Nature Communications

https://doi.org/10.1038/s41467-026-73353-0

Article in Press

Total syntheses of (+)-dalesconols A and B enabled by triple-relayed remote chirality transfer

Received: 17 November 2025

Accepted: 29 April 2026

Cite this article as: Guo, Y., Liu, J., Gao, W. *et al.* Total syntheses of (+)-dalesconols A and B enabled by triple-relayed remote chirality transfer. *Nat Commun* (2026). https://doi.org/10.1038/s41467-026-73353-0

Yun Guo, Jingjing Liu, Wen Gao, Yicong Ge, Jingyun Ren & Xinjun Luan

Total Syntheses of (+)-Dalesconols A and B Enabled by Triple-Relayed Remote Chirality Transfer

Yun Guo[1,§], Jingjing Liu[1,§], Wen Gao[1], Yicong Ge[1], Jingyun Ren[1,*] & Xinjun Luan[1,*]

[1]Key Laboratory of Synthetic and Natural Functional Molecule of the Ministry of Education, College of Chemistry & Materials Science, Northwest University, Xi'an, 710127, China.
[§]These authors contributed equally.
*e-mail: xluan@nwu.edu.cn, jyrenchem@nwu.edu.cn.

Abstract: Dalesconols A and B, featuring unique and highly congested polycyclic carbon frameworks and notable biological activities, have attracted sustained attention. However, their structural complexity constitutes a significant challenge for total synthesis. Herein, we present the asymmetric total syntheses of (+)-dalesconols A and B via a remote chirality transfer strategy. Central to this approach is the implementation of our palladium/norbornene-catalyzed trifunctionalization method, which enables one-step construction of the chiral polycyclic core skeleton via a triple relay of point-to-axial, axial-to-axial, and axial-to-point chirality transfer. Combined with intramolecular Michael addition, C–H oxidation/retro-Michael elimination, and global demethylation, this triple-relayed remote chirality transfer strategy allows concise and modular access to (+)-dalesconols A and B.

Introduction

Dalesconols A and B (Fig. 1), first isolated in 2008 by Tan and co-workers from mantis-associated fungus *Daldinia eschscholzii*, exhibited comparable level of immunosuppressive activity as to that of clinically utilized cyclosporine A, but with superior selectivity indexes (SI) for reduced cytotoxicity (dalesconol A: IC_{50} = 0.16 μg mL^{-1}, SI > 500; dalesconol B: IC_{50} = 0.25 μg mL^{-1}, SI > 320; cyclosporine A: IC_{50} = 0.06 μg mL^{-1}, SI = 187).[1] These compounds are biosynthetically produced as scalemic mixtures and have been reported to show enhanced biological activities relative to their enantiopure counterparts.[2] Independently, She, Lin, and co-workers isolated the same metabolites in 2009 from a mangrove-derived endophytic fungus (*Sporothrix* sp. #4335), where they were designated sporothrins A and B.[3] Biological evaluation revealed moderate antitumor activity for both compounds, while dalesconol A additionally exhibits potent acetylcholinesterase inhibition (IC_{50} = 1.05 μM).

Structurally, the unique and highly dense all-carbon skeleton, characterized by seven rings of varying sizes and two adjacent stereocenters, renders the dalesconols A and B attractive targets for total syntheses. Like biosyntheses,[4] arene dearomatization[5-35] has proven essential for installing the highly congested all-carbon quaternary center.[36-39] The first total syntheses of dalesconols A and B were beautifully achieved by the Snyder group in 2010 via a one-pot cascade combining Friedel–Crafts alkylation and oxidative dearomatization to construct the polycyclic skeleton (Fig. 1a).[36] Shi's group further advanced the field by using carbocation-triggered dearomatization to assemble the dalesconol core.[37] In 2017, the Tang group realized the asymmetric total syntheses of (+)-dalesconols A and B with a sophisticated Pd(0)-catalyzed enantioselective dearomatization–kinetic resolution strategy (Fig. 1b).[38] Our group contributed to this area in 2021 with the synthesis of racemic dalesconol A,[39] capitalizing our Pd(0)/NBE-catalyzed three-fold domino reaction involving C–H alkylation, alkyne insertion, and arene dearomatization (Fig. 1c).[40-41] Herein, we report the asymmetric total syntheses of (+)-dalesconols A and B, which leverage mechanism-guided stereochemical innovations in the domino process to enable remote chirality transfer for the one-step construction of chiral polycyclic architectures.

Results

Retrosynthetic design

As depicted in Fig. 2a, our synthetic design centers on the stereoselective construction of the quaternary carbon center via remote chirality transfer across a trans-configured double bond. The key advancement is the involvement of chiral propargylic fragment **5**, readily accessible from naturally occurring *L*-malic acid, to innovate the Pd(0)/NBE-catalyzed trifunctionalization reaction for stereoselective assembly of chiral dalesconol core **3**. Then, it can be elaborated by straightforward transformations, including a Michael addition to establish the entire heptacyclic skeleton, a benzylic oxidation/retro-Michael sequence to install the enone functionality, and demethylation to release three or four hydroxyl groups, thereby culminating in the asymmetric total syntheses of dalesconols A and B.

Proposed triple-relayed chirality transfer

The success of this proposed synthetic plan depends critically on establishing effective remote stereochemical induction in the domino reaction.[42] Detailed mechanistic analysis suggests that an attractive triple-relayed chirality transfer may be operative, as proposed in Fig. 2b. At the outset, palladacycle **A**, in situ formed with **4**, can enable the incorporation of chiral building block **5** to give intermediate **B** after the extrusion of NBE.[40] Then, a triple relay of chirality transfer is envisioned: **(i) point-to-axial chirality:** the chiral propargylic unit affects the alkyne insertion step, favoring the generation of sterically minimized vinyl-Pd(II) intermediate **C** bearing new axial chirality, while avoiding the formation of undesired intermediate **C'** with severe steric repulsion between the OR^1 and acetyl units; **(ii) axial-to-axial chirality:** stereo-recognition of two enantiomers of biaryl moiety can be rendered by the coordination with such an axially chiral vinyl-Pd(II) unit, enabling the formation of **D** with a preferred axial conformation, in which the acetyl-substituted phenyl ring is aligned trans to the naphthyl ring; **(iii) axial-to-point chirality:** Heck-type dearomatization of the naphthyl ring via 5-*exo*-trig cyclization, but not through 6-*endo*-trig route to give undesired **3'**, can produce the envisioned chiral product **3** by converting that conformationally favored biaryl axis into a centrally chiral spirocyclic carbon center.

Model studies for the triple-relayed chirality transfer strategy

To assess the feasibility of the triple-relayed chirality transfer, we first examined model reactions between readily accessible naphthylamide-based biaryl **6** and bromo-alkyl-alkynes **7a-e** (Fig. 3). To our delight, substrate **7a**, bearing an *ortho*-Me-substituted phenyl group, participated well in the Pd(0)/NBE-catalyzed reaction, delivering the product **8a** with discernible stereocontrol (2:1 dr) mediated by the remote propargylic stereocenter. This stereochemical communication was further enhanced by employing the sterically bulkier **7b**, which yielded product **8b** with improved diastereoselectivity (4:1 dr). Notably, the relative configuration of the major diastereomer of **8b** aligns fully with the stereochemistry proposed in the triple-relayed chirality transfer model (Supplementary Table S2). Further control studies featuring direct chirality transfer—conducted by systematically varying the size of the propargyl alcohol protecting group—resulted in no stereocontrol, highlighting the essential role of the relayed chirality transfer. Collectively, these results establish a solid foundation for applying this strategy to the asymmetric total syntheses of dalesconols A and B.

Asymmetric total synthesis of (+)-dalesconol A

With a successful model, we proceeded to the total synthesis of (+)-dalesconol A. Naphthylamide-based biaryl **4**, which features a high oxidation state, was prepared by starting from commercially available naphthylamine **9** (Fig. 4a). Boc-protection followed by a Cu(I)-catalyzed etherification afforded methoxy-substituted **10** in 80% yield. Regioselective bromination and subsequent Pd(0)-catalyzed borylation with B_2Pin_2 led to highly functionalized building block **11**. A Suzuki–Miyaura cross-coupling between **11** and aryl halide **12** proceeded smoothly to furnish biaryl diamine **13** in 77% yield. Finally, a selective diazotization/Sandmeyer iodination of **13** delivered the key aryl iodide **4** in 71% yield.

We next moved to the synthesis of key chiral fragment **5** that bears a secondary propargylic stereogenic center. After extensive attempts, the benzyl-substituted oxime ether **5a** was identified as the optimal target substrate (Fig. 4b). Following a known procedure,[43-44] enantiomerically pure compound **15** was efficiently prepared from a commercial source of (*S*)-α-hydroxy-γ-butyrolactone (**14**)—itself derived from *L*-malic acid. In parallel, oxime ether **17** was prepared in a single step with 87% yield, although the most common acetal protecting group could not be incorporated for the bulky ketone **16**. A Sonogashira cross-coupling between **15** and **17**, followed by an Appel reaction to convert the primary alcohol into the envisioned alkyl bromide, afforded the target compound **5a** in 65% overall yield.

With key fragments **4** and **5a** in hand, we investigated the pivotal triple domino reaction by using Pd(0)/NBE cooperative catalysis[45-56] (Table 1, and detailed optimization data see Supplementary Table S1). Gratifyingly, the desired product **18** was obtained in 69% yield as a single diastereomer under the optimal conditions (entry 1). The absolute configuration of **18** was unambiguously assigned by single-crystal X-ray diffraction analysis, confirming that the bulky oxime ether moiety adopts a trans orientation relative to both the propargylic and naphthylamide units (Supplementary Table S3). This stereochemical outcome is fully consistent with the proposed triple-relayed remote chirality transfer. Control experiments by varying reaction parameters didn't lead to improved efficiency (entries 2-12), but excellent stereoselectivities were maintained for all the cases (dr > 20:1). These results indicate that the high stereochemical control is entirely attributed to the deliberate structural design of substrate **5a**.

The endgame of asymmetric total synthesis of (+)-dalesconol A was accomplished through downstream transformations of advanced intermediate **18** (Fig. 5). The entire polycyclic skeleton core **19** was constructed via hydrolysis and a Michael addition, mediated by concentrated HCl and $Fe_2(SO_4)_3$. Next, using the $Co(acac)_2$/TBHP oxidation system,[57] the enone moiety was successfully introduced by a sequential benzylic oxidation and retro-Michael elimination, yielding product **20** in 64% yield.

Finally, a global demethylation of **20** with BBr_3 furnished (+)-dalesconol A in 75% yield, thus completing its asymmetric total synthesis.

Asymmetric total synthesis of (+)-dalesconol B

We next pursued the total synthesis of (+)-dalesconol B using the triple-relayed remote chirality transfer strategy (Fig. 6). The key chiral fragment **5b**, prepared analogously to **5a**, participated well in the Pd(0)/NBE-catalyzed polycyclization with biaryl fragment **4**. Treatment of the crude product under strong acidic conditions induced further cyclization, affording product **21**, which contains the complete heptacyclic framework of (+)-dalesconol B, in 57% total yield and with >20:1 dr. Subsequently, an oxidation/retro-Michael elimination sequence successfully generated enone **22**. Global demethylation of **22** then delivered (+)-dalesconol B, completing a concise and efficient total synthesis.

Discussion

In summary, we have achieved the concise and efficient total syntheses of (+)-dalesconol A and B starting from a commercial chiral precursor derived from *L*-malic acid. This success was enabled by stereochemical innovations to our prior Pd(0)/NBE-catalyzed trifunctionalization methodology, which established an innovative remote point-to-point chirality transfer strategy via triple relayed transmission. Owing to its modularity and high stereochemical fidelity, this strategy provides a general and robust platform for the rapid assembly of diverse dalesconol analogs. Related work is currently in progress in our laboratory and will be reported in due course.

Methods

Asymmetric synthesis of polycyclic compound 18 via triple-relayed chirality transfer strategy

In a glovebox, a 5.0 mL vial equipped with a stirring bar was charged with $PdCl_2$ (1.8 mg, 0.01 mmol), $P(4\text{-}F\text{-}C_6H_4)_3$ (6.3 mg, 0.02 mmol), NBE (37.7 mg, 0.4 mmol), Cs_2CO_3 (130.3 mg, 0.4 mmol), compound **4** (101.1 mg, 0.20 mmol), compound **5a** (151.9 mg, 0.30 mmol) and CH_3CN (2.0 mL). The vial was sealed with a Teflon screw cap, removed from the glovebox, and the reaction mixture was heated at 90 °C for 10 h. Upon cooling to room temperature, the mixture was filtered through a Celite pad, and the filtrate was concentrated under reduced pressure. Then, the resulting crude product was dissolved in THF (2.0 mL), treated with 2N HCl (0.5 mL), and stirred at room temperature for another 3 h. The reaction was quenched with saturated $NaHCO_3$ solution, and the mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (petroleum ether: ethyl acetate = 30:1) to afford the target product **18** as a white solid (97.1 mg, 69% yield, 99% ee).

Data availability

The data supporting the findings of this study, including figures, tables, experimental procedures, characterization data, NMR spectra, and HPLC spectra, are available within this article and its Supplementary Information. The X-ray crystallographic coordinates for structures reported in this study have been deposited at the Cambridge Crystallographic Data Center (CCDC), under deposition numbers 2478098 (**8b**) and 2478097 (**18**). These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures. All data are available from the corresponding authors upon request.

References

1. Zhang, Y. et al. Unprecedented Immunosuppressive Polyketides from *Daldinia eschscholzii*, A Mantis-Associated Fungus. *Angew. Chem. Int. Ed.* **47**, 5823-5826 (2008).
2. Zhang, Y. et al. Immunosuppressive Polyketides from Mantis-Associated *Daldinia eschscholzii*. *J. Am. Chem. Soc.* **133**, 5931-5940 (2011).
3. Wen, L. et al. Three Metabolites from the Mangrove Endophytic Fungus *Sporothrix* sp. (#4335) from the South China Sea. *J. Org. Chem.* **74**, 1093-1098 (2009).
4. Fang, W. et al. Naphthol Radical Couplings Determine Structural Features and Enantiomeric Excess of Dalesconols in *Daldinia eschscholzii*. *Nat. Commun.* **3**, 1039-1047 (2012).
5. Roche, S. P. & Porco, J. A., Jr. Dearomatization Strategies in the Synthesis of Complex Natural Products. *Angew. Chem. Int. Ed.* **50**, 4068-4093 (2011).
6. Zhuo, C., Zhang, W. & You, S. Catalytic Asymmetric Dearomatization Reactions. *Angew. Chem. Int. Ed.* **51**, 12662-12686 (2012).
7. Zheng, C. & You, S. Catalytic Asymmetric Dearomatization (CADA) Reaction-Enabled Total Synthesis of Indole-Based Natural

Products. *Nat. Prod. Rep.* **36**, 1589-1605 (2019).
8. George, J. H. Biomimetic Dearomatization Strategies in the Total Synthesis of Meroterpenoid Natural Products. *Acc. Chem. Res.* **54**, 1843-1855 (2021).
9. Huck, C. J., Boyko, Y. D. & Sarlah, D. Dearomative Logic in Natural Product Total Synthesis. *Nat. Prod. Rep.* **39**, 2231-2291 (2022).
10. Xiao, Q., Jackson, J. J., Basak, A., Bowler, J. M., Miller, B. G. & Zakarian, A. Enantioselective Synthesis of Tatanans A-C and Reinvestigation of Their Glucokinase-Activating Properties. *Nat. Chem.* **5**, 410-416 (2013).
11. Ren, W., Wang, Q. & Zhu, J. Total Synthesis of (±)-Aspidophylline A. *Angew. Chem. Int. Ed.* **53**, 1818-1821 (2014).
12. Du, K., Guo, P., Chen, Y., Cao, Z., Wang, Z. & Tang, W. Enantioselective Palladium-Catalyzed Dearomative Cyclization for the Efficient Synthesis of Terpenes and Steroids. *Angew. Chem. Int. Ed.* **54**, 3033-3037 (2015).
13. Pritchett, B. P., Donckele, E. J. & Stoltz, B. M. Enantioselective Catalysis Coupled with Stereodivergent Cyclization Strategies Enables Rapid Syntheses of (+)-Limaspermidine and (+)-Kopsihainanine A. *Angew. Chem. Int. Ed.* **56**, 12624-12627 (2017).
14. Ni, D., Wei, Y. & Ma, D. Thiourea-Catalyzed Asymmetric Michael Addition of Carbazolones to 2-Chloroacrylonitrile: Total Synthesis of 5,22-Dioxokopsane, Kopsinidine C, and Demethoxycarbonylkopsin. *Angew. Chem. Int. Ed.* **57**, 10207-10211 (2018).
15. Tu, H. F., Zhang, X., Zheng, C., Zhu, M. & You, S. Enantioselective Dearomative Prenylation of Indole Derivatives. *Nat. Catal.* **1**, 601-608 (2018).
16. Li, L., Yuan, K., Jia, Q. & Jia, Y. Eight-Step Total Synthesis of Phalarine by Bioinspired Oxidative Coupling of Indole and Phenol. *Angew. Chem. Int. Ed.* **58**, 6074-6078 (2019).
17. Powers, Z. et al. Biomimetic Synthesis of Meroterpenoids by Dearomatization-Driven Polycyclization. *Angew. Chem. Int. Ed.* **58**, 16141-16146 (2019).
18. Mu, X., Yu, H., Peng, H., Xiong, W., Wu, T. & Tang, W. Construction of Various Bridged Polycyclic Skeletons by Palladium-Catalyzed Dearomatization. *Angew. Chem. Int. Ed.* **59**, 8143-8147 (2020).
19. Li, G., Wang, Q. & Zhu, J. Unified Divergent Strategy towards the Total Synthesis of the Three Sub-Classes of Hasubanan Alkaloids. *Nat. Commun.* **12**, 36-42 (2021).
20. Magnani, C. S. H. & Maimone, T. J. Dearomative Synthetic Entry into the Altemicidin Alkaloids. *J. Am. Chem. Soc.* **143**, 7935-7939 (2021).
21. Hwang, T., Tuccinardi, J. P., Beard, A. A., Jackson, A. C., Jung, M. J. & Wood, J. L. Total Syntheses of (±)-Dracocephalone A and (±)-Dracocequinones A and B. *Angew. Chem. Int. Ed.* **61**, e202210821 (2022).
22. Qin, B., Lu, Z. & Jia, Y. Divergent Total Synthesis of Four Kopsane Alkaloids: *N*-Carbomethoxy-10,22-dioxokopsane, Epikopsanol-10-lactam, 10,22-Dioxokopsane, and N-Methylkopsanone. *Angew. Chem. Int. Ed.* **61**, e202201712 (2022).
23. Xu, B., Liu, C. & Dai, M. Catalysis-Enabled 13-Step Total Synthesis of (−)-Peyssonnoside A. *J. Am. Chem. Soc.* **144**, 19700-19703 (2022).
24. Zhu, W., Yin, Q., Lou, Z. & Yang, M. Modular Total Syntheses of *trans*-Clerodanes and Sesquiterpene (Hydro)Quinones via Tail-to-Head Cyclization and Reductive Coupling Strategies. *Nat. Commun.* **13**, 6633-6639 (2022).
25. Bulthaupt, H. H. et al. Enantioselective Total Syntheses of Cassane Furanoditerpenoids and Their Stimulation of Cellular Respiration in Brown Adipocytes. *J. Am. Chem. Soc.* **145**, 21562-21568 (2023).
26. Jiang, D. et al. A Homo-Mannich Reaction Strategy Enables Collective Access to Ibophyllidine, Aspidosperma, Kopsia, and Melodinus Alkaloids. *Angew. Chem. Int. Ed.* **62**, e202307286 (2023).
27. Sun, J. et al. Total Syntheses of Polyhydroxylated Steroids by An Unsaturation-Functionalization Strategy. *Angew. Chem. Int. Ed.* **62**, e202303639 (2023).
28. Zhu, A. et al. Divergent Synthetic Approach to Grayanane Diterpenoids. *J. Am. Chem. Soc.* **145**, 8540-8549 (2023).
29. Wiesler, S. et al. Late-Stage Benzenoid-to-Troponoid Skeletal Modification of The Cephalotanes Exemplified by The Total Synthesis of Harringtonolide. *Nat. Commun.* **15**, 4125-4132 (2024).
30. Xu, B., Zhang, Z., Tantillo, D. J. & Dai, M. Concise Total Syntheses of (−)-Crinipellins A and B Enabled by a Controlled Cargill Rearrangement. *J. Am. Chem. Soc.* **146**, 21250-21256 (2024).
31. Forster, D., Wang, Q. & Zhu, J. Total Synthesis of (±)-Crokonoid A. *J. Am. Chem. Soc.* **147**, 36090-36096 (2025).
32. Liu, C., Gong, H., Sheng, Y., Wang, W., Xia, Q. & Ding, H. Divergent Total Syntheses of Elisapterane and Relevant Diterpenoids Assisted by *In Silico* Structure Reassignment. *J. Am. Chem. Soc.* **147**, 33136-33152 (2025).

33. Zhang, J. et al. Enantioselective Total Syntheses of Sannamycins A and B. *J. Am. Chem. Soc.* **147**, 31476-31481 (2025).
34. Zhao, W., Al-Ahmad, R. & Dai, M. Total Synthesis of (−)-Psathyrin A Enabled by Radical Cyclization. *J. Am. Chem. Soc.* **147**, 32365-32369 (2025).
35. Zhong, L. et al. Total Synthesis of (−)-Neocucurbol C Enabled by Pattern Recognition and MHAT Cyclization. *J. Am. Chem. Soc.* **147**, 28589-28594 (2025).
36. Snyder, S. A., Sherwood, T. C. & Ross, A. G. Total Syntheses of Dalesconol A and B. *Angew. Chem. Int. Ed.* **49**, 5146-5150 (2010).
37. Fan, Y., Feng, P., Liu, M., Pan, H. & Shi, Y. A Concise Approach to the Dalesconol Skeleton. *Org. Lett.* **13**, 4494-4497 (2011).
38. Zhao, G., Xu, G., Qian, C. & Tang, W. Efficient Enantioselective Syntheses of (+)-Dalesconol A and B. *J. Am. Chem. Soc.* **139**, 3360-3363 (2017).
39. Zhao, P., Guo, Y. & Luan, X. Total Synthesis of Dalesconol A by Pd(0)/Norbornene-Catalyzed Three-Fold Domino Reaction and Pd(II)-Catalyzed Trihydroxylation. *J. Am. Chem. Soc.* **143**, 21270-21274 (2021).
40. Bai, L., Liu, J., Hu, W., Li, K., Wang, Y. & Luan, X. Palladium/Norbornene-Catalyzed C−H Alkylation/Alkyne Insertion/Indole Dearomatization Domino Reaction: Assembly of Spiroindolenine-Containing Pentacyclic Frameworks. *Angew. Chem. Int. Ed.* **57**, 5151-5155 (2018).
41. Nan, J., Yuan, Y., Bai, L., Liu, J. & Luan, X. Highly Chemoselective Construction of Spiro[4,5]decane-Embedded Polycyclic Scaffolds by A Palladium/Norbornene-Catalyzed C−H Activation/Arene Dearomatization Reaction. *Org. Lett.* **20**, 7731-7734 (2018).
42. Brandstatter, M., Freis, M., Huwyler, N. & Carreira, E. M. Total Synthesis of (−)-Merochlorin A. *Angew. Chem. Int. Ed.* **58**, 2490-2494 (2019).
43. Furstner, A. et al. Total Synthesis of Iejimalide B. *Angew. Chem. Int. Ed.* **45**, 5837-5842 (2006).
44. Liu, H., El-Salfiti, M. & Lautens, M. Expeditious Synthesis of Tetrasubstituted Helical Alkenes by A Cascade of Palladium-Catalyzed C-H Activations. *Angew. Chem. Int. Ed.* **51**, 9846-9850 (2012).
45. Ye, J. & Lautens, M. Palladium-Catalysed Norbornene-Mediated C–H Functionalization of Arenes. *Nat. Chem.* **7**, 863-870 (2015).
46. Della Ca', N., Fontana, M., Motti, E. & Catellani, M. Pd/Norbornene: A Winning Combination for Selective Aromatic Functionalization via C–H Bond Activation. *Acc. Chem. Res.* **49**, 1389-1400 (2016).
47. Wang, J. & Dong, G. Palladium/Norbornene Cooperative Catalysis. *Chem. Rev.* **119**, 7478-7528 (2019).
48. Dong, S. & Luan, X. Catellani Reaction: An Enabling Technology for Vicinal Functionalization of Aryl Halides by Palladium(0)/Norbornene Cooperative Catalysis. *Chin. J. Chem* . **39**, 1690-1705 (2021).
49. Sui, X., Zhu, R., Li, G., Ma, X. & Gu, Z. Pd-Catalyzed Chemoselective Catellani *ortho*-Arylation of Iodopyrroles: Rapid Total Synthesis of Rhazinal. *J. Am. Chem. Soc.* **135**, 9318-9321 (2013).
50. Weinstabl, H., Suhartono, M., Qureshi, Z. & Lautens, M. Total Synthesis of (+)-Linoxepin by Utilizing the Catellani Reaction. *Angew. Chem. Int. Ed.* **52**, 5305-5308 (2013).
51. Li, R. & Dong, G. Direct Annulation between Aryl Iodides and Epoxides through Palladium/Norbornene Cooperative Catalysis. *Angew. Chem. Int. Ed.* **57**, 1697-1701 (2018).
52. Liu, F., Dong, Z., Wang, J. & Dong, G. Palladium/Norbornene-Catalyzed Indenone Synthesis from Simple Aryl Iodides: Concise Syntheses of Pauciflorol F and Acredinone A. *Angew. Chem. Int. Ed.* **58**, 2144-2148 (2019).
53. Cheng, H. et al. A Concise Total Synthesis of (−)-Berkelic Acid. *Angew. Chem. Int. Ed.* **60**, 5141-5146 (2021).
54. Richardson, A. D., Vogel, T. R., Traficante, E. F., Glover, K. J. & Schindler, C. S. Total Synthesis of (+)-Cochlearol B by An Approach Based on A Catellani Reaction and Visible-Light-Enabled [2+2] Cycloaddition. *Angew. Chem. Int. Ed.* **61**, e202201213 (2022).
55. Li, X., Lu, Z., Liu, S., Sun, M., Duan, S. & Xie, Z. Asymmetric Total Synthesis of Benzenoid Cephalotane-Type Diterpenoids through A Cascade C(sp^2) & C(sp^3)–H Activation. *Nat. Commun.* **16**, 4674-4681 (2025).
56. Liu, X., Zhou, Y., Meng, Y., Zhu, Q., Li, R. & Dong, G. Concise Total Syntheses of Leuconoxine-Type Alkaloids Enabled by Palladium/Norbornene-Catalyzed Pyrrole Difunctionalization. *Angew. Chem. Int. Ed.* **64**, e202502736 (2025).
57. Wang, D., Cheng, P., Yang, T., Wu, P., Qu, G. & Guo, H. Asymmetric Domino Heck/Dearomatization Reaction of *β*-Naphthols to Construct Indole-Terpenoid Frameworks. *Org. Lett.* **23**, 7865-7872 (2021).

Acknowledgements

Funding

We acknowledge financial support from the National Natural Science Foundation of China (22371227, U24A20486, 22171225), Key Research and Development Program of Shaanxi (2024SF2-GJHX-66), and Shaanxi Fundamental Science Research Project for Chemistry & Biology (22JHZ001, 23JHQ010).

Author contributions

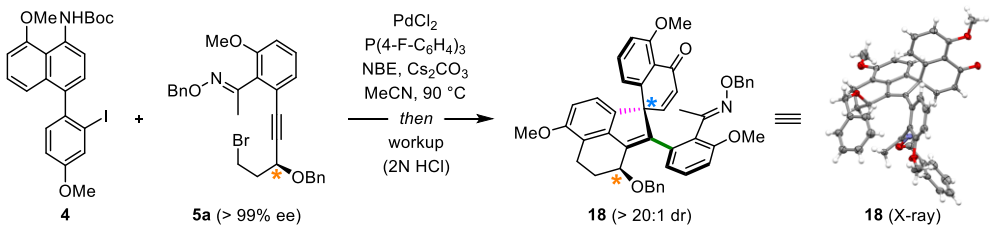
X.L. and J.R. conceived and directed the project. Y.G., J.L., and W.G. conducted the experimental work and analysed the data. X.L., J.R., and Y.G., co-wrote the manuscript with proofreading from all authors.

Competing interests

The authors declare no competing interests.

Tables

Table 1 | Results for the remote chirality transfer[a]



Entry	Variation from Standard Conditions	Yield (%)[b]
1	none	69
2	$Pd(OAc)_2$ instead of $PdCl_2$	21
3	$Pd(CH_3CN)_2Cl_2$ instead of $PdCl_2$	45
4	$Pd_2(dba)_3$ instead of $PdCl_2$	0
5	PPh_3 instead of $P(4\text{-F-}C_6H_4)_3$	48
6	$P(2\text{-furyl})_3$ instead of $P(4\text{-F-}C_6H_4)_3$	31
7	$P(4\text{-MeO-}C_6H_4)_3$ instead of $P(4\text{-F-}C_6H_4)_3$	44
8	K_2CO_3 instead of Cs_2CO_3	48
9	Na_2CO_3 instead of Cs_2CO_3	39
10	K_3PO_4 instead of Cs_2CO_3	27
11	Dioxane instead of CH_3CN	< 5
12	DMF instead of CH_3CN	26

[a]Optimal conditions: **4** (0.2 mmol), **5a** (0.3 mmol), $PdCl_2$ (0.01 mmol), $P(4\text{-F-}C_6H_4)_3$ (0.02 mmol), NBE (0.4 mmol), Cs_2CO_3 (0.4 mmol), CH_3CN (2 mL), 90 °C, 10 h. [b]Yield of isolated product; dr was determined by ^1H NMR. dba = dibenzylideneacetone.

Figure Legends/Captions

Fig. 1 | Previous studies on the total syntheses of dalesconols A and B. a) Total syntheses of (±)-dalesconols A and B by Snyder in 2010. b) Total syntheses of (+)-dalesconols A and B by Tang in 2017. c) Total synthesis of (±)-Dalesconol A by our group in 2021.

Fig. 2 | Design plan for total syntheses of (+)-dalesconols A and B. a) Retrosynthetic analysis of (+)-dalesconols A and B. b) Proposed triple-relayed chirality transfer.

Fig. 3 | Model reaction studies. Reaction conditions: **6** (0.2 mmol), **7** (0.3 mmol), $PdCl_2$ (0.01 mmol), PPh_3 (0.02 mmol), NBE (0.4 mmol), Cs_2CO_3 (0.4 mmol), CH_3CN (2 mL), 90 °C, 10 h. Yield of isolated product; dr was determined by ^1H NMR.

Fig. 4 | Preparation of two coupling partners 4 and 5a. a) Naphthylamide-based biaryl fragment **4**. b) Chiral propargylic fragment **5a**.

Fig. 5 | Completion of the total synthesis of (+)-dalesconol A.

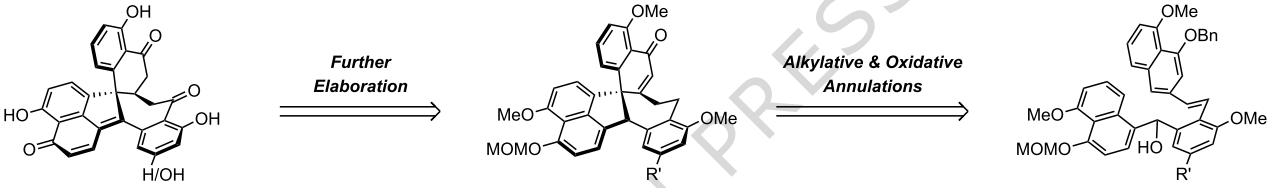
Fig. 6 | Total synthesis of (+)-dalesconol B.

Editor's Summary

Natural products with densely fused polycyclic frameworks, such as dalesconols A and B, pose longstanding challenges for asymmetric synthesis due to their intricate stereochemistry. Here, the authors report concise, enantioselective total syntheses via a triple-relayed remote chirality transfer strategy using palladium/norbornene catalysis.

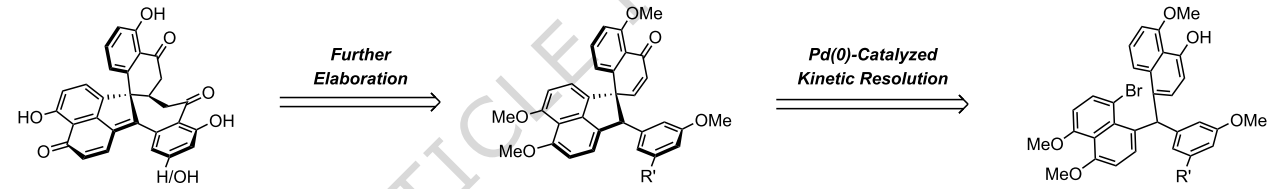
Peer Review Information: *Nature Communications* thanks the anonymous reviewer(s) for their contribution to the peer review of this work. A peer review file is available.

a) Total syntheses of (±)-dalesconols A and B by Snyder (2010)



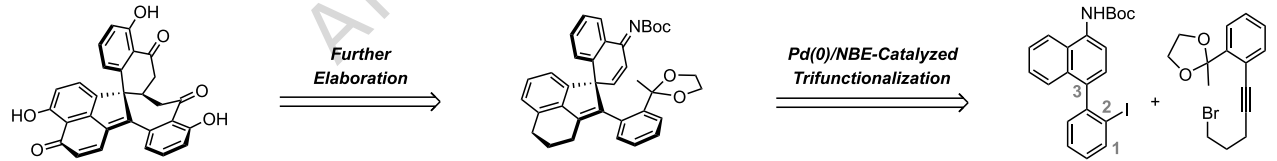
(±)-Dalesconol A-B

b) Total syntheses of (+)-dalesconols A and B by Tang (2017)



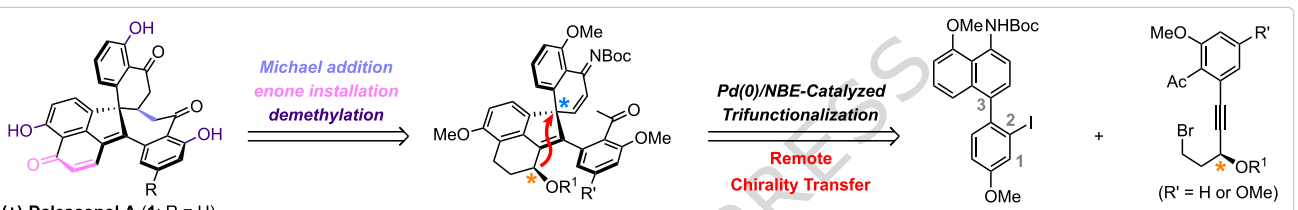
(+)-Dalesconol A-B

c) Total synthesis of (±)-dalesconol A by our group (2021)

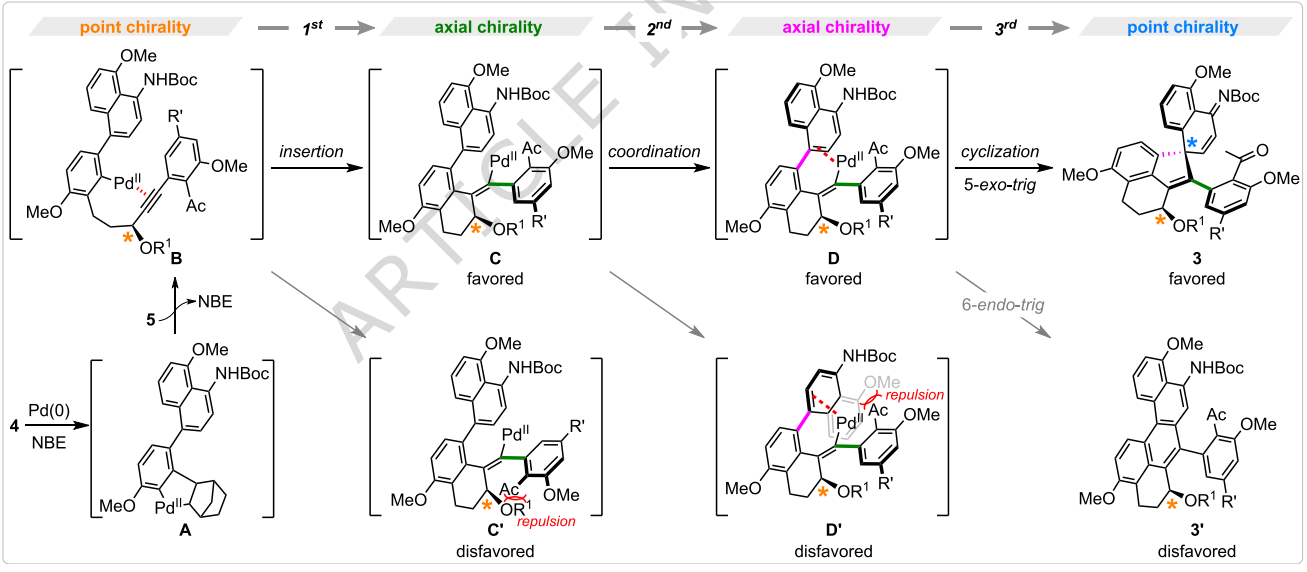


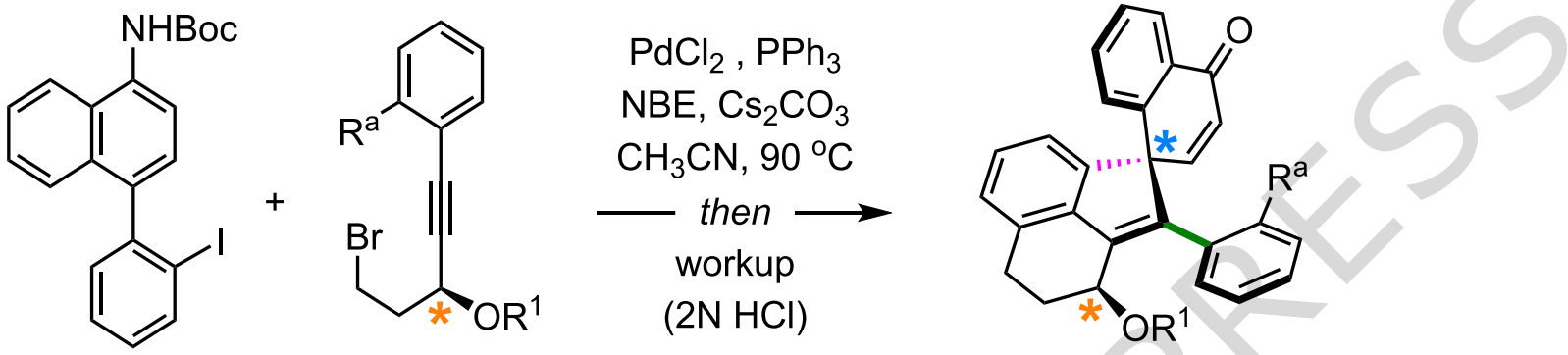
(±)-Dalesconol A

a) Retrosynthetic analysis of (+)-dalesconols A and B



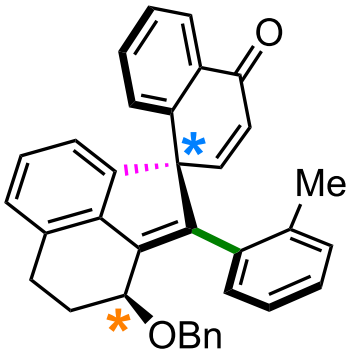
b) Proposed triple-relayed chirality transfer



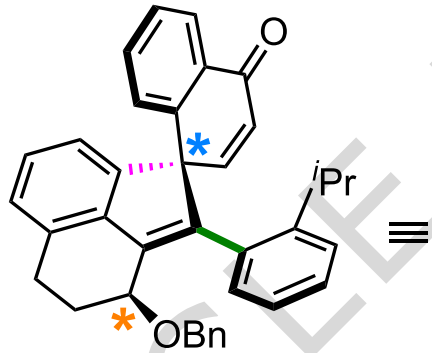


6 **7** **8**

Relayed Chirality Transfer

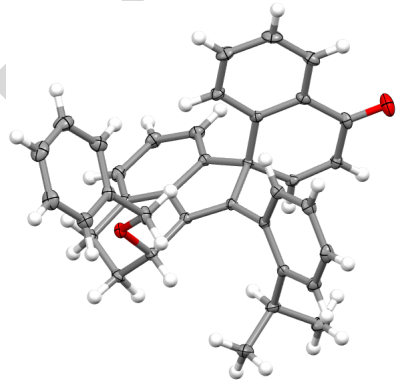


8a
72%, 2:1 dr



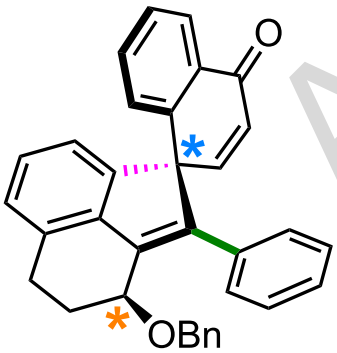
8b
67%, 4:1 dr

≡

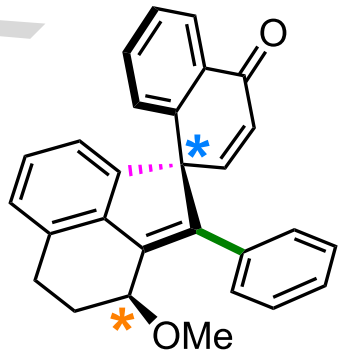


$8b_{major}$
(X-ray)

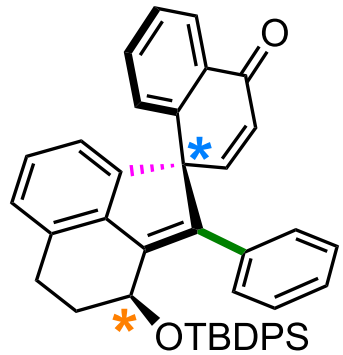
Direct Chirality Transfer



8c
76%, 1:1 dr

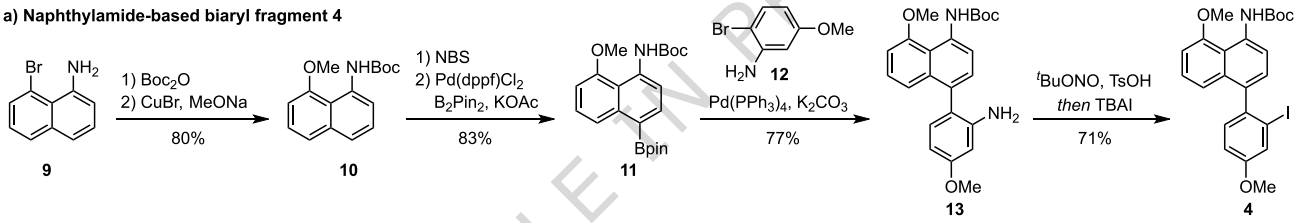


8d
83%, 1:1 dr



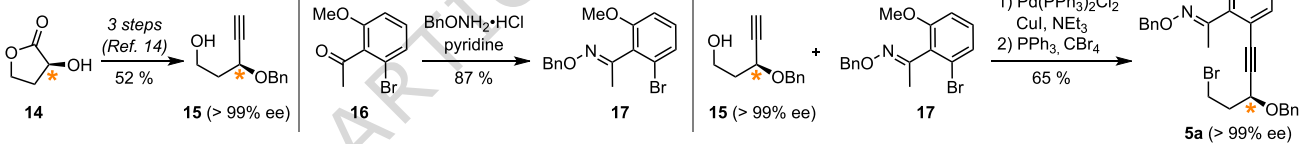
8e
59%, 1:1 dr

a) Naphthylamide-based biaryl fragment 4



9 **10** **11** **13** **4**

b) Chiral propargylic fragment 5a



14 **15** (> 99% ee) **16** **17** **15** (> 99% ee) **17** **5a** (> 99% ee)