

RESEARCH ARTICLE

View Article Online
View Journal

Cite this: DOI: 10.1039/d5qo01443c

Bridging terpenyl aldehydes and terpenes with hydrazine

Li-Ming Zhang,^{a,b} Su-Yang Xu,^{a,b} Xue-Ting Li,^{a,b} Ting-Ting Song,^a Ding-Wei Ji,^a Yanhua Lu,^c Boshun Wan^{a,b} and Qing-An Chen^{a,b}*Received 16th October 2025,
Accepted 2nd December 2025

DOI: 10.1039/d5qo01443c

rsc.li/frontiers-organic

In nature, terpenoids are typically biosynthesized through the catalysis of specific enzymes, while the artificial synthesis of unnatural terpenoids has garnered increasing attention. Herein, we have developed a molecular-bridging strategy that enables the preparation of unnatural terpenoids from natural terpenyl aldehydes and terpenes, expanding the potential applications of natural terpenoids. This reactivity hinges on the strategic use of Ts-hydrazine as a crucial mediator, which enables molecular bridging through pyrazole formation. More importantly, the modular molecular synthesis strategy could significantly expand the structural diversity space of the terpenoid family through precisely tunable building-block assembly. Furthermore, the resulting pyrazole moiety can be subjected to further modification, enhancing the synthetic utility of this strategy.

Introduction

Terpenoids, widely distributed in nature, exhibit diverse biological activities and serve as important industrial chemicals.¹ They have long been the focus of pharmaceutical and synthetic chemists.² In general, the chemically and structurally diverse terpenoids originate from simple isoprene precursors, dimethylallyl diphosphate (DMAPP) and isopentenyl diphosphate (IPP). Under the catalysis of enzymes, they can be converted into hemiterpenoids or condensed into geranyl diphosphate (GPP), farnesyl diphosphate (FPP), and geranylgeranyl diphosphate (GGPP), and thereby could be further derived into monoterpenoids, sesquiterpenoids, diterpenoids, and other terpenoids³ (Fig. 1A). In nature, terpenyl aldehydes and terpenes are the two main forms of terpenoids, such as prenal, isoprene (hemiterpenoids), citronellal, myrcene (monoterpenoids), farnesal, farnesene (sesquiterpenoids), retinal, neophytadiene (diterpenoids), *etc.* However, the synthesis of unnatural terpenoids⁴ from these readily available natural sources remains a challenging yet highly rewarding task for the enrichment of the terpenoid molecular library.⁵

Given the structural diversity and natural abundance of terpenoid aldehydes and terpenes, catalytic post-functionalization strategies have been extensively explored.⁶ However, traditional methods typically rely on additional functionalizing reagents, expensive catalysts, and harsh conditions, which are

not conducive to the advancement of green chemistry.⁷ In contrast, strategies that leverage both natural terpenyl aldehydes and terpenes to directly accomplish molecular bridging of natural terpenoids using readily accessible reagents remain scarce (Fig. 1B). Although this strategy is highly attractive for upgrading naturally abundant terpenoids, how to conveniently and effectively integrate two terpenoid compounds under catalyst-free conditions poses a great challenge.

The [3 + 2] cycloaddition of diazo compounds represents a versatile strategy for constructing five-membered N-heterocycles.⁸ Over the past decades, its extensive utility has been well demonstrated in the synthesis of pyrazoles and pyrazolines using alkynes or electron-deficient alkenes.⁹ However, the application of this powerful reaction to terpenoid compounds remains largely unexplored. Here, in line with our long-standing interest in terpenoid chemistry,¹⁰ we propose the development of a streamlined molecular-assembly approach utilizing terpenyl aldehydes and terpenes. Given the inherent derivatization potential of carbonyl groups, terpenyl aldehydes can directly condense with amines to form imine analogues, which subsequently undergo cycloaddition with terpenes to achieve molecular assembly (Fig. 1C). Such a cycloaddition approach is highly appealing if pharmaceutically interesting nitrogen-containing heterocyclic scaffolds¹¹ could be rapidly accessed while preserving the characteristic isoprenoid units of terpenoid skeletons. This protocol not only opens new avenues for constructing bioactive nitrogen heterocycles, but also provides a novel perspective for the synthesis of unnatural terpenoids. Importantly, this dual-functional strategy could significantly expand the structural diversity space of terpenoid architectures through programmed molecular fusion.

^aDalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, China. E-mail: qachen@dicp.ac.cn

^bUniversity of Chinese Academy of Sciences, Beijing 100049, China

^cHubei Institute of Aerospace Chemotechnology, Xiangyang, 441003, China



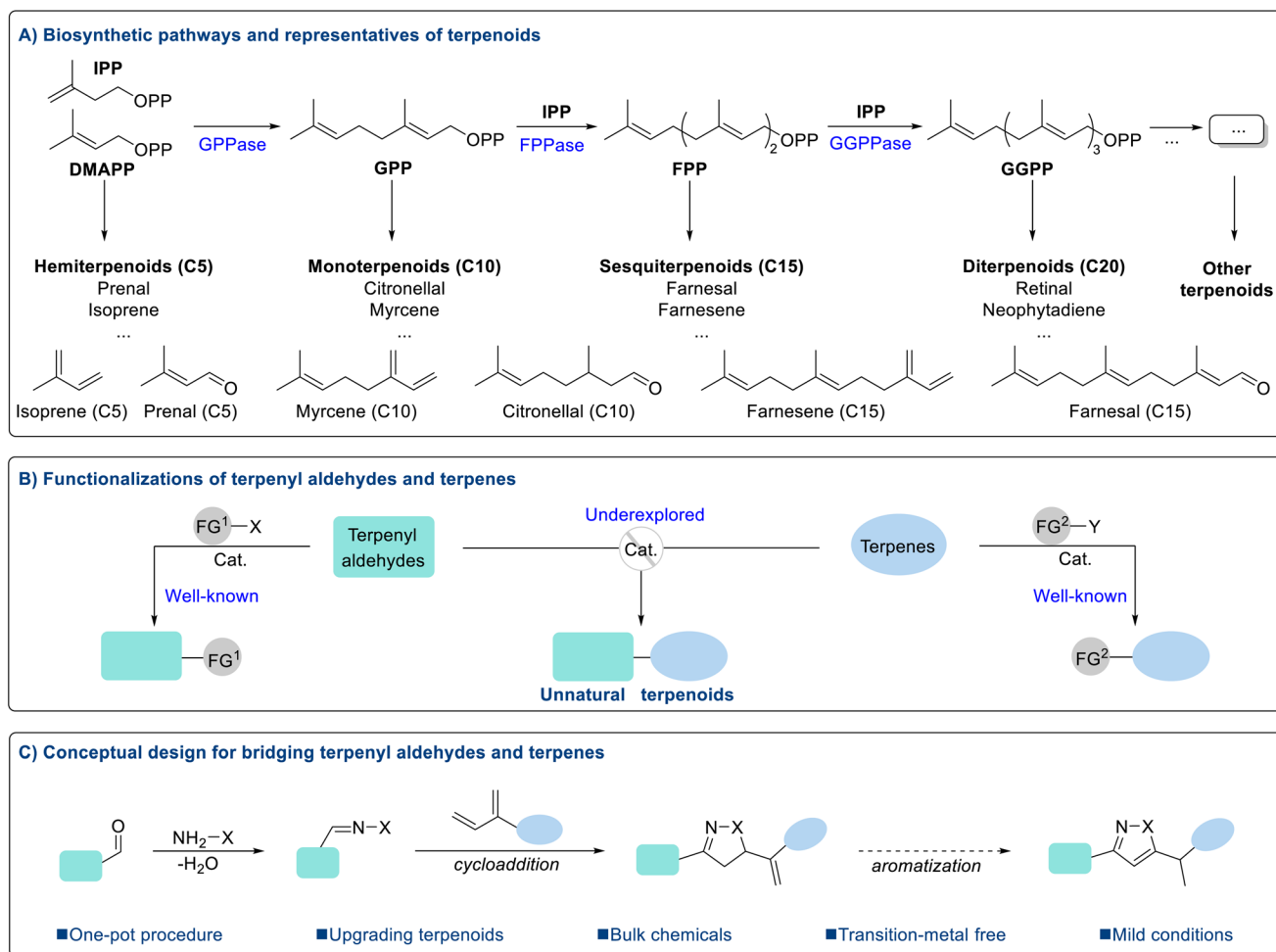


Fig. 1 Synthesis and transformation of terpenoids.

Results and discussion

We commenced the exploration of the molecular-bridging strategy by using citronellal (**1a**) and isoprene (**2a**) as the model substrates. The key challenge lies in identifying suitable linkers that can promote the reaction efficiently and with high chemo- and regioselectivity. This inherent difficulty stems from the presence of multiple potentially reactive alkenyl units in terpenoid structures. Additionally, a possible aromatization of the resulting five-membered nitrogen heterocycle *via* alkene migration introduces further complexity into the reaction system (Fig. 2A, top).

Considering the activation ability of the carbonyl group, various nitrogen-containing reagents were evaluated under the initial reaction conditions (Fig. 2A, bottom). First, inexpensive hydroxylamine (**L1**) was employed as the linker, but the oxime derived from it exhibited low reactivity and failed to effectively react with isoprene. Subsequently, the nitron derived from *N*-Me hydroxylamine (**L2**), as a highly reactive 1,3-dipole, reacted with isoprene to yield a mixture of isooxazoline isomers with less than 10% yield. These

results prompted us to explore alternative 1,3-dipole precursors. Notably, diazo compounds generated from hydrazones¹² attracted our attention, as hydrazones can be conveniently prepared from carbonyl compounds and hydrazines. Therefore, various substitution patterns of hydrazine were evaluated to implement the molecular-bridging strategy, including hydrazine hydrate (**L3**), phenylhydrazine (**L4**), and methyl sulfonylhydrazine (**L5**). Pleasingly, methyl sulfonylhydrazine (**L5**) as the linker afforded pyrazole **3a** with exclusive selectivity, albeit with 23% yield. In view of the pyrazole fragment being a versatile lead molecule in pharmaceutical development,¹³ and pyrazole-based terpenoids have been reported to possess both antifungal activity and low toxicity,¹⁴ we further explored other sulfonylhydrazines (**L6–L10**).¹⁵ Notably, *p*-toluenesulfonylhydrazine (**L9**) demonstrated optimal reaction efficiency through the formation of *N*-tosylhydrazone, which is an emerging building block in current organic chemistry (Fig. 2B, a).¹⁶

After determining the appropriate linker, it was essential to optimize other reaction parameters to further improve the reaction efficiency and selectivity. Alkoxide bases significantly



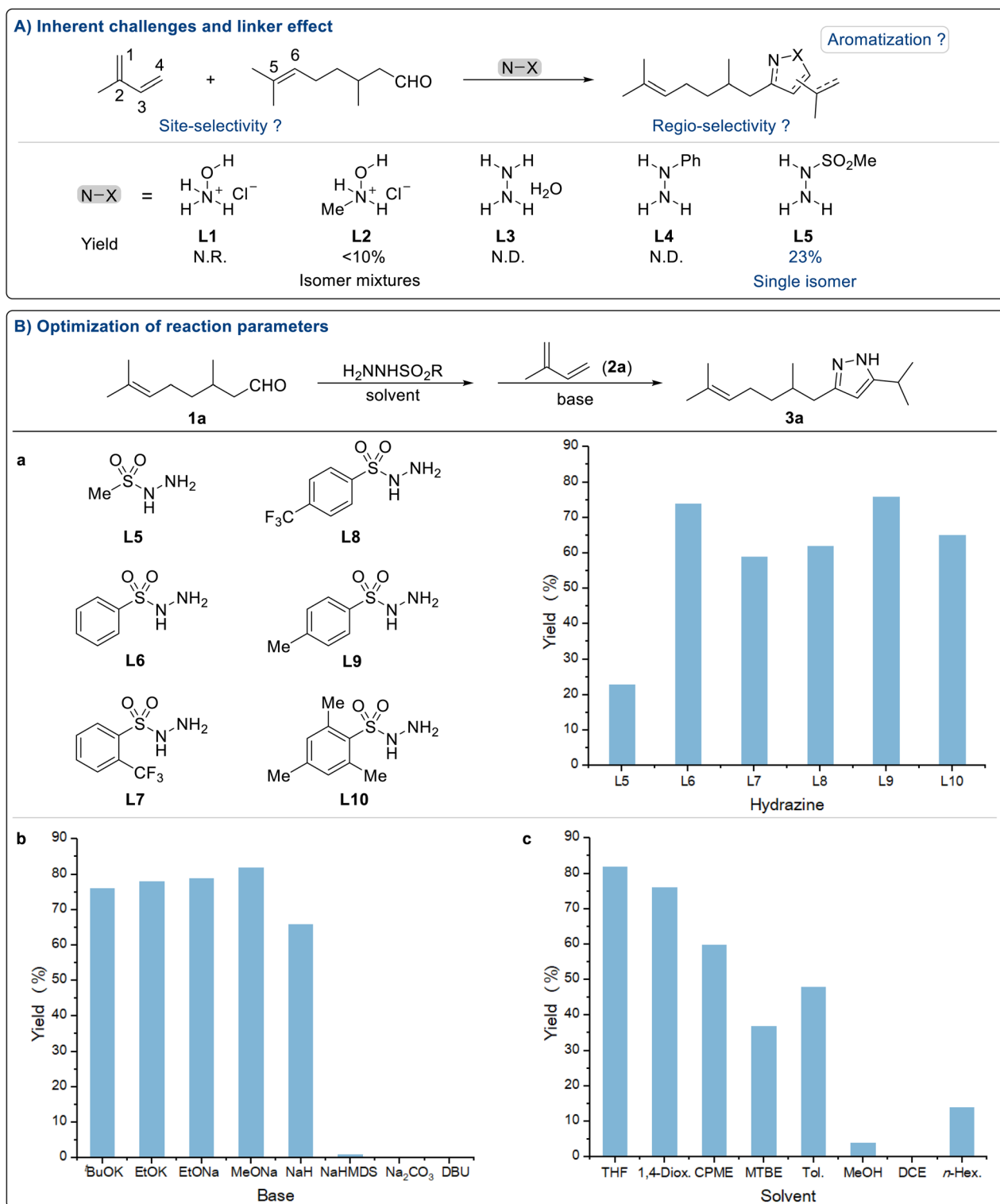


Fig. 2 Reaction development. (A) Inherent challenges and linker effects. (B) Optimization of reaction parameters. Reaction conditions: **1a** (0.21 mmol), linker (0.20 mmol), **2a** (0.80 mmol), base (0.5 mmol), solvent (0.5 mL), 70 °C, 16 h. (a) ^tBuOK as base, THF as solvent. (b) **L9** as linker, THF as solvent. (c) **L9** as linker, MeONa as base. The yields were determined by GC-FID analysis of the crude mixture with 1,3,5-trimethoxybenzene as the internal standard.

enhanced the reaction. Specifically, MeONa exhibited superior performance, affording a higher yield of 84%. In contrast, other inorganic and organic bases, including NaHMDS,

Na₂CO₃, and DBU, failed to effectively produce the desired product (Fig. 2b). When THF was replaced with other ether solvents, decreased yields were observed. Toluene provided only



moderate yields, and the use of alcoholic or hydrocarbon solvents led to a substantial yield reduction. Moreover, no target product was detected when a halogenated alkane was employed as solvent (Fig. 2c).

With the optimized reaction conditions in hand, we subsequently explored the substrate scope of this operationally simple molecular-bridging protocol for terpenyl aldehydes and terpenes (Fig. 3). Initially, a series of terpenyl aldehydes were

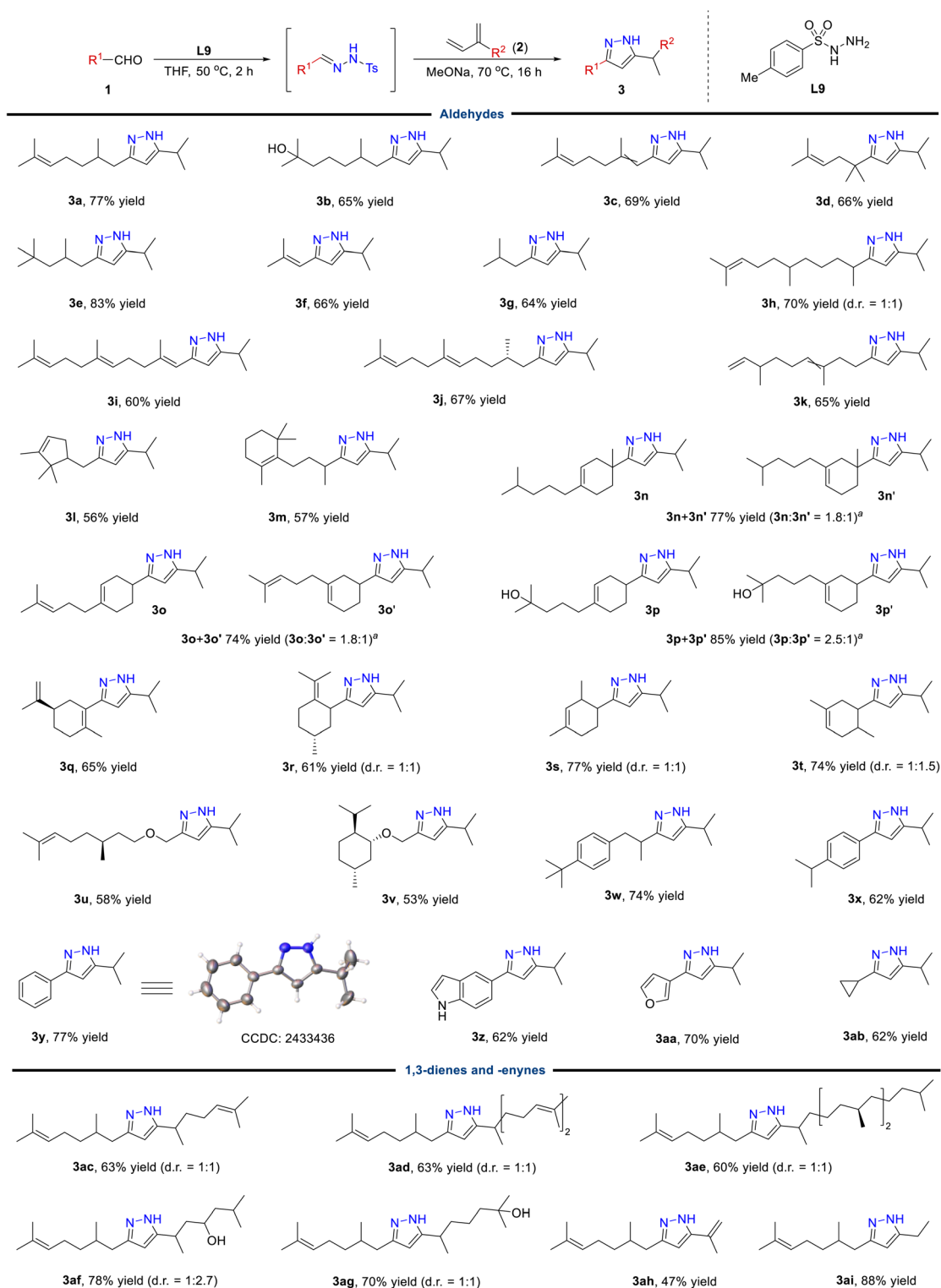


Fig. 3 Substrate scope. Reaction conditions: **1** (0.21 mmol), **L9** (0.20 mmol), **2** (0.80 mmol), MeONa (0.50 mmol), THF (0.5 mL). Isolated yields are given in all cases. ^a From the mixtures of regioisomeric aldehydes.



explored using isoprene as the linking partner. Naturally occurring linear monoterpene aldehydes, such as citronellal, hydroxycitronellal, and citral, all reacted efficiently to afford the corresponding products in good yields (**3a–3c**). Steric hindrance exhibited minimal impact on the reaction (**3d** and **3e**). Both smaller hemiterpene (C5) aldehydes and longer-chain sesquiterpene (C15) aldehydes worked well under this protocol (**3f–3k**). A variety of cyclic terpenyl aldehydes were also suitable for this reaction, successfully achieving molecular assembly with isoprene (**3l–3t**). Notably, aldehydes bearing sensitive functional groups, such as hydroxyl groups, were also suitable for this protocol, affording the expected products **3b** and **3p** in 65% and 85% yields, respectively. Additionally, aldehyde derivatives of geraniol and menthol were also compatible with this reaction system, further broadening the scope of this method (**3u** and **3v**). Aromatic aldehydes, heteroaromatic aldehydes, and alkyl aldehydes containing strained rings also reacted efficiently (**3w–3ab**), which underscored the versatility and broad applicability of this reaction. The structure of compound **3y** was unambiguously confirmed by single-crystal X-ray crystallography analysis (CCDC: 2433436).

Next, we systematically investigated terpenes containing different numbers of isoprene units. Myrcene (C10), farnesene (C15), and neophytadiene (C20) all efficiently underwent this reaction with citronellal in good yields (**3ac–3ae**). It provided an effective approach for the structural modification and functionalization of terpenoids. Notably, monoterpene dienes bearing reactive hydroxyl groups were well tolerated in the reaction system regardless of their substitution positions (**3af** and

3ag). Furthermore, when valylene was employed, the reaction proceeded smoothly, affording the molecular combination product **3ah**, which was structurally analogous to compound **3a** but with a different oxidation state. Remarkably, butadiene, the simplest diene as a widely used molecular building block, also exhibited excellent reactivity in this reaction (**3ai**), further highlighting the practical value and generality of this method in synthetic chemistry. Aryl 1,3-dienes and 1,3-enynes were capable of reacting with aromatic aldehydes but failed to undergo reaction with alkyl aldehydes (see Fig. S1, page S3 in the SI for details).

To illustrate the practical utility of this molecular-bridging strategy, a scale-up experiment (20 mmol) was performed using citronellal and isoprene (Fig. 4), and no significant decrease in yield (77%) was observed. Given the significant biological activity of terpenoid compounds, further prenylation of compound **3a** was attempted. Treatment of **3a** with NaH and prenyl bromide successfully introduced a prenyl group onto the nitrogen atom, yielding **4** with high efficiency.^{8a} Under palladium catalysis, precise ligand modulation enabled the formation of two different reverse-prenylated pyrazoles, **5** and **6**, in moderate yields.^{8c,17} Additionally, CAN-mediated cycloaddition of 1,3-dicarbonyl compounds with alkenes successfully generated the fused-ring product **7**.¹⁸ Intriguingly, oxidation of the alkene to an aldehyde *via* Lemieux–Johnson oxidation¹⁹ triggered a rapid intramolecular nucleophilic addition, leading to the formation of the aza-hemiacetal **8** (CCDC: 2433435). Furthermore, hydrogenation of the alkene smoothly produced **9** in 83% yield. Treatment of **3a** with

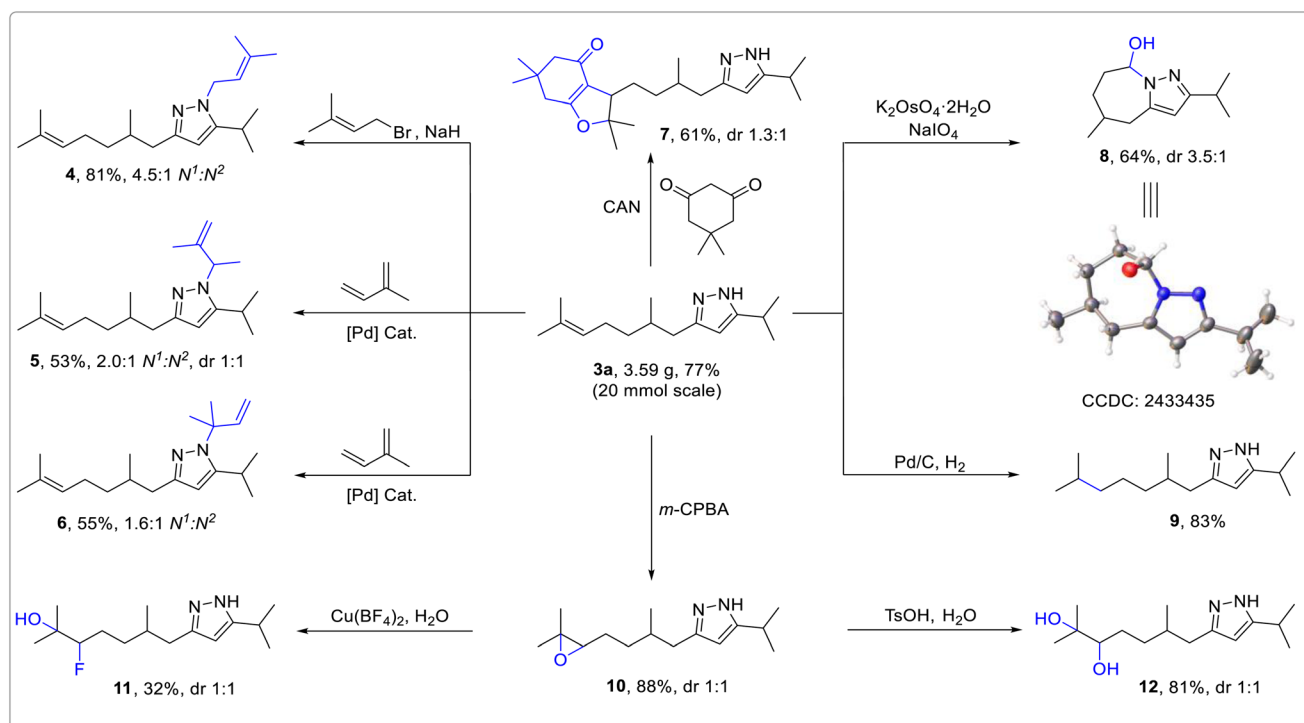


Fig. 4 Synthetic transformations.



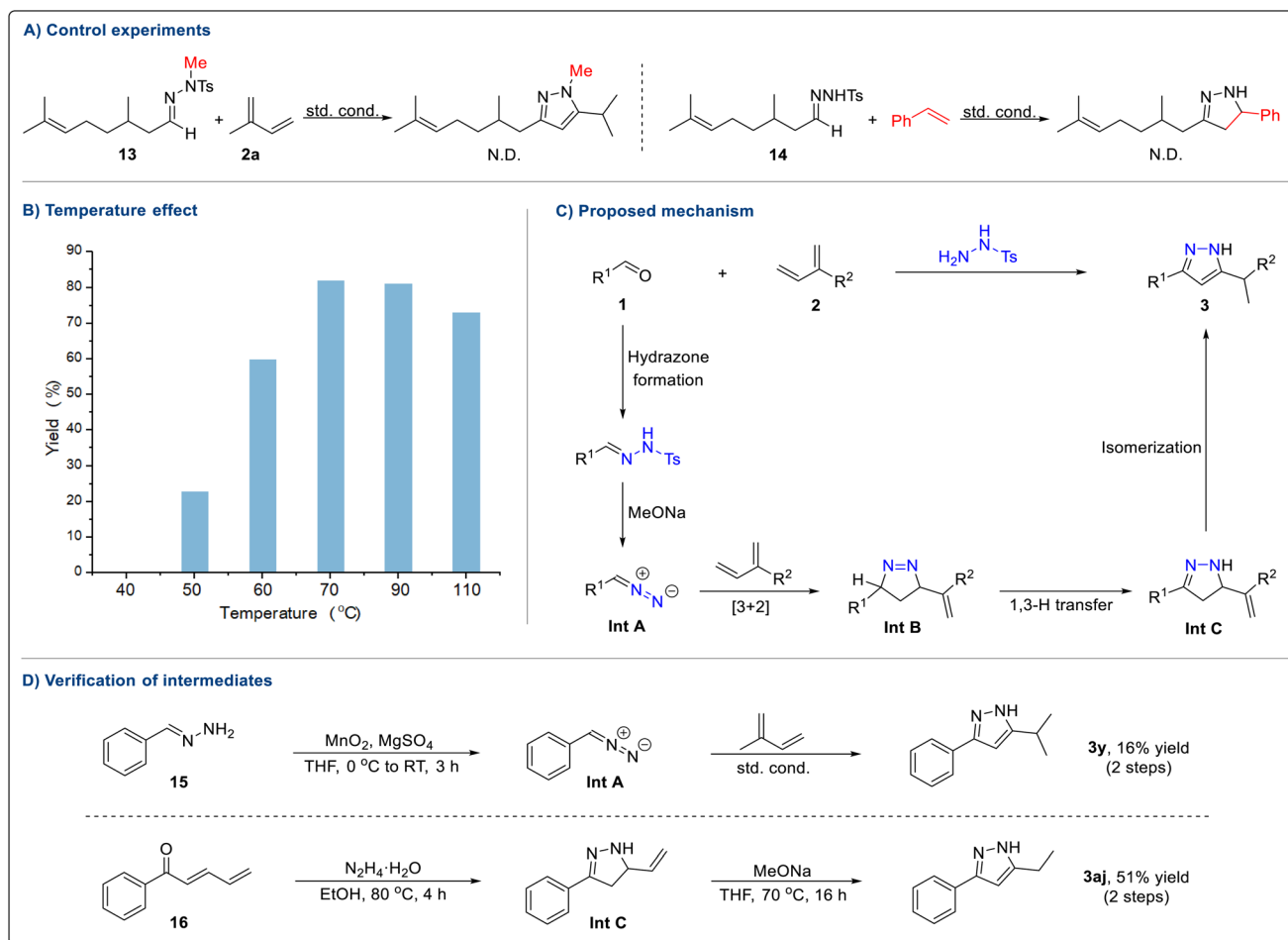


Fig. 5 Mechanistic investigations.

m-CPBA rapidly yielded epoxide **10** in 88% yield. Subsequent ring-opening of the epoxide **10** resulted in the hydroxyfluorinated product **11** and the dihydroxylated product **12**.

To elucidate the reaction mechanism of this bridging protocol, several control experiments were designed and performed (Fig. 5A). First, the *N*-methyl-protected tosylhydrazone (**13**), which is inert to the formation of the diazo 1,3-dipole, was subjected to the standard reaction with isoprene (**2a**), and no pyrazole product was observed. Furthermore, replacing isoprene (**2a**) with styrene failed to initiate the reaction, demonstrating that conjugated diene structural units are essential for this protocol. Temperature-controlled experiments of the model reaction revealed that efficient reaction progression requires a temperature above 50 °C (Fig. 5B), which is consistent with the reported decomposition temperature of *N*-tosylhydrazones into diazo intermediates.²⁰ Based on these findings, a plausible reaction mechanism is proposed (Fig. 5C). The hydrazone, prepared by condensation of aldehyde **1** and *N*-tosylhydrazine **L9**, can form diazo intermediate **A** upon treatment with a base. Subsequently, the reactive diazo **A** undergoes 3 + 2 cycloaddition with the terminal double bond of the terpene **2** to generate intermediate **B**. A 1,3-hydrogen transfer produces the nonaromatic pyrazoline intermedi-

ate **C**, which rapidly aromatizes *via* olefin isomerization²¹ to yield the pyrazole **3**.

In addition, verification experiments of potential intermediates have essentially confirmed the above-mentioned mechanism (Fig. 5D). First, the diazo intermediate **A** was synthesized *in situ* and directly subjected to reaction with isoprene under standard conditions, which smoothly generated the pyrazole product, albeit in low yield. This reduced yield might be attributed to the inherent instability of the diazo intermediate and the tendency of excess diazo compounds to undergo dimerization.²² Consequently, the slow release of the diazo intermediate emerges as a key factor for the success of our protocol. From the reaction of **16** with $N_2H_4 \cdot H_2O$, the labile intermediate **C** was obtained and it effectively underwent double-bond isomerization under standard reaction conditions, ultimately yielding the stable pyrazole compound **3aj**.

Conclusions

In summary, we have developed a catalyst-free molecular-bridging strategy that enables the combination of naturally abundant terpenyl aldehydes and terpenes for the upgrading of



natural terpenoids. Ts-hydrazide acted as a molecular linker through the formation of pyrazole. This protocol features readily available starting materials, mild reaction conditions, and simple experimental procedures. The scalability and practicality of this protocol were demonstrated through gram-scale synthesis and a series of diverse derivatizations. Owing to the structural importance and versatility of the resulting products, it is hoped that this highly efficient and operationally simple protocol will become a powerful tool for the synthetic community.

Author contributions

Q.-A. C. conceived and supervised the project. Q.-A. C. and L.-M. Z. designed the experiments and wrote the paper. L.-M. Z., S.-Y. X., X.-T. L., T.-T. S., D.-W. J., Y. L. and B. W. performed the experiments and analyzed the data. All authors discussed the results and commented on the manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data underlying this study are available in the article and its supplementary information (SI). Supplementary information is available. See DOI: <https://doi.org/10.1039/d5qo01443c>.

CCDC 2433435 and 2433436 contain the supplementary crystallographic data for this paper.^{23a,b}

Acknowledgements

We thank Prof. Zhi-Shi Ye (DUT) for helpful discussions and manuscript revisions.

References

- 1 E. Breitmaier, *Terpenes: Flavors, Fragrances, Pharmaca, Pheromones*, Wiley-VCH, Weinheim, 2006.
- 2 (a) Y. Gao, R. B. Honzatko and R. J. Peters, Terpenoid synthase structures: a so far incomplete view of complex catalysis, *Nat. Prod. Rep.*, 2012, **29**, 1153–1175; (b) J. Gershenzon and N. Dudareva, The function of terpene natural products in the natural world, *Nat. Chem. Biol.*, 2007, **3**, 408–414.
- 3 F. J. Leeper and J. C. Vederas, *Biosynthesis: Aromatic Polyketides, Isoprenoids, Alkaloids*, Springer-Verlag, Berlin, Heidelberg, 2000.
- 4 (a) C. Oberhauser, V. Harms, K. Seidel, B. Schröder, K. Ekramzadeh, S. Beutel, S. Winkler, L. Lauterbach, J. S. Dickschat and A. Kirschning, Exploiting the synthetic potential of sesquiterpene cyclases for generating unnatural terpenoids, *Angew. Chem., Int. Ed.*, 2018, **57**, 11802–11806; (b) W. Wang, D. Huang, Y. Yu, H. Qian and S. Ma, A modular approach for the synthesis of natural and artificial terpenoids, *Angew. Chem., Int. Ed.*, 2023, **62**, e202307626; (c) T. Nishimura, J. Kawai, Y. Oshima and H. Kikuchi, Removal of the *E*-olefin barrier of humulene leading to unnatural terpenoid-like skeletons, *Org. Lett.*, 2018, **20**, 7317–7320.
- 5 T. Zeng, Z. Liu, H. Liu, W. He, X. Tang, L. Xie and R. Wu, Exploring chemical and biological space of terpenoids, *J. Chem. Inf. Model.*, 2019, **59**, 3667–3678.
- 6 (a) D. J. Jansen and R. A. Shenvi, Synthesis of medicinally relevant terpenes: reducing the cost and time of drug discovery, *Future Med. Chem.*, 2014, **6**, 1127–1148; (b) W. P. Teh, D. C. Obenschain, B. M. Black and F. E. Michael, Catalytic metal-free allylic C–H amination of terpenoids, *J. Am. Chem. Soc.*, 2020, **142**, 16716–16722; (c) S. Wang, D. Ren, Z. Liu, D. Yang, P. Wang, Y. Gao, X. Qi and A. Lei, Cobalt-catalysed allylic fluoroalkylation of terpenes, *Nat. Synth.*, 2023, **2**, 1202–1210; (d) B. Aberle, D. Kowalczyk, S. Massini, A.-N. Egler-Kemmerer, S. Gergel, S. C. Hammer and B. Hauer, Methylation of unactivated alkenes with engineered methyltransferases to generate non-natural terpenoids, *Angew. Chem., Int. Ed.*, 2023, **62**, e202301601; (e) Y. C. Kang, R. T. Wetterer, R. R. Karimov, M. Kojima, M. Surke, I. Martín-Torres, J. Nicolai, M. Elkin and J. F. Hartwig, Substitution, elimination, and integration of methyl groups in terpenes initiated by C–H bond functionalization, *ACS Cent. Sci.*, 2024, **10**, 2016–2027.
- 7 (a) J. H. Clark, Green chemistry: challenges and opportunities, *Green Chem.*, 1999, **1**, 1–8; (b) J. D. Lasso, D. J. Castillo-Pazos and C.-J. Li, Green chemistry meets medicinal chemistry: a perspective on modern metal-free late-stage functionalization reactions, *Chem. Soc. Rev.*, 2021, **50**, 10955–10982.
- 8 (a) A. Ford, H. Miel, A. Ring, C. N. Slattery, A. R. Maguire and M. A. McKerver, Modern organic synthesis with α -diazocarbonyl compounds, *Chem. Rev.*, 2015, **115**, 9981–10080; (b) Y. Xia, D. Qiu and J. Wang, Transition-metal-catalyzed cross-couplings through carbene migratory insertion, *Chem. Rev.*, 2017, **117**, 13810–13889; (c) Z. Zhang and V. Gevorgyan, Visible light-induced reactions of diazo compounds and their precursors, *Chem. Rev.*, 2024, **124**, 7214–7261.
- 9 For selected reviews, see: (a) Q. Xiao, Y. Zhang and J. Wang, Diazo compounds and *N*-tosylhydrazones: novel cross-coupling partners in transition-metal-catalyzed reactions, *Acc. Chem. Res.*, 2013, **46**, 236–247; (b) D. Arunprasath, B. D. Bala and G. Sekar, Luxury of *N*-tosylhydrazones in transition-metal-free transformations, *Adv. Synth. Catal.*, 2019, **361**, 1172–1207; (c) S. P. Chandrasekharan, A. Dhami, S. Kumar and K. Mohanan, Recent advances in pyrazole synthesis employing diazo compounds and synthetic analogues, *Org. Biomol. Chem.*, 2022, **20**, 8787–8817.



- 10 (a) Y.-C. Hu, D.-W. Ji, C.-Y. Zhao, H. Zheng and Q.-A. Chen, Catalytic prenylation and reverse prenylation of indoles with isoprene: regioselectivity manipulation through choice of metal hydride, *Angew. Chem., Int. Ed.*, 2019, **58**, 5438–5442; (b) C.-S. Kuai, D.-W. Ji, C.-Y. Zhao, H. Liu, Y.-C. Hu and Q.-A. Chen, Ligand-regulated regiodivergent hydrosilylation of isoprene under iron catalysis, *Angew. Chem., Int. Ed.*, 2020, **59**, 19115–19120; (c) W.-S. Jiang, D.-W. Ji, W.-S. Zhang, G. Zhang, X.-T. Min, Y.-C. Hu, X.-L. Jiang and Q.-A. Chen, Orthogonal regulation of nucleophilic and electrophilic sites in Pd-catalyzed regiodivergent couplings between indazoles and isoprene, *Angew. Chem., Int. Ed.*, 2021, **60**, 8321–8328; (d) C.-Y. Zhao, Y.-Y. Liu, X.-X. Zhang, G.-C. He, H. Liu, D.-W. Ji, Y.-C. Hu and Q.-A. Chen, Bioinspired and ligand-regulated unnatural prenylation and geranylation of oxindoles with isoprene under Pd catalysis, *Angew. Chem., Int. Ed.*, 2022, **61**, e202207202; (e) G. Zhang, C.-Y. Zhao, X.-T. Min, Y. Li, X.-X. Zhang, H. Liu, D.-W. Ji, Y.-C. Hu and Q.-A. Chen, Nickel-catalysed asymmetric heteroarylate cyclotomerization of isoprene, *Nat. Catal.*, 2022, **5**, 708–715; (f) W.-S. Zhang, D.-W. Ji, Y. Yang, T.-T. Song, G. Zhang, X.-Y. Wang and Q.-A. Chen, Nucleophilic aromatization of monoterpenes from isoprene under nickel/iodine cascade catalysis, *Nat. Commun.*, 2023, **14**, 7087.
- 11 (a) A. F. Pozharskii, A. Soldatenkov and A. R. Katritzky, *Heterocycles in Life and Society: An Introduction to Heterocyclic Chemistry, Biochemistry and Applications*, Wiley-VCH, Weinheim, 2011; (b) S. Minakata, Utilization of N-X bonds in the synthesis of N-heterocycles, *Acc. Chem. Res.*, 2009, **42**, 1172–1182; (c) 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; (d) K. R. Dvorak and J. J. Tepe, Advances in the total synthesis of bis- and trisindole alkaloids containing N-heterocyclic linker moieties, *Nat. Prod. Rep.*, 2024, **41**, 1264–1293.
- 12 (a) A. Padwa and H. Ku, Intramolecular cycloaddition reactions of olefinic tosylhydrazones, *J. Org. Chem.*, 1980, **45**, 3756–3766; (b) Y. Xia and J. Wang, N-Tosylhydrazones: versatile synthons in the construction of cyclic compounds, *Chem. Soc. Rev.*, 2017, **46**, 2306–2362.
- 13 (a) A. A. Bekhit, H. M. Ashour and A. A. Guemei, Novel pyrazole derivatives as potential promising anti-inflammatory antimicrobial agents, *Arch. Pharm.*, 2005, **338**, 167–174; (b) M. A. Alam, Antibacterial pyrazoles: tackling resistant bacteria, *Future Med. Chem.*, 2022, **14**, 343–362; (c) Y. Zhang, C. Wu, N. Zhang, R. Fan, Y. Ye and J. Xu, Recent advances in the development of pyrazole derivatives as anticancer agents, *Int. J. Mol. Sci.*, 2023, **24**, 12724–12758.
- 14 H. Huang, C. Huang, Q. Fang, Y. Wu, Y. Kuang, J. Zhang, G. Fan, Z. Wang, S. Chen and D. Peng, Novel design of pyrazolyl-containing monoterpene compounds to enhance antifungal efficacy against *Rhizoctonia solani*, *J. Agric. Food Chem.*, 2025, **73**, 7074–7086.
- 15 (a) C. C. Dudman and C. B. Reese, Preparation of aryldiazoalkanes from 2,4,6-triisopropylbenzenesulphonyl hydrazones, *Synthesis*, 1982, 419–421; (b) V. K. Aggarwal, E. Alonso, G. Hynd, K. M. Lydon, M. J. Palmer, M. Porcelloni and J. R. Studley, Catalytic asymmetric synthesis of epoxides from aldehydes using sulfur ylides with in situ generation of diazocompounds, *Angew. Chem., Int. Ed.*, 2001, **40**, 1430–1433; (c) Z. Liu, P. Sivaguru, G. Zanoni and X. Bi, N-Triflylsulfonylhydrazones: a new chapter for diazo-based carbene chemistry, *Acc. Chem. Res.*, 2022, **55**, 1763–1781.
- 16 (a) J. Barluenga, P. Moriel, C. Valdes and F. Aznar, N-Tosylhydrazones, as reagents for cross-coupling reactions: a route to polysubstituted olefins, *Angew. Chem., Int. Ed.*, 2007, **46**, 5587–5590; (b) J. Barluenga and C. Valdes, Tosylhydrazones: new uses for classic reagents in palladium-catalyzed cross-coupling and metal-free reaction, *Angew. Chem., Int. Ed.*, 2011, **50**, 7486–7500.
- 17 A. Y. Jiu, H. S. Slocumb, C. S. Yeung, X.-H. Yang and V. M. Dong, Enantioselective addition of pyrazoles to dienes, *Angew. Chem., Int. Ed.*, 2021, **60**, 19660–19664.
- 18 V. Nair, J. Mathew and L. G. Nair, Cerium(IV) ammonium nitrate mediated addition of 1,3-dicarbonyl compounds to Dienes, *Synth. Commun.*, 1996, **26**, 4531–4538.
- 19 R. Pappo, D. Allen, R. Lemieux and W. Johnson, Osmium tetroxide-catalyzed periodate oxidation of olefinic bonds, *J. Org. Chem.*, 1956, **21**, 478–479.
- 20 (a) J. R. Fulton, V. K. Aggarwal and J. de Vicente, The use of tosylhydrazone salts as a safe alternative for handling diazo compounds and their applications in organic synthesis, *Eur. J. Org. Chem.*, 2005, 1479–1492; (b) V. K. Aggarwal, J. de Vicente, B. Pelotier, I. P. Holmes and R. V. Bonner, A simple, user-friendly process for the homologation of aldehydes using tosylhydrazone salts, *Tetrahedron Lett.*, 2000, **41**, 10327–10331.
- 21 Y. Xu, X. Qi, P. Zheng, C. C. Berti, P. Liu and G. Dong, Deacylative transformations of ketones via aromatization-promoted C-C bond activation, *Nature*, 2019, **567**, 373–378.
- 22 (a) J. Barluenga, M. Tomás-Gamasa, F. Aznar and C. Valdés, Synthesis of sulfones by Iron-catalyzed decomposition of sulfonylhydrazones, *Eur. J. Org. Chem.*, 2011, 1520–1526.
- 23 (a) CCDC 2433435: Experimental Crystal Structure Determination, 2025, DOI: [10.5517/ccdc.csd.cc2mp5xf](https://doi.org/10.5517/ccdc.csd.cc2mp5xf); (b) CCDC 2433436: Experimental Crystal Structure Determination, 2025, DOI: [10.5517/ccdc.csd.cc2mp5yg](https://doi.org/10.5517/ccdc.csd.cc2mp5yg).

