **TS2'**, which leads endergonic intermediate to **IN4'**, further converted into another possible isomer **3a'**. Product **3a** is 6.4 kcal/mol and 15.7 kcal/mol more stable than **3a'**, and **3a''**, respectively. However, the transition state leading to **3a'** and **3a''** lies higher in energy than **TS1**/**TS2** (leads to **3a**). From these data, we conclude that the preference for the formation of product **3a** over **3a'** and **3a''** is governed by energetically favourable.[64, 65]

Conclusions

In summary, we have developed a dearomative formal [3+2] cycloaddition reaction between indole and aryl sulfonyl allenol for the peripheral editing of indoles along with the installation of diverse functionality such as consecutive three quaternary centers, sulfone, and prenyl units. The transformation proceeds under mild conditions, avoids precious metal catalysts, and demonstrates compatibility with a diverse range of functionalities with consistently high regio- and diastereocontrolled products. The protocol is compatible with a wide range of pharmaceutically relevant substrates, gram-scale scalability, and double cascade dearomative cyclization that provides rapid access to a structurally complex molecular scaffold. Late-stage functionalization and product diversification further highlight the synthetic versatility of the strategy. Additionally, we have undertaken extensive mechanistic investigations to unravel the underlying processes. This included a range of control experiments, such as reaction with deuterated solvents/additives and density functional theory (DFT) analysis, which have collectively backed the formation of diastereoselective cyclopenta[b]indole derivatives. Overall, this operationally simple strategy enables efficient construction of nonplanar, tricyclic cyclopenta[b]indole derivatives of potential relevance to medicinal chemistry and complex molecule synthesis.

Author contributions

A.C.S. K. K. and P.S. discovered, developed the reaction, designed the experiments, and analyzed the results. K. K., P.S., and R.D.T. performed synthesis. A.K.P. and M.V.M. performed DFT analysis. The manuscript was written through the contributions of all authors. All authors have given approval to the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

CCDC 2514415 (for 3a) contains the supplementary crystallographic data for this paper. The data supporting this article have been included as part of supplementary information (SI). Supplementary information: experimental procedures, optimization studies, mechanistic studies, and characterization data of new compounds.

Acknowledgements

Generous financial support by the Anusandhan National Research Foundation (ANRF), India, ANRF/PAIR/2025/000006/PAIR-A is gratefully acknowledged. We thank the Central Research Facilities and Department of Chemistry, IIT Ropar, for providing the necessary research facilities and infrastructure. We thank Kamlesh Satpute for the analysis of X-ray single-crystal data. M.V.M. thanks the financial support by the ANRF (ANRF/ECRG/ 2024/002337/CS) and CNMS, Jain University, Bangalore, India. PS, thank the University Grant Commission (UGC) for the Senior Research Fellowship. KK and RDT, thanks for the ANRF-PAIR grants and IIT Ropar for the fellowship, respectively.

Notes and references

(1) J. Chen, W. Zhang, D. Huang, J. Wu and X. Wu, *Asian J. Org. Chem.*, 2025, **14**, e00382.
(2) N. Kratena, B. Marinić and T. J. Donohoe, *Chem. Sci.*, 2022, **13**, 14213–14225.
(3) A. R. Pape, K. P. Kaliappan and E. P. Kündig, *Chem. Rev.*, 2000, **100**, 2917–2940.
(4) F. Lovering, J. Bikker and C. Humblet, *J. Med. Chem.*, 2009, **52**, 6752–6756.
(5) A. Palai, P. Rai and B. Maji, *Chem. Sci.*, 2023, **14**, 12004–12025.
(6) M. Zhu, X. Zhang, C. Zheng and S.-L. You, *Acc. Chem. Res.*, 2022, **55**, 2510–2525.
(7) B. Baruah, C. D. Pegu and M. L. Deb, Top. *Curr. Chem.*, 2024, **382**, 18.
(8) X. Mo, D. P. Rao, K. Kaur, R. Hassan, A. S. Abdel-Samea, S. M. Farhan, S. Bräse and H. Hashem, *Molecules*, 2024, **29**, 4770.
(9) C. Zheng and S.-L. You, *Nat. Prod. Rep.*, 2019, **36**, 1589–1605.
(10) S. P. Roche and J. A. Porco Jr., *Angew. Chem. Int. Ed.*, 2011, **50**, 4068–4093.
(11) M. Bandini and A. Eichholzer, *Angew. Chem. Int. Ed.*, 2009, **48**, 9608–9644.
(12) D. Ni, S. Hu, X. Tan, Y. Yu, Z. Li and L. Deng, *Angew. Chem. Int. Ed.*, 2023, **62**, e202308606.
(13) M. C. DiPoto, R. P. Hughes and J. Wu, *J. Am. Chem. Soc.*, 2015, **137**, 14861–14864.
(14) H. Xiong, H. Xu, S. Liao, Z. Xie and Y. Tang, *J. Am. Chem. Soc.*, 2013, **135**, 7851–7854.
(15) L. M. Repka, J. Ni and S. E. Reisman, *J. Am. Chem. Soc.*, 2010, **132**, 14418–14420.
(16) J. Yang, L. Yang, Y. Zhao, L. Hou, Y. Qiu, G. Pan, X. Liu, X. Feng and S. Dong, *J. Am. Chem. Soc.,* 2025, **147**, 35755–35766.
(17) L. Hou, L. Yang, G. Yang, Z. Luo, W. Xiao, L. Yang, F. Wang, L.-Z. Gong, X. Liu, W. Cao and X. Feng, *J. Am. Chem. Soc.*, 2024, **146**, 23457–23466.
(18) M. S. Oderinde, E. Mao, A. Ramirez, J. Pawluczyk, C. Jorge, L. A. M. Cornelius, J. Kempson, M. Vetrichelvan, M. Pitchai, A. Gupta, A. K. Gupta, N. A. Meanwell, A. Mathur and T. G. M. Murali Dhar, *J. Am. Chem. Soc.*, 2020, **142**, 3094–3103.
(19) Z. Xie, Y. Wang, Y. Li et al., *J. Am. Chem. Soc.*, 2015, **137**, 9423–9428.
(20) G. Mei, H. Yuan, Y. Gu, W. Chen, L. W. Chung and C.-C. Li, *Angew. Chem. Int. Ed.*, 2014, **53**, 11051–11055.
(21) S.-X. Feng, Q.-T. Lu, Y. Lu, L. Cui, L. Yang, A. S. Baghel and Q. Cai, *Angew. Chem. Int. Ed.*, 2025, **64**, e202512345.
(22) A. Shikari, C. Parida and S. C. Pan, *Org. Lett.*, 2024, **26**, 5057–5062.
(23) P.-Z. Dong, B. Qiu, X.-D. An and J. Xiao, *Green Chem.*, 2022, **24**, 3772–3777.
(24) H. Li, R. P. Hughes and J. Wu, *J. Am. Chem. Soc.*, 2014, **136**, 6288–6296.
(25) Z. Deng, L. Meng, X. Bing, S. Niu, X. Zhang, J. Peng, Y. Luan, L. Chen and P. Tang, *J. Am. Chem. Soc.,* 2024, **146**, 2325–2332.
(26) Y.-Z. Liu, H. Song, C. Zheng and S.-L. You, *Nat. Synth.*, 2022, **1**, 203–216.
(27) J. Winkelblech, A. Fan and S.-M. Li, Appl. *Microbiol. Biotechnol., 2015, **99**, 7379–7397.*
(28) B. Botta, A. Vitali, P. Menendez, D. Misiti and G. D. Monache, *Curr. Med. Chem.*, 2005, **12**, 713–739.
(29) M. Jost, A. Luzhetskyy and A. Bechthold, *ChemBioChem*, 2014, **15**, 1502–1510.
(30) Barry M. Trost and M. K. Brennan, *Synthesis*, 2009, 3003–3025.
(31) Y. Zhang and S.-M. Li, *Nat. Prod. Rep.*, 2012, **29**, 127–144.
(32) S.-M. Li, *Nat. Prod. Rep.*, 2010, **27**, 57–78.
(33) L. Sander, J. M. Müller and C. B. W. Stark, *J. Am. Chem. Soc.*, 2025, **147**, 26506–26517.
(34) X. Chang, F. Zhang, S. Zhu, Z. Yang, X. Feng and Y. Liu, *Nat. Commun.*, 2023, **14**, 3876.
(35) H.-F. Tu, X. Zhang, C. Zheng, M. Zhu and S.-L. You, *Nat. Catal.*, 2018, **1**, 601–608.
(36) P. Singh, M. V. Mane, S. K. Mahto and A. C. Shaikh, *Org. Lett.*, 2025, **27**, 8217–8222.
(37) P. Singh, Deepshikha, N. Lal, M. V. Mane and A. C. Shaikh, *Org. Lett.*, 2025, **27**, 1153–1158.
(38) N. Krause and A. S. K. Hashmi, *Chem. Rev.*, 2014, **114**, 11195–11249.
(39) N. Krause and C. Winter, *Chem. Rev.*, 2011, **111**, 1994–2009.
(40) X.-X. Li, L.-L. Zhu, W. Zhou and Z. L. Chen, *Org. Lett.*, 2012, **14**, 436–439.
(41) S. Ma, *Acc. Chem. Res.*, 2009, **42**, 1679–1688.
(42) J. Ye and S. Ma, *Acc. Chem. Res.*, 2014, **47**, 989–1000.
(43) N. Krause, *Chem. Soc. Rev.*, 2012, **41**, 2028–2041.
(44) M. S. Santos, D. C. Fernandes, M. T. Rodrigues, T. Regiani, A. D. Andricopulo, A. L. T. G. Ruiz, D. B. Vendramini-Costa, J. E. de Carvalho, M. N. Eberlin and F. Coelho, *J. Org. Chem.*, 2016, **81**, 6626–6639.
(45) T. Nakazawa, K. Ishiuchi, M. Sato, Y. Tsunematsu, S. Sugimoto, Y. Gotanda, H. Noguchi, K. Hotta and K. Watanabe, *J. Am. Chem. Soc.*, 2013, **135**, 13446–13455.
(46) J. E. Saxton, *Nat. Prod. Rep.*, 1997, **14**, 559–590.
(47) J. Börgel and T. Ritter, *Chem*, 2020, **6**, 1877–1887.
(48) D. C. Blakemore, L. Castro, I. Churcher, D. C. Rees, A. W. Thomas, D. M. Wilson and A. Wood, *Nat. Chem.*, 2018, **10**, 383–394.
(49) X. Liu and J. Zhang, *Chem. Eur. J.*, 2025, **31**, e202404640.
(50) A. B. Charette and C. Molinaro, *Chem. Rev.*, 2004, **104**, 2279–2298.
(51) R. R. Tata and M. Harmata, *Org. Lett.*, 2016, **18**, 5684–5687.
(52) A. Maestro and M. Zurro, *Org. Biomol. Chem.*, 2023, **21**, 7739–7755.
(53) C. G. S. Lima, F. P. Pauli, D. C. S. Costa, A. S. de Souza, L. S. M. Forezi, V. F. Ferreira and F. de Carvalho da Silva, *Eur. J. Org. Chem.*, 2020, 2650–2692.
(54) X. Li, Z. Li and J. Sun, *Nat. Synth.*, 2022, **1**, 426–438.
(55) S.-C. Zhan, J. Sun, Q. Sun, Y. Han and C.-G. Yan, *J. Org. Chem.*, 2023, **88**, 5440–5456.
(56) Z. Han, B. Zhu, Y. Zang, C. Zhang, X.-Q. Dong, H. Huang and J. Sun, *Chem. Sci.*, 2024, **15**, 720–725.
(57) H.-P. Pan, Z.-Q. Zhu, Z.-W. Qiu, H.-F. Liu, J.-D. Ma, B.-Q. Li, N. Feng, A.-J. Ma, J.-B. Peng and X.-Z. Zhang, *J. Org. Chem.*, 2021, **86**, 16518–16534.

View Article Online
DOI: 10.1039/D6SC03994D

(58) J. R. Wang, X.-L. Jiang, Q.-Q. Hang, S. Zhang, G.-J. Mei and F. Shi, *J. Org. Chem.*, 2019, **84**, 7829–7839.

(59) L.-Y. Mei, Y. Wei, X.-Y. Tang and M. Shi, *J. Am. Chem. Soc.*, 2015, **137**, 8131–8137.

(60) Y. Zhang, J. Wang and W. Su, *Angew. Chem. Int. Ed.*, 2010, **49**, 10189–10191.

(61) T. Vivekanand, B. Satpathi, S. K. Bankar and S. S. V. Ramasastry, *RSC Adv.*, 2018, **8**, 18576–18588.

(62) Y. Yuwen, J. Tang, Y. Qi, T. Zou, S. Zhang, Y.-Q. Zhang and Q.-W. Zhang, *Chem. Sci.*, 2026, **17**, 3171–3177.

(63) S. Dutta, C. G. Daniliuc, C. Mück-Lichtenfeld and A. Studer, *J. Am. Chem. Soc.*, 2025, **147**, 4249–4257.

(64) M. Chellegui, M. Trabelsi, B. Champagne and V. Liégeois, *ACS Omega*, 2025, **10**, 833–847.

(65) X. Yu, C. Zheng and S.-L. You, *J. Am. Chem. Soc.*, 2024, **146**, 25878–25887.

View Article Online
DOI: 10.1039/D6SC03994D

Stereoselective Dearomative Formal [3+2] cycloaddition of Indole with Allenols: Access to Structurally Diverse Cyclopenta[b]indoles

Kavneet Kaur,[a$] Puja Singh,[a$] Rahul D. Thombare,[a] Adithya K. P.,[b] Manoj V. Mane,[b] and Aslam C. Shaikh,[a*]

[a]Department of Chemistry, Indian Institute of Technology, Ropar (IIT Ropar), Rupnagar, Punjab – 140 001, India. E-mail: aslam.shaikh@iitrpr.ac.in.
[b]Centre of Nano and Material Sciences, Jain (Deemed-to-be University), Bangalore, Karnataka 562112, India.
[$] Both authors equally contributed to this work.

Data availability

CCDC 2514415 (for 3a) contains the supplementary crystallographic data for this paper. The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: experimental procedures, optimization studies, mechanistic studies, and characterization data of new compounds.