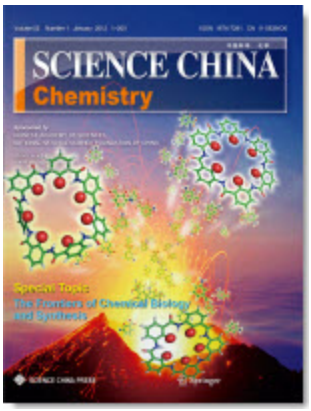


Deciphering fungal metabolon coupling tandem inverse-electron-demand Diels-Alder reaction and semipinacol rearrangement for the biosynthesis of fused polycyclic alkaloids

Journal:	*SCIENCE CHINA Chemistry*
Manuscript ID	SCC-2024-0423.R1
Manuscript Type:	Article
Date Submitted by the Author:	01-Jun-2024
Complete List of Authors:	Liu, Shuai; Kunming Institute of Botany Chinese Academy of Sciences, Key Laboratory of Phytochemistry and Natural Medicines Xu, Wenqiang; Peking University Shenzhen Graduate School Di, Ying-Tong Tang, Mancheng Chen, Ding-Kang; Kunming Institute of Botany Chinese Academy of Sciences, Key Laboratory of Phytochemistry and Natural Medicines mingming, cao; Kunming Institute of Botany Chinese Academy of Sciences, Key Laboratory of Phytochemistry and Natural Medicines Chang, Yao-Wen; Kunming Institute of Botany Chinese Academy of Sciences, Key Laboratory of Phytochemistry and Natural Medicines Tang, Hong-Yu; Kunming Institute of Botany Chinese Academy of Sciences, Key Laboratory of Phytochemistry and Natural Medicines Yuan, Chun-Mao; Guizhou Medical University, State Key Laboratory of Functions and Applications of Medicinal Plants Yang, Jun-Bo; Kunming Institute of Botany Chinese Academy of Sciences, Molecular Biology Experimental Center, Germplasm Bank of Wild Species in Southwest China Zuo, Zhi-Li; Kunming Institute of Botany Chinese Academy of Sciences, Key Laboratory of Phytochemistry and Natural Medicines Guo, Han; Kunming Institute of Botany Chinese Academy of Sciences, Yunnan Key Laboratory for Wild Plant Resources Xu, zhi-fei; Kunming Institute of Botany Chinese Academy of Sciences, Key Laboratory of Phytochemistry and Natural Medicines Zeng, Ying; Kunming Institute of Botany Chinese Academy of Sciences, Key Laboratory of Phytochemistry and Natural Medicines Wu, Yun-Dong; Peking University Shenzhen Graduate School, Lab of

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

	Computational Chemistry and Drug Design, State Key Laboratory of Chemical Oncogenomics XJ , Hao
Keywords:	Diels-Alder reaction, semipinacol rearrangement, biosynthesis, spiro polycyclic alkaloids, chemical computation, fungal metabolon
Speciality:	Chemical Biology

SCIENCE CHINA
Chemistry

• ARTICLES •

January 2024 Vol.59 No.1: 1–2
doi:

Deciphering fungal metabolon coupling tandem inverse-electron-demand Diels-Alder reaction and semipinacol rearrangement for the biosynthesis of spiro polycyclic alkaloids

Shuai Liu [1,4,†], Wen-Qiang Xu [2,3,†], Ying-Tong Di [1,†*], Man-Cheng Tang [5], Ding-Kang Chen [1,4], Ming-Ming Cao [1], Yao-Wen Chang [1], Hong-Yu Tang [1], Chun-Mao Yuan [6], Jun-Bo Yang [7], Zhi-Li Zuo [1], Han Guo [8], Zi-Fei Xu [1], Ying Zeng [1], Yun-Dong Wu [2,3*] & Xiao-Jiang Hao [1,6,8,9*]

[1] *Key Laboratory of Phytochemistry and Natural Medicine (Chinese Academy of Sciences), Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650201, China*

[2] *Lab of Computational Chemistry and Drug Design, State Key Laboratory of Chemical Oncogenomics, Peking University Shenzhen Graduate School, Shenzhen, 518055, China*

[3] *Shenzhen Bay Laboratory, Shenzhen, 518055, China*

[4] *University of Chinese Academy of Sciences, Beijing, 100049, China*

[5] *State Key Laboratory of Microbial Metabolism, School of Life Sciences & Biotechnology, Shanghai JiaoTong University, Shanghai, 200240, China*

[6] *State Key Laboratory of Functions and Applications of Medicinal Plants, Guizhou Medical University, Guiyang, 550014, China*

[7] *Molecular Biology Experimental Center, Germplasm Bank of Wild Species in Southwest China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650201, China*

[8] *Yunnan Key Laboratory for Wild Plant Resources, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650201, China.*

[9] *Research Unit of Chemical Biology of Natural Anti-Virus Products, Chinese Academy of Medical Sciences, Beijing, 100730, China*

Received (date)** accepted (date) **;

In the intricate process of natural product biosynthesis, a metabolon can enhance metabolic flux by associating sequential enzymes. A fungal metabolon, comprising of flavin-dependent monooxygenase SpeF and P450 monooxygenase SpeG, is identified in the biosynthesis of spiro polycyclic alkaloids (+)-notoamide B and its diastereomer (+)-versicolamide B. Using notoamide E as a substance, SpeF/SpeG metabolon can control the stereoselectivity of its 2,3-epoxidation, followed by hydrogen atom abstraction at C-17 to generate reactive epoxide tau-mA with dienyl iminium unit. Subsequently, (+)-notoamide B and (+)-versicolamide B are produced via tandem nonenzymatic inverse-electron-demand Diels-Alder reaction and semipinacol rearrangement. This provides the first example of metabolon in the biosynthesis of spiro-prenylated indole alkaloids.

metabolon, Diels-Alder reaction, semipinacol rearrangement, biosynthesis, notoamides, spiro polycyclic alkaloids

Citation: Liu S, Xu WQ, Di YT, Tang MC, Chen DK, Cao MM, Chang YW, Tang HY, Yuan CM, Yang JB, Zuo ZL, Guo H, Xu ZF, Zeng Y, Wu YD & Hao XJ. Title: Deciphering fungal metabolon coupling tandem inverse-electron-demand Diels-Alder reaction and semipinacol rearrangement for the biosynthesis of spiro polycyclic alkaloids. *Sci China Chem*, 2024, ??: ??, doi: ???

1 Introduction

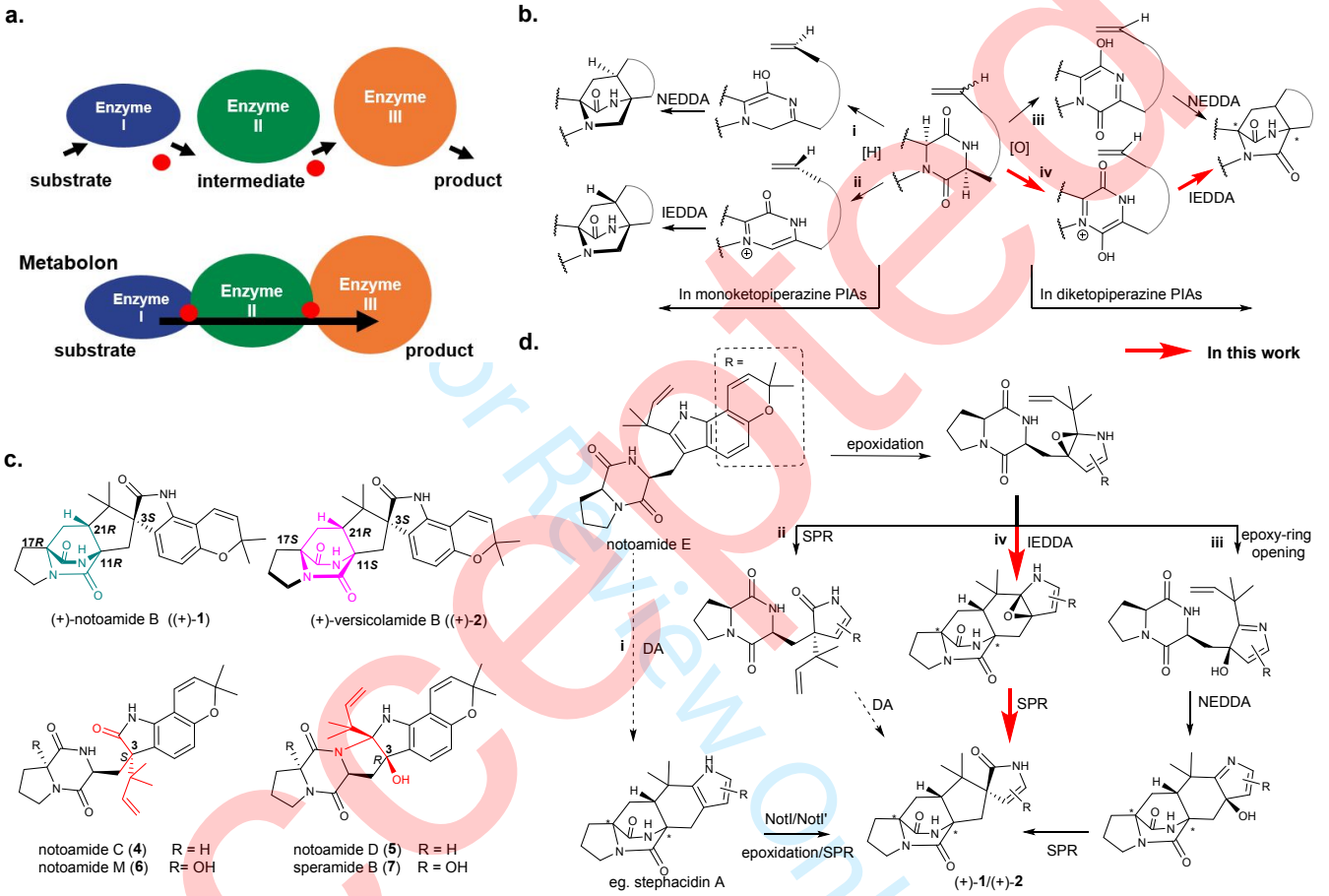
Metabolons are temporary protein complexes consisting of sequential enzymes, playing a crucial role in the

† These authors contributed equally to this work

*Corresponding authors (email: haoxj@mail.kib.ac.cn; ydwu@pku.edu.cn; diyt@mail.kib.ac.cn)

biosynthesis of natural products from various organisms [1-4]. These complexes could help transport unstable, toxic, or reactive intermediates and enhance metabolic flux (Figure 1a) [5, 6]. However, the reactive intermediates may be converted to off-pathway products via non-enzymatic reactions [7-9]. As a result, enzymatic and non-enzymatic steps are intertwined in natural product biosynthesis, making it challenging to understand their pathways [9, 10].

Figure 1. a). Two modes of substrate channeling in natural product biosynthesis; **b).** Biosynthesis of 2,5-bicyclo[2.2.2]diazaoctane core; **c).** The structures of diketopiperazine PIAs in this paper; **d).** Biosynthetic analysis of (+)-**1**/(+)-**2** (The highlighted pathway reported in this work) SPR: semipinacol rearrangement;



IEDDA: inverse-electron-demand Diels–Alder reaction; NEDDA: normal-electron-demand Diels–Alder reaction; DA: Diels–Alder reaction.

Aspergillus, *Penicillium*, and related genera are well-known for their impressive ability to produce structurally diversified prenylated indole alkaloids (PIAs) that feature a unique 2,5-bicyclo[2.2.2]diazaoctane core and a variety of biological activities (Figure S1) [11-13]. This is achieved through a critical step, Diels–Alder (DA) reaction, which forms their 2,5-bicyclo[2.2.2]diazaoctane ring system [14-18]. Two types of enzymatic reactions, the normal-electron-demand (NED) DA reaction and the inverse-electron-demand (IED) DA reaction, have been discovered in the construction of this core in monoketopiperazine PIAs (Figure 1bi-ii, S2) [16, 18]. Diketopiperazine PIAs, such as (+)-notoamide B ((+)-**1**) and (+)-versicolamide B ((+)-**2**), possess a 2*H*-pyran unit, a 3-spiro-2-oxindole moiety, and a diastereomeric 2,5-bicyclo[2.2.2]diazaoctane core, and are co-isolated from various fungi (Figure 1c) [11, 15, 19]. It is intriguing to understand the biogenesis of these enantiomers and diastereomers in different fungi (Figure 1d) [15]. While several enzymes have been identified to catalyze the formation of their spiro-2-oxindole functionality [20-23], the generation of the remaining 2,5-bicyclo[2.2.2]diazaoctane core has not been fully elucidated (Figure 1di-ii). Recently, the biosynthesis pathway of brevianamides X/Y, analogs of (+)-**1** and (+)-**2** but without 2*H*-pyran moiety, has been reported [17]. Specifically, neutral azadiene intermediate with 3-hydroxyindolenine moiety could convert to brevianamides X/Y via nonenzymatic NEDDA and semipinacol rearrangement (SPR) reaction (Figures 1biii, 1diii). Nevertheless, the biosynthetic pathway of 2,5-bicyclo[2.2.2]diazaoctane core in notoamides remains uncharacterized.

In our investigation of the chemical constituents of *A.*

ochraceus CGMCC 3.4414 (*Ao*), we identified enantiomers (+)-**1** and (+)-**2** (Figure 1c). The gene cluster for the biosynthesis of (+)-**1** and (+)-**2**, named *spe* cluster, was identified by antiSMASH (Figure S3) [24]. Notably, SpeF and SpeG are similar to BvnB and BvnD, respectively. However, since notoamides C (**4**) and M (**6**), which contain the same spiro-2-oxindole and individual dioxopiperazine rings, are coproduced in the same microbe, along with that **4** and notoamide D (**5**) could not be converted to their 17-hydroxylated products, **6** and speramide B (**7**), in feeding experiments (Figures 1c, S4), the putative indole 2,3-epoxy moiety might be maintained in notoamides biosynthesis (Figure 1div). Moreover, recent chemical computation of brevianamides has suggested an IEDDA biosynthesis (Figure 1biv) [25]. We conjectured that the reactive epoxide with dienyl iminium unit might be generated, followed by nonenzymatic IEDDA and SPR reaction to construct both alkaloids (+)-**1** and (+)-**2** (Figure 1div).

Herein, we report the metabolon SpeF/SpeG for the biosynthesis of (+)-**1** and (+)-**2** via gene knockout, heterologous expression, DFT calculation, colocalization, and yeast two-hybrid analysis. The conversion begins with the epoxidation of the indol moiety in **3** by SpeF, coupling oxidation of its diketopiperazine unit at C-17 by SpeG. Then, (+)-**1** and (+)-**2** were constructed via ketone-enol isomerization, IEDDA, and SPR reactions.

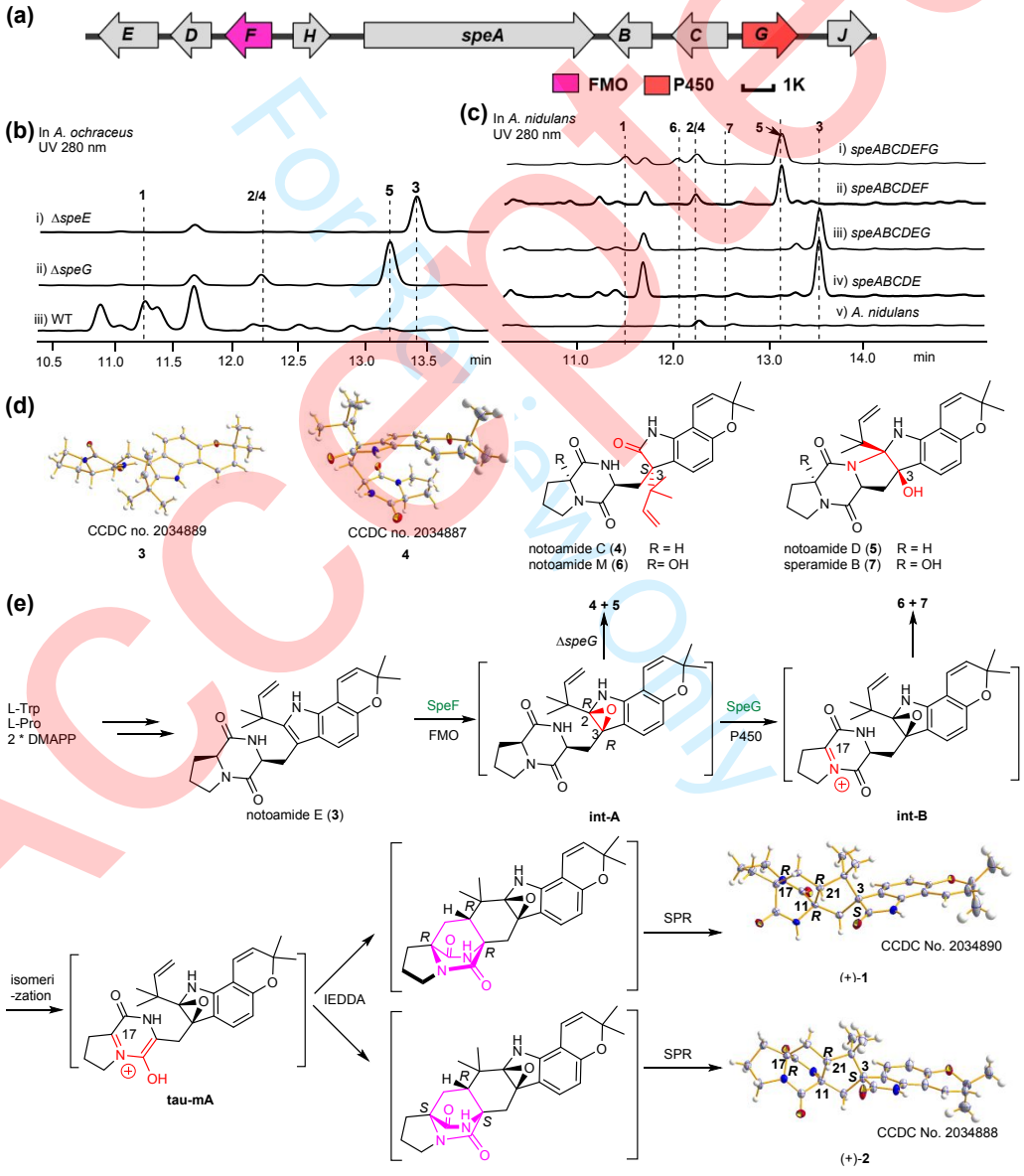


Figure 2. Characterization of (+)-1/(+)-2 biosynthesis. a). Notoamides biosynthetic gene cluster (*spe*) from *A. ochraceus*; **b).** HPLC analysis (280 nm) of *Ao* knockout mutants; **c).** HPLC analysis (280 nm) of the recombinant *A. nidulans* (An) strains expressing different *spe* genes; **d).** Crystal structures of compounds **1 - 4**; **e).** Proposed biosynthetic pathway for (+)-**1**/(+)-**2** in this work.

2 Experimental

General information, general procedures, heterologous expression, gene deletion, high-performance liquid chromatography (HPLC) traces, nuclear magnetic resonance (NMR) spectra, crystallographic data, mechanism studies, characterization data, computational methods, confocal microscopy, yeast two-hybrid assays and are listed in the Supporting Information online.

3 Results and discussion

3.1 Probing the *spe* gene cluster in *A. ochraceus*

The gene cluster for the biosynthesis of (+)-**1** and (+)-**2** in *Ao* was identified through bioinformatic analysis with antiSMASH [24], which shares high similarities with that of notoamides (*not/not'*) (Figure 2a, S3, Table S1) [26]. This region, referred to as *spe* cluster, contains seven genes: *speA* (a two-module NRPS), *speB* and *speD* (two prenyltransferases, PT), *speC* and *speG* (two cytochrome P450 monooxygenases, P450), *speE* (a berberine bridge enzyme, BBE-like) [27, 28], and *speF* (a flavin-dependent monooxygenase, FMO). Subsequently, using the recombination approach, we abolished *speE* and *speG* in *Ao*, and the mutants abolished the production of (+)-**1**/(+)-**2** (Figure 2b, S5) [29].

3.2 Unraveling the biosynthesis pathway of (+)-1/(+)-2

We heterologously expressed the seven *spe* genes in *A. nidulans* A1145 (*An*), followed by isolation and structural characterization [30, 31]. Co-expression of *speABCDE* in *An*, we observed the production of notoamide E (**3**), and its structure was determined via NMR and X-ray diffraction analysis (Figures 2civ, 2d, S16, Tables S6, S15) [32]. When *speF*, a homologue of *notB*, was added to the strain, it produced the expected **4** and **5** (Figures 2cii, Tables S7-8). This is consistent with the *in vitro* assay of SpeF (Figure S6) [33]. X-ray diffraction analysis indicated that the absolute configuration at C-3 of compound **4** is *S* (Figures 2d, S17, Table S16). Alkaloids **4** and **5** are believed to be rearranged shunt products derived from intermediate **int-A** with 2*R*,3*R*-epoxy moiety (Figures 2e, S7) [21]. Finally, when *speG* was coexpressed with *speABCDEF*, two new prominent products were observed (Figure 2ci). Structure characterization by NMR and X-ray single-crystal analysis demonstrated them as (+)-**1** and its diastereomer (+)-**2** (Figures 1c, 2e, S14-15, Tables S4-5, S13-14) [19]. Additionally, two minor compounds with a molecular weight of 447 Da were identified as notoamide M (**6**) and speramide B (**7**). (Figure 2d, Tables S9-10) [34, 35].

Based on the results of gene heterologous reconstruction and knockout, we established the biosynthesis pathway of (+)-**1** and (+)-**2** (Figure 2e). Both systems showed a SpeG-dependent change of metabolic profile, indicating that SpeG mediates the diketopiperazine ring's oxidation and directly impacts the diastereo-outcome of the presumed DA reactions. Concerning the SpeG *in vitro* assay, intensive attempts to produce this P450 enzyme in *E. coli* and *S. cerevisiae* were unsuccessful, thus preventing direct functional analysis. Nonetheless, the *in vivo* results showed that the *An-speFG* transformed **3** but not their rearranged products **4**-**7** into DA cycloadducts **1** and **2** (Figures 3ai-vi) and that *An-speABCDEG* was unable to recognize **3** as a substrate (Figure 2ciii), along with the principles for P450 enzymes and Diels–Alder reactions, together suggest that SpeG might oxidize a non-isolable intermediate, **int-A**, between **3** and **4**/**5** to azadiene moiety required for DA cyclization (Figure 2e). Considering that **6** and **7** possessed one more hydroxyl at C-17 than **4** and **5**, it's reasonable that SpeG involved the oxidation at C-17 in the diketopiperazine unit of **int-A**. But **4** and **5** could not be converted to their 17-hydroxylated products, **6** and **7**, in *An-speFG* feeding experiments (Figures 3av-vi). Although we cannot exclude the possibility that the dioxopiperazine ring of the **int-A** suffers 17-hydroxylation and dehydration, it's more likely that SpeG might directly desaturate the N–C bond in the dioxopiperazine ring of **int-A** to generate **int-B**. Then, **int-B** could be tautomerized to azadiene species, followed by DA and SPR reaction to form (+)-**1** and (+)-**2** (Figure 2e).

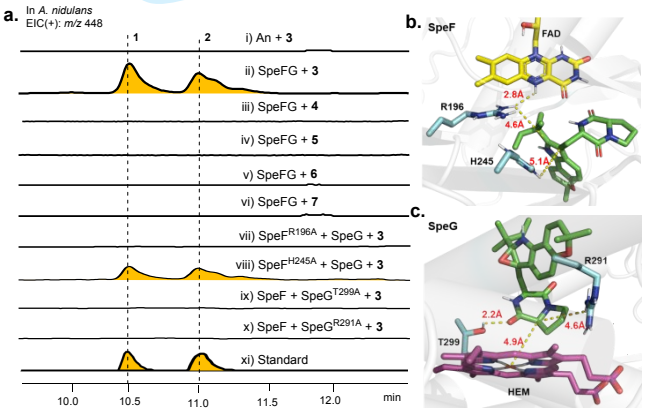


Figure 3. Functional characterization of SpeF and SpeG. a). The HPLC analysis of the *in vitro* assay of SpeF and SpeG and their mutants. **b).** Binding model of **3** in the substrate-binding domain of SpeF; **c).** Binding

model of **int-A** in the substrate-binding domain of SpeG.

To further understand the catalytic mechanism, model structures of SpeF and SpeG with their cofactors were generated by AlphaFold2 and I-TASSER. Molecular docking with substrate was performed to infer critical amino acid residues in the catalytic active site. Since the intermediate **int-A** was too labile to be assayed enzymatically, the attribution of the conserved tetrad to the catalytic activity in SpeF and SpeG was detected by LC-MS analysis after feeding **3** in *An-speFG,* including their mutants. The major residues surrounding the active site of substrate **3** in SpeF are shown in Figure 3b. The conserved R196 residue was located near the isoalloxazine moiety of FAD. The SpeF mutant R196A completely abolished the enzymatic activity of SpeF, possibly due to stabilizing the noncatalytic "out" FAD conformation (Figure 3avii). This result is consistent with those reported FMOs, such as CtdE (PDB: 7kpq) [22], PhqK (PDB: 6pvi) [36], 3HB6H (PDB: 4bk3) [37], and PhzS (PDB: 2rgj) [38]. Moreover, the residue H245 in the SpeF–FAD-**3** complex formed the hydrogen bond interaction with N1 (5.1 Å) to stabilize the substrate. Therefore, we mutated the H245 residue to alanine, and SpeF retained 25% activity with **3** (Figure 3aviii). The model of SpeG complexed with heme was then generated (Figure 3c). Molecular docking with **int-A** showed that C-17 was close to the porphyrin unit in SpeG. The SpeG variants T299A and R291A completely lose enzymatic activity (Figure 3aix-x).

3.3 Computation studies on the mechanism of the DA reaction and the epoxy-opening reaction

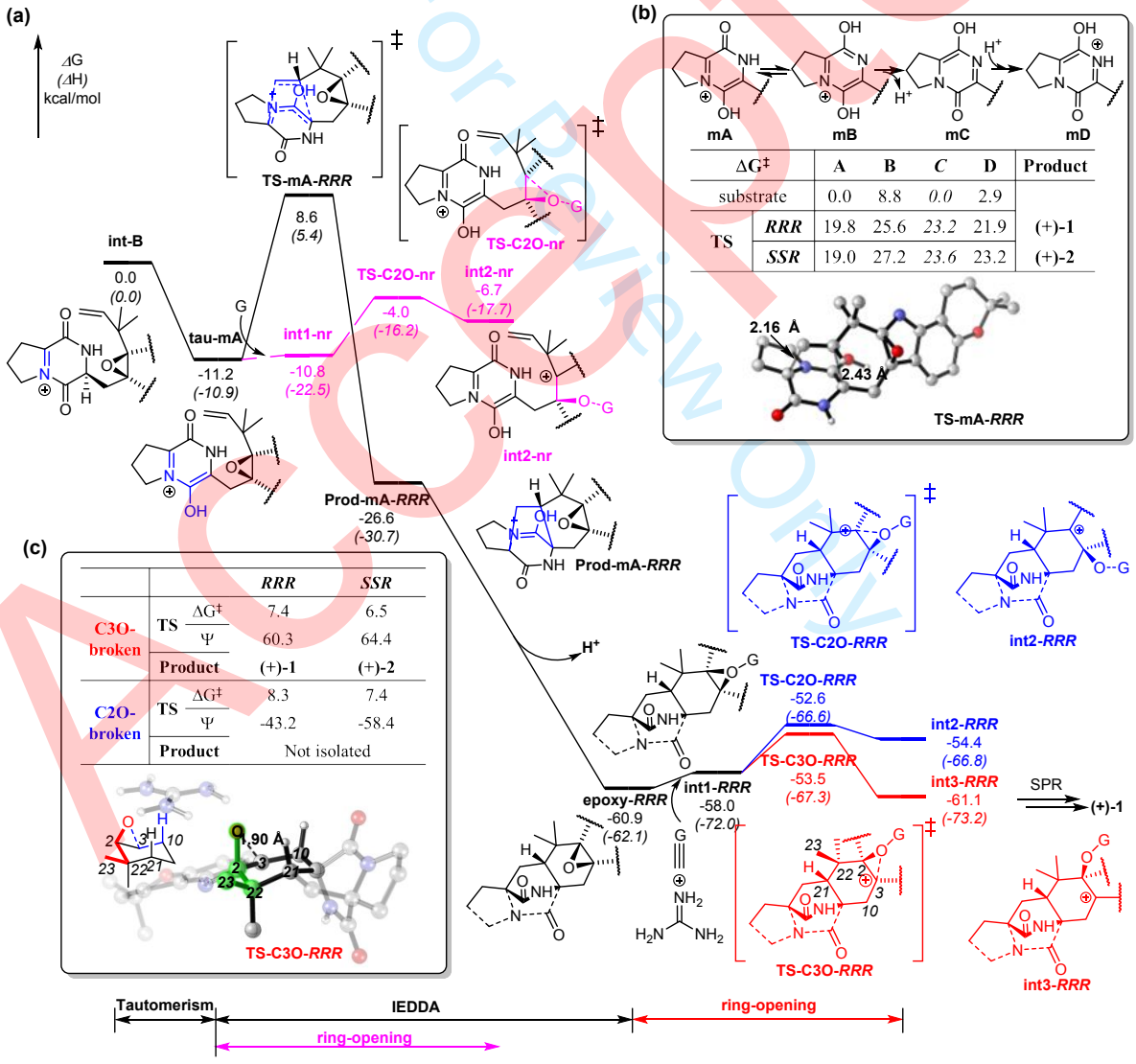


Figure 4. DFT calculation results of Diels-Alder (DA) reaction and epoxy-ring opening reaction to (+)-1/(+)-2. a). The potential energy surface of the

possible biosynthesis pathway from **int-B**, through tautomerization reaction, DA reaction, and ring-opening reaction to the final product; **b).** Several possible azadienes forms of **tau-mA**, the energy barrier when DA reaction occurs and their selectivity, and a schematic diagram of the three-dimensional structure of **TS-mA-*SSR***. The free energy is in kcal/mol, and the bond length is in Angstrom; **c).** The energy barrier of the transition states and the dihedral angles (in degree) for twisting when the ***RRR*** and ***SSR*** configurations of epoxy intermediates undergo ring-opening reactions and the resulting product. A schematic diagram of the three-dimensional structure of TS-C3O-SSR, in which the twisted dihedral angle is highlighted, is also included.

To explore the innate regio- and stereochemical preferences associated with critical steps in the notoamide biosynthetic pathway, we performed density functional theory (DFT) calculations at the B3LYP-D3/6-311++G(d,p), IEFPCM (H_2O)//B3LYP-D3/6-31+G(d), IEFPCM(H_2O) levels, evaluating intermediate and transition-state (TS) structures [39]. Our findings indicated that the keto-enol tautomerization process, which converts **int-B** to the zwitterionic form **tau-mA**, occurs spontaneously with a barrier of 10.1 kcal/mol (Figure 4a). The subsequent transformation of **tau-mA** into the IEDDA adducts **Prod-mA-*RRR*** and **Prod-mA-*SSR*** faced energy barriers of 19.0 and 19.8 kcal/mol, respectively (Figures 4a, 4b, S8, Table S12). These computational results align with our experimental observations, where the ratio of (+)-**1** and (+)-**2** was found to be 2:3. This alignment is particularly noteworthy since (+)-**1** and (+)-**2** are derived from **Prod-mA-*RRR*** and **Prod-mA-*SSR***, respectively. Moreover, our analysis reveals that DA barriers encountered by the other three possible azadiene species (**B-D**) are significantly higher, ranging from 2 to 8.2 kcal/mol, compared to the barrier associated with **tau-mA** (Figures 4b, S8). Based on these findings, we proposed a mechanism for the IEDDA reaction involving **tau-mA**, which plays a crucial role in the biosynthesis of the 2,5-bicyclo[2.2.2]diazaoctane core found in notoamides. This proposed mechanism also aligns well with our analysis of the frontier molecular orbitals (Figure S9) [40]. Thus, the formation of the 2,5-bicyclo[2.2.2]diazaoctane core in (+)-**1** and (+)-**2** might not require enzymatic catalysis due to their low barriers. Nevertheless, enzymes are still needed to form DA substances, which is also the case in the biosynthesis of brevianamides [12, 17].

Next, we investigated the regioselectivity of the epoxy-ring-opening reaction involving the intermediate **epoxy-*RRR***, utilizing protonated guanidine as the catalyst, following the approach used by Houk [17]. As shown in Figures 4a and 4c, our results demonstrate that the protonation of **epoxy-*RRR*** initially yields **int1-*RRR***. The reaction preferred C3O-bond cleavage (the red route) over C2O-bond cleavage (the blue route) due to a lower barrier ($\Delta\Delta G^{\ddagger}$ = 0.9 kcal/mol) (Figures 4c, S10). This preference is further emphasized by the significant energetic difference (~ 6.7 kcal/mol) favoring the formation of the C3O-cleaved product **int3-*RRR*** over its C2O-cleaved counterpart **int2-*RRR***. As shown in Figure 4c, in the **epoxy-*RRR*** structure, the central six-membered ring was found to be in a half-chair conformation, with 21-H pointing upward and axial. At the same time, 23-Me and 10-H were equatorial and axial, respectively. This would make the C3-O bond breaking more favorable than the C2-O bond breaking, consistent with the Houk torsional model [41]. Moreover, similar regioselectivity of the epoxy-ring-opening reaction was also observed for the intermediate **epoxy-*SSR*** (Figure S10).

The ring-opening process of the intermediate **tau-mA** before forming a bicyclic structure was investigated, as shown in the purple route in Figure 4a. At this time, although the energy barrier of the ring opening is low, it is an endothermic reaction. DA competes more favorably due to the intense exotherm. When the bicyclic structure is formed, the ring-opening process is transformed into an exothermic reaction due to the stabilizing effect of the newly formed six-membered ring. This also verifies from the mechanism that the epoxy intermediate first undergoes the DA reaction and then epoxy-ring-opens.

3.4 SpeFG is a fungal metabolon

In our proposed biosynthetic pathway for (+)-**1** and (+)-**2**, the unstable intermediate **int-A** undergoes the hydrogen atom abstraction at C-17 catalyzed by SpeG, overwhelming the epoxy-ring opening reaction (Figure 2e). This implied that **int-A**, generated by SpeF, can be efficiently transferred to SpeG [6]. To test this hypothesis, we fused SpeF with the green fluorescent protein (GFP) and SpeG with the red fluorescent protein (mCherry), respectively (Figure 5a). Then, they were co-transformed into the *An*, creating a transformant called An-speF-gfp-speG-mcherry (*Asgsm*). When compound **3** was fed to the transformant *Asgsm*, compounds

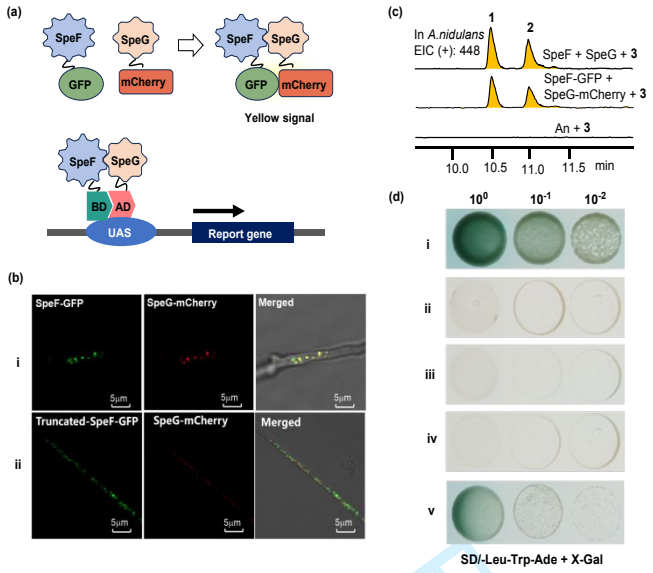


Figure 5. Result of colocalization experiments. a). Colocalization and yeast two-hybrid of SpeF and SpeG. **b).** LC-MS analysis of feeding results of alkaloid **3** in *An-speF-gfp-speG-mcherry*. **c)**. Colocalization experiments of SpeF and truncated SpeF, with SpeG. **d).** Protein–protein interaction of SpeF and SpeG using yeast two-hybrid analysis. i: BD-p53 and AD-T (positive controls); ii: BD-Lam and AD-T (negative controls); iii: BD-SpeG and AD; iv: BD and AD-SpeF; v: BD-SpeG and AD-SpeF.

(+)-**1** and (+)-**2** were detected *via* LC-MS analysis (Figure 5b); simultaneously, yellow fluorescence, caused by the red and green fluorescence overlap, was observed (Figure 5ci). These results indicated that SpeF and SpeG were close to each other. Then, through TMHMM and Phyre2 predictions, we found that SpeF has a possible membrane structure at its N-terminus (Figure S11). To further understand the interaction of SpeF and SpeG, we truncated the N-terminal 40 amino acids of SpeF, constructing the An-truncated-speF-GFP-speG-mCherry transformant (*Asgsm**), in which truncated-SpeF was observed to be diffused throughout the cell (Figure 5cii). Feeding experiments showed that **3** could be converted to **4**-**5** rather than (+)-**1**/(+)-**2** (Figure S12). These data indicated that the N-terminal region does not affect the catalytic activity of the FMO SpeF, but affects its distribution. As a result, **int-A**, generated by SpeF, could not be efficiently transferred to the P450 SpeG, which impeded the formation of (+)-**1**/(+)-**2**. Then, fluorescence-labeled *An* transformants were generated with SpeF/SpeC, SpeG/SpeB, and SpeF/SpeB, respectively. However, there colocalizations were not observed (Figure S13).

Subsequently, yeast two-hybrid assays were conducted (Figures 5a, 5d). As depicted in Figure 5di-iv, neither SpeF nor SpeG showed auto-activation. When *speF* and *speG* were co-transformed, yeast strains grew on the QDO plate and delivered a blue color (similar to positive controls) (Figure 5dv) [42, 43]. These results also support the presume that SpeF and SpeG are close to each other. However, the precise transportation mechanism of the unstable **int-A** remains to be elucidated due to a lack of information on the cocrystal structure for SpeF and SpeG.

The spatial organization of reactants within the enzyme cascade is crucial for the sequential occurrence of reactions in natural product biosynthesis. This organization helps to direct the flow of intermediates and enhance the selectivity of the overall process [44]. The control of reactive intermediates often involves the exquisite design of reaction conditions and the selection of suitable catalysts [45]. The rapid generation and consumption are critical for achieving the desired selectivity and avoiding side reactions. Metabolons represent a form of spatial organization in cellular metabolism. The metabolon enzymes involved in a specific pathway are physically associated, allowing for efficient substrate channeling. This organization aids in regulating metabolic pathways and prevents the escape of intermediates into the broader cellular environment. The spatial organization of enzymes within metabolons ensures the efficient and regulated flow of metabolites, contributing to the efficient biosynthesis of natural products.

Recent research has shown that the epoxidation of C2-C3 of (+)-6-epi-stephacidin A or (+)-stephacidin A (Figure S2), along with the semi-pinacol rearrangement, is facilitated by NotI/I′, resulting in the formation of the spiro-oxindole center in (+)-**1** and (+)-**2** [36]. However, our study discovered that (+)-**1** and (+)-**2** could also be produced from **3** through catalysis by SpeFG metabolon. Therefore, the findings of this paper exemplify the diverse biosynthetic pathways leading to a specific natural product in different microbial species.

According to the experimental results of Greshock and our previous theoretical calculations [25, 46, 47], if DA addition occurs in **4**, according to the experimental results [48], ***SSR*** and ***RRS*** are generated in a ratio of 1.2:1. Our previous theoretical calculations indicate that the energy barrier difference (5.3 kcal/mol) for the generation of ***RRR*** is large.[25] These indicate that the ***RRR*** conformation is challenging to generate, suggesting that **3** does not follow the "epoxidation-migration-DA" route. These phenomena also confirm the correctness and novelty of our proposed "epoxidation-DA-ring-opening & migration" route.

4 Conclusion

A significant challenge in studying PIA biosynthesis is the presence of unstable intermediates, such as those with epoxy and azadiene moieties. Enzyme co-localization experiments

suggest that SpeF and SpeG may form metabolon that work together to perform catalytic roles. The metabolon helps stabilize the labile intermediates and facilitate the reaction in the biosynthesis of (+)-**1** and (+)-**2**, which involves sequential epoxidation by FMO SpeF, desaturation of the dioxopiperazine ring by P450 SpeG, followed by spontaneous intramolecular DA reaction and semi-pinacol rearrangement. Protein interaction may also exist in other cascade reactions in the dynamic natural product biosynthesis process. Identifying and characterizing this metabolon-mediated biosynthetic pathway could lead to new biomimetic strategies to produce these pharmaceutically important molecules and the discovery of new biologically active compounds [49].

Acknowledgments We thank Prof. Y. Tang, from the Department of Chemical and Biomolecular Engineering, University of California, Los Angeles (UCLA), for providing the *Aspergillus indulans* A1145 heterologous expression system and the plasmid of XW55. The calculations were carried out at the SZBL supercomputing center. We are grateful to Prof. Li Sheng-Ying (Shandong University), Li Li (Fujian Normal University), and Yi Zou (Southwest University) for worthy discussion and the Germplasm Bank of Wild Species in Southwest China, Kunming Institute of Botany, Chinese Academy of Sciences (KIB, CAS) for supporting of experimental equipment and space. This work was supported by the National Natural Science Foundation of China (U1812403 to X.J.H, 2193304 to Y.D.W, 81573323 and 31770392 to Y.T.D, and 22177050 to M.M.C.), and the Yunnan Provincial Science and Technology Department (202003AD150012 to X.J.H, 202201AS070040 and 202302AA310035 to Y.T.D).

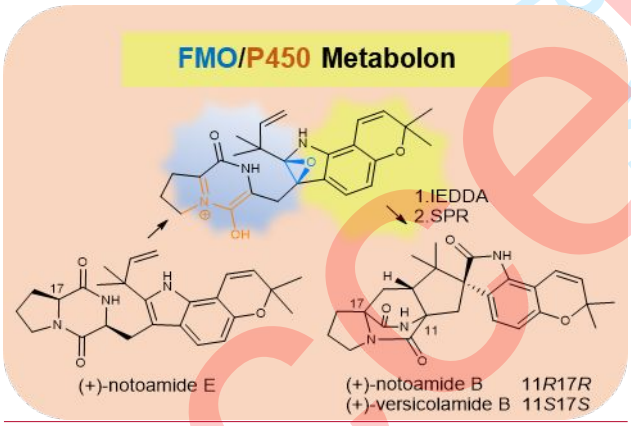
Conflict of interest The authors declare that they have no conflict of interest.

Supporting information The supporting information is available online at http://chem.scichina.com and http://link.springer.com/journal/11426. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accuracy and content remains entirely with the authors.

[1] Mo C, Valachovic M, Randall SK, et al. *Proc Natl Acad Sci USA*, 2002, 99(15): 9739-9744
[2] Jaremko MJ, Davis TD, Corpuz JC, et al.. *Nat Prod Rep*, 2020, 37(3): 355-379
[3] Zhang Y, Fernie AR. *Plant Commun*, 2021, 2(1): 100081
[4] Pedley AM, Pareek V, Benkovic SJ. *Annu Rev Biochem*, 2022, 91(1): 89-106
[5] Welch GR, Easterby JS. *Trends Biochem Sci*, 1994, 19(5): 193-197
[6] Pareek V, Sha Z, He J, et al. *Mol Cell*, 2021, 81(18): 3775-3785
[7] Zhang YHP. *Biotechnol Adv*, 2011, 29(6): 715-725
[8] Ohashi M, Jamieson CS, Cai Y, et al. *Nature*, 2020, 586(7827): 64-69
[9] Zou Y, Garcia-Borras M, Tang MC, et al. *Nat Chem Biol*, 2017, 13(3): 325-332
[10] Muchowska KB, Varma SJ, Moran J. *Chem Rev*, 2020, 120(15): 7708-7744
[11] Finefield JM, Frisvad JC, Sherman DH, et al. *J Nat Prod*, 2012, 75(4): 812-833
[12] Godfrey RC, Green NJ, Nichol GS, et al. *Nat Chem*, 2020, 12(7): 615-619
[13] Mukai K, de Sant'Ana DP, Hirooka Y, et al. *Nat Chem*, 2018, 10(1): 38-44
[14] Kato H, Nakahara T, Sugimoto K, et al. *Org Lett*, 2015, 17(3): 700-703
[15] Klas KR, Kato H, Frisvad JC, et al. *Nat Prod Rep*, 2018, 35(6): 532-558
[16] Dan Q, Newmister SA, Klas KR, et al. *Nat Chem*, 2019, 11(11): 972-980
[17] Ye Y, Du L, Zhang X, et al. *Nat Catal*, 2020, 3(6): 497-506
[18] Liu Z, Rivera S, Newmister SA, et al. *Nat Chem*, 2023, 15(4): 526-534
[19] Greshock TJ, Grubbs AW, Jiao P, et al. *Angew Chem, Int Ed*, 2008, 47(19): 3573-3577
[20] Fraley AE, Tran HT, Kelly SP, et al. *ChemBioChem*, 2020, 21(17): 2449-2454
[21] Li S, Finefield JM, Sunderhaus JD, et al. *J Am Chem Soc*, 2012, 134(2): 788-791
[22] Liu Z, Zhao F, Zhao B, et al. *Nat Commun*, 2021, 12(1): 4158
[23] Fraley AE, Caddell Haatveit K, Ye Y, et al. *J Am Chem Soc*, 2020, 142(5): 2244-2252
[24] Blin K, Shaw S, Augustijn HE, et al. *Nucleic Acids Res*, 2023, 51(W1): W46-W50
[25] Xu W, Sun T-Y, Di Y, et al. *Chem Asian J*, 2023, 18(7): e202300063
[26] Li S, Srinivasan K, Tran H, et al. *MedChemComm*, 2012, 3(8): 987-996
[27] Zhang JM, Liu X, Wei Q, et al. *Nat Commun*, 2022, 13(1): 225
[28] Daniel B, Konrad B, Toplak M, et al. *Arch Biochem Biophys*, 2017, 632(88-103
[29] Szewczyk E, Nayak T, Oakley CE, et al. *Nat Protoc*, 2006, 1(6): 3111-3120
[30] Kato H, Tsunematsu Y, Yamamoto T, et al. *J Antibiot*, 2016, 69(7): 561-566
[31] Zhu Y, Wang J, Mou P, et al. *Org Biomol Chem*, 2021, 19(9): 1985-1990
[32] Tsukamoto S, Kato H, Greshock TJ, et al. *J Am Chem Soc*, 2009, 131(11): 3834-3835
[33] Kato H, Yoshida T, Tokue T, et al. *Angew Chem, Int Ed*, 2007, 46(13): 2254-2256
[34] Chang Y-W, Yuan C-M, Zhang J, et al. *Tetrahedron Lett*, 2016, 57(45): 4952-4955
[35] Tsukamoto S, Kawabata T, Kato H, et al. *Org Lett*, 2009, 11(6): 1297-1300
[36] Fraley AE, Haatveit KC, Ye Y, et al. *J Am Chem Soc*, 2020, 142(5): 2244−2252
[37] Montersino S, Orru R, Barendregt A, et al. *J Biol Chem*, 2013, 288(36): 26235−26245
[38] Greenhagen BT, Shi K, Robinson H, et al. *Biochemistry*, 2008, 47(19): 5281−5289
[39] Frisch MJT, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 09*, 2009, Revision D.01(Gaussian, Inc.: Wallingford, CT):
[40] Zhang Z, Jamieson CS, Zhao YL, et al. *Am Chem Soc*, 2019, 141(14):

5659-5663
[41] Houk KN, Paddon-Row MN, Rondan NG, et al. *Science*, 1986, 231(4742): 1108-1117
[42] Aleman F, Yazaki J, Lee M, et al. *Sci Rep*, 2016, 6(1): 28941
[43] Li M, Lv M, Wang X, et al. *New Phytol*, 2023, 238(1): 186-201
[44] Li X, Awakawa T, Mori T, et al. *J Am Chem Soc*, 2021, 143(50): 21425-21432
[45] Liu J, Lu J, Zhang C, et al. *Nat Chem*, 2023, 15(8): 1083-1090
[46] Greshock TJ, Williams RM. *Org Lett*, 2007, 9(21): 4255-4258
[47] Greshock TJ, Grubbs AW, Tsukamoto S, et al. *Angew Chem, Int Ed*, 2007, 46(13): 2262-2265
[48] Miller KA, Tsukamoto S, Williams RM. *Nat Chem*, 2009, 1: 63-68
[49] Xiao X, Xu K, Gao Z-H, et al. *Sci China Chem*, 2023, 66(6): 1553-1633

Table of Contents graphic



Supplementary information

Deciphering fungal metabolon coupling tandem inverse-electron-demand Diels-Alder reaction and semipinacol rearrangement for the biosynthesis of spiro polycyclic alkaloids

Shuai Liu [1,4,†], Wen-Qiang Xu [2,3,†], Ying-Tong Di [1,†*], Man-Cheng Tang [5], Ding-Kang Chen [1,4], Ming-Ming Cao [1], Yao-Wen Chang [1], Hong-Yu Tang [1], Chun-Mao Yuan [6], Jun-Bo Yang [7], Zhi-Li Zuo [1], Han Guo [8], Zi-Fei Xu [1], Ying Zeng [1], Yun-Dong Wu [2,3*] & Xiao-Jiang Hao [1,6,8,9*]

[1]*Key Laboratory of Phytochemistry and Natural Medicine (Chinese Academy of Sciences), Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650201, China*
[2]*Lab of Computational Chemistry and Drug Design, State Key Laboratory of Chemical Oncogenomics, Peking University Shenzhen Graduate School, Shenzhen, 518055, China*
[3]*Shenzhen Bay Laboratory, Shenzhen, 518055, China*
[4]*University of Chinese Academy of Sciences, Beijing, 100049, China*
[5]*State Key Laboratory of Microbial Metabolism, School of Life Sciences & Biotechnology, Shanghai JiaoTong University, Shanghai, 200240, China*
[6]*State Key Laboratory of Functions and Applications of Medicinal Plants, Guizhou Medical University, Guiyang, 550014, China*
[7]*Molecular Biology Experimental Center, Germplasm Bank of Wild Species in Southwest China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650201, China*
[8]*Yunnan Key Laboratory for Wild Plant Resources, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, 650201, China.*
[9]*Research Unit of Chemical Biology of Natural Anti-Virus Products, Chinese Academy of Medical Sciences, Beijing, 100730, China*

[†] These authors contributed equally to this work

*Corresponding authors (email: haoxj@mail.kib.ac.cn; ydwu@pku.edu.cn; diyt@mail.kib.ac.cn)

*e-mail: haoxj@mail.kib.ac.cn; ydwu@pku.edu.cn; diyt@mail.kib.ac.cn

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Experimental Procedures

1. Strains and culture conditions

Aspergillus ochraceus 3.4414 were bought from CGMCC. *A. ochraceus* and its mutants were cultivated in YM (5 g/L yeast extract, 10 g/L peptone, 10 g/L maltose) at 28 ℃ for both sporulation and production of secondary metabolite. *Saccharomyces cerevisiae* BJ5464-NpgA (*MATα ura3-52 his3-Δ200 leu2-Δ1 trp1 pep4::HIS3 prb1 Δ1.6R can1 GAL*) was used for *in vivo* homologous recombination to construct the *A. nidulans* A1145 overexpression plasmids.[1] Yeast Extract Peptone Dextrose (YPD) medium (20 g/L peptone, 10 g/L yeast extract, 20 g/L dextrose) was used for routine growth. In contrast, the uracil-dropout semisynthetic medium was used to select plasmids, which were transformed into *S. cerevisiae*. *Escherichia coli* BL21 (DE3) (Tiangen, Beijing) and *E. coli* stbl3 (AngyuBio, Shanghai) were grown in LB media and used for the standard DNA manipulation. *A. nidulans* A1145 was used as the host of heterologous expression of *spe* gene cluster.

2. Preparation of protoplasts of *A. ochraceus*

Fresh spores of *A. ochraceus* were inoculated into 500 mL YG in 1 L Erlenmeyer flask and germinated at 28℃ and 250 rpm for approximately 16 h. Harvest the hyphae by filtration through Miracloth sterilized by autoclaving. Then, the mycelia were transferred into TF1 (1% (w/v) Yatalase, 0.6 M $(NH_4)_2SO_4$ in 50 mM Maleic acid, pH 7.5) and incubated for 3 h at 30 °C with 60 rpm. The resulting solution is briefly filtered through a syringe filled with cotton and collected in a centrifugation tube. Centrifuge at 200 × *g* for 10 min and discard the supernatant. Add 20 mL of TF Solution 2 (1.2 M Sorbitol (Glucitol), 50 mM $CaCl_2 \cdot 2H_2O$, 35 mM NaCl, 10 mM Tris–HCl (pH 7.5)) and mix by gently inverting the tube. Centrifuge at 200 × *g* for 10 min and discard the supernatant.[2] Resuspend the pelleted protoplasts in TF Solution 2 to a final concentration of 1.0 - 5.0 × 10^7/mL.

3. Fungal Transformation and Gene Deletion in *A. ochraceus*

Deletion cassettes were generated using a fusion PCR technique. They followed the zeocin resistance marker approach for gene deletion previously described using *ble* cassette encodes zeocin binding proteins as the selectable marker.[3] Briefly, approximately 1.0 - 2.0 kb of 5' flanking region and 3' flanking region were PCR amplified from each targeted loci in the *A. ochraceus* genomic DNA using the corresponding primer pairs p1 & p3 and p4 & p6. Ble cassette was PCR amplified from Pan8.1 using the corresponding primer pairs pbleF and pbleR. The two initial fragments containing a 5' flanking region and a 3' flanking region were fused to the *ble* fragment using the corresponding primer pairs p2 and p5. All primers used in this study are listed in Table S1. Phusion High-Fidelity DNA Polymerase was used for all PCR amplification. The constructed gene knock-out cassettes were transformed into *A. ochraceus* by polyethylene glycol (PEG) mediated protoplast transformation. The lyophilized DNA fragments were incubated with 100 μL of the protoplasts, then 50 μL of room temperature,

freshly filtered PEG solution (25% PEG average molecular weight 3,350, 0.6 M KCl, 50 mM $CaCl_2$, 10 mM Tris-HCI, pH 7.5) was added and gently mixed and place in an ice water bath for 25 min. Add 1 mL at room temperature, filtered PEG solution. Mix the PEG solution with the protoplast suspension by gently drawing it into the micropipette tip and expelling it. Draw in and expel at least ten times. Leave at room temperature for 25 min. Plate transformation mixture onto selective plates.[2]

4. Heterologous expression in *A. nidulans* A1145

The genes in the *spe* cluster were amplified by PCR and cloned into vectors by recombination in yeast. The genomic DNA of *A. ochraceus* was used as the templates of PCR for the *spe* genes; pYTU, pYTR, and pYTP were used to amplify *glaA*, *gpdA*, and *amyB* promoters, respectively.[4] The overlapping DNA fragments and PacI/SwaI-digested expression vectors pYTU, pYTP, and pYTR were co-transformed into yeast and generated pSPE1-9s by yeast homologous recombination. The primers used for the heterologous expression are listed in Table S1.

Preparation of the protoplasts of *A. nidulans* A1145 was similar to that of *A. ochraceus* .[2] Fresh spores of *A. nidulans* were inoculated into 25 mL liquid CD media (10 g/L glucose, 50 mL 20 × nitrate salts, 1 mL trace elements, pH 6.5) in 250 mL flask and germinated at 37 ˚C and 250 rpm for approximately 9 h. To prepare 20 × nitrate salts, 120 g $NaNO_3$, 10.4 g KCl, 10.4 g $MgSO_4$·•$7H_2O$, and 30.4 g KH_2PO_4 were dissolved in 1 L double distilled water. The 100 mL trace elements with pH 6.5 contained 2.20 g $ZnSO_4$•$7H_2O$, 1.10 g H_3BO_3, 0.50 g $MnCl_2$•$4H_2O$, 0.16 g $FeSO_4$•$7H_2O$, 0.16 g $CoCl_2$•$5H_2O$, 0.16 g $CuSO_4$•$5H_2O$, and 0.11 g $(NH_4)_6Mo_7O_{24}$•$4H_2O$. The selection markers of the three expression vectors were uridine, pyridoxine, and riboflavin in *A. nidulans* A1145. *A. nidulans* A1145 was initially grown on CD agar plates containing 10 mM uridine, 5 mM uracil, 0.5 μg/mL pyridoxine HCl and 2.5 μg/mL riboflavin at 37 °C for five days. Mycelia were harvested by centrifugation at 3,500 rpm, 10 min, and washed with 10 mL Osmotic buffer (1.2 M $MgSO_4$, 10 mM sodium phosphate, pH 5.8). Then, the mycelia were transferred into 10 mL of Osmotic buffer containing 30 mg lysing enzymes from Trichoderma and 20 mg Yatalase in a 125 mL flask. The flask was kept in a shaker at 80 rpm overnight at 30 °C. The resulting solution is briefly filtered through a Miracloth and collected in a centrifugation tube. Centrifuge at 200 × g for 10 min and discard the supernatant. The protoplasts were washed with 10 mL STC buffer (1.2 M sorbitol, 10 mM $CaCl_2$, 10 mM Tris-HCI, pH 7.5). The protoplasts were resuspended in 1 mL STC buffer for transformation. CDST media (20 g/L starch, 20 g tryptone, 50 mL 20 × nitrate salts, 1 mL trace elements, pH 6.5) produced secondary metabolites. As described above, the constructed plasmid for heterologous expression was transformed into protoplasts of *A. nidulans* A1145 by polyethylene glycol (PEG) mediated protoplast transformation.

5. Chemical complementation assays

For precursor feeding in *A. ochraceus* mutants and *A. nidulans* A1145, 1 mg precursors were dissolved in DMSO and added to 20 mL of liquid YM or CDST cultures of respective strain. After further cultivation at 30 °C for 20 days, the secondary metabolites were extracted with ethyl acetate, dissolved in MeOH, and analyzed on LC-MS.

6. Expression and purification of SpeF from *E. coli* and *in vitro* assays

To construct the plasmid for expressing SpeF in *E. coli*, the intron-free *speF* was amplified by PCR using the *A. ochraceus* cDNA as the template. The recovered DNA fragment was ligated into the vector pET-28a that was digested with BamHI/HindIII by Gibson assembly, yielding the expression plasmid pSPE10. After being confirmed by sequencing, the plasmid was transferred into Rosetta (DE3) for protein expression and purification.

Overexpression and subsequent protein purification of SpeF was performed as follows: *E. coli* Rosetta (DE3) harboring the plasmid pSPE10 was grown overnight in 5 mL of LB with 50 μg/mL kanamycin at 37 °C. 250 mL of fresh LB with 50 μg/mL kanamycin was inoculated with 2.5 mL overnight culture and incubated at 37 °C until the optical density at 600 nm reached 0.6. The protein was overexpressed at 16 °C for 16 h with 0.1 mM IPTG. Cells were harvested by centrifugation (3000 × g, 15 min). All subsequent procedures were performed at 4 °C or on ice. Harvested cells were resuspended in disruption buffer (50 mM Tris-HCl (pH 7.8), 200 mM NaCl). The supernatant was subjected to His-Tag affinity purification after sonication and centrifugation (17000 g, 60 min, 4 °C).

An assay of SpeF was performed in 100 μL volume containing 50 mM Tris-HCl (pH 7.8), 0.2 mM notoamide E (**3**), 2 μM SpeF, 2.5 mM NADPH, and 2 mM DTT. The mixture was incubated at 30 °C for 20 min and extracted twice with ethyl acetate. The organic phases were dried and dissolved in 20 μL MeOH and subjected to analysis by LC-MS as described in Chemical Analysis.

7. General procedures for chemical analyses

The *A. nidulans* and *A. ochraceus* strains were grown in CDST or YM and then extracted with ethyl acetate to analyze the metabolites. The organic phase was dried by speed Vacuum and dissolved in methanol for analysis. LC-MS analysis were performed on an LC-MS with a Waters T3 C18 color (5 μM, 2.0 × 100 mm). Chromatographic separation was achieved with a linear gradient of 5 - 95% MeCN-H_2O in 15 minutes, followed by 95% MeCN for 5 minutes with a flow rate of 0.5 mL/min.

8. Isolation and structural characterization of metabolites

For isolation compounds, *A. nidulans* A1145 were grown in CDST at 30 °C for 5 days and then extracted by mixed solvent (MeOH: EtOAc = 90: 10) at room temperature. After the evaporation of the solvent under reduced pressure, the residue was suspended in water and extracted with EtOAc three times. The EtOAc extract (15 g) was then fractionated using C18 gel column chromatography, using a stepwise gradient of MeOH-H_2O (2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, 9:1, and 10:0, v/v), to yielded pooled fractions. The fractions containing the target compounds were combined and used for further purification by HPLC with a Waters Xselect HSS T3 OBD Semi-Prep coloum (5 μM, 10 × 150 mm) to obtain compounds **1** (40 mg), **2** (70 mg), **3**(125 mg), **4** (32 mg), **5** (107 mg), **6** (0.4 mg), and **7** (1.4 mg). For the chemical structural elucidation, 1D and 2D NMR spectra were obtained on Bruker AV-500 DRX-600, ASC-800

spectrometers with tetramethylsilane as internal standard, at the Analytical & Testing Center of Kunming Institute of Botany, CAS.

9. X-ray Crystal Structure Analysis

Compounds **1**, **2**, **3**, and **4** were crystallized using the solvent vapor diffusion method. A suitable crystal was selected on a SuperNova, Dual, Cu at 0, AtlasS2 diffractometer. The crystal was kept at 100.01(10) K during data collection. Using Olex2, the structure was solved with the ShelXT.[5] Structure solution program using intrinsic phasing refined with the ShelXL. The refinement package was measured by least squares minimization. The crystallographic data for compounds **1**, **2**, **3**, and **4** (CCDC 2034890 (**1**), 2034888 (**2**), 2034887 (**3**) and 2034889 (**4**)) have been deposited in the Cambridge Crystallographic Data Centre. Copies of the data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK (fax: +44-1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

10. Computational methods

All quantum mechanical calculations were performed with Gaussian 09.[6] Geometry optimizations with the B3LYP-D37 density functional with the IEFPCM model (H2O),8, and the 6-31+G(d) basis set.[7] Single point energies were calculated using B3LYP-D3 with the IEFPCM model (H_2O), and the 6-311++G(d,p) basis set.[8] Structure graphics were generated using CYLview.[9] Multiwfn and vmd were used for orbital plots.[10]

11. Yeast two-hybrid assays

The ORF of SpeG and SpeF were amplified by PCR and cloned into the pGBKT7 (bait vector) and pGADT7 (prey vector), respectively. Plasmids were co-transformed into the AH109 yeast strain and cultured on a DDO (SD/-Trp/-Leu) medium. Positive clones were transferred to QDO medium (SD/-Leu/-Trp/-His/-Ade+ X-α-gal). Yeast cells containing pGBKT7-53 and pGADT7-T were used as positive controls, while pGBKT7-Lam and pGADT7-T were used as negative controls. Yeast strain was cultured at 30 ℃ and observed after 2–4 d.

12. Confocal microscopy.

The plasmids used for the subcellular localization of SpeB, SpeC, SpeF, truncated-SpeF, and SpeG in *A. nidulans* were constructed by the method similar to heterologous expression. The green fluorescent protein (GFP), mCherry sequence, and their terminators were synthesized by GENEWIZ and used for amplification. *speB*, *speC*, *speF*, truncated-*speF*, and *speG* genes were amplified from the genomic DNA of *A. ochraceus* with overhang primers. The overlapping DNA fragments and PacI/SwaI-digested expression vectors pYTU, pYTP, and pYTR were co-transformed into yeast and generated pSPE11-20s by yeast homologous recombination. The primers used for the heterologous expression are listed in Table S1.

The transformant bearing GFP or RFP fusion constructs was grown for 3-5 d at 30 ℃ in CDST medium to induce protein expression in a 250 mL Erlenmeyer flask. Hyphae were washed with

distilled water and examined by a Leica TCS SP8X laser scanning confocal microscope (Leica Microsystems, Germany). The green and red fluorescence signals were recorded at 488 nm and 588 nm, respectively.

Data availability

All data generated and analyzed during this study are included in this article and its Supplementary Information files. Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC) as CCDC 2034890 (**1**), 2034888 (**2**), 2034887 (**3**), and 2034889 (**4**) can be obtained free of charge from the CCDC via https://www.ccdc.cam.ac.uk/.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Supplementary Tables

Table S1 Features of the *spe* Gene Products

Protein	Size (aa)	Predicted function	Homologs (identities/positives [%])	Accession number	Strain
SpeA	2252	non-ribosomal peptide synthetase	NotE (61/74)	E1ACQ0.1	*Aspergillus sp.* MF297-2
SpeB	451	Reverse prenyltransferase	NotF (69/82)	E0Y3X1.1	*Aspergillus sp.* MF297-2
SpeC	524	cytochrome P450 monooxygenase	NotG (71/81)	E1ACQ2.1	*Aspergillus sp.* MF297-2
SpeD	428	prenyltransferase	NotC (75/88)	E0Y3X0.1	*Aspergillus sp.* MF297-2
SpeE	620	Flavin-dependent monooxygenase	NotD (67/78)	E1ACP9.1	*Aspergillus sp.* MF297-2
SpeF	453	Flavin-dependent monooxygenase	NotB (70/81)	E1ACP7.2	*Aspergillus sp.* MF297-2
SpeG	500	cytochrome P450 monooxygenase	NotH (68/82)	E1ACQ3.1	*Aspergillus sp.* MF297-2

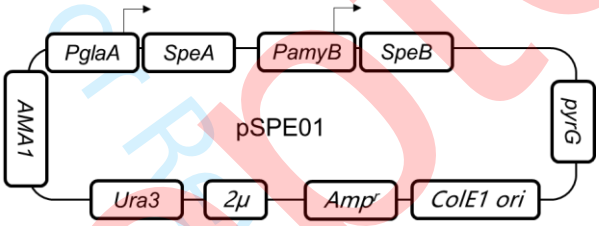
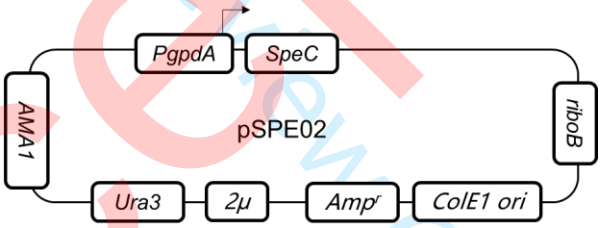
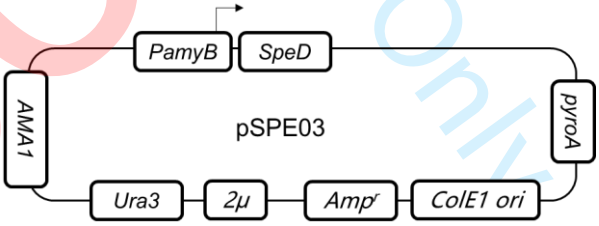
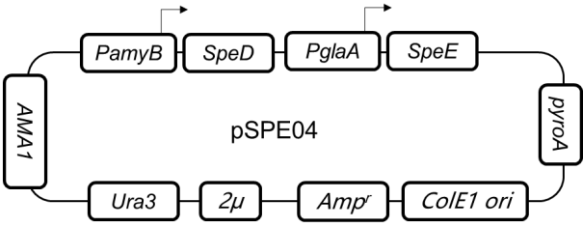
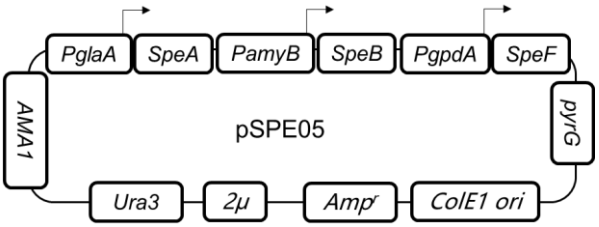
Table S2 Primers used in this study

Primer name	Sequence (5'→3')
speE-KO-P1	GCTGCGAGGGTTGTGATA
speE-KO-P2	TGTTCTTCTTCGGCATCA
speE-KO-P3	GGAGTTGAGACAAATGGTGTTCAGGACGAAGAAATGTAGACTTAGGGA
speE-KO-P4	AATGGTGGAGGCGGCGGATTGTTGACGGATGGACAGAAT
speE-KO-P5	TTTCTGTTCTATCTCGGGTAT
speE-KO-P6	AGGCGATGATAGAAAGAAAA
speG-KO-P1	CCGTAGAAGGTGTGGAAGCAGTC
speG-KO-P2	CGGTAATGACCTCGTCTCCAACAAT
speG-KO-P3	AATGGTGGAGGCGGCGGATTGAGTGAGGAGAAGAGAGGAGGAAGT
speG-KO-P4	GGAGTTGAGACAAATGGTGTTCAGGACCGTCAGCAAGGAGATACAGGAA
speG-KO-P5	CACGCACCACAGGACCATATTCTT
speG-KO-P6	GGCAGCATTCAGGCGATGGAA
KO-ble-F	AATCCGCCGCCTCCACCATT
KO-ble-R	TCCTGAACACCATTTGTCTCAACTCC
YZ-speE-1F	GGACCGACTGAGAATGTGTC
YZ-speE-1R	GGGTCCCAGGAGCTTGAGAT
YZ-speE-2F	CGTCTCTCCGCATGCCAGA
YZ-speE-2R	CTGACGGAGGCTCACTCTAG
YZ-speG-1F	CCGTCAGCAAGGAGATACAGGAA
YZ-speG-1R	GGAGTTGAGACAAATGGTGTTCAGGA
YZ-speG-2F	AATGGTGGAGGCGGCGGATT
YZ-speG-2R	AATGGTGGAGGCGGCGGATT
U-speAB-1F	GCCTGAGCTTCATCCCCAGCATCATTACACCTCAGCAATGGTTTCTTCGAAGATCAAC
U-speAB-1R	GGCAAATGGGCACGAACGACCC

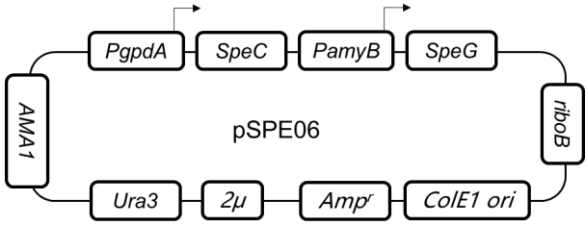
U-speAB-2F	CTGGCCGTATTCGCCTGGGATG
U-speAB-2R	CTCGTTCGGCACCTTTAATCGCCGCATCGTTGGTGTTTCCACGCACAGCTTTGTGCC
U-speAB-3F	GGCACAAAGCTGTGCGTGGAAACACCAACGATGCGGCGATTAAAGGTGCCGAACGAG
U-speAB-3R	GTGGAGGACATACCCGTAATTTTCTGGGCATTTAAATCAGGCAGGTGCTGTATTCAGC
R-speC-F	ACTAACCATTACCCCGCCACATAGACACATCTAAACAATGAGTCTCGCACATGTCCTC
R-speC-R	TAAAGGGTATCATCGAAAGGGAGTCATCCAATTTAAATGCCACTGAGAACTAATACAG
P-speD-F	TCCCTTCTCTGAACAATAAACCCCACAGAAGGCATTTATGACGATCCAAGGCAACCAA
P-speD-R	ATGAGACCCAACAACCATGATACCAGGGGATTTAAATTAGATGGTCTGGCCTCTTAGGT
P-speDE-1F	TCCCTTCTCTGAACAATAAACCCCACAGAAGGCATTTATGACGATCCAAGGCAACCAA
P-speDE-1R	CATAGGTCGCCAGGTACGACCAGTTCGGAAGATCAGGTAGATGGTCTGGCCTCTTAGG
P-speDE-2F	CCTAAGAGGCCAGACCATCTACCTGATCTTCCGAACTGGTCGTACCTGGCGACCTATG
P-speDE-2R	GCCCGAGACTGCAGTACATTGCTGAGGTGTAATGATGCTGGGGATGAAGCTCAGGCTC
P-speDE-3F	GAGCCTGAGCTTCATCCCCAGCATCATTACACCTCAGCAATGTACTGCAGTCTCGGGC
P-speDE-3R	ATGAGACCCAACAACCATGATACCAGGGGATTTAAATAGCGGCAAACAATGCGGGATC
U-speABF-1F	GCCTGAGCTTCATCCCCAGCATCATTACACCTCAGCAATGGTTTCTTCGAAGATCAAC
U-speABF-1R	GGCAAATGGGCACGAACGACCC
U-speABF-2F	CTGGCCGTATTCGCCTGGGATG
U-speABF-2R	CTCGTTCGGCACCTTTAATCGCCGCATCGTTGGTGTTTCCACGCACAGCTTTGTGCC
U-speABF-3F	GGCACAAAGCTGTGCGTGGAAACACCAACGATGCGGCGATTAAAGGTGCCGAACGAG
U-speABF-3R	CTTGGGTCTCTCCCGTCACCCAAATCAATTCACCGGAGTCAGGCAGGTGCTGTATTCAG
U-speABF-4F	CTGAATACAGCACCTGCCTGACTCCGGTGAATTGATTTGGGTGACGGGAGAGACCCAAG
U-speABF-4R	GCTGGGCGTCGCTCTGTAATTTAGTCATTGTTTAGATGTGTCTATGTGGCGGGGTAAT
U-speABF-5F	ATTACCCCGCCACATAGACACATCTAAACAATGACTAAATTACAGAGCGACGCCCAGC
U-speABF-5R	GTGGAGGACATACCCGTAATTTTCTGGGCATTTAAATCGCGCAGTAAGGGAATGACAG
R-speCG-1F	ACTAACCATTACCCCGCCACATAGACACATCTAAACAATGAGTCTCGCACATGTCCTC
R-speCG-1R	GTTATATCATTTATAGCTCGTTCGGCACCTTTAATCGCCACTGAGAACTAATACAGTG
R-speCG-2F	CACTGTATTAGTTCTCAGTGGCGATTAAAGGTGCCGAACGAGCTATAAATGATATAAC
R-speCG-2R	GCGCAGCGACAGTGGCCATAAATGCCTTCTGTGGGGTTTATTGTTCAGAGAAGGGAG
R-speCG-3F	CTCCCTTCTCTGAACAATAAACCCCACAGAAGGCATTTATGGCCACTGTCGCTGCGC
R-speCG-3R	AGGGTATCATCGAAAGGGAGTCATCCAATTTAAATGTGGAGGGGTATTCATGCAATTC
P-speE-F	TCCCTTCTCTGAACAATAAACCCCACAGAAGGCATTTATGTACTGCAGTCTCGGGCTTG
P-speE-R	ATGAGACCCAACAACCATGATACCAGGGGATTTAAATAGCGGCAAACAATGCGGGATC
P-speF-F	TCCCTTCTCTGAACAATAAACCCCACAGAAGGCATTTATGACTAAATTACAGAGCGACG
P-speF-R	ATGAGACCCAACAACCATGATACCAGGGGATTTAAATCGCGCAGTAAGGGAATGACAG
R-speG-F	ACTAACCATTACCCCGCCACATAGACACATCTAAACAATGGCCACTGTCGCTGCGCTAG
R-speG-R	AGGGTATCATCGAAAGGGAGTCATCCAATTTAAATGTGGAGGGGTATTCATGCAATTC
28a-speF-F	TGGTGGTGGTGCTCGAGTCAGACCATGTCACCCTGATTGC
28a-speF-R	TGCCGCGCGGCAGCCATATGACTAAATTACAGAGCGACGC
R-mCherry-F	ACTAACCATTACCCCGCCACATAGACACATCTAAACAATGGCCTCCTCCGAGGACGT
R-mCherry-R	AAGGGTATCATCGAAAGGGAGTCATCCAATTTAAATCCGGTAGAGGTGTGGTCAAT
P-GFP-F	TCCCTTCTCTGAACAATAAACCCCACAGAAGGCATTTATGGTGAGCAAGGGCGAGGAG
P-GFP-R	ATGAGACCCAACAACCATGATACCAGGGGATTTAAATGTATTGGGATGAATTTTGTA
R-SpeC-mCherry-1F	ACTAACCATTACCCCGCCACATAGACACATCTAAACAATGAGTCTCGCACATGTCCTC
R-SpeC-mCherry-1R	ACGTCCTCGGAGGAGGCCATTCCACCTCCACCTCCACCCAGCTGACGCCTAGTGAAGA
R-SpeC-mCherry-2F	TCTTCACTAGGCGTCAGCTGGGTGGAGGTGGAGGTGGAATGGCCTCCTCCGAGGACGT
R-SpeC-mCherry-2R	AAGGGTATCATCGAAAGGGAGTCATCCAATTTAAATCCGGTAGAGGTGTGGTCAAT
R-SpeG-mCherry-1F	ACTAACCATTACCCCGCCACATAGACACATCTAAACAATGGCCACTGTCGCTGCGCT
R-SpeG-mCherry-1R	ACGTCCTCGGAGGAGGCCATTCCACCTCCACCTCCACCTAAGTCAACTTCCTCCTCTCT
R-SpeG-mCherry-2F	AGAGAGGAGGAAGTTGACTTAGGTGGAGGTGGAGGTGGAATGGCCTCCTCCGAGGACGT
R-SpeG-mCherry-2R	AGGGTATCATCGAAAGGGAGTCATCCAATTTAAATCCGGTAGAGGTGTGGTCAATA
P-SpeF-GFP-1F	TCCCTTCTCTGAACAATAAACCCCACAGAAGGCATTTATGACTAAATTACAGAGCGACG
P-SpeF-GFP-1R	CTCCTCGCCCTTGCTCACCATTCCACCTCCACCTCCACCGACCATGTCACCCTGATTGC
P-SpeF-GFP-2F	GCAATCAGGGTGACATGGTCGGTGGAGGTGGAGGTGGAATGGTGAGCAAGGGCGAGGAG

P-SpeF-GFP-2R	GATGAGACCCAACAACCATGATACCAGGGGATTTAAATGTATTGGGATGAATTTTGTA
U-SpeB-GFP-1F	TCCCTTCTCTGAACAATAAACCCCACAGAAGGCATTTATGACGATCACCTCGAACCATT
U-SpeB-GFP-1R	CTCCTCGCCCTTGCTCACCATTCCACCTCCACCTCCACCCGCCTCACCTGCCTCCCAAA
U-SpeB-GFP-2F	TTTGGGAGGCAGGTGAGGCGGGTGGAGGTGGAGGTGGAATGGTGAGCAAGGGCGAGGAG
U-SpeB-GFP-2R	GATGAGACCCAACAACCATGATACCAGGGGATTTAAATGTATTGGGATGAATTTTGTA
U-SpeR-mCherry-SpeFtun-GFP-1F	CCTGAGCTTCATCCCCAGCATCATTACACCTCAGCAATGGCCACTGTCGCTGCGCTAG
U-SpeR-mCherry-SpeFtun-GFP-1R	CAGTGGAGGACATACCCGTAATTTTCTGGGCATTTAAATGTATTGGGATGAATTTTGTA
U-SpeR-mCherry-SpeFtun-GFP-2F	CAGTGGAGGACATACCCGTAATTTTCTGGGCATTTAAATGTATTGGGATGAATTTTGTA
U-SpeR-mCherry-SpeFtun-GFP-2R	CAGTGGAGGACATACCCGTAATTTTCTGGGCATTTAAATGTATTGGGATGAATTTTGTA
AD-SpeF-F	ATACGACGTACCAGATTACGCTATGACTAAATTACAGAGCGA
AD-SpeF-R	ATCTGCAGCTCGAGCTCGATCTAGACCATGTCACCCTGATT
BD-SpeG-F	AGGAGGACCTGCATATGTCGGCCATGGCCACTGTCGCTGCGCTA
BD-SpeG-R	TATGCGGCCGCTGCAGGTCGAGGGCCCTATAAGTCAACTTCCTCCTCTCTT

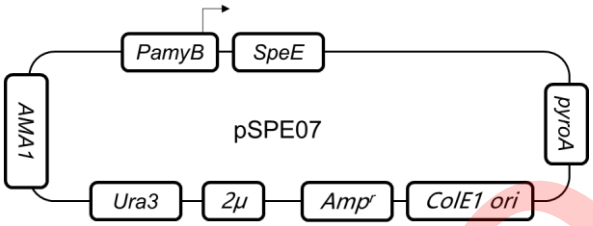
Table S3 Plasmids used in this study

Name	Plasmid map	Vector
pSPE01		pYTU
pSPE02		pYTR
pSPE03		pYTP
pSPE04		pYTP
pSPE05		pYTU

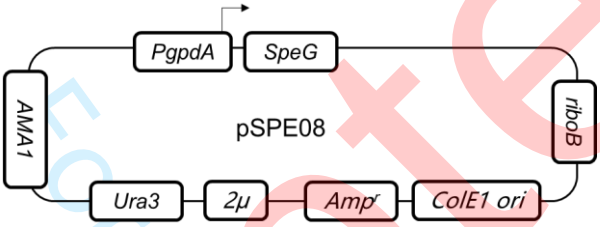
pSPE06 pYTR



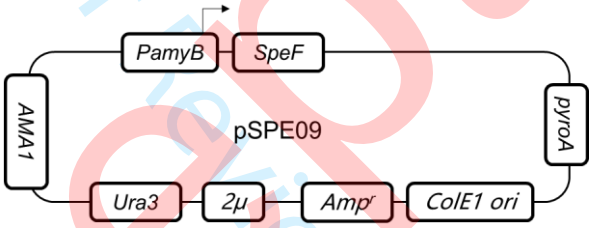
pSPE07 pYTP



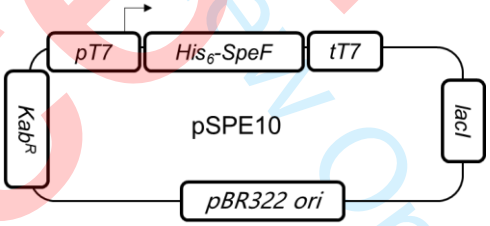
pSPE08 pYTR



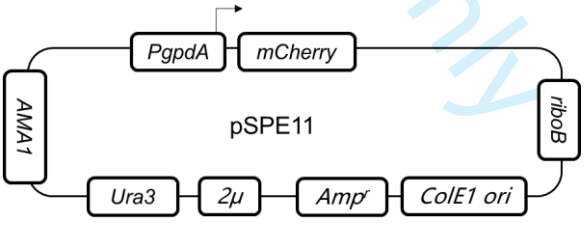
pSPE09 pYTP



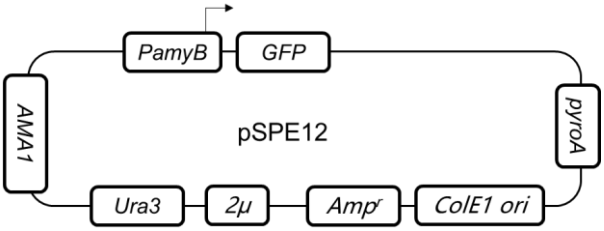
pSPE10 pET28A



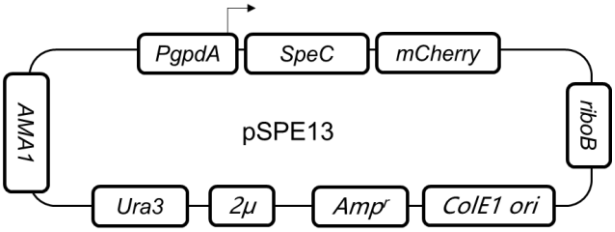
pSPE11 pYTR



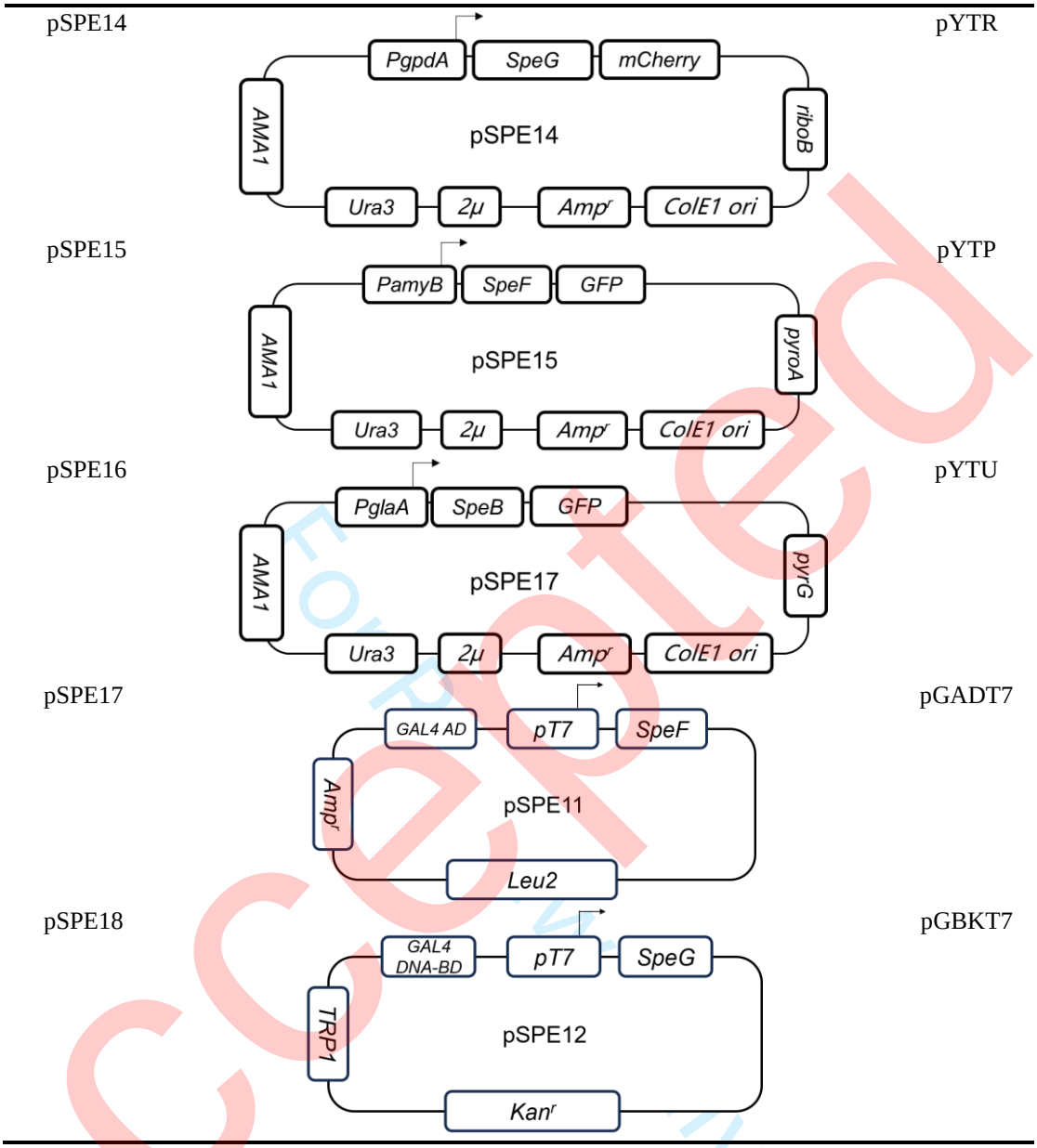
pSPE12 pYTP



pSPE13 pYTR



https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english



https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S4 NMR data of (+)-notoamide B ((+)-1) in acetone-d_6

no.	1[a]		Reported Notoamide B[11]	
	δ_C type	δ_H mult (J in Hz)	δ_C type	δ_H mult (J in Hz)
1		9.58 br s		9.47 br s
2	184.0, C		184.0 C	
3	62.4, C		62.6 C	
4	127.3, CH	7.09, d (8.1)	127.4, CH	7.08, d (8.5)
5	109.5, CH	6.42, d (8.1)	109.6, CH	6.41, d (8.5)
6	153.6, C		153.7, C	
7	105.7, C		105.8, C	
8	139.1, C		139.2, C	
9	123.4, C		123.5, C	
10	34.7, CH_2	2.22, d (14.4) 3.05, d (14.4)	34.8, CH_2	2.21, d (14.5) 3.04, d (14.5)
11	67.0, C		67.1, C	
12	170.3, C		170.0, C	
14	44.2, CH_2	3.49, (2H), m	44.3, CH_2	3.45, dt (11.5, 6.5) 3.49, ddd (11.5, 7.5, 5.0)
15	25.3, CH_2	1.91, m 2.06, m	25.4, CH_2	1.83, m 1.90, m
16	30.1, CH_2	1.84, m 2.66, m	30.4, CH_2	1.83, m 2.65, m
17	69.3, C		69.3, C	
18	174.1, C		174.1, C	
19		8.09, br s		7.99, br s
20	30.9, CH_2	1.84, m 2.02, m	31.0, CH_2	1.83, m 2.02, m
21	56.7, CH	3.37, m	56.8, CH	3.36, m
22	43.3, C		46.4, C	
23	23.8, CH_3	0.80, s	23.8, CH_3	0.80, s
24	20.2, CH_3	0.80, s	20.3, CH_3	0.83, s
25	117.6, CH_2	6.66, d (9.9)	117.6, CH_2	6.64, d (10.0)
26	131.1, CH	5.77, d (9.9)	131.2, CH	5.74, d (10.0)
27	76.5, C		76.6, C	
28	28.0, CH_3	1.41, s	28.0, CH_3	1.39, s
29	28.0, CH_3	1.42, s	28.0, CH_3	1.40, s

[a] 600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S5 NMR data of (+)-versicolamide B ((+)-2) in DMSO-d_6

	2[a]		Reported (+)-Versicolamide B[12]	
no.	δ_C type	δ_H mult (J in Hz)	δ_C type	δ_H mult (J in Hz)
1		10.60, s		9.84 br s
2	183.0, C		183.3 C	
3	62.1, C		62.5 C	
4	126.5, CH	7.11, d (8.1)	126.9, CH	7.13, d (8.1)
5	108.3, CH	6.35, d (8.1)	108.7, CH	6.38, d (8.1)
6	152.4, C		152.7, C	
7	104.6, C		104.9, C	
8	138.5, C		139.0, C	
9	121.7, C		122.1, C	
10	33.8, CH_2	2.06, d (15.2) 3.77, d (15.2)	34.3, CH_2	2.08, d (15.2) 2.79, d (15.2)
11	67.2, C		67.6, C	
12	169.4, C		169.7, C	
14	43.5, CH_2	3.27, m	43.8, CH_2	3.30 m
15	24.6, CH_2	1.78, m 1.95, m	25.0, CH_2	1.80, m 1.98, m
16	28.6, CH_2	1.77, m 2.43, m	29.0, CH_2	1.78, m 2.46, m
17	68.7, C		69.1, C	
18	172.8, C		173.1, C	
19		8.75, s		8.77, s
20	28.1, CH_2	1.61, dd (13.1, 7.3) 1.90, dd (13.0, 10.3)	28.5, CH_2	1.64, m 1.93, m
21	50.2, CH	3.11, dd, (10.3, 7.3)	50.5, CH	3.09, dd, (8.8, 8.6)
22	47.0, C		47.4, C	
23	23.1, CH_3	0.67, s	23.5, CH_3	0.97, s
24	20.5, CH_3	0.94, s	20.9, CH_3	0.69, s
25	116.8, CH	6.54, d (10.0)	117.3, CH	6.58, d (10.1)
26	130.4, CH	5.71, d (10.0)	130.7, CH	5.74, d (10.1)
27	76.0, C		76.3, C	
28	27.8, CH_3	1.33, s	28.2, CH_3	1.36, s
29	27.7, CH_3	1.33, s	28.1, CH_3	1.37, s

[a] 600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S6 NMR data of notoamide E (3) in acetone-d_6

	3[a]		Reported Notoamide E[13]	
no.	δ_C type	δ_H mult (J in Hz)	δ_C type	δ_H mult (J in Hz)
1		9.59, br s		7.34 br s
2	141.3, C		141.3 C	
3	106.2, C		106.4, C	
4	118.7, CH	7.28, d (8.4)	118.7, CH	7.26, d (8.5)
5	110.8, CH	6.56, d (8.4)	110.6, CH	6.54, d (8.5)
6	149.5, C		149.4, C	
7	105.9, C		106.0, C	
8	132.5, C		132.5, C	
9	124.9, C		125.1, C	
10	26.4, CH_2	3.04, dd (15.2, 11.2) 3.61, dd (15.3, 4.1)	26.0, CH_2	3.03, dd (15.0, 11.0) 3.60, dd (15.0, 4.5)
11	56.0, CH	4.40, dd (11.2, 4.1)	56.0, CH	4.38, dd (11.0, 4.5)
12	166.3, C		166.3, C	
14	45.7, CH_2	3.46, m 3.56, m	45.5, CH_2	3.45, m 3.55, m
15	23.2, CH_2	1.88, m 1.96, m	22.8, CH_2	1.94, m 1.94, m
16	28.9, CH_2	1.92, m 2.20, m	28.5, CH_2	1.94, m 2.19, m
17	59.6, CH	4.18, m	59.1, CH	4.16, m
18	169.9, C		171.8, C	
19				5.61, s
20	111.8, CH_2	5.07, d (10.6) 5.12, d (17.4)	111.6, CH_2	5.05, dd (10.5, 1.0) 5.11, dd (17.5, 1.5)
21	147.4, CH	6.25, dd (17.4, 10.6)	147.1, CH	6.24, dd (17.5, 10.5)
22	40.0, C		40.0, C	
23	28.3, CH_3	1.58, s	27.8, CH_3	1.57, s
24	28.4, CH_3	1.58, s	27.8, CH_3	1.57, s
25	118.6, CH	6.94, d (9.8)	118.3, CH	6.93, d (9.8)
26	129.8, CH	5.69, d (9.8)	129.6, CH	5.24, d (9.8)
27	76.0, C		76.0, C	
28	27.6, CH_3	1.40, s	27.2, CH_3	1.38, s
29	27.7, CH_3	1.40, s	27.2, CH_3	1.39, s

[a] 600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S7 NMR data of notoamide C (4) in acetone-d_6

	4[a]		Reported Notoamide C[11]	
no.	δ_C type	δ_H mult (*J* in Hz)	δ_C type	δ_H mult (*J* in Hz)
1		10.40, br s		10.30, br s
2	182.4 C		182.3 C	
3	56.5, C		56.6, C	
4	128.9, CH	7.00, d (8.2)	128.8, CH	7.00, d (8.3)
5	108.7, CH	6.34, d (8.2)	108.8, CH	6.34, d (8.3)
6	153.7, C		153.8, C	
7	105.6, C		105.7, C	
8	139.8, C		139.9, C	
9	121.1, C		121.3, C	
10	32.8, CH_2	2.65, dd (14.7, 5.2) 2.76, dd (14.7, 5.2)	32.9, CH_2	2.65, dd (14.7, 4.9) 2.76, dd (14.7, 4.9)
11	54.7, CH	4.01, br t 5.2	54.7, CH	3.99, br t 4.9
12	164.7, C		164.8, C	
14	45.5, CH_2	3.19, m 3.41, dt (11.7, 8.3)	45.5, CH_2	3.19, dt (11.7, 5.9) 3.40, dt (11.7, 8.3)
15	22.0, CH_2	1.71, m 1.71, m	22.1, CH_2	1.71, m 1.71, m
16	29.1, CH_2	1.27, m 1,99. m	29.1, CH_2	1.30, m 2.00, m
17	58.9, CH	3.89, m	59.0, CH	3.89 dd (10.3, 6.4)
18	168.9, C		169.0, C	
19		6.27, br s		6.27, br s
20	113.7, CH_2	4.98, d (17.5, 1.1) 5.04, d (10.8, 1.1)	113.7, CH_2	4.98, dd (17.6, 1.0) 5.04, dd (10.3, 1.0)
21	144.3, CH	6.12, dd (17.4, 10.8)	144.4, CH	6.13, dd (17.6, 10.3)
22	43.2, C		43.3, C	
23	21.8, CH_3	1.00, s	21.8, CH_3	1.00, s
24	22.7, CH_3	1.08, s	22.8, CH_3	1.07, s
25	117.6, CH_2	6.59, d (10.0)	117.6, CH_2	6.59, d (10.7)
26	130.9, CH	5.73, d (10.0)	131.0, CH	5.73, d (10.7)
27	76.7, C		76.7, C	
28	28.0, CH_3	1.39, s	28.0, CH_3	1.39, s
29	28.4, CH_3	1.42, s	28.4, CH_3	1.42, s
6-OH				

[a] 600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S8 NMR data of notoamide D (5) in acetone-d_6

	5[a]		Reported Notoamide D[11]	
no.	δ_C type	δ_H mult (J in Hz)	δ_C type	δ_H mult (J in Hz)
1		6.60, br s		6.60, br s
2	92.6, C		92.7 C	
3	89.2, C		89.4, C	
4	124.7, CH	7.02, d (8.1)	124.7, CH	7.01, d (8.0)
5	108.3, CH	6.15, d (8.1)	108.3, CH	6.15, d (8.0)
6	155.2, C		155.3, C	
7	106.5, C		106.5, C	
8	146.7, C		146.8, C	
9	124.9, C		124.9, C	
10	35.9, CH_2	2.47, dd (12.9, 7.6) 2.73, dd (12.9, 11.2)	36.1, CH_2	2.65, dd (13.0, 8.0) 2.75, dd (13.0, 11.0)
11	60.0, CH	3.81, dd (11.2, 7.6)	60.0, CH	3.82, dd (11.0, 8.0)
12	166.7, C		166.5, C	
14	45.2, CH_2	3.37, m 3.47, dt (11.2, 7.6)	45.7, CH_2	3.35, ddd (11.0, 8.0, 5.0) 3.47, dt (11.0, 8.0)
15	24.3, CH_2	1.88, m 1.88, m	24.3, CH_2	1.88, m 1.88, m
16	28.9, CH_2	2.05, m 2.19, m	29.0, CH_2	2.05, m 2.18, ddd (18.0, 7.0, 6.0)
17	62.2, CH	4.07 t (7.9)	62.2, CH	4.07 t (8.0)
18	173.8, C		173.2, C	
20	111.7, CH_2	4.87, dd (10.8, 1.4) 4.92, dd (17.6, 1.4)	111.7, CH_2	4.88, dd (11.0, 1.5) 4.93, dd (17.5, 1.5)
21	146.4, CH	6.33, dd (17.6, 10.8)	146.4, CH	6.34, dd (17.5, 11.0)
22	45.7, C		45.3, C	
23	24.7, CH_3	1.24, s	24.8, CH_3	1.25, s
24	25.1, CH_3	1.27, s	25.2, CH_3	1.28, s
25	117.8, CH_2	6.41, d (9.9)	117.9, CH_2	6.40, d (10.0)
26	129.5, CH	5.62, d (9.9)	129.5, CH	5.63, d (10.0)
27	76.4, C		76.5, C	
28	27.8, CH_3	1.35, s	27.9, CH_3	1.36, s
29	28.4, CH_3	1.37, s	28.4, CH_3	1.38, s
6-OH		4.47, s		4.33, br s

[a] 500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S9 NMR data of notoamide M (6) in pyridine-d_5

no.	6[a]		Reported Notoamide M[14, 15,b]	
	δ_C type	δ_H mult (J in Hz)	δ_C type	δ_H mult (J in Hz)
1				
2	182.2 C		183.8 C	
3	56.0, C		57.1, C	
4	128.6, CH	7.23, d (8.2)	129.7, CH	6.89, d (8.5)
5	108.0, CH	6.62, d (8.2)	109.3, CH	6.31, d (8.5)
6	153.1, C		154.3, C	
7	105.0, C		106.3, C	
8	140.4, C		140.1, C	
9	120.9, C		121.0, C	
10	33.2, CH_2	2.99, dd (14.8, 4.1) 3.10, dd (14.8, 5.8)	33.7, CH_2	2.69, dd (15.0, 6.5) 2.81, dd (15.0, 3.0)
11	54.4, CH	4.50, dd (4.1, 5.8)	55.3, CH	4.15, dd (6.5, 3.0)
12	167.9, C		167.4, C	
14	45.0, CH_2	3.67, m 3.73, m	45.7, CH_2	3.36, m 3.37, m
15	19.5, CH_2	1.71, m 2.05, m	19.7, CH_2	1.68, m 1.91, m
16	36.5, CH_2	1.94, td, (12.1, 8.6, 1.0) 2.39, ddd, (12.3, 7.1, 1.0)	36.4, CH_2	1.35, m 1.95, m
17	87.1, C		87.6, C	
18	167.9, C		168.7, C	
19				
20	113.4, CH_2	4.99, (overlapped) 5.06, (overlapped)	114.3, CH_2	4.99, dd (17.5, 1.0) 5.07, dd (10.5, 1.0)
21	143.8, CH	6.36, dd (17.0, 10.8)	144.4, CH	6.05, dd (17.5, 10.5)
22	42.8, C		43.7, C	
23	21.5, CH_3	1.12, s	21.9, CH_3	0.99, s
24	22.3, CH_3	1.22, s	22.7, CH_3	1.08, s
25	117.5, CH_2	6.83, d (9.9)	117.6, CH_2	6.46, d (10.0)
26	130.0, CH	5.56, d (9.9)	131.5, CH	5.69, d (10.0)
27	76.1, C		77.3, C	
28	28.0, CH_3	1.39, s	27.9, CH_3	1.38, s
29	27.7, CH_3	1.41, s	27.8, CH_3	1.41, s

[a] 800 MHz for ^{1}H NMR and 201 MHz for ^{13}C NMR.

[b] Data reported in the literature measured in methanol-d_4.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S10 NMR data of speramide B (7) in DMSO-d_6

	7[a]		Reported Speramide B[16]	
no.	δ_C type	δ_H mult (J in Hz)	δ_C type	δ_H mult (J in Hz)
1		6.72, br s		6.72, br s
2	91.3 C		91.3 C	
3	87.4, C		87.4, C	
4	123.9, CH	6.99, d (7.9)	124.7, CH	7.00, d (8.1)
5	106.4, CH	6.12, d (7.9)	106.3, CH	6.13, d (8.1)
6	153.7, C		153.7, C	
7	104.6, C		104.6, C	
8	145.8, C		145.8, C	
9	123.9, C		122.9, C	
10	34.9, CH_2	2.40, m 2.49, m	34.9, CH_2	1.60, dd (7.6, 12.5) 2.49, (overlapped)
11	57.2, CH	4.00, dd (10.3, 8.7)	57.2, CH	4.01, dd (11.4, 7.8)
12	167.0, C		167.1, C	
14	44.1, CH_2	3.42, m 3.31, m	44.3, CH_2	3.42, m 3.31, m
15	20.5, CH_2	1.96, m 1.78, m	20.6, CH_2	1.95, m 1.79, m
16	36.8, CH_2	1.99, m 1.96, m	36.7, CH_2	2.00, m 1.95, m
17	89.7, C	4.08, br s	89.8, C	4.07 t (8.0)
18	170.3, C		170.3, C	
19				
20	110.8, CH_2	4.83, d (17.0, 2.4) 4.81, d (11.0, 2.4)	110.8, CH_2	4.82, dd (17.0, 2.4) 4.81, dd (11.0, 2.4)
21	145.5, CH	6.29, dd (17.0, 11.0)	145.6, CH	6.30, dd (17.0, 11.0)
22	44.7, C		44.8, C	
23	24.6, CH_3	1.16, s	24.7, CH_3	1.17, s
24	24.0, CH_3	1.20, s	24.0, CH_3	1.21, s
25	117.3, CH_2	6.54, d (11.1)	117.5, CH_2	6.54, d (9.8)
26	128.2, CH	5.60, m	128.2, CH	5.61, d (9.8)
27	75.5, C		75.6, C	
28	27.4, CH_3	1.32, s	27.5, CH_3	1.33, s
29	28.0, CH_3	1.35, s	28.0, CH_3	1.36, s
3-OH		5.40, s		5.60, s
17-OH		6.51, s		6.51, s

[a] 600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S11 Specific rotations for compounds (1-7)

compound	specific rotations in this paper	specific rotations in literature	reference
(+)-notoamide B (**1**)	+148.9 (*c* 0.15, MeOH)	+102 (*c* 0.05, MeOH) –118 (*c* 0.064, MeOH)	17, 18
(+)-versicolamide B (**2**)	+38.2 (*c* 0.22, MeOH)	+26 (*c* 0.1, acetone) -34 (*c* 0.1, acetone)	17 19
(–)-notoamide E (**3**)	-68.0 (*c* 0.17, MeOH)	-28 (*c* 0.013, MeOH)	13
(+)-notoamide C (**4**)	+33.0 (*c* 0.16, MeOH)	+97 (*c* 0.40, MeOH) +23 (*c* 0.255, MeOH)	11, 20
(–)-notoamide D (**5**)	-173.0 (*c* 0.2, MeOH)	-163 (c 0.32, MeOH)	11
(+)-notoamide M (**6**)	+106.4 (*c* 0.02, MeOH)	+51 (*c* 1.7, MeOH)	14
(–)-speramide B (**7**)	-83.3 (*c* 0.2, MeOH)	-95(*c* 0.09, MeOH)	16

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Table S12 Thermodynamic data (in atomic units) of all species.

	TCG[a]	TCH[b]	E(solv)	ifreq[c]	ΔG	ΔH
4a	0.467815	0.562	-1399.822178	-	0.0	0.0
TS-6π	0.468842	0.560318	-1399.808452	-298.334	9.3	7.6
5	0.475129	0.563197	-1399.847632	-	-11.4	-15.2
tua-mA	0.466329	0.555765	-1474.259743	-	0.0	0.0
TS-mA-SSR	0.471002	0.554786	-1474.234121	-400.455	19.0	15.5
TS-mA-RRR	0.470218	0.554827	-1474.232040	-369.316	19.8	16.8
Prod-mA-SSR	0.475206	0.558901	-1474.291509	-	-14.4	-18.0
Prod-mA-RRR	0.475947	0.55903	-1474.293833	-	-15.4	-19.3
tau-mB	0.465833	0.555066	-1474.245248	-	8.8	8.7
TS-mB-SSR	0.470336	0.554172	-1474.220385	-451.848	27.2	23.7
TS-mB-RRR	0.470303	0.554394	-1474.222921	-421.201	25.6	22.2
Prod-mB-SSR	0.474188	0.558116	-1474.266443	-	0.7	-2.7
Prod-mB-RRR	0.475737	0.558495	-1474.273796	-	-2.9	-7.1
tau-mC	0.451115	0.541643	-1473.823400	-	0.0	0.0
TS-mC-SSR	0.456375	0.540916	-1473.791007	-459.667	23.6	19.9
TS-mC-RRR	0.457171	0.541071	-1473.792498	-450.184	23.2	19.0
Prod-mC-SSR	0.461747	0.545005	-1473.851415	-	-10.9	-15.5
Prod-mC-RRR	0.46167	0.545055	-1473.853393	-	-12.2	-16.7
tau-mD	0.46563	0.555516	-1474.254496	-	2.9	3.1
TS-mD-SSR	0.470119	0.555072	-1474.226598	-371.443	23.2	20.4
TS-mD-RRR	0.470733	0.554947	-1474.229180	-353.676	21.9	18.7
Prod-mD-SSR	0.475617	0.559065	-1474.290242	-	-13.3	-17.1
Prod-mD-RRR	0.475555	0.559057	-1474.291826	-	-14.3	-18.1
int-B'	0.450932	0.541988	-1473.814541	-	-	-
int-B	0.46659	0.555611	-1474.242160	-	-	-
guanidine	0.049283	0.081243	-205.463413	-	-	-
guanidine-H+	0.059117	0.094343	-205.931880	-	-	-
epoxy-SSR	0.461865	0.545649	-1473.875798	-	0.0	0.0
int1-SSR	0.542627	0.642647	-1679.826224	-	1.9	-10.0
TS-C2O-SSR	0.542772	0.641688	-1679.817631	-193.972	7.4	-5.2
TS-C3O-SSR	0.541184	0.640922	-1679.817572	-305.288	6.5	-5.6
int2-SSR	0.542526	0.642614	-1679.819831	-	5.9	-6.0
int3-SSR	0.540272	0.641624	-1679.828438	-	-0.9	-12.0
epoxy-RRR	0.461703	0.5455	-1473.877562	-	0.0	0.0
int1-RRR	0.542535	0.64256	-1679.827892	-	2.0	-9.9
TS-C2O-RRR	0.543079	0.641819	-1679.818538	-136.292	8.3	-4.5
TS-C3O-RRR	0.541997	0.640992	-1679.818807	-299.142	7.4	-5.2
int2-RRR	0.541157	0.64234	-1679.819380	-	6.5	-4.7
int3-RRR	0.540271	0.641364	-1679.828615	-	0.2	-11.1
epoxy-nr	0.47809	0.56756	-1475.056337	-	0.0	0.0
int1-nr	0.559274	0.664794	-1681.009591	-	0.4	-11.6
TS-C2O-nr	0.558696	0.663468	-1680.998242	-252.629	7.2	-5.3
int2-nr	0.55756	0.664259	-1681.001372	-	4.5	-6.8

a. Thermal correction to Free Energy.; b. Thermal correction to Enthalpy.; c. imaginary frequency

Supplementary Figures

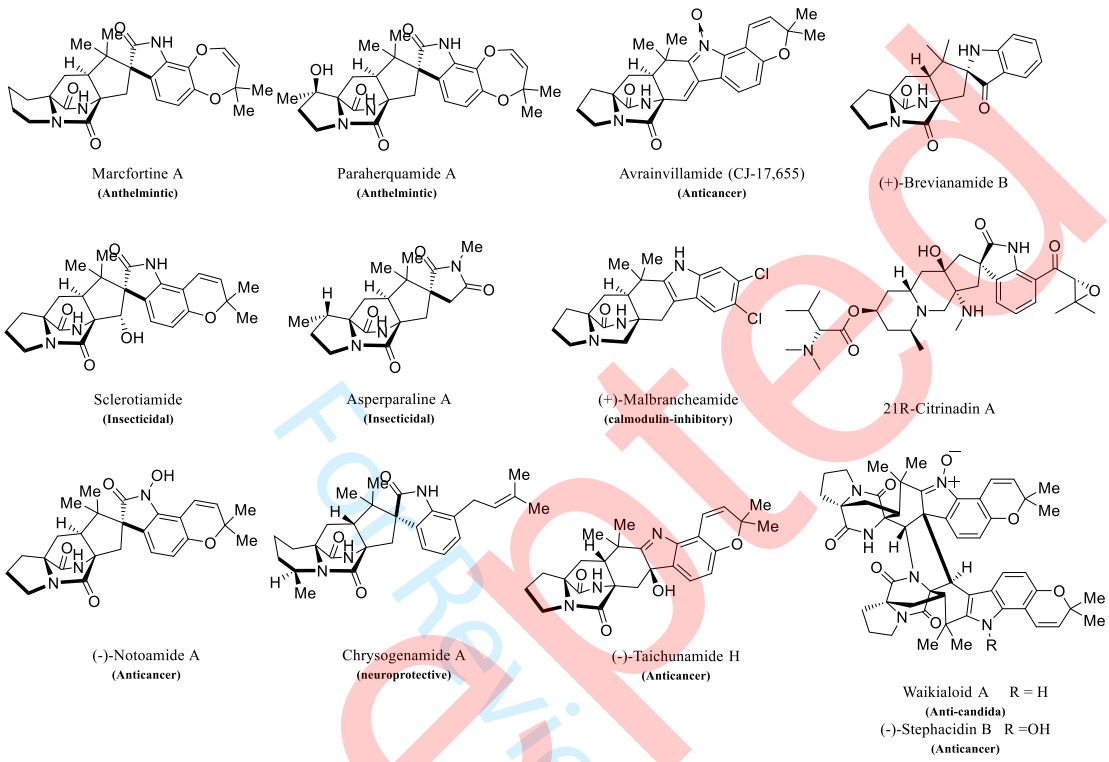


Figure S1 Examples of prenylated indole alkaloids with bicyclo[2.2.2]diazaoctane core.

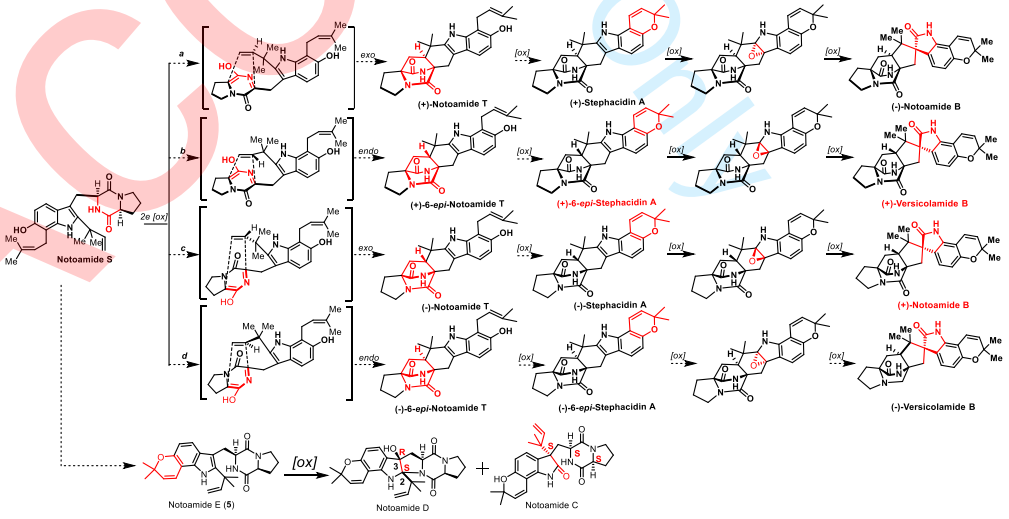


Figure S2 Biosynthesis pathway of notoamides proposed in the literature.[21]

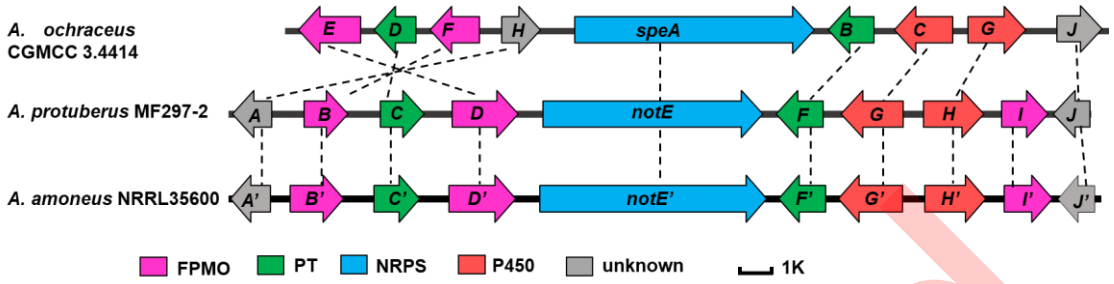


Figure S3 The comparison of gene clusters for the biosynthesis of notoamides in *A. ochraceus*, *A. protuberus*, and *A. amoneus*.

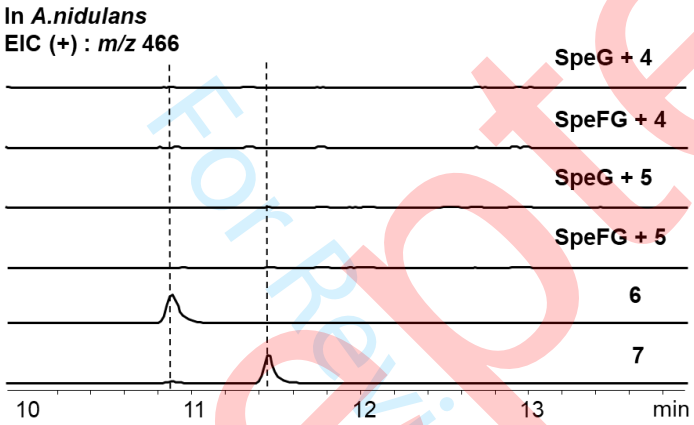


Figure S4 The results of feeding of 4 and 5 to the *An-speG* and *An-speFG*

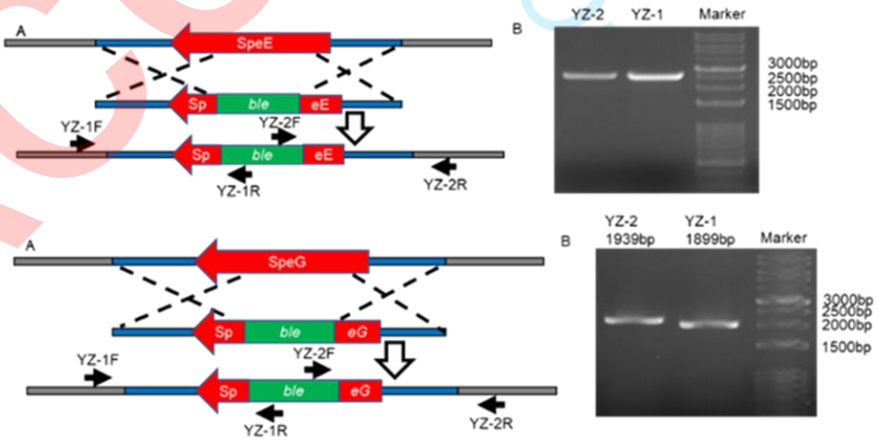


Figure S5 Gene knock-out results of *speE* and *speG* in *A. ochraceus*.

(A) Knockout strategy and PCR results used to inactivate *speE* and *speG*
Result: No *m/z* of 448 (**1-2**) detection of Δ*speE* and Δ*speG* mutant in LC-MS experiment.

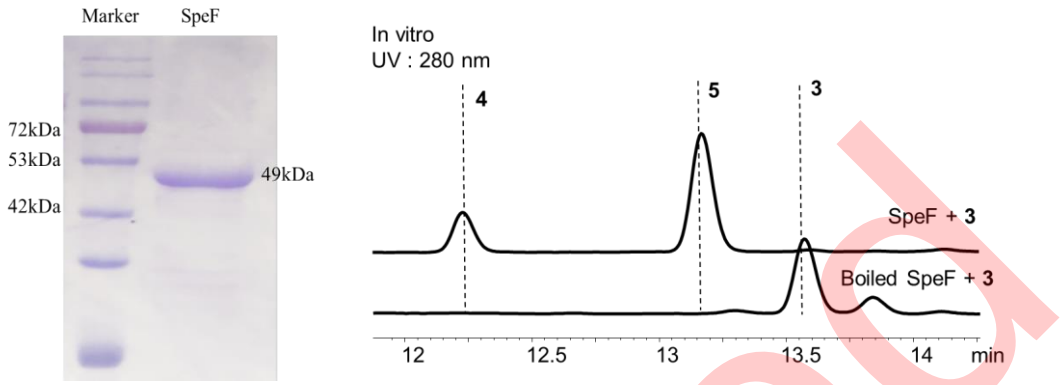


Figure S6 In vitro assay of SpeF.

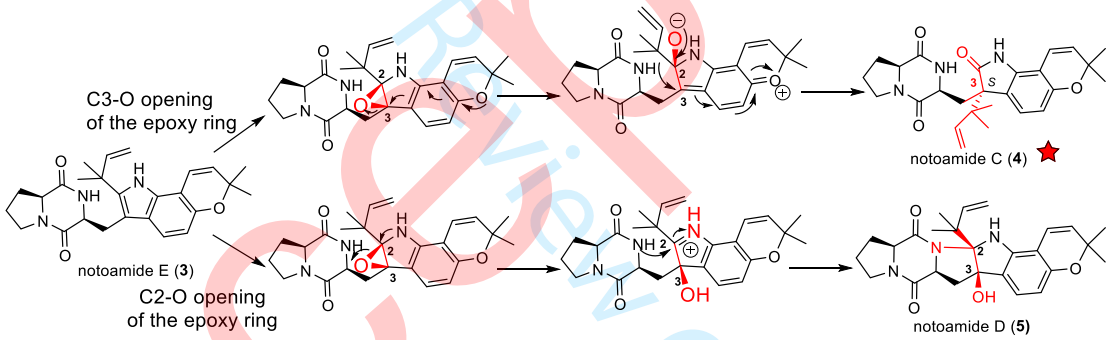
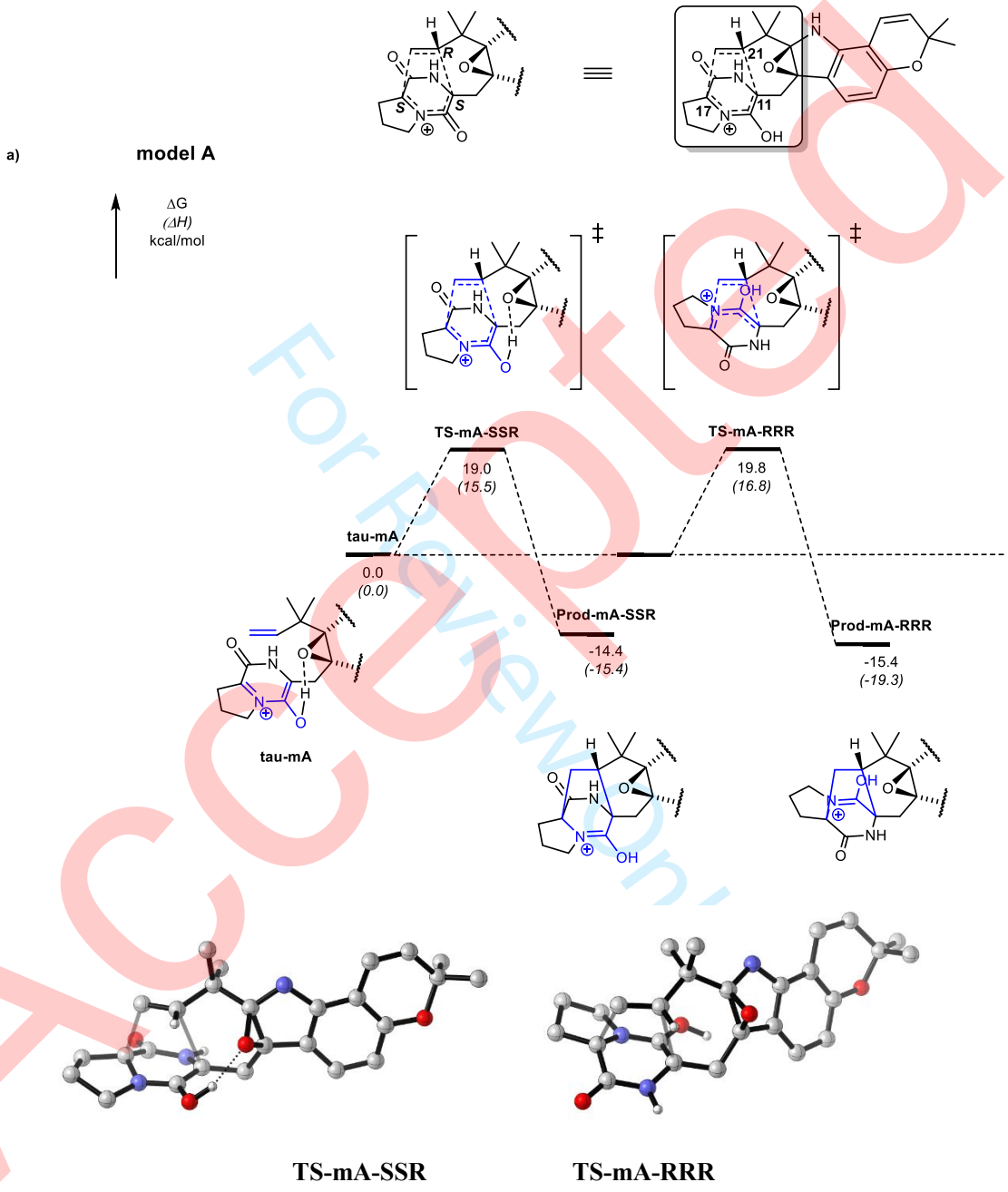


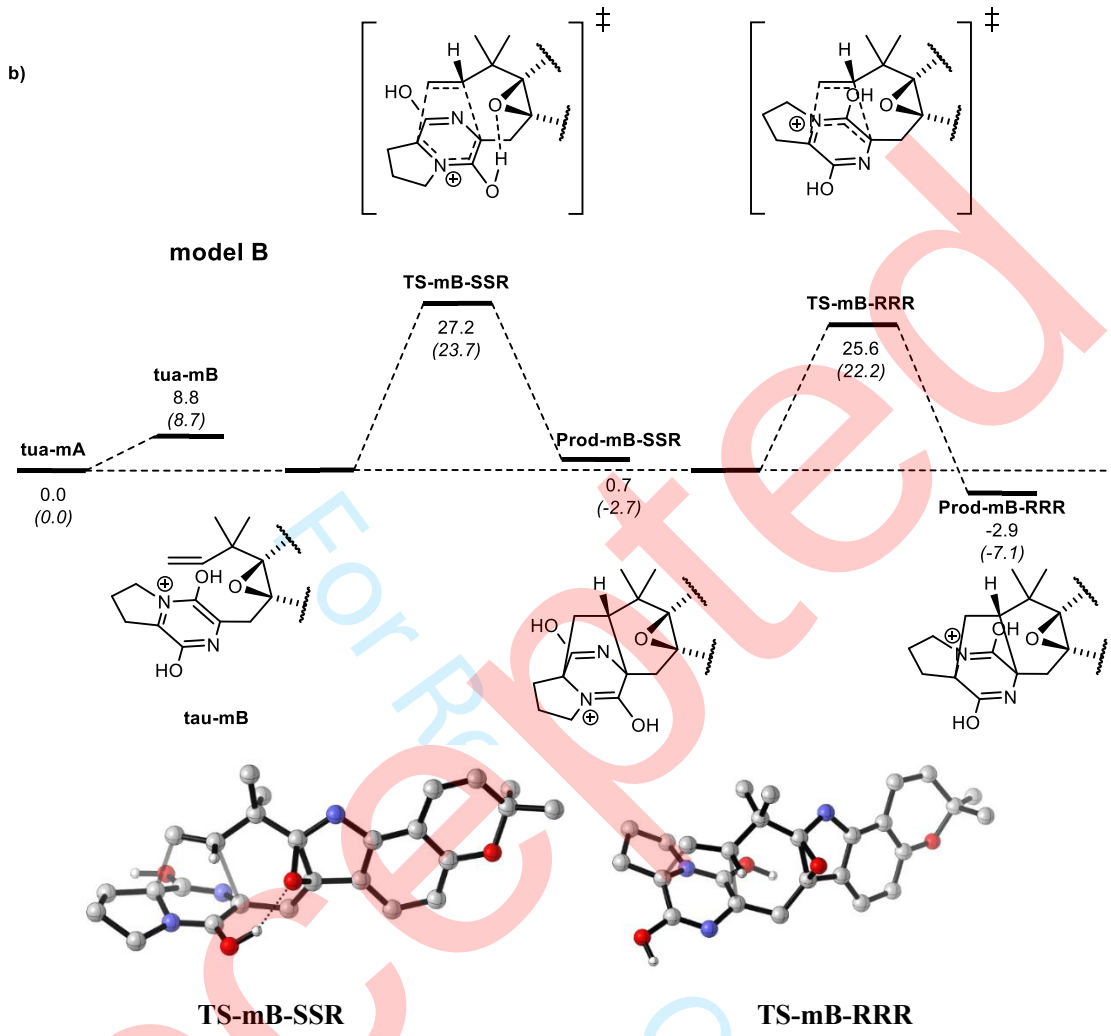
Figure S7 The mechanism for the formation of 4 and 5 from 3.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Figure S8 Energy barriers for the transition states of the 4 models (A-D) and two different Diels-Alder addition reactions (SSR and RRR conformations), where models A-D have the same number of atoms.



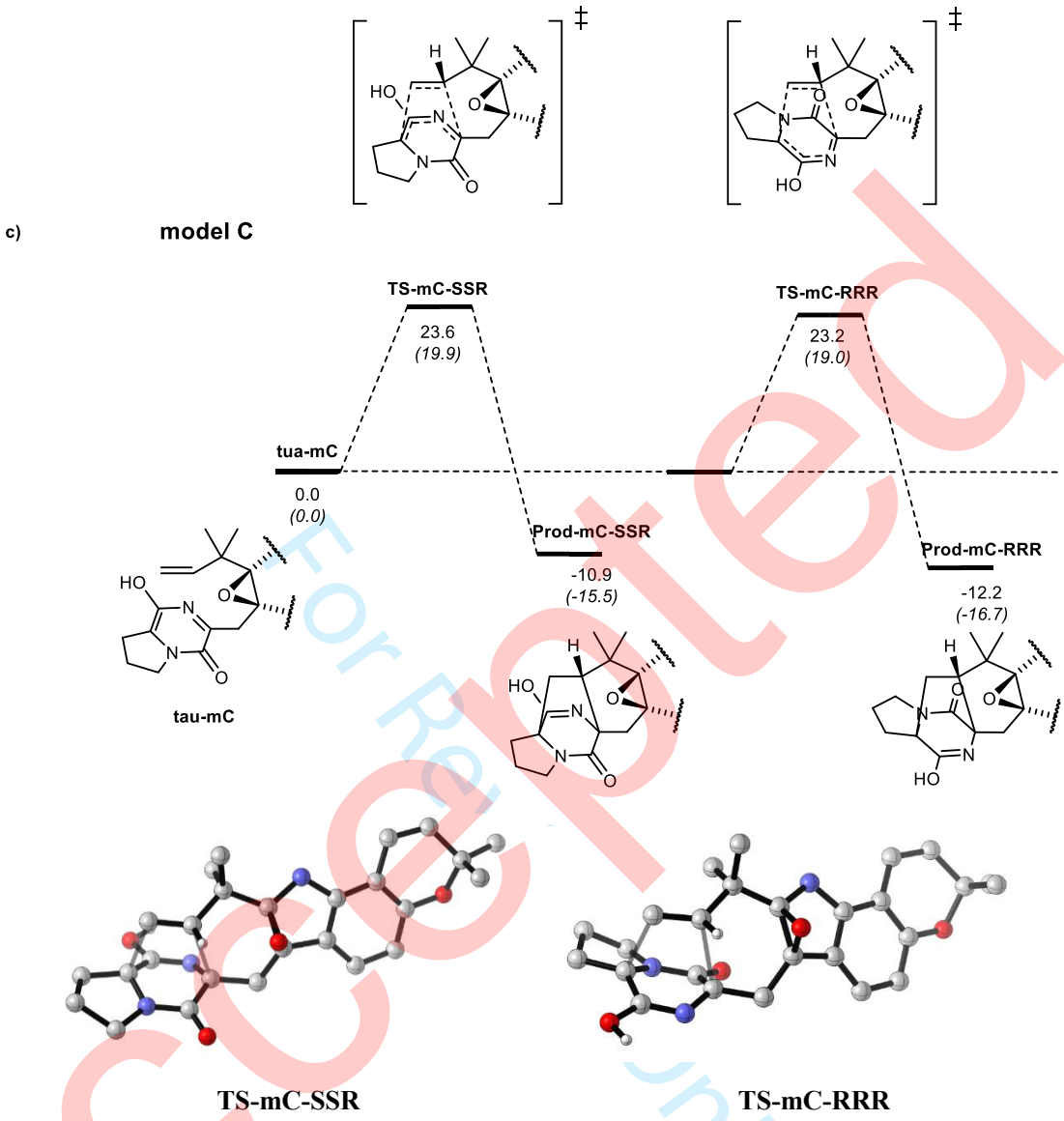
https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english



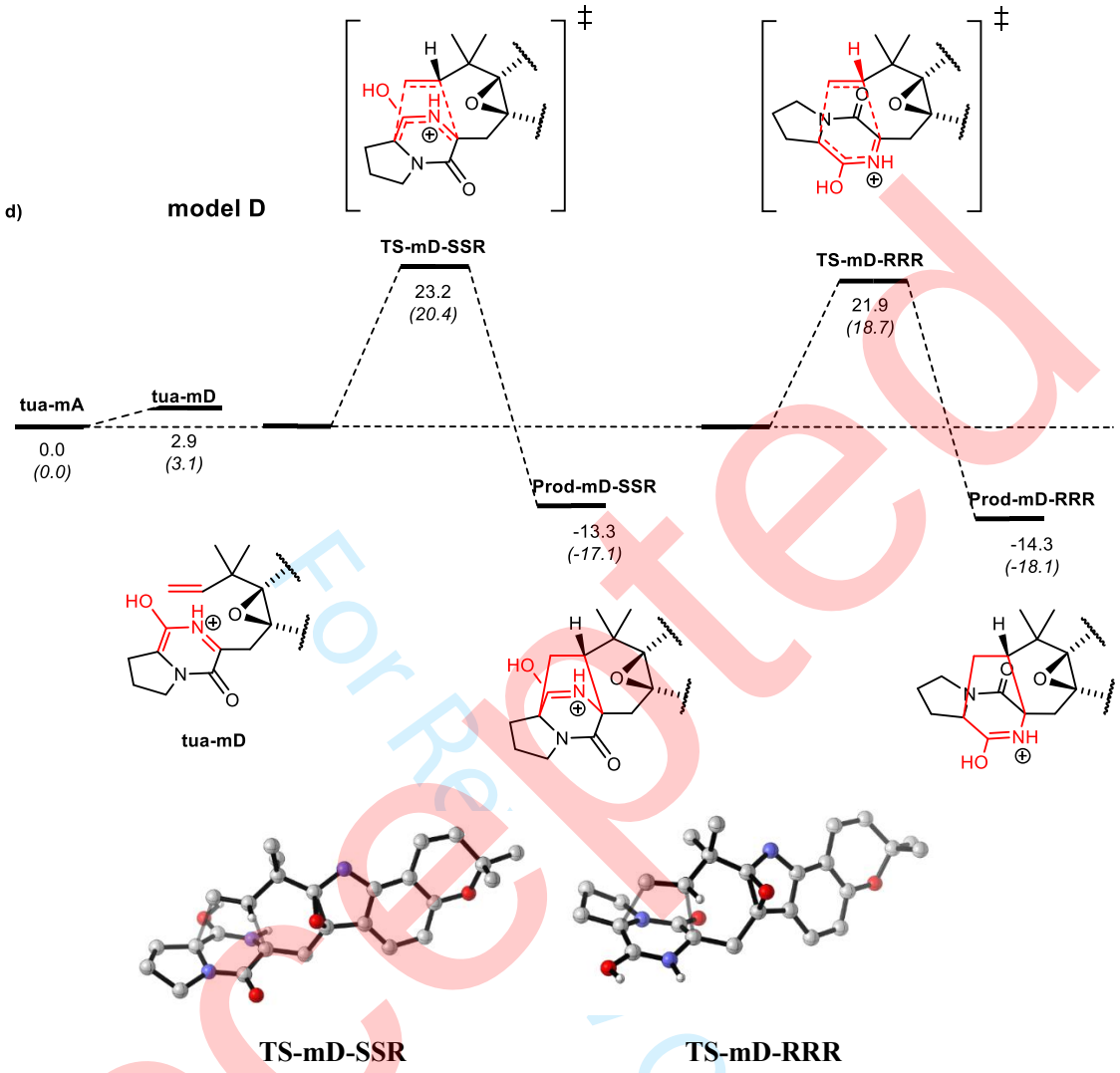
TS-mB-SSR

TS-mB-RRR

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english



https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english



TS-mD-SSR TS-mD-RRR

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

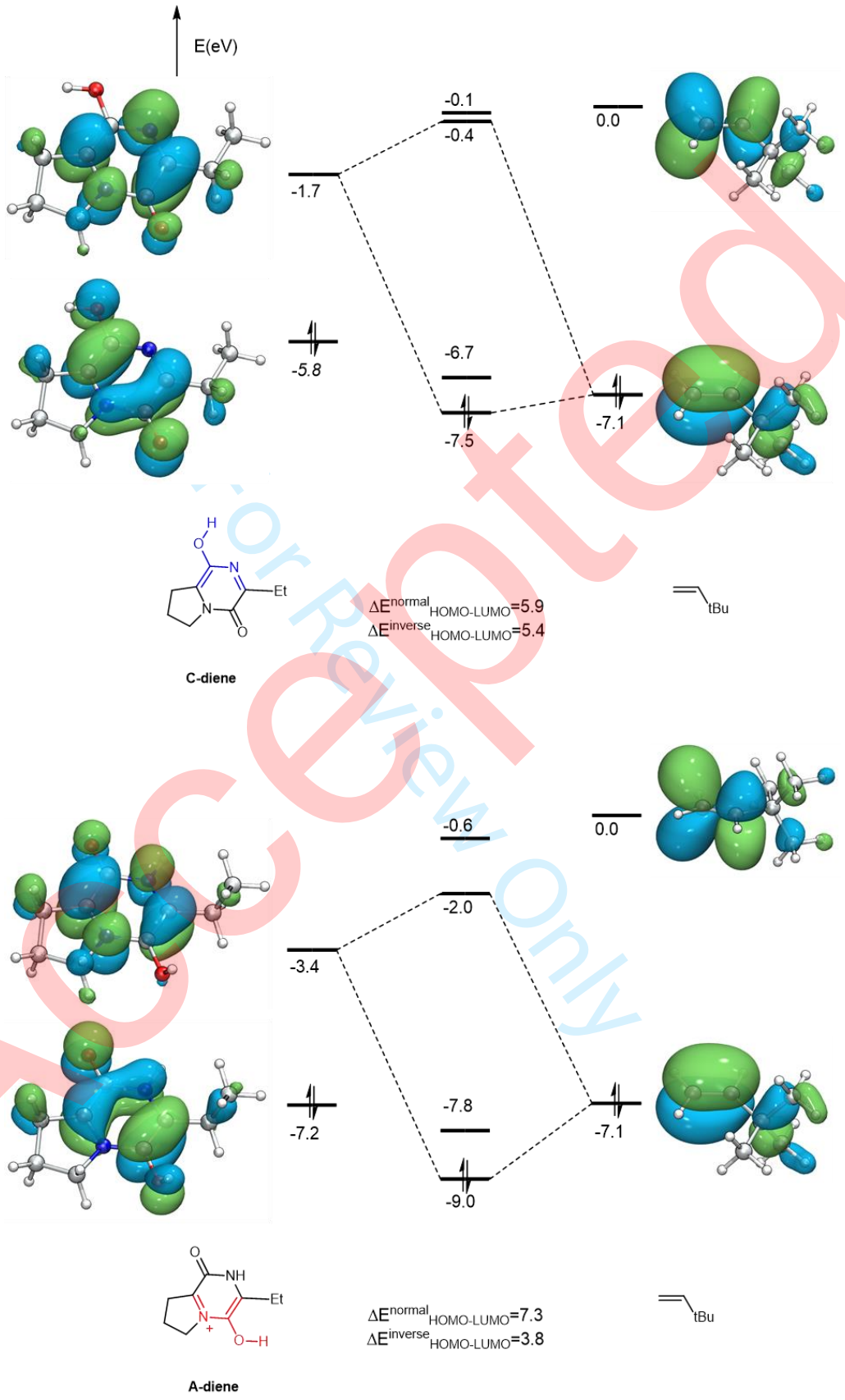
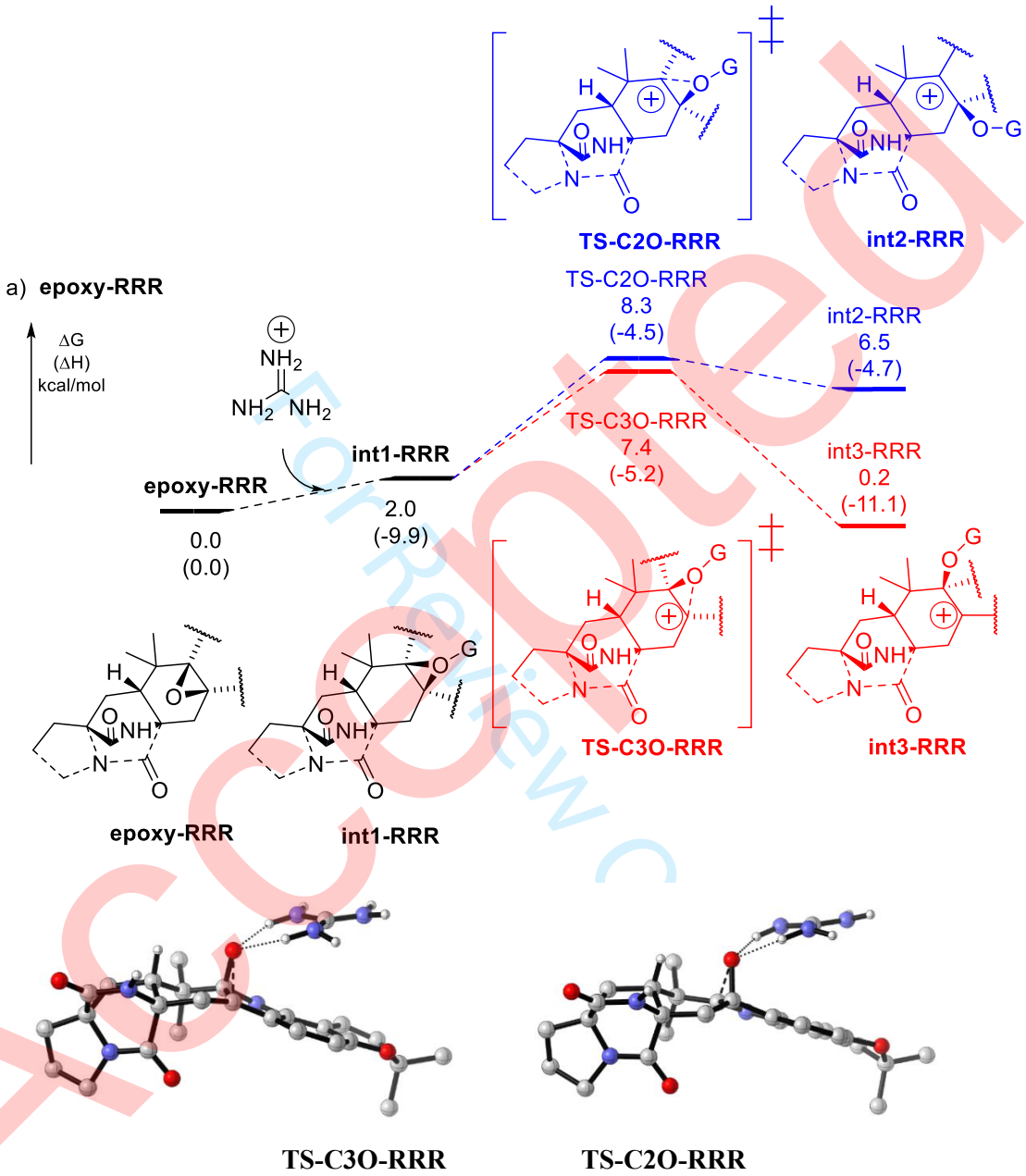
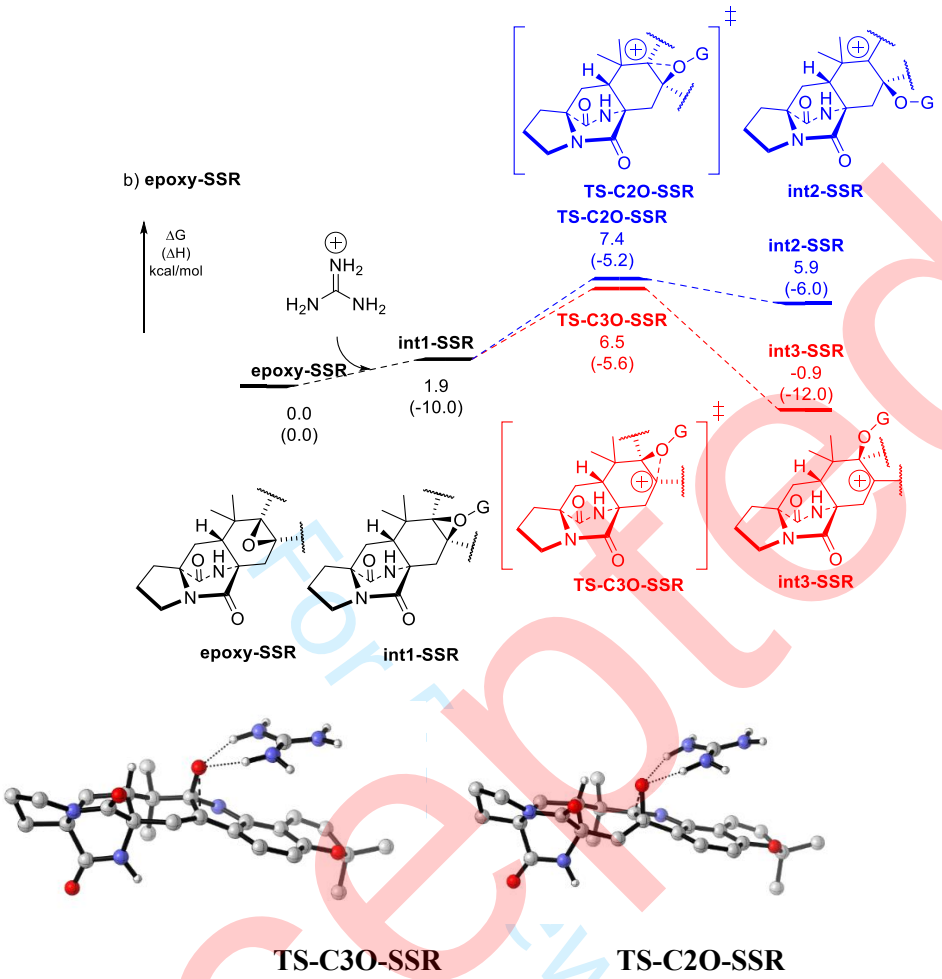


Figure S9 Molecular orbital analysis of two types of DA reactions.

Figure S10 Potential energy surfaces of the ring-opening step and their structures of the transition states (a) epoxy-RRR and (b) epoxy-SSR



https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english



TS-C3O-SSR TS-C2O-SSR

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

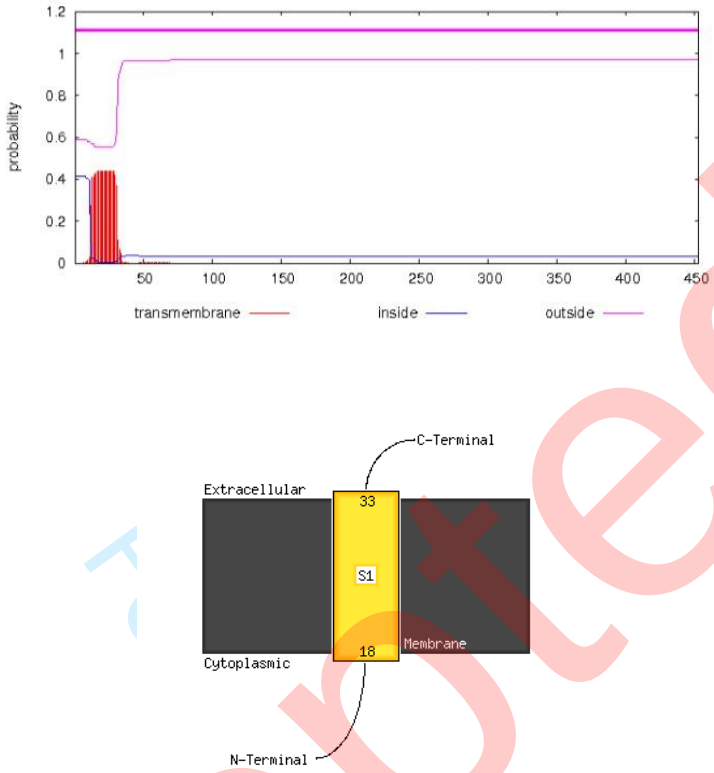


Figure S11 The analysis of membrane structure of SpeF via TMHMM and Phyre2.

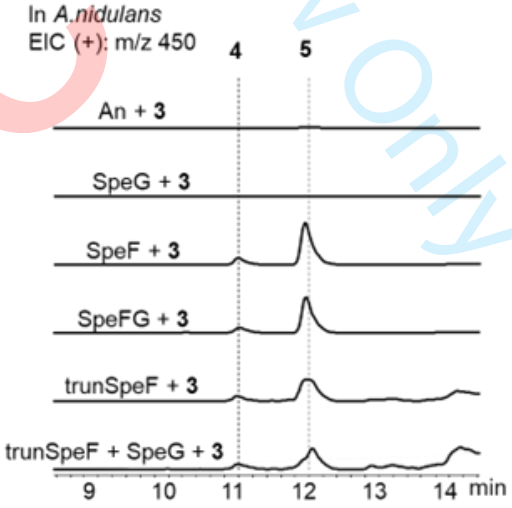


Figure S12 The results of feeding of **3** to the *An-trunSpeF and An-SpeG*.

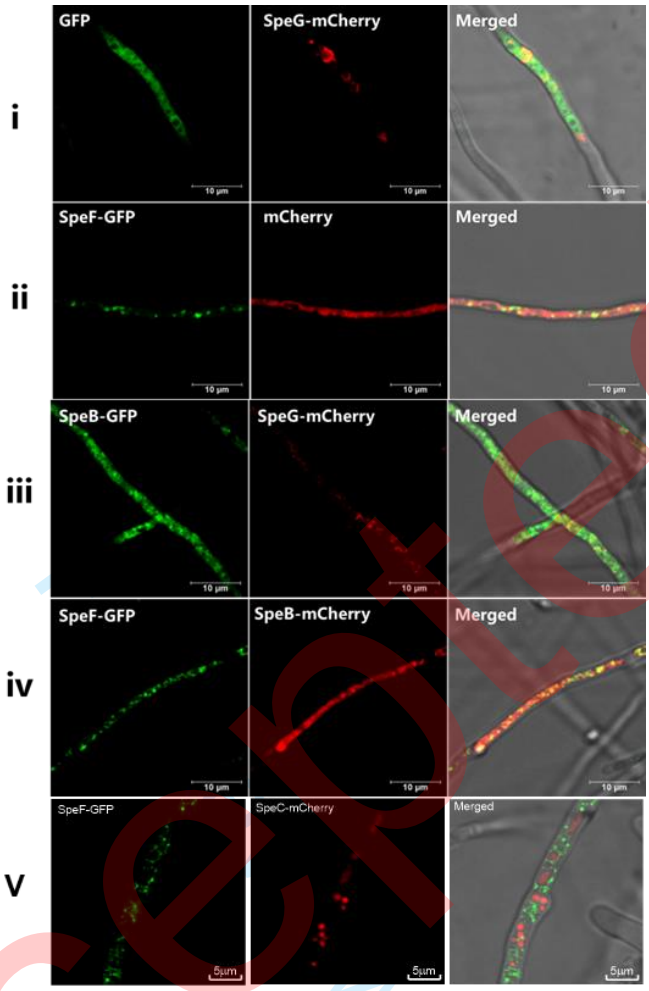


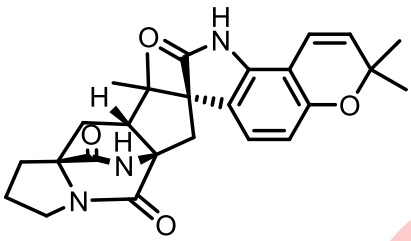
Figure S13 Colocalization experiments of SpeF and SpeG. i). GFP and SpeG-mcherry; ii). SpeF-GFP and mcherry; iii). SpeB-GFP and SpeG-mcherry; iv). SpeF-GFP and SpeB-mcherry; v) SpeF-GFP and SpeC-mcherry

Results: The colocalization of GFP/SpeG-mCherry, SpeF-GFP/mcherry, SpeB-GFP/SpeG-mcherry, and SpeF-GFP/SpeB-mcherry, SpeF-GFP/SpeB-mcherry was not observed.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

X-ray Crystallographic Analysis

X-ray Crystallographic Data of (+)-notoamide B ((+)-1)



Compound (+)-1 was recrystallized from CH_3OH/H_2O (20: 1) to obtain colorless crystals. Crystallographic data (excluding structure factor tables) for (+)-notoamide B (CCDC 2034890) have been deposited in the Cambridge Crystallographic Data Centre. Flack parameter = -0.07(4).

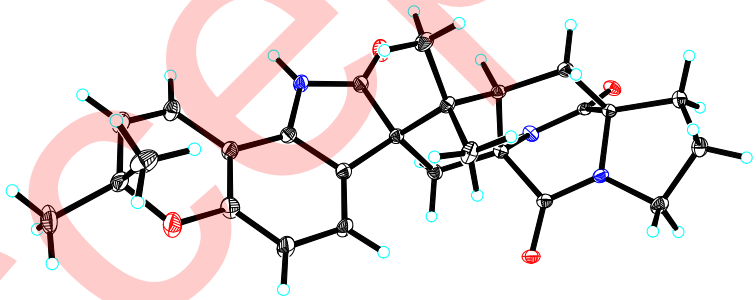


Figure S14 ORTEP drawing of the X-ray crystal structure of (+)-1

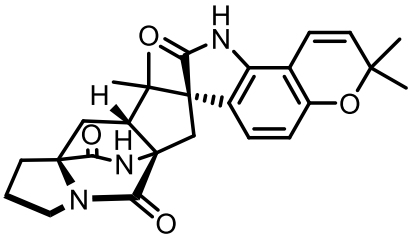
(Displacement ellipsoids are drawn at the 30% probability level).

Table S13 Crystal data and structure refinement for (+)-**1**

Identification code	global	
Empirical formula	C26 H31 N3 O5	
Formula weight	465.54	
Temperature	101(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.14950(10) Å	α= 90°.
	b = 17.6125(3) Å	β= 90°.
	c = 18.4238(3) Å	γ= 90°.
Volume	2319.94(6) $Å^3$	
Z	4	
Density (calculated)	1.333 Mg/m^3	
Absorption coefficient	0.758 mm^{-1}	
F(000)	992	
Crystal size	0.580 x 0.200 x 0.100 mm^3	
Theta range for data collection	3.47 to 72.61°.	
Index ranges	-7<=h<=8, -21<=k<=21, -22<=l<=22	
Reflections collected	50691	
Independent reflections	4601 [R(int) = 0.0442]	
Completeness to theta = 72.61°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.93 and 0.75	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	4601 / 263 / 406	
Goodness-of-fit on F^2	1.057	
Final R indices [I>2sigma(I)]	R1 = 0.0362, wR2 = 0.0943	
R indices (all data)	R1 = 0.0370, wR2 = 0.0951	
Absolute structure parameter	-0.07(4)	
Largest diff. peak and hole	0.426 and -0.346 $e.Å^{-3}$	

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

X-ray Crystallographic Data of (+)-versicolamide B ((+)-2)



Compound (+)-**2** was recrystallized from CH_3OH/H_2O (10 : 1) to obtain colorless crystals. Crystallographic data (excluding structure factor tables) for (+)-versicolamide B (CCDC 2034888) have been deposited in the Cambridge Crystallographic Data Centre. Flack parameter = 0.05(3).

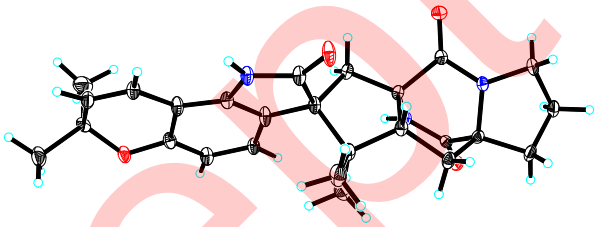


Figure S15 ORTEP drawing of the X-ray crystal structure of (+)-**2**

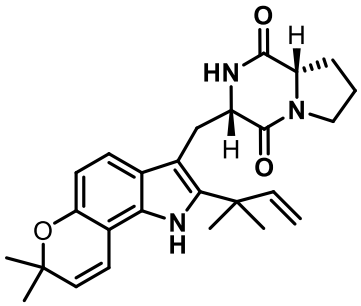
(Displacement ellipsoids are drawn at the 30% probability level).

Table S14 Crystal data and structure refinement for (+)-**2**

Identification code	global	
Empirical formula	C26 H29 N3 O4	
Formula weight	447.52	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.6011(2) Å	α= 90°.
	b = 13.0005(3) Å	β= 90°.
	c = 23.4328(6) Å	γ= 90°.
Volume	2315.58(10) $Å^3$	
Z	4	
Density (calculated)	1.284 Mg/m^3	
Absorption coefficient	0.707 mm^{-1}	
F(000)	952	
Crystal size	0.300 x 0.220 x 0.180 mm^3	
Theta range for data collection	3.77 to 72.42°.	
Index ranges	-9<=h<=9, -14<=k<=16, -28<=l<=28	
Reflections collected	41114	
Independent reflections	4587 [R(int) = 0.0354]	
Completeness to theta = 72.42°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.88 and 0.78	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	4587 / 240 / 368	
Goodness-of-fit on F^2	1.041	
Final R indices [I>2sigma(I)]	R1 = 0.0312, wR2 = 0.0841	
R indices (all data)	R1 = 0.0315, wR2 = 0.0844	
Absolute structure parameter	0.05(3)	
Largest diff. peak and hole	0.514 and -0.151 $e.Å^{-3}$	

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

X-ray Crystallographic Data of notoamide E (3)



Compound **3** was recrystallized from CH_3OH/H_2O (20 : 1) to obtain colorless crystals. Crystallographic data (excluding structure factor tables) for notoamide E (CCDC 2034887) have been deposited in the Cambridge Crystallographic Data Centre. Flack parameter = 0.03(2).

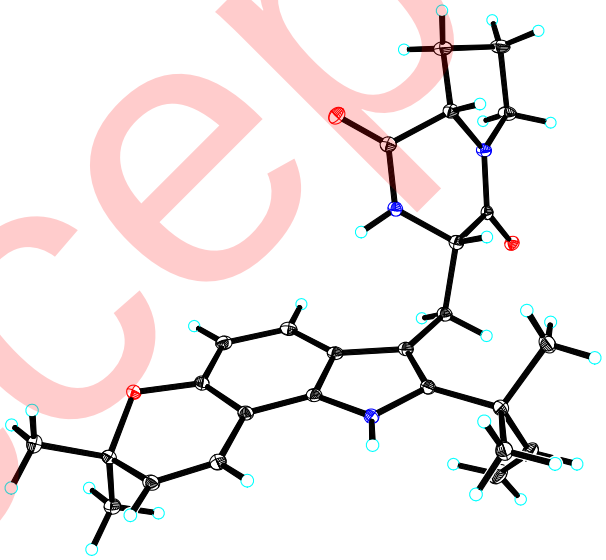


Figure S16 ORTEP drawing of the X-ray crystal structure of **3**

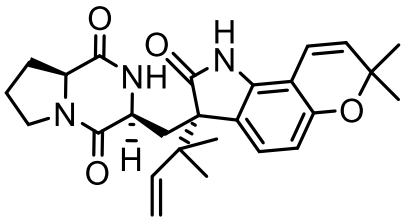
(Displacement ellipsoids are drawn at the 30% probability level).

Table S15 Crystal data and structure refinement for **3**

Identification code	global	
Empirical formula	C_{26} H_{29} N_3 O_4	
Formula weight	447.52	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.6011(2) Å	α= 90°.
	b = 13.0005(3) Å	β= 90°.
	c = 23.4328(6) Å	γ= 90°.
Volume	2315.58(10) $Å^3$	
Z	4	
Density (calculated)	1.284 Mg/m^3	
Absorption coefficient	0.707 mm^{-1}	
F(000)	952	
Crystal size	0.300 x 0.220 x 0.180 mm^3	
Theta range for data collection	3.77 to 72.42°.	
Index ranges	-9<=h<=9, -14<=k<=16, -28<=l<=28	
Reflections collected	41114	
Independent reflections	4587 [R(int) = 0.0354]	
Completeness to theta = 72.42°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.88 and 0.78	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	4587 / 240 / 368	
Goodness-of-fit on F^2	1.041	
Final R indices [I>2sigma(I)]	R1 = 0.0312, wR2 = 0.0841	
R indices (all data)	R1 = 0.0315, wR2 = 0.0844	
Absolute structure parameter	0.05(3)	
Largest diff. peak and hole	0.514 and -0.151 $e.Å^{-3}$	

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

X-ray Crystallographic Data of (+)-notoamide C (4)



Compound **4** was recrystallized from CH_3OH/H_2O (15 : 1) to obtain colorless crystals. Crystallographic data (excluding structure factor tables) for (+)-notoamide C (CCDC 2034889)) have been deposited in the Cambridge Crystallographic Data Centre. Flack parameter = 0.15(5).

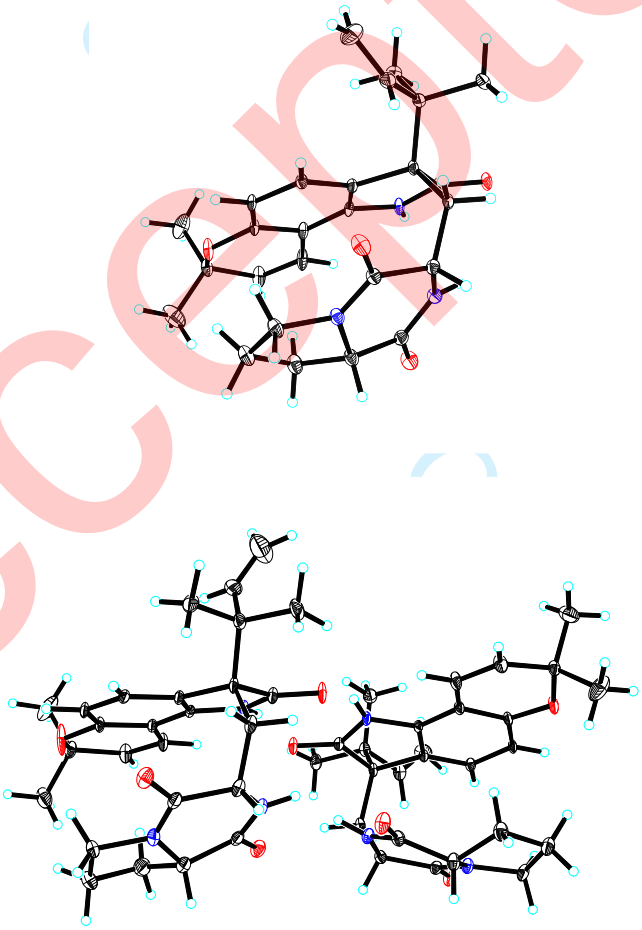


Figure S177 ORTEP drawing of the X-ray crystal structure of **4**

(Displacement ellipsoids are drawn at the 30% probability level).

Table S16 Crystal data and structure refinement for **4**

Identification code	global	
Empirical formula	C26 H31 N3 O4	
Formula weight	449.54	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 14.8956(3) Å	α= 90°.
	b = 10.3642(2) Å	β= 92.7740(10)°.
	c = 15.2100(3) Å	γ= 90°.
Volume	2345.38(8) $Å^3$	
Z	4	
Density (calculated)	1.273 Mg/m^3	
Absorption coefficient	0.698 mm^{-1}	
F(000)	960	
Crystal size	0.640 x 0.350 x 0.240 mm^3	
Theta range for data collection	2.91 to 72.35°.	
Index ranges	-18<=h<=18, -12<=k<=12, -18<=l<=15	
Reflections collected	41160	
Independent reflections	9231 [R(int) = 0.0517]	
Completeness to theta = 72.35°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.85 and 0.61	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	9231 / 1 / 603	
Goodness-of-fit on F^2	1.029	
Final R indices [I>2sigma(I)]	R1 = 0.0414, wR2 = 0.1102	
R indices (all data)	R1 = 0.0419, wR2 = 0.1108	
Absolute structure parameter	0.15(5)	
Largest diff. peak and hole	0.890 and -0.267 $e.Å^{-3}$	

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

NMR spectra of the alkaloids 1-7

NMR spectra of (+)-notoamide B ((+)−1) in acetone-d_6

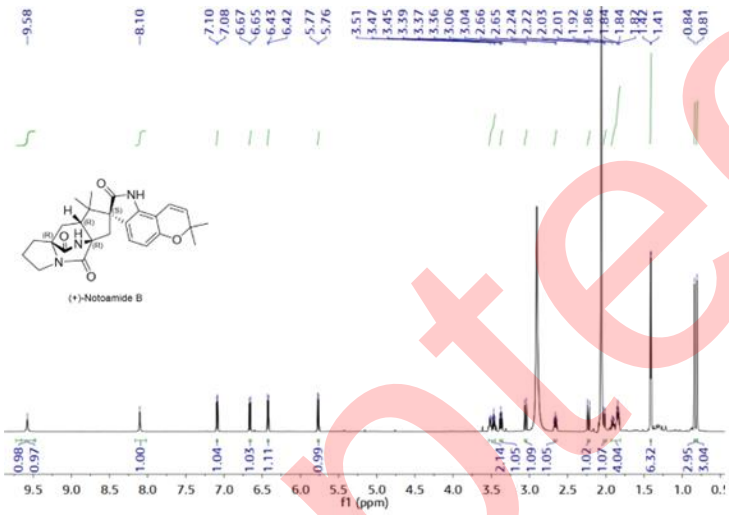


Figure S18 ^{1}H NMR (600 MHz) spectrum of (+)-notoamide B ((+)-**1**))

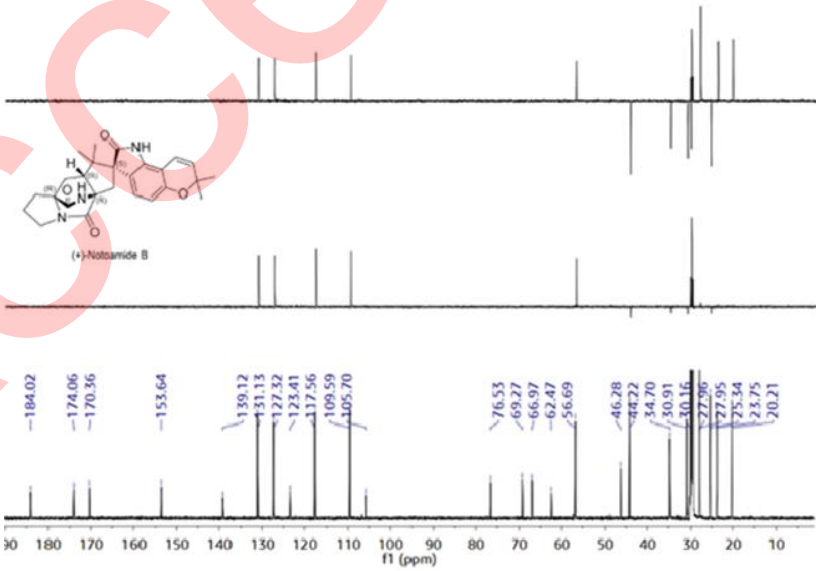


Figure S19 ^{13}C NMR (150 MHz) spectrum of (+)-notoamide B ((+)-**1**))

NMR spectra of (+)-versicolamide B ((+)-2) in DMSO-d_6

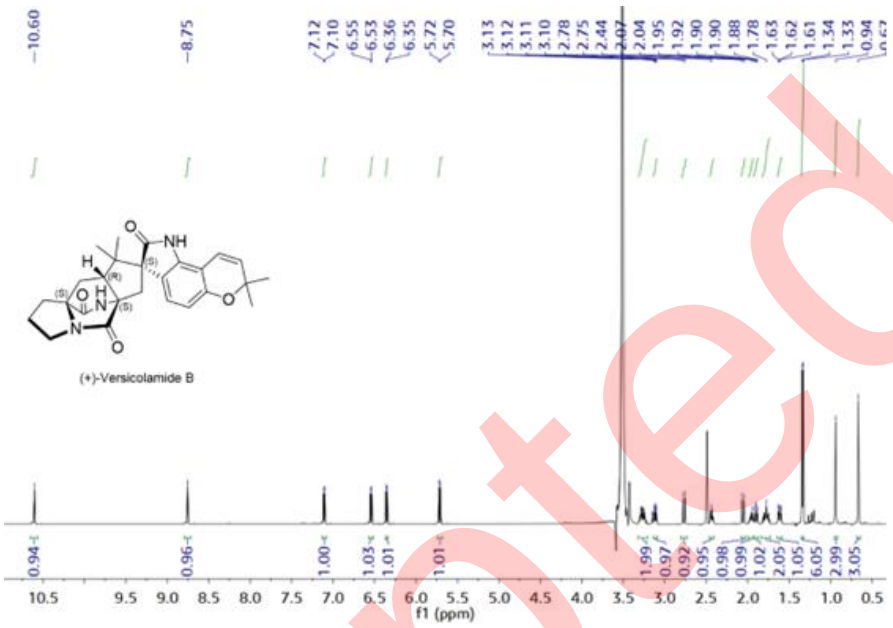


Figure S20 ^{1}H NMR (600 MHz) spectrum of (+)-versicolamide B ((+)-**2**)

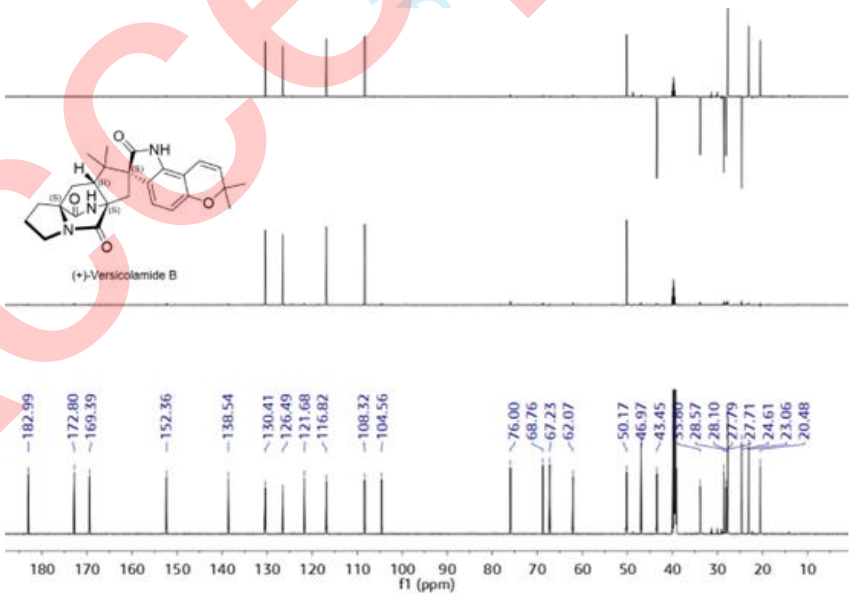


Figure S21 ^{13}C NMR (150 MHz) spectrum of (+)-versicolamide B ((+)-**2**)

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

NMR spectra of notoamide E (3) in acetone-d_6

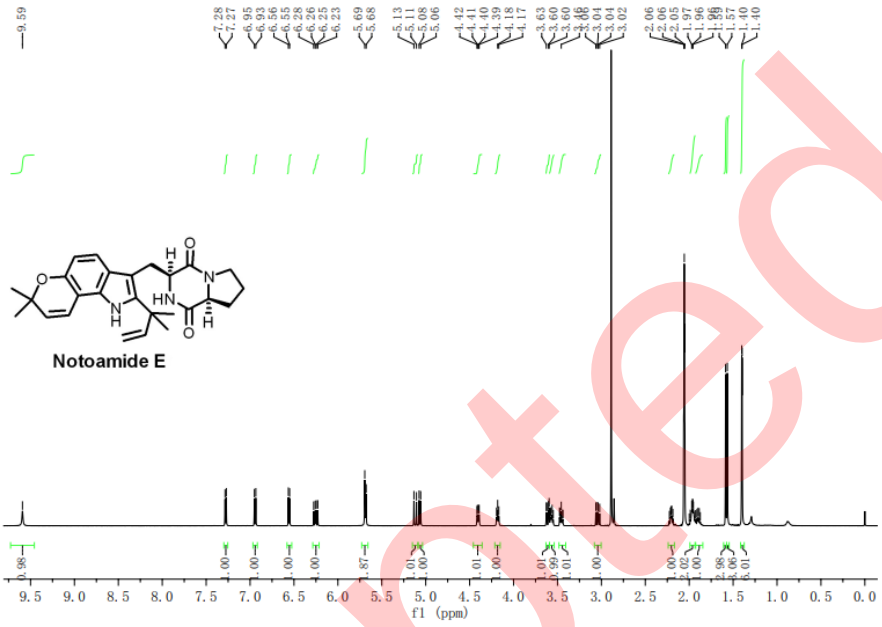


Figure S22 ^{1}H NMR (600 MHz) spectrum of notoamide E (**3**)

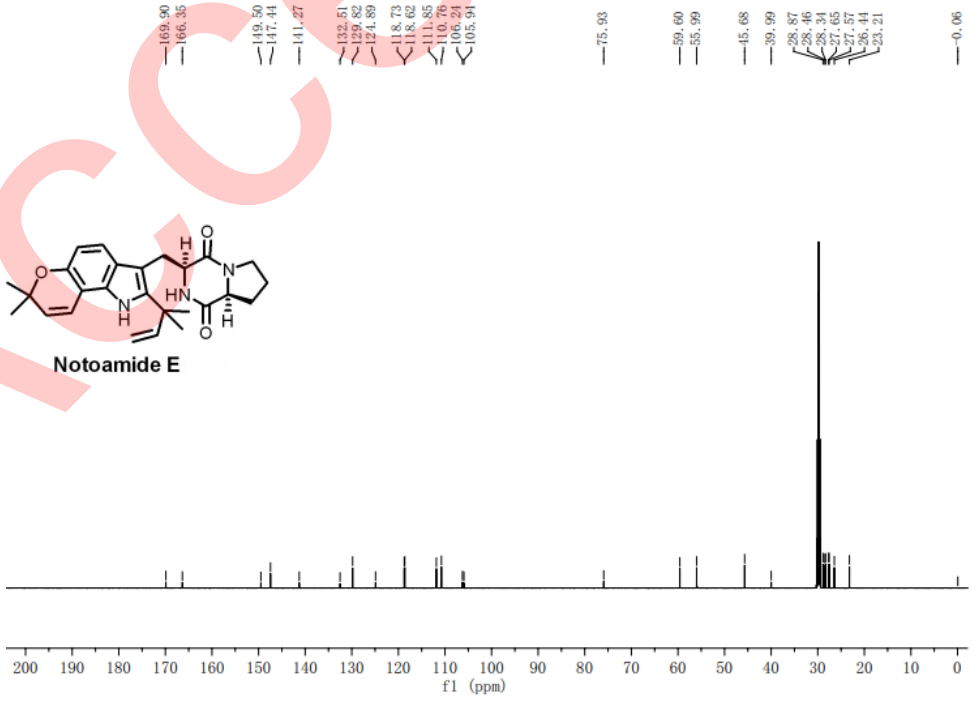


Figure S23 ^{13}C NMR (150 MHz) spectrum of notoamide E (**3**)

NMR spectra of notoamide C (4) in acetone-d_6

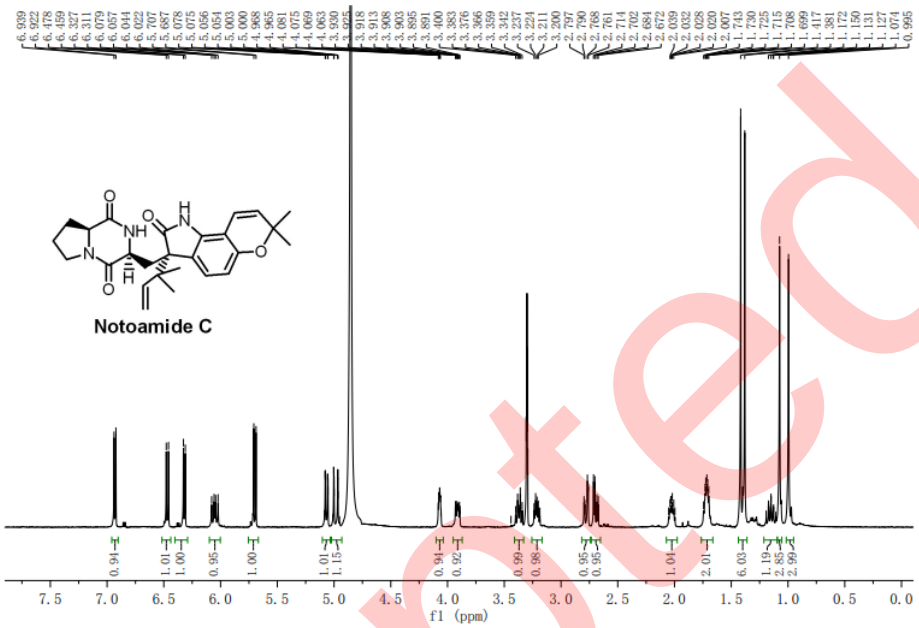


Figure S24 ^{1}H NMR (600 MHz) spectrum of notoamide C (**4**)

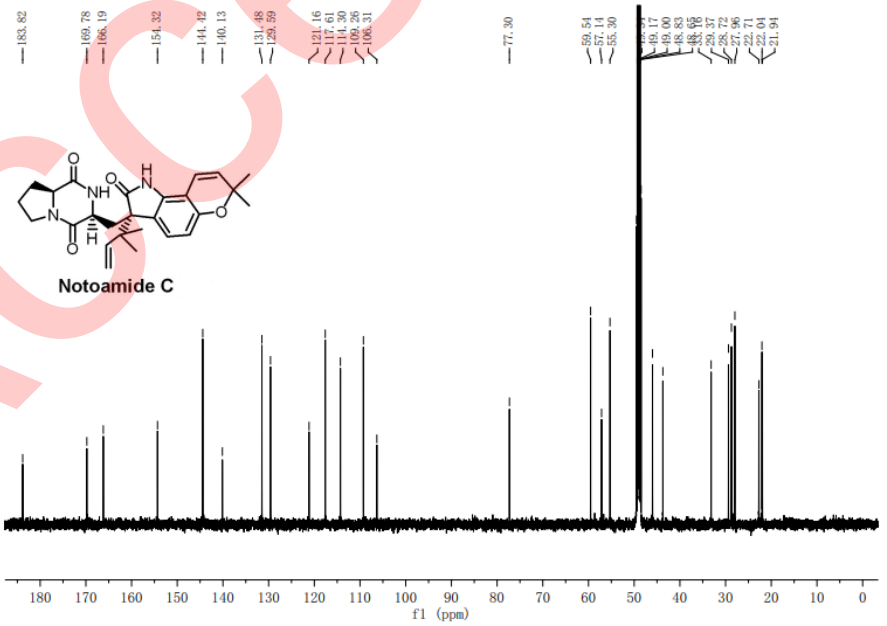


Figure S25 ^{13}C NMR (150 MHz) spectrum of notoamide C (**4**)

NMR spectra of notoamide D (5) in acetone-d_6

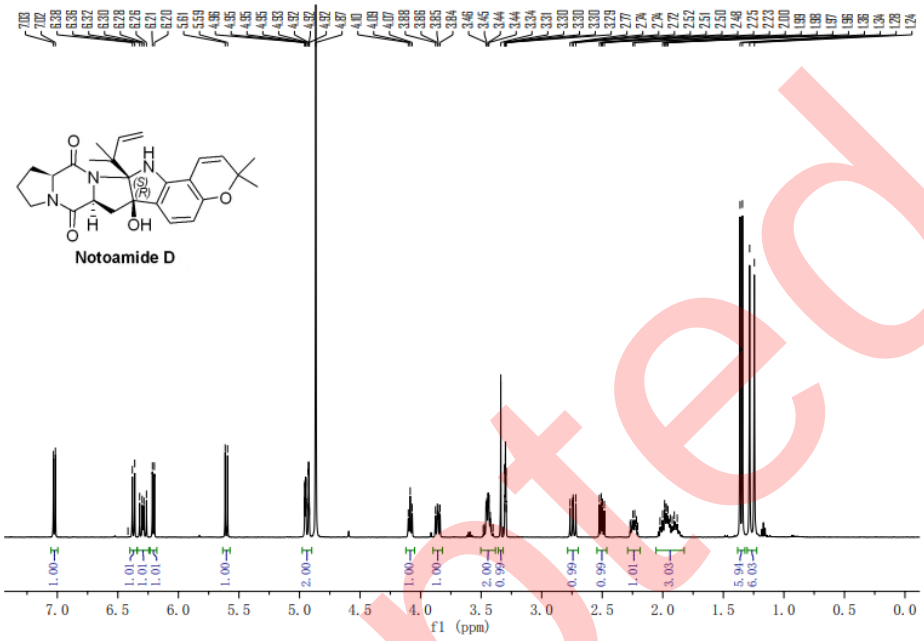


Figure S26 ^{1}H NMR (500 MHz) spectrum of notoamide D (**5**)

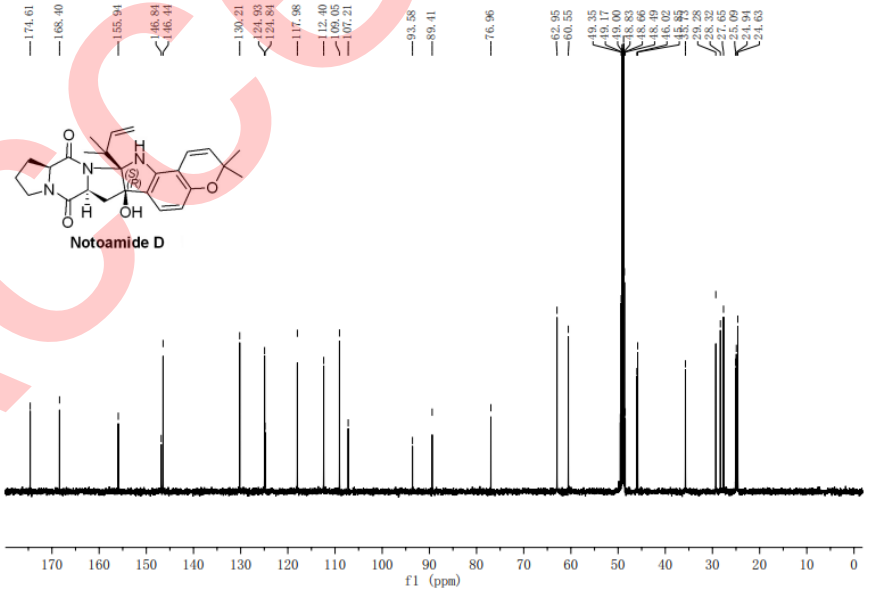


Figure S27 ^{13}C NMR (125 MHz) spectrum of notoamide D (**5**)

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

NMR spectra of notoamide M (6) in pyridine-d_5

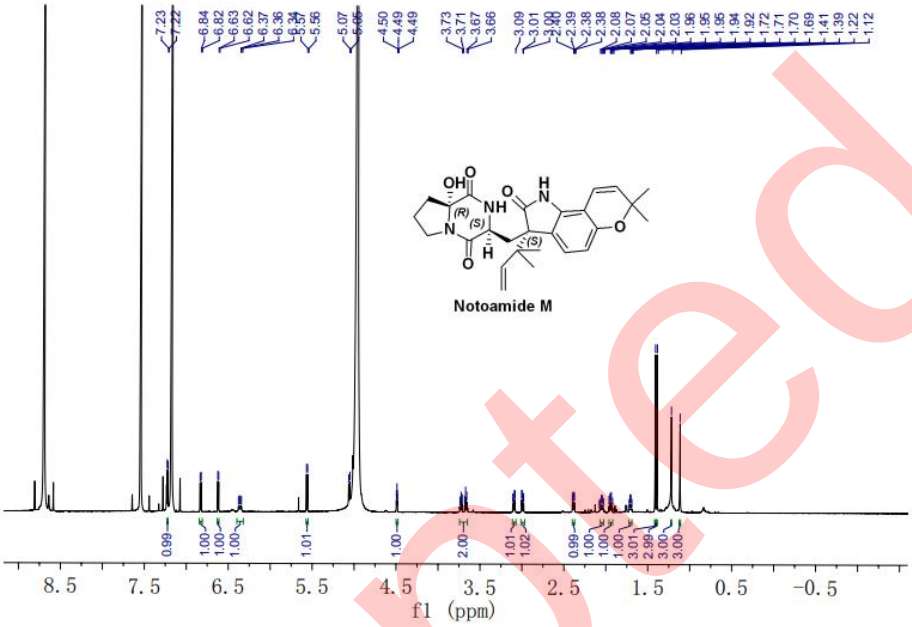


Figure S28 ^{1}H NMR (800 MHz) spectrum of notoamide M (**6**)

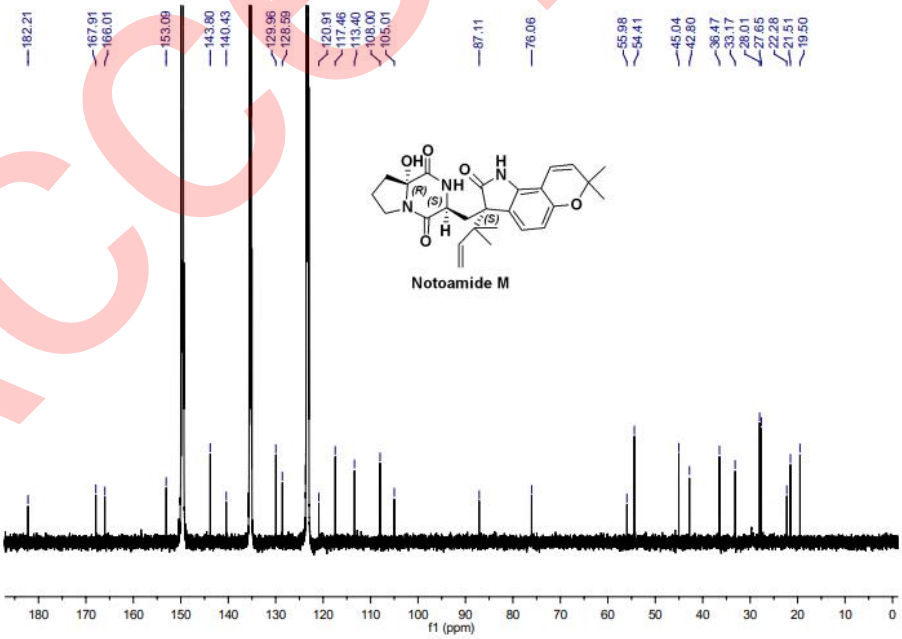


Figure S29 ^{13}C NMR (200 MHz) spectrum of notoamide M (**6**)

NMR spectra of speramide B (7) in DMSO-d_6

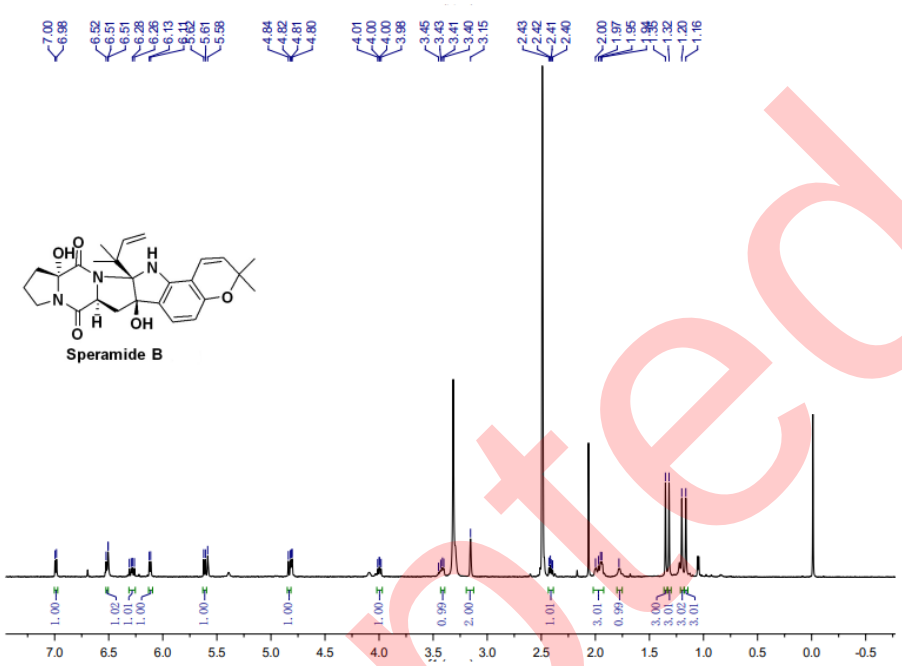


Figure S30 ^{1}H NMR (600 MHz) spectrum of speramide B (**7**)

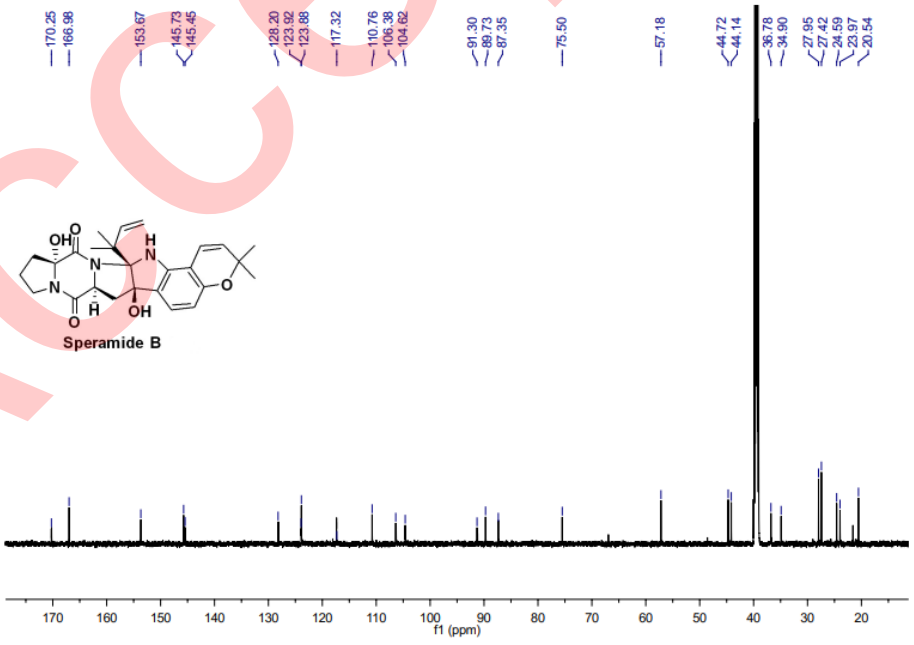
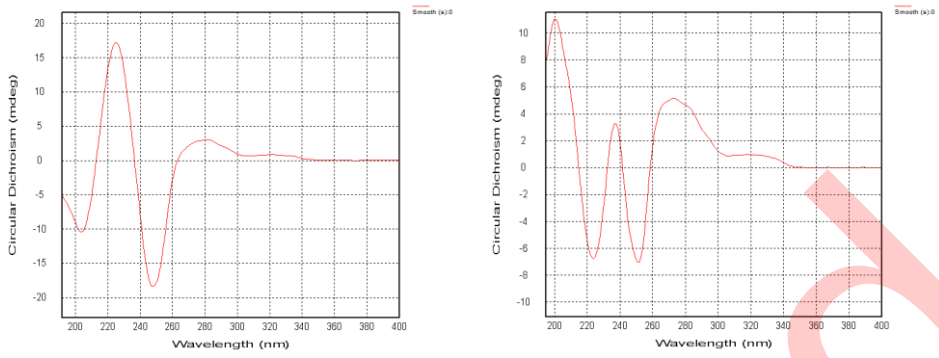


Figure S31 ^{13}C NMR (150 MHz) spectrum of speramide B (**7**)

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english



(+)-(1) **(+)-(2)**

Figure S32 CD spectrum of alkaloids (+)-notoamide B (**(+)-1**) and (+)-versicolamide B (**(+)-2**), in MeOH

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Cartesian coordinates of all species

4a

C	-2.276683	-2.251754	-1.611836
C	-3.487709	-1.699587	-1.001967
C	-3.429247	-0.287240	-0.486918
C	-2.140888	0.363604	-0.621488
C	-1.009251	-0.226567	-1.187418
C	-1.103708	-1.560622	-1.700700
N	-1.770013	1.617618	-0.214771
C	-0.434347	1.862149	-0.504358
C	0.071660	0.717263	-1.116266
C	1.469731	0.429706	-1.590734
C	2.192109	-0.626449	-0.725545
N	2.180154	-0.228656	0.684416
C	3.021868	-0.693262	1.631026
C	4.125337	-1.600746	1.106941
N	4.488351	-1.295063	-0.287625
C	3.630943	-0.845001	-1.218390
O	2.909033	-0.431442	2.834596
C	5.468630	-1.500744	1.839584
C	6.458995	-2.037139	0.791038
C	5.927612	-1.484477	-0.543564
C	0.194627	3.223053	-0.188991
C	1.436937	3.006093	0.671094
C	1.598470	3.322295	1.960031
O	-4.535781	-2.374742	-0.980565
C	-4.532925	0.436277	-0.084399
C	-5.869957	0.057403	0.294106
C	-6.281931	-0.974740	1.082578
C	-0.815540	4.151270	0.514963
C	0.622252	3.908066	-1.515067
H	-2.364636	-3.263926	-1.995734
H	-0.238257	-2.023610	-2.169575
H	-2.372106	2.270941	0.263342
H	1.452678	0.041887	-2.614000
H	2.080594	1.333488	-1.618549
H	5.470612	-2.069253	2.771775
H	5.678899	-0.451070	2.075159
H	7.488673	-1.723670	0.982198
H	6.435529	-3.133062	0.780020
H	6.077712	-2.163864	-1.387577
H	6.374338	-0.517125	-0.801230
H	2.272830	2.537624	0.154850
H	2.535632	3.106877	2.467381
H	-4.397335	1.520381	-0.078404
H	-6.626429	0.796814	0.025785
H	-1.670092	4.364450	-0.136825
H	-0.334314	5.106271	0.746267
H	-1.188350	3.733261	1.456821
H	1.059906	4.891137	-1.304757
H	1.363377	3.316187	-2.059553
H	-0.247389	4.044892	-2.167524
H	1.387026	0.320582	1.005081
H	1.667464	-1.587819	-0.831667
H	3.742613	-2.632386	1.167343
C	-5.367216	-1.971919	1.721567
H	-4.325561	-1.639465	1.736348
H	-5.692951	-2.188190	2.746729
H	-5.395651	-2.911780	1.153764
C	-7.741828	-1.133003	1.415393
H	-8.082509	-2.140362	1.136912
H	-7.906693	-1.039669	2.497760
H	-8.371809	-0.400268	0.901658
O	3.957475	-0.625552	-2.394009
H	0.823282	3.793744	2.557796

TS-6π

C	-2.447148	-2.132532	-1.322118
C	-3.542851	-1.556360	-0.574878
C	-3.428439	-0.151052	-0.170258
C	-2.152276	0.459408	-0.368263
C	-1.060258	-0.173187	-0.982713
C	-1.239709	-1.489378	-1.483575
N	-1.749721	1.729017	-0.045350
C	-0.422323	1.937069	-0.418723
C	0.034324	0.765938	-1.009568
C	1.394775	0.435065	-1.557813
C	2.133368	-0.620497	-0.708203
N	2.247086	-0.168473	0.681387

C	3.118770	-0.661930	1.585238
C	4.114698	-1.663125	1.016722
N	4.408699	-1.412035	-0.404776
C	3.520272	-0.931923	-1.290900
O	3.111975	-0.354257	2.783283
C	5.505744	-1.653067	1.661595
C	6.385739	-2.276127	0.563608
C	5.812586	-1.703781	-0.745039
C	0.243567	3.297531	-0.188423
C	1.527176	3.091846	0.611797
C	1.759118	3.439900	1.881830
O	-4.582438	-2.268762	-0.342849
C	-4.597816	0.626390	-0.001769
C	-5.872153	0.105637	0.188521
C	-6.122062	-1.168088	0.732731
C	-0.712086	4.269896	0.532607
C	0.610773	3.926898	-1.559272
H	-2.589578	-3.146046	-1.685731
H	-0.428050	-1.996373	-2.000721
H	-2.311972	2.396319	0.460863
H	1.308255	0.022655	-2.568373
H	2.028055	1.319891	-1.643050
H	5.525356	-2.207158	2.602289
H	5.806996	-0.618914	1.864585
H	7.445785	-2.037970	0.684700
H	6.280652	-3.367242	0.573881
H	5.862358	-2.402268	-1.585268
H	6.308763	-0.773400	-1.045253
H	2.331871	2.602783	0.065287
H	2.719729	3.228492	2.345174
H	-4.520279	1.687333	-0.245407
H	-6.716901	0.661398	-0.218495
H	-1.597927	4.471576	-0.079840
H	-0.204456	5.224744	0.699703
H	-1.039653	3.895723	1.509012
H	1.076491	4.908214	-1.408946
H	1.310488	3.301108	-2.120431
H	-0.290309	4.057469	-2.169065
H	1.515248	0.444612	1.031449
H	1.557478	-1.557751	-0.734854
H	3.659076	-2.660788	1.125236
C	-5.451852	-1.626109	1.998090
H	-4.472139	-1.167754	2.141744
H	-6.098091	-1.328639	2.837903
H	-5.353731	-2.715169	2.020106
C	-7.406809	-1.872360	0.408330
H	-7.195820	-2.930808	0.218757
H	-8.089194	-1.832678	1.268926
H	-7.908105	-1.447739	-0.465646
O	3.781204	-0.759754	-2.490590
H	1.020466	3.934637	2.506572

5

C	-2.983546	-0.979031	-1.926651
C	-3.733008	-0.460159	-0.854712
C	-3.217323	0.510325	0.020581
C	-1.887919	0.908263	-0.213616
C	-1.102841	0.397283	-1.278102
C	-1.674649	-0.554156	-2.145675
N	-1.100344	1.806386	0.460797
C	0.162702	1.898006	-0.124123
C	0.199505	1.026412	-1.202655
C	1.303736	0.645605	-2.154783
C	2.216510	-0.538247	-1.711637
N	1.485440	-1.485986	-0.866041
C	2.026710	-2.334206	0.029604
C	3.540599	-2.269306	0.137828
N	4.066813	-0.930052	-0.167919
C	3.520254	-0.068734	-1.040731
O	4.049357	1.010656	-1.340593
O	1.358394	-3.130385	0.702353
C	4.119700	-2.556700	1.527291
C	5.502939	-1.884655	1.455398
C	5.263407	-0.608157	0.627411
C	1.204433	2.810336	0.509850
C	2.151571	2.028273	1.413242
C	2.005048	0.769614	1.834126
O	-5.036160	-0.877485	-0.730816
C	-4.095541	1.044463	1.053685
C	-5.260917	0.430145	1.318076
C	-5.631797	-0.856206	0.607933
C	2.025400	3.559728	-0.569622
C	0.531272	3.895397	1.396671
C	-7.136697	-0.952136	0.364836
C	-5.112330	-2.073666	1.388971
H	-3.447536	-1.717007	-2.574274
H	-1.108547	-0.964427	-2.978374

H	-1.395711	2.343372	1.261108
H	0.838953	0.355474	-3.103202
H	1.964107	1.480105	-2.388056
H	4.167077	-3.626943	1.738618
H	3.491821	-2.083903	2.290387
H	5.914605	-1.659426	2.442812
H	6.210684	-2.541435	0.936714
H	6.101612	-0.353359	-0.027919
H	5.043837	0.264291	1.253298
H	3.008676	2.608955	1.759673
H	2.727081	0.317283	2.508832
H	1.175914	0.145427	1.511864
H	-3.809387	1.948559	1.585973
H	-5.948211	0.805884	2.071694
H	2.690240	4.284476	-0.084596
H	1.356593	4.106742	-1.243731
H	2.650105	2.882014	-1.150098
H	-0.171330	4.500901	0.811757
H	0.006252	3.467248	2.258095
H	1.300260	4.564014	1.797350
H	-7.669708	-0.975677	1.321427
H	-7.489355	-0.090327	-0.211290
H	-7.372868	-1.867496	-0.187946
H	-5.552301	-2.094214	2.392270
H	-5.379514	-3.000023	0.867334
H	-4.022971	-2.025320	1.491020
H	0.473877	-1.512737	-0.948994
H	2.543603	-1.054343	-2.627360
H	3.942759	-2.993796	-0.588983

tau-mA

C	-1.909109	-2.261382	0.427422
C	-3.075513	-1.688519	-0.093386
C	-3.148420	-0.325919	-0.468936
C	-1.993445	0.435574	-0.261383
C	-0.809861	-0.129171	0.250191
C	-0.763781	-1.476102	0.597653
N	-1.821818	1.807904	-0.456077
C	-0.467820	2.173669	-0.239143
C	0.213868	0.946338	0.263089
C	1.404000	0.907541	1.201686
C	2.479279	-0.057735	0.767443
N	2.775347	-1.132136	1.560984
C	3.761266	-2.089282	1.335125
C	4.519588	-1.825929	0.129197
N	4.224135	-0.784289	-0.638964
C	3.216750	0.113649	-0.387621
O	3.092656	1.099367	-1.282956
O	3.953485	-3.042581	2.094275
C	5.638050	-2.632622	-0.432278
C	6.232343	-1.692633	-1.508393
C	5.094038	-0.719055	-1.856653
C	-0.174081	3.652350	0.058124
C	-0.340477	3.946221	1.541885
C	-0.859433	3.152630	2.483258
O	-4.145978	-2.509467	-0.294269
C	-4.390833	0.162781	-1.054790
C	-5.496280	-0.597218	-1.002641
C	-5.493614	-1.923820	-0.274290
C	1.249030	4.054273	-0.394656
C	-1.169564	4.556423	-0.719766
C	-6.372143	-2.956552	-0.976999
C	-5.907852	-1.735436	1.192727
H	-1.911921	-3.314867	0.687240
H	0.142575	-1.929726	0.986088
H	-2.386420	2.317259	-1.122336
H	1.845487	1.902112	1.293247
H	1.046917	0.640264	2.199701
H	5.227378	-3.558978	-0.858438
H	6.349282	-2.925963	0.344752
H	4.478320	-1.039205	-2.701822
H	5.405528	0.313078	-2.012646
H	-0.011017	4.948037	1.821409
H	-0.942075	3.491990	3.512422
H	-1.227888	2.151292	2.275483
H	-4.406417	1.132661	-1.545087
H	-6.436543	-0.267747	-1.436657
H	1.405755	5.116243	-0.180082
H	1.367797	3.903158	-1.471696
H	2.037763	3.499772	0.117924
H	-1.098903	4.379729	-1.799965
H	-2.202197	4.402254	-0.393607
H	-0.922547	5.606911	-0.536696
H	-7.414774	-2.621650	-0.976914
H	-6.048918	-3.095690	-2.013716
H	-6.314916	-3.917934	-0.456078
H	-6.918716	-1.316856	1.247788

H	-5.895351	-2.698554	1.715466
H	-5.221865	-1.047174	1.698012
H	2.248318	-1.259953	2.423302
O	0.492484	1.446418	-1.111346
H	2.151078	1.431519	-1.301165
H	7.078541	-1.138896	-1.092781
H	6.574989	-2.233768	-2.391569

TS-mA-SSR

C	-3.710600	-2.187341	0.307389
C	-4.394009	-1.011653	-0.025349
C	-3.721884	0.192203	-0.348909
C	-2.325564	0.154065	-0.290167
C	-1.627307	-1.025670	0.022828
C	-2.310896	-2.197154	0.329583
N	-1.424002	1.213495	-0.464176
C	-0.091049	0.722600	-0.419214
C	-0.180506	-0.715171	-0.083508
C	0.837942	-1.557292	0.648118
C	2.253399	-1.057900	0.556016
N	2.908423	-0.767432	1.735772
C	4.175292	-0.227243	1.795973
C	4.733451	-0.012867	0.447988
N	4.321660	-0.884552	-0.549200
C	3.024708	-1.236256	-0.600172
O	2.549803	-1.724817	-1.752928
O	4.731354	0.082966	2.847338
C	6.190727	0.294997	0.223609
C	6.364559	0.058120	-1.292557
C	5.308194	-1.004416	-1.654277
C	1.003175	1.737383	-0.048660
C	3.605368	1.661618	0.037049
O	-5.755446	-1.070813	-0.091434
C	-4.523305	1.348556	-0.731635
C	-5.852017	1.331516	-0.540773
C	-6.525203	0.159219	0.139449
C	0.760024	3.058275	-0.842088
C	0.900845	2.038457	1.458394
C	-7.900138	-0.128969	-0.459431
C	-6.608157	0.389560	1.655894
H	-4.283556	-3.079062	0.539859
H	-1.777023	-3.110074	0.578115
H	-1.651047	1.979676	-1.085193
H	0.535424	-1.631598	1.696626
H	0.793819	-2.575380	0.238655
H	6.789986	-0.404720	0.819562
H	6.449854	1.305989	0.544804
H	6.171278	0.980952	-1.847304
H	7.371761	-0.278579	-1.544702
H	5.702930	-2.023853	-1.638029
H	4.810336	-0.831242	-2.609534
H	-4.038880	2.209409	-1.184843
H	-6.479731	2.172806	-0.822408
H	1.569659	3.763597	-0.635123
H	-0.176805	3.527876	-0.524023
H	0.724207	2.880589	-1.922318
H	-0.116765	2.357386	1.700249
H	1.134686	1.164443	2.069802
H	1.582231	2.846865	1.739282
H	-8.564425	0.726341	-0.296982
H	-7.821100	-0.311875	-1.535971
H	-8.342741	-1.009444	0.017890
H	-7.192413	1.291557	1.868783
H	-7.090128	-0.466219	2.142052
H	-5.605940	0.520467	2.077749
H	2.409688	-0.857133	2.616448
O	0.212092	-0.306648	-1.456381
H	1.631220	-1.374966	-1.877366
H	4.359926	1.975437	-0.679381
H	3.631830	2.208661	0.976181
C	2.370517	1.266141	-0.503109
H	2.381337	0.961347	-1.547051

TS-mA-RRR

C	-3.425564	-2.199150	0.196171
C	-4.048282	-0.954384	0.354576
C	-3.379868	0.265199	0.094113
C	-2.061603	0.166526	-0.364149
C	-1.434722	-1.079598	-0.566874
C	-2.108435	-2.263191	-0.269781
N	-1.166376	1.204096	-0.619064
C	0.044745	0.678868	-1.169328
C	-0.083254	-0.813998	-1.127361
C	1.017596	-1.859914	-1.027610
C	2.256613	-1.357917	-0.346360
N	3.486386	-1.843741	-0.764709

C	4.683040	-1.291813	-0.363466
C	4.477220	-0.191819	0.593856
N	3.367333	-0.264626	1.404568
C	2.218440	-0.764863	0.926476
O	1.131467	-0.564812	1.681021
O	5.779739	-1.639952	-0.800363
C	5.591725	0.467547	1.355906
C	4.840161	1.261310	2.446225
C	3.549910	0.460362	2.693774
C	1.274379	1.604130	-1.122371
C	3.821443	1.177576	-0.942860
O	-5.314444	-0.944115	0.858860
C	-4.073909	1.510656	0.396433
C	-5.390637	1.492634	0.658074
C	-6.181847	0.205678	0.563309
C	1.138179	2.599780	-2.314331
C	1.307714	2.408571	0.190987
C	-6.747994	0.019702	-0.852096
C	-7.280856	0.138373	1.621341
H	-3.985564	-3.099910	0.425191
H	-1.637771	-3.230848	-0.420437
H	-1.502458	2.110861	-0.918694
H	0.640835	-2.746941	-0.503467
H	1.269996	-2.185967	-2.040732
H	6.216189	1.089434	0.710803
H	6.234655	-0.312820	1.783218
H	5.424662	1.367642	3.361652
H	4.591303	2.262931	2.083209
H	2.673887	1.074492	2.902442
H	3.653947	-0.292982	3.479638
H	-3.508412	2.438332	0.434604
H	-5.937689	2.398932	0.903764
H	1.986656	3.290681	-2.318191
H	0.219721	3.190624	-2.219506
H	1.110684	2.069650	-3.270623
H	0.414849	3.030875	0.281230
H	1.344339	1.767072	1.071911
H	2.170372	3.080305	0.206196
H	-7.418825	0.849260	-1.101185
H	-5.937215	-0.001064	-1.588029
H	-7.309537	-0.919382	-0.914323
H	-8.005376	0.943409	1.459338
H	-7.805766	-0.820574	1.560030
H	-6.856132	0.245982	2.624693
H	3.518482	-2.495107	-1.544201
O	-0.121244	-0.079755	-2.397631
H	0.380920	-1.130430	1.422579
H	4.676051	0.951065	-1.574068
H	3.945006	2.048280	-0.307000
C	2.549271	0.818650	-1.390263
H	2.495868	0.191655	-2.277054

Prod-mA-SSR

C	-3.690337	-2.213487	0.146380
C	-4.391612	-1.010291	0.012192
C	-3.755528	0.206189	-0.336426
C	-2.367665	0.154702	-0.509819
C	-1.654454	-1.059614	-0.409073
C	-2.307018	-2.239893	-0.073575
N	-1.486725	1.217824	-0.745493
C	-0.185560	0.690231	-1.003645
C	-0.244349	-0.760756	-0.756936
C	0.941794	-1.581715	-0.326848
C	2.194667	-0.734295	-0.036134
N	2.283983	-0.387822	1.390659
C	3.367156	0.311522	1.819491
C	4.349969	0.498291	0.646283
N	4.564347	-0.854415	0.049187
C	3.505412	-1.490755	-0.331963
O	3.647780	-2.650881	-0.923223
O	3.539602	0.743000	2.953002
C	5.764931	0.946567	1.016700
C	6.680910	0.154049	0.060854
C	5.992942	-1.211716	-0.084281
C	1.042979	1.547706	-0.752888
C	3.626842	1.325401	-0.446143
O	-5.748276	-1.050409	0.167073
C	-4.586364	1.391846	-0.509847
C	-5.867098	1.375820	-0.107192
C	-6.441894	0.168620	0.601760
C	1.153660	2.612497	-1.867792
C	0.864429	2.247225	0.613981
C	-7.903493	-0.066223	0.225415
C	-6.267604	0.301065	2.122232
H	-4.236177	-3.113152	0.411615
H	-1.759345	-3.174477	0.013332
H	-1.794272	2.051654	-1.230257

H	0.699841	-2.192795	0.548016
H	1.127400	-2.276817	-1.153021
H	5.963492	0.683477	2.059974
H	5.878983	2.027695	0.912396
H	6.739784	0.645504	-0.915602
H	7.695736	0.050093	0.450315
H	6.247360	-1.899169	0.728441
H	6.158244	-1.707683	-1.041966
H	-4.166926	2.274183	-0.986439
H	-6.516889	2.237717	-0.233923
H	2.040402	3.239114	-1.726141
H	0.281612	3.275762	-1.855817
H	1.215642	2.143899	-2.855660
H	0.067775	2.992344	0.541471
H	0.585831	1.548134	1.404813
H	1.770943	2.772419	0.925506
H	-8.513515	0.784813	0.546138
H	-8.008187	-0.183810	-0.858058
H	-8.279428	-0.969318	0.717467
H	-6.792107	1.192072	2.484883
H	-6.677711	-0.580435	2.628215
H	-5.207068	0.397017	2.378381
H	1.553485	-0.649692	2.043279
O	-0.102818	-0.226508	-2.129800
H	2.800824	-3.071787	-1.158439
H	4.301217	1.426160	-1.300130
H	3.455496	2.327952	-0.053007
C	2.305822	0.616953	-0.864296
H	2.374780	0.318767	-1.913261

Prod-mA-RRR

C	-3.551583	-2.170249	0.249229
C	-4.186888	-0.928320	0.366916
C	-3.521894	0.292196	0.096158
C	-2.193038	0.196414	-0.328342
C	-1.555031	-1.051211	-0.492322
C	-2.222172	-2.233033	-0.185933
N	-1.297102	1.244241	-0.578779
C	-0.081340	0.697671	-1.095382
C	-0.197737	-0.776894	-1.023503
C	0.990048	-1.693797	-0.870017
C	2.266101	-0.934936	-0.485708
N	3.446139	-1.727345	-0.866308
C	4.680790	-1.253859	-0.556329
C	4.525233	0.102367	0.158393
N	3.581603	-0.129264	1.298994
C	2.441450	-0.670977	1.010426
O	1.576267	-0.906775	1.967122
O	5.747942	-1.790969	-0.824827
C	5.778121	0.652625	0.843347
C	5.269223	1.238825	2.177187
C	4.134316	0.296674	2.603218
C	1.220584	1.476614	-0.944240
C	3.810981	1.038992	-0.854340
O	-5.464797	-0.916553	0.844500
C	-4.231731	1.537661	0.359954
C	-5.553711	1.514614	0.593346
C	-6.332834	0.219713	0.505034
C	1.290402	2.568720	-2.034329
C	1.224506	2.150166	0.445971
C	-6.864038	0.002574	-0.919570
C	-7.457014	0.165214	1.537264
H	-4.109395	-3.070412	0.486258
H	-1.734586	-3.196933	-0.303984
H	-1.636737	2.125020	-0.946858
H	0.785778	-2.504595	-0.161864
H	1.165053	-2.175398	-1.837288
H	6.275424	1.398005	0.218835
H	6.481418	-0.167354	1.016264
H	6.054147	1.284982	2.934995
H	4.878019	2.250816	2.031730
H	3.350191	0.765715	3.199801
H	4.500725	-0.594591	3.122400
H	-3.673121	2.469769	0.392818
H	-6.112598	2.421054	0.810428
H	2.230132	3.127205	-1.965117
H	0.472596	3.288153	-1.915793
H	1.221763	2.129711	-3.034774
H	0.442563	2.912352	0.485076
H	1.016573	1.452620	1.260532
H	2.173356	2.651732	0.648302
H	-7.535128	0.821904	-1.200003
H	-6.035975	-0.025459	-1.635775
H	-7.416850	-0.941985	-0.977248
H	-8.183059	0.961320	1.341446
H	-7.973454	-0.798735	1.482681
H	-7.057805	0.296147	2.548320

H	3.339293	-2.637999	-1.300029
O	-0.219012	-0.070266	-2.318870
H	0.754042	-1.324387	1.647460
H	4.435683	1.107776	-1.748155
H	3.763761	2.039144	-0.421812
C	2.403085	0.475468	-1.196593
H	2.375537	0.218118	-2.258408

tau-mB

C	-3.375088	-2.160459	0.776159
C	-4.208840	-1.194467	0.202481
C	-3.701737	-0.013684	-0.388631
C	-2.312109	0.154163	-0.347512
C	-1.458318	-0.819788	0.200193
C	-1.987151	-1.972343	0.773359
N	-1.571385	1.258942	-0.763279
C	-0.169207	0.975149	-0.681183
C	-0.052333	-0.363094	-0.015838
C	0.999103	-0.953878	0.919116
C	2.437966	-0.936460	0.483262
N	2.813183	-1.820054	-0.439991
C	4.084929	-1.911775	-0.819267
C	5.070459	-1.094539	-0.260934
N	4.668165	-0.202027	0.675266
C	3.389275	-0.078434	1.078946
O	3.170193	0.839327	2.018617
O	4.339524	-2.849737	-1.753633
C	6.551229	-1.004407	-0.477438
C	6.904634	0.360231	0.162439
C	5.808299	0.599577	1.210869
C	0.758141	2.207865	-0.671304
C	1.034125	2.684761	0.745058
C	0.386640	2.338944	1.867846
O	-5.549508	-1.454825	0.168550
C	-4.646599	0.908124	-1.007207
C	-5.964367	0.751745	-0.801962
C	-6.483415	-0.322409	0.129666
C	2.077608	1.924093	-1.421720
C	0.084455	3.406499	-1.401880
C	-7.794737	-0.921524	-0.374651
C	-6.626760	0.224504	1.558084
H	-3.821263	-3.049366	1.210366
H	-1.344959	-2.732116	1.209707
H	-1.915200	1.849631	-1.508830
H	0.880980	-0.502803	1.908459
H	0.751597	-2.013661	1.039131
H	6.820583	-1.053453	-1.537055
H	7.047551	-1.840742	0.032921
H	7.897331	0.362100	0.614850
H	6.867192	1.146651	-0.596621
H	5.492481	1.637121	1.314959
H	6.051415	0.195879	2.197817
H	1.817315	3.442119	0.808779
H	0.630991	2.808079	2.817987
H	-0.427397	1.619154	1.875450
H	-4.276760	1.705172	-1.647287
H	-6.696098	1.414469	-1.256493
H	2.728583	2.802971	-1.369770
H	1.871774	1.704794	-2.473185
H	2.623468	1.074453	-1.016869
H	-0.148110	3.147136	-2.441827
H	-0.827715	3.732679	-0.895422
H	0.776054	4.254853	-1.420789
H	-8.572097	-0.150585	-0.400653
H	-7.669593	-1.327098	-1.383886
H	-8.123914	-1.725712	0.291693
H	-7.331148	1.063540	1.572422
H	-6.998150	-0.559679	2.227629
H	-5.659510	0.580027	1.929064
O	0.264211	-0.198826	-1.434125
H	2.266908	1.235387	1.945318
H	5.285373	-2.896899	-1.974828

TS-mB-SSR

C	-3.723616	-2.174749	0.362076
C	-4.406054	-1.007932	-0.000595
C	-3.733233	0.188095	-0.351387
C	-2.336843	0.151837	-0.289524
C	-1.638845	-1.020803	0.052286
C	-2.323319	-2.183564	0.386744
N	-1.434602	1.207503	-0.486650
C	-0.103167	0.711757	-0.430472
C	-0.191484	-0.713267	-0.060315
C	0.838740	-1.502274	0.704486
C	2.258657	-1.002495	0.589972
N	2.890655	-0.733097	1.770768

C	4.101481	-0.260122	1.710025
C	4.703463	0.014392	0.423758
N	4.301237	-0.896874	-0.569961
C	3.015505	-1.246752	-0.591337
O	2.536815	-1.813609	-1.698411
O	4.689813	0.080526	2.867329
C	6.167044	0.320143	0.177200
C	6.324881	0.060009	-1.338578
C	5.288014	-1.031033	-1.667651
C	1.001303	1.714938	-0.061563
C	3.610226	1.626288	-0.017685
O	-5.768183	-1.068498	-0.069327
C	-4.534459	1.335090	-0.761691
C	-5.863497	1.322852	-0.571982
C	-6.537117	0.166304	0.134454
C	0.774868	3.039572	-0.849696
C	0.909314	2.006257	1.448816
C	-7.912393	-0.134781	-0.457491
C	-6.620461	0.430990	1.645351
H	-4.296990	-3.060530	0.615583
H	-1.788853	-3.089347	0.659255
H	-1.659393	1.957571	-1.128086
H	0.569513	-1.493920	1.763579
H	0.791786	-2.548025	0.368693
H	6.789605	-0.373534	0.756891
H	6.431572	1.340342	0.465796
H	6.105941	0.969495	-1.904890
H	7.336817	-0.258238	-1.595148
H	5.704735	-2.040840	-1.624045
H	4.789314	-0.893426	-2.628639
H	-4.049351	2.185414	-1.233770
H	-6.490808	2.157592	-0.873428
H	1.589472	3.737452	-0.635740
H	-0.160475	3.515864	-0.536715
H	0.744053	2.866705	-1.931087
H	-0.105402	2.329825	1.698502
H	1.149701	1.125068	2.048777
H	1.595633	2.811635	1.728692
H	-8.576671	0.723909	-0.313931
H	-7.833750	-0.341687	-1.529727
H	-8.354973	-1.004366	0.039448
H	-7.205389	1.337237	1.837465
H	-7.102019	-0.413813	2.150806
H	-5.618444	0.571946	2.064397
O	0.197628	-0.340238	-1.446894
H	1.596503	-1.525508	-1.806746
H	4.326786	1.953675	-0.767172
H	3.645960	2.212446	0.897966
C	2.356954	1.208546	-0.517097
H	2.348668	0.891575	-1.557358
H	5.621069	0.331509	2.741328

TS-mB-RRR

C	-3.441580	-2.197181	0.234162
C	-4.067722	-0.951260	0.367362
C	-3.400672	0.265148	0.088750
C	-2.079778	0.161698	-0.360840
C	-1.449178	-1.086715	-0.539145
C	-2.121833	-2.266264	-0.224510
N	-1.185530	1.197189	-0.629184
C	0.027740	0.661413	-1.168270
C	-0.095821	-0.829835	-1.100385
C	1.014939	-1.857955	-0.978457
C	2.274629	-1.333300	-0.345936
N	3.466364	-1.865577	-0.775399
C	4.550844	-1.303715	-0.327310
C	4.470552	-0.158296	0.540511
N	3.367184	-0.202255	1.394002
C	2.231677	-0.724400	0.944369
O	1.167761	-0.603825	1.738900
O	5.771574	-1.674170	-0.736526
C	5.609807	0.496316	1.281355
C	4.885448	1.318240	2.370610
C	3.594200	0.533342	2.664500
C	1.263738	1.574258	-1.120900
C	3.813782	1.152655	-0.947479
O	-5.336623	-0.934447	0.865696
C	-4.098974	1.514187	0.365270
C	-5.417090	1.498057	0.620117
C	-6.204746	0.207600	0.544078
C	1.144768	2.569953	-2.312829
C	1.290281	2.379284	0.192847
C	-6.762266	-0.005421	-0.870992
C	-7.310059	0.157338	1.596524
H	-4.000689	-3.094971	0.476807
H	-1.646698	-3.234564	-0.355611
H	-1.523174	2.095488	-0.951954

H	0.654291	-2.726858	-0.412328
H	1.268693	-2.225036	-1.976149
H	6.232009	1.103561	0.620363
H	6.246590	-0.282479	1.718087
H	5.491076	1.438860	3.270493
H	4.637324	2.314472	1.993192
H	2.730945	1.160440	2.889947
H	3.715099	-0.207722	3.459646
H	-3.535492	2.443606	0.389749
H	-5.967456	2.407324	0.846781
H	2.000170	3.252576	-2.312596
H	0.231776	3.170723	-2.225707
H	1.118629	2.038845	-3.268773
H	0.411040	3.023511	0.261701
H	1.288645	1.739590	1.076300
H	2.167980	3.030062	0.228721
H	-7.434395	0.817319	-1.138564
H	-5.947267	-0.036599	-1.601884
H	-7.320372	-0.947365	-0.919651
H	-8.035469	0.957352	1.414850
H	-7.832321	-0.803898	1.550260
H	-6.891784	0.285019	2.600244
O	-0.136129	-0.113186	-2.383902
H	0.385869	-1.076251	1.397112
H	4.656992	0.958011	-1.604563
H	3.923777	2.046726	-0.341371
C	2.533707	0.769350	-1.379336
H	2.483215	0.160284	-2.278320
H	5.683844	-2.375490	-1.410461

Prod-mB-SSR

C	-3.694401	-2.209814	0.204664
C	-4.394085	-1.010312	0.037115
C	-3.756495	0.195252	-0.345110
C	-2.368698	0.137173	-0.518764
C	-1.656756	-1.074406	-0.384111
C	-2.310584	-2.243301	-0.014316
N	-1.486564	1.192313	-0.783178
C	-0.184410	0.654505	-1.023879
C	-0.244249	-0.788074	-0.735455
C	0.937426	-1.598994	-0.280332
C	2.189567	-0.745287	-0.002910
N	2.223514	-0.346987	1.419990
C	3.285830	0.297482	1.714982
C	4.338821	0.487242	0.626144
N	4.556557	-0.869720	0.056029
C	3.485559	-1.510337	-0.287955
O	3.617625	-2.700404	-0.823009
O	3.415305	0.841430	2.932724
C	5.758433	0.937552	0.995039
C	6.665485	0.147683	0.027319
C	5.982167	-1.222833	-0.096052
C	1.043784	1.519700	-0.798200
C	3.627450	1.300644	-0.493338
O	-5.751648	-1.043611	0.193399
C	-4.585392	1.377741	-0.546717
C	-5.865041	1.375174	-0.139924
C	-6.440213	0.187168	0.600823
C	1.152224	2.552243	-1.943367
C	0.866463	2.255861	0.548359
C	-7.903953	-0.052518	0.236043
C	-6.259854	0.356584	2.117017
H	-4.240973	-3.101043	0.495850
H	-1.762934	-3.174909	0.100550
H	-1.792704	2.007559	-1.299593
H	0.695524	-2.156717	0.628029
H	1.109582	-2.328847	-1.080789
H	5.997393	0.650574	2.026098
H	5.874875	2.019289	0.901708
H	6.702566	0.637840	-0.950402
H	7.686824	0.056015	0.401669
H	6.256448	-1.903438	0.715949
H	6.135938	-1.722403	-1.053834
H	-4.165117	2.247135	-1.045907
H	-6.513150	2.235329	-0.285857
H	2.041708	3.180094	-1.823858
H	0.282369	3.218758	-1.946077
H	1.208390	2.056377	-2.918281
H	0.049713	2.978146	0.466459
H	0.628196	1.565447	1.359624
H	1.765395	2.813457	0.826052
H	-8.510220	0.808258	0.537391
H	-8.013019	-0.196972	-0.843762
H	-8.280826	-0.941812	0.751974
H	-6.780767	1.257516	2.459813
H	-6.670195	-0.511219	2.646025
H	-5.198087	0.456001	2.366624

O	-0.104362	-0.291235	-2.125482
H	2.761628	-3.115800	-1.034995
H	4.304792	1.367847	-1.348159
H	3.465319	2.315183	-0.127283
C	2.305301	0.585404	-0.883420
H	2.369135	0.254965	-1.922777
H	4.276013	1.279496	3.044881

Prod-mB-RRR

C	-3.581249	-2.165873	0.300640
C	-4.220073	-0.923403	0.382222
C	-3.553812	0.292457	0.093306
C	-2.218499	0.190563	-0.309934
C	-1.576334	-1.058837	-0.437719
C	-2.245142	-2.234590	-0.114334
N	-1.320234	1.234688	-0.571013
C	-0.097945	0.675318	-1.062565
C	-0.210585	-0.795683	-0.954417
C	0.976617	-1.703735	-0.766433
C	2.272086	-0.950168	-0.434802
N	3.421748	-1.778706	-0.875697
C	4.541960	-1.234362	-0.590477
C	4.532272	0.098298	0.131126
N	3.627403	-0.104221	1.300955
C	2.482818	-0.654925	1.041647
O	1.647131	-0.887444	2.027658
O	5.731972	-1.726556	-0.937729
C	5.821296	0.625416	0.771127
C	5.352047	1.267804	2.093434
C	4.211630	0.358600	2.576419
C	1.201921	1.459260	-0.921951
C	3.791651	1.049285	-0.856216
O	-5.504903	-0.903431	0.843141
C	-4.271012	1.541438	0.317733
C	-5.596467	1.519935	0.531595
C	-6.370416	0.220571	0.461823
C	1.260168	2.544507	-2.019844
C	1.211684	2.141293	0.463719
C	-6.878093	-0.032780	-0.965525
C	-7.511733	0.187322	1.476208
H	-4.140456	-3.061944	0.549849
H	-1.752921	-3.199271	-0.203819
H	-1.658308	2.101864	-0.971447
H	0.771201	-2.481902	-0.021455
H	1.157331	-2.238094	-1.703062
H	6.331186	1.332762	0.113496
H	6.501796	-0.208231	0.967376
H	6.154539	1.329493	2.831324
H	4.971663	2.279128	1.918774
H	3.447726	0.863442	3.170009
H	4.575534	-0.516888	3.123421
H	-3.715492	2.475867	0.337033
H	-6.160963	2.429513	0.719162
H	2.197999	3.107455	-1.960988
H	0.440222	3.261905	-1.901954
H	1.187262	2.097994	-3.016802
H	0.411973	2.884357	0.512257
H	1.036846	1.442041	1.284851
H	2.152145	2.666034	0.648103
H	-7.547558	0.776856	-1.276412
H	-6.038639	-0.075053	-1.667642
H	-7.426518	-0.980685	-1.009119
H	-8.237524	0.974976	1.248030
H	-8.023311	-0.780011	1.437334
H	-7.130329	0.345339	2.490283
O	-0.224593	-0.119191	-2.269551
H	0.817110	-1.302276	1.726493
H	4.397654	1.140300	-1.760565
H	3.740824	2.039481	-0.401686
C	2.389061	0.462593	-1.170528
H	2.351255	0.186792	-2.227418
H	5.605381	-2.542419	-1.460802

tau-mC

C	2.817615	-0.979940	1.942926
C	3.579857	-0.536471	0.857060
C	3.113671	0.452886	-0.040089
C	1.827316	0.954834	0.199359
C	1.057769	0.533050	1.298593
C	1.543702	-0.438914	2.164068
N	1.101194	1.855689	-0.577442
C	-0.119677	2.207765	0.096357
C	-0.205329	1.326174	1.298958
C	-1.437453	0.817544	2.027416
C	-2.134474	-0.301978	1.293155
N	-1.467756	-1.408462	1.037081

C	-2.018041	-2.389826	0.299395
C	-3.277505	-2.270945	-0.228512
N	-3.981035	-1.134580	0.071235
C	-3.517179	-0.102448	0.862234
O	-4.238600	0.877895	1.143648
O	-1.282178	-3.519705	0.066785
C	-4.097565	-3.174894	-1.100592
C	-5.187578	-2.216408	-1.639374
C	-5.317511	-1.132745	-0.554474
C	-1.205888	2.833336	-0.789941
C	-1.841074	1.812254	-1.719800
C	-1.532496	0.521759	-1.875376
O	4.842508	-1.046103	0.715380
C	4.002789	0.885908	-1.110710
C	5.118812	0.187608	-1.377149
C	5.426029	-1.093070	-0.630132
C	-2.323664	3.489340	0.052839
C	-0.564208	3.951646	-1.657688
C	6.925581	-1.263771	-0.394975
C	4.831548	-2.303786	-1.366198
H	3.228989	-1.740132	2.599547
H	0.945466	-0.787491	3.000757
H	1.582810	2.558240	-1.122559
H	-1.121823	0.465239	3.018323
H	-2.133735	1.638872	2.186090
H	-4.532350	-3.982902	-0.496160
H	-3.499565	-3.640639	-1.888790
H	-6.062510	-1.380273	0.210100
H	-5.532873	-0.133538	-0.936650
H	-2.653360	2.230071	-2.317733
H	-2.084627	-0.101937	-2.574440
H	-0.735864	0.038389	-1.318882
H	3.763554	1.784007	-1.675206
H	5.808698	0.488331	-2.161334
H	-3.023400	3.999792	-0.619106
H	-1.903728	4.229290	0.739886
H	-2.895301	2.754650	0.621476
H	-0.073038	4.699377	-1.023180
H	0.163501	3.556886	-2.374031
H	-1.342891	4.460080	-2.236161
H	7.447517	-1.345491	-1.354367
H	7.329505	-0.405246	0.151515
H	7.116679	-2.173406	0.184002
H	5.256718	-2.379567	-2.373144
H	5.054149	-3.226803	-0.818462
H	3.745191	-2.198178	-1.457607
O	0.076355	2.769611	1.425710
H	-0.405149	-3.383095	0.468054
H	-4.846859	-1.759543	-2.574430
H	-6.137468	-2.720535	-1.829897

TS-mC-SSR

C	-1.644757	-0.976028	0.133804
C	-2.355224	0.223752	-0.056297
C	-3.744242	0.290791	0.099109
C	-4.396680	-0.909854	0.470663
C	-3.697761	-2.098016	0.705333
C	-2.305516	-2.130432	0.536207
C	-0.215905	-0.704598	-0.192433
C	-0.155464	0.730546	-0.539383
H	-1.760105	-3.056961	0.694991
N	-1.474299	1.274068	-0.346459
H	-1.781744	2.007451	-0.974311
C	0.880902	-1.572775	0.372250
H	0.897653	-2.505170	-0.203679
H	0.602374	-1.821730	1.401750
C	1.021284	1.693849	-0.387029
C	0.807667	2.882276	-1.368405
H	-0.093498	3.453312	-1.113802
H	1.659179	3.567494	-1.308720
H	0.721623	2.532438	-2.403582
C	1.040312	2.231252	1.057402
H	0.096981	2.739881	1.276537
H	1.175608	1.421420	1.777785
H	1.849126	2.956342	1.194387
H	-4.250059	-2.983772	1.003080
C	-4.544971	1.503256	-0.014373
C	-5.885167	1.417404	-0.035753
H	-4.043923	2.467586	-0.050873
H	-6.515802	2.300239	-0.101103
C	-6.570099	0.066536	-0.026278
C	-6.775873	-0.448019	-1.459136
C	-7.886954	0.106541	0.746375
H	-5.813810	-0.538340	-1.974537
H	-7.264041	-1.429272	-1.442553
H	-7.405052	0.249524	-2.023026
H	-7.721620	0.453237	1.771733

H	-8.588044	0.789327	0.254625
H	-8.336790	-0.891275	0.778535
O	-5.746003	-0.909537	0.696772
C	2.321933	1.016147	-0.821808
H	2.233479	0.503508	-1.775084
C	2.271803	-0.980931	0.405097
C	3.584068	1.541002	-0.503975
H	3.675541	2.363214	0.201037
H	4.340961	1.535848	-1.282040
C	4.709241	0.054430	0.527129
C	3.868404	0.049205	1.669410
C	6.161381	0.455602	0.461855
H	6.707919	-0.033653	1.278113
H	6.296614	1.534476	0.573242
N	4.511435	-1.020266	-0.341866
N	2.675188	-0.478857	1.614012
C	3.262353	-1.546043	-0.533303
O	3.020858	-2.391868	-1.417666
C	5.673122	-1.272677	-1.209898
H	6.118981	-2.233999	-0.933253
H	5.347606	-1.333362	-2.251456
C	6.608593	-0.079391	-0.919589
O	4.288131	0.716568	2.774688
H	3.539712	0.764893	3.397973
O	-0.063950	-0.267201	-1.595955
H	7.659485	-0.377345	-0.926592
H	6.478387	0.693417	-1.683552

TS-mC-RRR

C	-1.506493	-1.099269	-0.360119
C	-2.143525	0.153122	-0.267377
C	-3.483331	0.273704	0.119919
C	-4.163821	-0.929764	0.423295
C	-3.533147	-2.176726	0.374235
C	-2.189506	-2.260720	-0.019521
C	-0.128057	-0.865596	-0.873552
C	-0.013837	0.608534	-1.033454
H	-1.703585	-3.231039	-0.079075
N	-1.239529	1.180147	-0.549562
H	-1.573720	2.041637	-0.964071
C	0.981744	-1.875600	-0.670362
H	1.119858	-2.434139	-1.601001
H	0.659158	-2.587577	0.099781
C	1.222732	1.513377	-1.033277
C	1.043646	2.536028	-2.192016
H	0.148948	3.153446	-2.043698
H	1.909858	3.204739	-2.228508
H	0.956203	2.026621	-3.157086
C	1.320580	2.289186	0.294472
H	0.453615	2.945204	0.412262
H	1.348285	1.623400	1.157577
H	2.211764	2.923921	0.304660
H	-4.101189	-3.065048	0.631986
C	-4.193191	1.532527	0.307699
C	-5.523096	1.526841	0.495930
H	-3.629262	2.462253	0.322532
H	-6.083426	2.443898	0.658420
C	-6.303895	0.230566	0.431858
C	-6.771008	-0.051199	-1.004457
C	-7.477094	0.228479	1.409922
H	-5.911381	-0.115369	-1.680001
H	-7.325297	-0.995993	-1.043879
H	-7.424383	0.756109	-1.353428
H	-7.127091	0.407242	2.431888
H	-8.189226	1.015731	1.140577
H	-7.994813	-0.735889	1.377036
O	-5.458115	-0.887824	0.865342
C	2.466779	0.688734	-1.373015
H	2.334037	0.087540	-2.268206
C	2.305642	-1.291748	-0.251213
C	3.773626	1.116125	-1.104237
H	3.940563	2.010236	-0.511584
H	4.560468	0.902201	-1.821788
C	4.601735	-0.188623	0.435812
C	4.571419	-1.305017	-0.438934
C	5.806184	0.503495	1.021673
H	6.367133	1.064914	0.270006
H	6.483856	-0.244957	1.452545
N	3.575315	-0.159829	1.376946
N	3.434640	-1.857968	-0.778094
C	2.349894	-0.694899	1.096290
O	1.391008	-0.659489	1.893891
C	3.914833	0.642204	2.563146
H	3.077942	1.294306	2.822190
H	4.102549	-0.032164	3.406035
C	5.182862	1.397813	2.118739
H	4.907925	2.370427	1.698276

H	5.866029	1.573309	2.952700
O	5.735272	-1.681222	-1.026913
H	5.524022	-2.327020	-1.726581
O	-0.164648	-0.231944	-2.211486

Prod-mC-SSR

C	-1.658780	-1.006586	-0.098657
C	-2.361065	0.215591	-0.154935
C	-3.733974	0.286917	0.105212
C	-4.377885	-0.928970	0.442272
C	-3.684830	-2.138857	0.545103
C	-2.309304	-2.176879	0.271976
C	-0.257976	-0.726667	-0.508849
C	-0.200720	0.722028	-0.759412
H	-1.768769	-3.118143	0.327476
N	-1.484790	1.274668	-0.433454
H	-1.818141	2.070257	-0.965329
C	0.934590	-1.552668	-0.119985
H	1.082678	-2.324852	-0.880925
H	0.732210	-2.066110	0.824885
C	1.052600	1.560365	-0.570015
C	1.094615	2.660772	-1.652965
H	0.233744	3.333616	-1.560791
H	1.997478	3.273164	-1.554193
H	1.084252	2.224501	-2.658065
C	0.979296	2.212243	0.828073
H	0.156327	2.932277	0.858642
H	0.812562	1.467029	1.608948
H	1.900246	2.753091	1.065768
H	-4.229412	-3.035685	0.823202
C	-4.520668	1.513634	0.135065
C	-5.860061	1.445545	0.208395
H	-4.007379	2.472220	0.128027
H	-6.478658	2.338177	0.251803
C	-6.565039	0.105528	0.175908
C	-6.882478	-0.305277	-1.270123
C	-7.821437	0.106321	1.044261
H	-5.961589	-0.371841	-1.859099
H	-7.385626	-1.278966	-1.285762
H	-7.537770	0.438133	-1.737502
H	-7.576006	0.377228	2.076357
H	-8.544721	0.830365	0.654319
H	-8.284575	-0.885914	1.039593
O	-5.706784	-0.927854	0.767387
C	2.284298	0.612660	-0.784173
H	2.250857	0.317444	-1.836508
C	2.233208	-0.743440	0.042906
C	3.651217	1.298279	-0.501707
H	3.542430	2.286948	-0.049521
H	4.222911	1.425671	-1.425172
C	4.476331	0.395273	0.456436
C	3.577132	0.168799	1.651877
C	5.934928	0.809559	0.682171
H	6.267900	0.471790	1.668832
H	6.060868	1.894506	0.635581
N	4.591461	-0.925142	-0.198246
N	2.457790	-0.418138	1.474873
C	3.450002	-1.574794	-0.474470
O	3.376624	-2.658894	-1.068792
C	5.964878	-1.282840	-0.556034
H	6.353579	-2.029522	0.148004
H	5.992267	-1.708595	-1.562702
C	6.701490	0.062728	-0.431122
O	3.989118	0.640351	2.843454
H	3.286480	0.471739	3.500898
O	-0.200027	-0.186202	-1.893578
H	7.760755	-0.066298	-0.194285
H	6.630211	0.613250	-1.375688

Prod-mC-RRR

C	-1.584383	-1.067428	-0.357177
C	-2.229567	0.184071	-0.272673
C	-3.572128	0.295101	0.105881
C	-4.243534	-0.912613	0.416300
C	-3.603384	-2.155119	0.378973
C	-2.258227	-2.232080	-0.011288
C	-0.208740	-0.819445	-0.860626
C	-0.100455	0.643863	-1.014728
H	-1.760965	-3.197114	-0.062567
N	-1.328527	1.221139	-0.548744
H	-1.662607	2.072907	-0.983875
C	0.973716	-1.720556	-0.632740
H	1.110025	-2.344491	-1.521509
H	0.775249	-2.384842	0.213248
C	1.199185	1.427913	-0.890074
C	1.238820	2.516081	-1.985425

H	0.418292	3.232381	-1.858387
H	2.175739	3.082037	-1.937048
H	1.156642	2.071934	-2.983345
C	1.227451	2.103831	0.498811
H	0.434680	2.854751	0.560079
H	1.064558	1.390425	1.309334
H	2.177667	2.615348	0.674282
H	-4.165378	-3.045195	0.643800
C	-4.293535	1.549001	0.283216
C	-5.623562	1.533338	0.469484
H	-3.737554	2.483541	0.291161
H	-6.191868	2.446946	0.623458
C	-6.393723	0.230383	0.415586
C	-6.860350	-0.065845	-1.017924
C	-7.565492	0.225905	1.395432
H	-6.001035	-0.128545	-1.694010
H	-7.407275	-1.015211	-1.049361
H	-7.520443	0.733597	-1.372257
H	-7.215481	0.415409	2.415459
H	-8.284679	1.005023	1.121235
H	-8.075018	-0.743059	1.370699
O	-5.538610	-0.878120	0.855905
C	2.376705	0.424516	-1.152089
H	2.303366	0.140313	-2.205718
C	2.279946	-0.958329	-0.377818
C	3.788413	1.024711	-0.902448
H	3.747169	2.025695	-0.468172
H	4.360505	1.100942	-1.831931
C	4.546913	0.100252	0.090805
C	4.540472	-1.248484	-0.596511
C	5.863347	0.643090	0.661100
H	6.356830	1.324727	-0.036810
H	6.548350	-0.185936	0.865283
N	3.693037	-0.062974	1.288488
N	3.415950	-1.799844	-0.844033
C	2.501160	-0.664390	1.125730
O	1.701818	-0.928249	2.033913
C	4.312824	0.430292	2.518175
H	3.574098	0.963951	3.122224
H	4.704707	-0.408711	3.107701
C	5.439609	1.327796	1.978074
H	5.049580	2.331701	1.776736
H	6.268249	1.422423	2.684585
O	5.724468	-1.770490	-0.961705
H	5.561263	-2.604769	-1.443107
O	-0.229772	-0.180586	-2.202794

tua-mD

C	2.792026	-1.232596	1.776595
C	3.501004	-0.851843	0.630826
C	3.018307	0.130314	-0.267776
C	1.797211	0.728648	0.059264
C	1.087907	0.377999	1.224816
C	1.575376	-0.608726	2.080166
N	1.077161	1.665869	-0.679287
C	-0.079479	2.089062	0.056398
C	-0.119608	1.249164	1.287580
C	-1.346199	0.785301	2.059911
C	-2.128540	-0.243067	1.304378
N	-1.529552	-1.341963	0.845217
C	-2.108023	-2.293205	0.054645
C	-3.421433	-2.102946	-0.299838
N	-4.079056	-1.014753	0.189529
C	-3.544918	-0.044740	1.025265
O	-4.216536	0.897277	1.459944
O	-1.278647	-3.288790	-0.300396
C	-4.330079	-2.922917	-1.167259
C	-5.468303	-1.923442	-1.485555
C	-5.479160	-0.955610	-0.291710
C	-1.216466	2.718456	-0.763004
C	-1.979550	1.672690	-1.566764
C	-1.596756	0.438034	-1.909501
O	4.654808	-1.521451	0.352061
C	3.776679	0.383688	-1.486168
C	5.020078	-0.106991	-1.609872
C	5.676363	-0.852433	-0.467876
C	-2.216558	3.475442	0.140051
C	-0.613752	3.749192	-1.758026
C	6.451732	0.115383	0.438280
C	6.568153	-1.985129	-0.971135
H	3.208939	-1.996681	2.424257
H	1.047017	-0.877237	2.992201
H	1.560807	2.330728	-1.268611
H	-1.027025	0.376740	3.028464
H	-2.005123	1.624003	2.274626
H	-4.694139	-3.788726	-0.598625
H	-3.825887	-3.296876	-2.062643

H	-6.131330	-1.280673	0.525594
H	-5.720797	0.077826	-0.543693
H	-2.950487	2.027464	-1.916142
H	-2.243729	-0.193666	-2.513352
H	-0.635458	0.021515	-1.624063
H	3.312615	0.944074	-2.293732
H	5.608684	0.047260	-2.510282
H	-2.940826	3.999556	-0.493115
H	-1.699509	4.213719	0.757910
H	-2.783751	2.805593	0.788787
H	-0.048921	4.520590	-1.220849
H	0.038329	3.273949	-2.497177
H	-1.421316	4.243007	-2.308127
H	7.235445	0.622149	-0.135454
H	5.779932	0.876191	0.849793
H	6.917852	-0.432601	1.264960
H	7.390628	-1.574934	-1.566583
H	6.991590	-2.536398	-0.125221
H	5.995387	-2.678551	-1.595407
O	0.216771	2.666908	1.366945
H	-1.751759	-4.017220	-0.738007
H	-0.530242	-1.468965	1.044096
H	-5.232966	-1.375566	-2.403011
H	-6.431065	-2.420263	-1.615381

TS-mD-SSR

C	-1.665730	-0.943676	0.181727
C	-2.392409	0.237466	-0.056672
C	-3.782538	0.288502	0.085639
C	-4.418315	-0.908618	0.495997
C	-3.702347	-2.076937	0.778236
C	-2.309939	-2.095203	0.619444
C	-0.242865	-0.656523	-0.146384
C	-0.201408	0.764271	-0.540471
H	-1.752920	-3.008084	0.812764
N	-1.524801	1.293107	-0.380142
H	-1.838727	1.996731	-1.038527
C	0.869622	-1.468585	0.471345
H	0.893783	-2.444659	-0.025002
H	0.608554	-1.648320	1.520410
C	0.967770	1.734614	-0.389587
C	0.790303	2.889268	-1.415495
H	-0.128055	3.452275	-1.214863
H	1.629541	3.587690	-1.339802
H	0.751753	2.506892	-2.441301
C	0.947762	2.320236	1.035351
H	0.034355	2.903045	1.179365
H	0.952713	1.541883	1.802693
H	1.797564	2.986954	1.208186
H	-4.243511	-2.959747	1.103323
C	-4.601627	1.482911	-0.078722
C	-5.939770	1.373745	-0.105002
H	-4.116305	2.453175	-0.149896
H	-6.583713	2.243028	-0.209499
C	-6.604785	0.014498	-0.047249
C	-6.799781	-0.554976	-1.460475
C	-7.922887	0.062845	0.722587
H	-5.835468	-0.650399	-1.970761
H	-7.273890	-1.541769	-1.408523
H	-7.437609	0.112361	-2.050532
H	-7.764167	0.449452	1.734584
H	-8.633462	0.716294	0.205433
H	-8.357436	-0.939843	0.790853
O	-5.767189	-0.923570	0.711545
C	2.278684	1.036737	-0.777675
H	2.207898	0.519187	-1.730282
C	2.256603	-0.873726	0.391837
C	3.525591	1.599430	-0.475123
H	3.623889	2.405473	0.245641
H	4.317224	1.546257	-1.213636
C	4.820570	-0.047320	0.503010
C	4.009295	0.143902	1.631181
C	6.268559	0.321398	0.349226
H	6.843743	-0.173706	1.142030
H	6.432561	1.397091	0.444904
N	4.506219	-1.070563	-0.362536
N	2.789419	-0.411674	1.590475
C	3.218171	-1.526622	-0.528255
O	2.904131	-2.349043	-1.390332
C	5.635126	-1.417006	-1.254332
H	6.047015	-2.377733	-0.930915
H	5.267153	-1.517750	-2.276716
C	6.614109	-0.244819	-1.048282
O	4.481537	0.822718	2.673941
H	3.787622	1.176175	3.260478
O	-0.069211	-0.272760	-1.557133
H	2.167614	-0.309395	2.388404

H	7.653851	-0.570341	-1.113079
H	6.451846	0.518059	-1.815628

TS-mD-RRR

C	-1.511118	-1.094138	-0.406310
C	-2.148533	0.156397	-0.297390
C	-3.481287	0.272833	0.111852
C	-4.153554	-0.933850	0.420519
C	-3.520407	-2.179741	0.355277
C	-2.184763	-2.260279	-0.061178
C	-0.144896	-0.849508	-0.939506
C	-0.033392	0.625512	-1.086542
H	-1.699325	-3.229900	-0.133874
N	-1.250401	1.189232	-0.587907
H	-1.592079	2.053433	-0.990881
C	0.980482	-1.847935	-0.747214
H	1.126937	-2.387101	-1.688577
H	0.678508	-2.577797	0.012558
C	1.209353	1.520454	-1.089147
C	1.053383	2.527284	-2.264236
H	1.926187	3.186783	-2.304031
H	0.963934	2.006581	-3.222589
H	0.164403	3.153235	-2.125360
C	1.316303	2.313283	0.226999
H	0.456401	2.979855	0.330389
H	1.330618	1.666518	1.104496
H	2.213193	2.939573	0.229403
H	-4.082436	-3.070071	0.618603
C	-4.190667	1.529389	0.317169
C	-5.516463	1.518852	0.530375
H	-3.629702	2.460828	0.323692
H	-6.075891	2.434186	0.704844
C	-6.296756	0.222116	0.478949
C	-6.799932	-0.052099	-0.946343
C	-7.443246	0.212380	1.487993
H	-5.957833	-0.110272	-1.644154
H	-7.353148	-0.997767	-0.976830
H	-7.463827	0.755804	-1.273376
H	-7.066076	0.385823	2.501130
H	-8.163434	0.999981	1.242431
H	-7.960095	-0.752638	1.463269
O	-5.438694	-0.898992	0.883257
C	2.445037	0.675278	-1.423654
H	2.309775	0.089180	-2.330392
C	2.264882	-1.212869	-0.295947
C	3.752267	1.103014	-1.174133
H	3.949648	1.959700	-0.538949
H	4.549672	0.848517	-1.864334
C	4.596971	-0.223385	0.588911
C	4.627544	-1.216450	-0.399812
C	5.760943	0.491083	1.213727
H	6.337162	1.058589	0.479275
H	6.433877	-0.248961	1.665511
N	3.513057	-0.177884	1.435899
N	3.453078	-1.788002	-0.721736
C	2.283115	-0.676300	1.082748
O	1.291904	-0.632497	1.815430
C	3.797881	0.597059	2.664004
H	2.941326	1.230328	2.899742
H	3.954829	-0.106004	3.487922
C	5.074499	1.370122	2.285382
H	4.808131	2.342225	1.859217
H	5.716160	1.542400	3.151228
O	5.785484	-1.537567	-0.972490
H	5.687356	-1.976896	-1.837435
O	-0.183242	-0.213696	-2.269085
H	3.416098	-2.468555	-1.478555

Prod-mD-SSR

C	-1.692910	-0.986750	-0.008781
C	-2.399909	0.229436	-0.105570
C	-3.779593	0.296653	0.110836
C	-4.426281	-0.918772	0.444718
C	-3.728764	-2.122603	0.588387
C	-2.346431	-2.157325	0.358055
C	-0.286764	-0.701598	-0.393436
C	-0.232347	0.742294	-0.666735
H	-1.804634	-3.095706	0.440478
N	-1.522509	1.292343	-0.381445
H	-1.849027	2.069390	-0.944608
C	0.900129	-1.509642	0.052956
H	1.032962	-2.352531	-0.631735
H	0.697676	-1.944701	1.037279
C	1.014712	1.586425	-0.456940
C	1.052105	2.719731	-1.504929
H	0.185428	3.380078	-1.390453

H	1.948226	3.337495	-1.385256
H	1.045856	2.315122	-2.522881
C	0.949677	2.189509	0.961785
H	0.109273	2.885131	1.028160
H	0.795645	1.424320	1.727548
H	1.857512	2.748144	1.207682
H	-4.276907	-3.018800	0.860941
C	-4.575043	1.518223	0.094467
C	-5.915370	1.440033	0.121579
H	-4.069093	2.480534	0.090536
H	-6.541553	2.328313	0.128788
C	-6.609517	0.094686	0.084934
C	-6.872543	-0.340469	-1.364629
C	-7.895078	0.098637	0.909145
H	-5.931156	-0.408522	-1.920027
H	-7.368019	-1.317945	-1.382635
H	-7.516393	0.390789	-1.865728
H	-7.688209	0.388120	1.944603
H	-8.609796	0.810271	0.482380
H	-8.349867	-0.897381	0.904154
O	-5.764119	-0.923432	0.722076
C	2.245329	0.651895	-0.705150
H	2.192105	0.358679	-1.755888
C	2.220551	-0.720358	0.082242
C	3.618830	1.333576	-0.452122
H	3.529002	2.281422	0.083225
H	4.130101	1.540523	-1.394805
C	4.533383	0.378679	0.367357
C	3.792804	0.143787	1.660912
C	6.011566	0.776544	0.467050
H	6.431598	0.423528	1.413429
H	6.137174	1.860431	0.421452
N	4.561735	-0.927789	-0.318234
N	2.628671	-0.419998	1.493791
C	3.393901	-1.556827	-0.535274
O	3.241640	-2.604035	-1.159856
C	5.902792	-1.301673	-0.788916
H	6.332083	-2.054775	-0.118354
H	5.834079	-1.721938	-1.794774
C	6.659667	0.034646	-0.721185
O	4.317023	0.528396	2.787666
H	3.756428	0.380128	3.576115
O	-0.189297	-0.193875	-1.780816
H	2.019346	-0.660567	2.273074
H	7.733444	-0.106427	-0.579139
H	6.510103	0.596137	-1.649447

Prod-mD-RRR

C	-1.605946	-1.065648	-0.327523
C	-2.254965	0.184324	-0.261813
C	-3.599433	0.296776	0.106351
C	-4.269074	-0.909215	0.426557
C	-3.624275	-2.150588	0.408561
C	-2.277800	-2.229459	0.027152
C	-0.231829	-0.815611	-0.830356
C	-0.126195	0.647626	-0.997046
H	-1.778635	-3.193959	-0.010513
N	-1.355639	1.222936	-0.545640
H	-1.691116	2.067708	-0.993316
C	0.949448	-1.717338	-0.583961
H	1.061538	-2.365647	-1.460146
H	0.761587	-2.353327	0.284716
C	1.168333	1.441618	-0.877471
C	1.204882	2.520980	-1.981757
H	2.141731	3.087255	-1.942717
H	1.114750	2.070906	-2.976007
H	0.386306	3.237666	-1.851485
C	1.203427	2.124378	0.507024
H	0.403376	2.866647	0.567657
H	1.051771	1.417864	1.325546
H	2.148178	2.649803	0.670716
H	-4.185543	-3.038789	0.680598
C	-4.325428	1.551022	0.262680
C	-5.656342	1.532743	0.440153
H	-3.772861	2.487489	0.262036
H	-6.228545	2.446477	0.577651
C	-6.422901	0.227472	0.398865
C	-6.883070	-0.086956	-1.032630
C	-7.597760	0.231618	1.374841
H	-6.021138	-0.155831	-1.704789
H	-7.427982	-1.037666	-1.054593
H	-7.543422	0.706795	-1.398878
H	-7.251837	0.434641	2.393622
H	-8.317882	1.005416	1.088422
H	-8.104601	-0.738889	1.360043
O	-5.566120	-0.874593	0.854908
C	2.344864	0.441563	-1.145166

H	2.262411	0.148085	-2.194791
C	2.237751	-0.921943	-0.351217
C	3.761467	1.034003	-0.908513
H	3.728870	2.029780	-0.464419
H	4.322236	1.116008	-1.843302
C	4.542975	0.123723	0.086797
C	4.592598	-1.216789	-0.607423
C	5.865867	0.679700	0.632804
H	6.324550	1.379713	-0.069015
H	6.571424	-0.137865	0.807889
N	3.711582	-0.066791	1.292510
N	3.412474	-1.732212	-0.808798
C	2.501133	-0.638779	1.154219
O	1.703148	-0.884181	2.056705
C	4.360514	0.410277	2.520488
H	3.625687	0.918913	3.148476
H	4.775159	-0.439310	3.075726
C	5.457825	1.334230	1.969577
H	5.050693	2.335717	1.796334
H	6.303117	1.425277	2.655289
O	5.734130	-1.712924	-0.984029
H	5.671029	-2.548667	-1.489961
O	-0.236666	-0.197232	-2.175403
H	3.267895	-2.616653	-1.291893

int-B'

C	2.781128	-1.197856	1.919418
C	3.614691	-0.725838	0.901092
C	3.225262	0.320130	0.032034
C	1.946872	0.854011	0.232235
C	1.110123	0.405294	1.269761
C	1.517643	-0.625555	2.105062
N	1.290407	1.816335	-0.534850
C	0.057341	2.188780	0.105766
C	-0.115211	1.253069	1.255028
C	-1.405918	0.773651	1.894942
C	-2.120416	-0.274424	1.082088
N	-1.469489	-1.284189	0.622796
C	-2.145290	-2.199554	-0.217130
C	-3.627495	-2.387185	0.031958
N	-4.261345	-1.090523	0.319030
C	-3.603883	-0.026454	0.805770
O	-4.128498	1.073036	1.008976
O	-1.531390	-2.818630	-1.063301
C	-4.460735	-2.927153	-1.133982
C	-5.873548	-2.416665	-0.792614
C	-5.639604	-1.017719	-0.191118
C	-0.967084	2.905020	-0.785594
C	-1.642796	1.954287	-1.760426
C	-1.357204	0.674253	-2.004038
O	4.861668	-1.273803	0.800920
C	4.183524	0.776116	-0.966650
C	5.293115	0.062228	-1.203160
C	5.526502	-1.259811	-0.503164
C	-2.057660	3.605301	0.056044
C	-0.235723	4.001329	-1.607876
C	7.004202	-1.472579	-0.178987
C	4.960043	-2.418731	-1.336944
O	0.215468	2.667763	1.468565
H	3.135700	-2.003904	2.552930
H	0.866714	-0.992813	2.893228
H	1.828298	2.533314	-1.002818
H	-1.164185	0.337656	2.874023
H	-2.069152	1.616610	2.074228
H	-3.729700	-3.043670	0.911141
H	-4.399176	-4.014077	-1.215121
H	-4.097646	-2.489623	-2.070107
H	-6.531406	-2.379516	-1.663939
H	-6.337108	-3.072087	-0.047552
H	-6.335115	-0.768809	0.615395
H	-5.692211	-0.221432	-0.941988
H	-2.452790	2.425297	-2.320038
H	-1.926718	0.106455	-2.735661
H	-0.562225	0.142261	-1.492956
H	3.997641	1.705843	-1.498588
H	6.033975	0.379239	-1.931772
H	-2.695067	4.199145	-0.608555
H	-1.605448	4.274908	0.791788
H	-2.700363	2.888947	0.569512
H	0.284444	4.701700	-0.943562
H	0.484196	3.572513	-2.311635
H	-0.963566	4.570763	-2.194705
H	7.589614	-1.519131	-1.102840
H	7.382295	-0.649518	0.435264
H	7.138596	-2.411458	0.367440
H	5.446466	-2.456479	-2.317478
H	5.127055	-3.371671	-0.822718

H	3.884613	-2.282423	-1.490108

int-B

C	2.881210	-0.720539	2.052947
C	3.579932	-0.388893	0.886827
C	3.045200	0.478180	-0.095981
C	1.752501	0.962476	0.136752
C	1.037128	0.637716	1.304805
C	1.600999	-0.194181	2.268712
N	0.973581	1.764989	-0.692464
C	-0.231881	2.154022	-0.016283
C	-0.255639	1.381748	1.264089
C	-1.413325	0.928307	2.130340
C	-2.158299	-0.370632	1.722583
N	-1.297040	-1.377787	1.104339
C	-1.677860	-2.328449	0.228907
C	-3.097323	-2.207274	-0.253668
N	-3.847572	-1.191883	0.060100
C	-3.421023	-0.106896	0.915761
O	-4.145998	0.842819	1.044200
O	-0.966663	-3.219881	-0.225107
C	-3.775559	-3.138838	-1.179847
C	-5.242746	-2.642627	-1.172425
C	-5.168715	-1.198477	-0.638270
C	-1.363689	2.675291	-0.913280
C	-2.038281	1.547440	-1.678102
C	-1.588638	0.303077	-1.874982
O	4.847540	-0.875778	0.751033
C	3.880406	0.820837	-1.240520
C	5.011361	0.134647	-1.470258
C	5.395387	-1.043610	-0.601484
C	-2.416648	3.456955	-0.097471
C	-0.774500	3.663005	-1.961425
C	6.906763	-1.125874	-0.397579
C	4.833134	-2.349431	-1.183001
O	-0.018136	2.834683	1.251502
H	3.350906	-1.373983	2.780736
H	1.074568	-0.427669	3.191238
H	1.409442	2.405856	-1.341598
H	-1.016817	0.774833	3.139179
H	-2.153138	1.723667	2.215582
H	-2.569744	-0.797148	2.652949
H	-0.337123	-1.443621	1.435178
H	-3.631408	-4.177088	-0.864006
H	-3.286108	-3.050859	-2.161803
H	-5.693196	-2.677153	-2.164754
H	-5.840188	-3.260816	-0.498099
H	-5.944697	-0.929766	0.078072
H	-5.121158	-0.434923	-1.420038
H	-2.979501	1.840505	-2.145587
H	-2.149270	-0.391425	-2.496067
H	-0.646303	-0.052072	-1.470282
H	3.588929	1.641944	-1.890660
H	5.661238	0.369102	-2.309172
H	-3.184399	3.841641	-0.777554
H	-1.952240	4.303694	0.414292
H	-2.919045	2.837897	0.645239
H	-0.240715	4.481565	-1.463990
H	-0.098900	3.164910	-2.663228
H	-1.588127	4.099633	-2.549691
H	7.404226	-1.292188	-1.358890
H	7.287755	-0.196579	0.038190
H	7.152847	-1.957547	0.270735
H	5.234204	-2.517328	-2.188579
H	5.110668	-3.197176	-0.546263
H	3.741194	-2.297762	-1.250877

C-diene

C	-1.171682	0.639919	0.050988
C	-0.111175	1.506233	0.034757
C	1.428060	-0.221887	0.009852
C	0.374294	-1.242806	0.057225
C	-2.121313	-1.525783	0.089321
C	-3.210974	-0.527748	-0.337011
C	-2.660443	0.854160	0.092516
H	-4.176501	-0.755480	0.119640
H	-3.329919	-0.555441	-1.425108
C	2.848952	-0.719324	-0.026827
H	2.938836	-1.418526	-0.870708
H	3.011599	-1.341300	0.865571
N	1.165853	1.065099	0.003113
N	-0.893959	-0.708065	0.051660
O	-0.229763	2.874447	0.043159
O	0.572873	-2.475853	0.091478
H	-2.008210	-2.381349	-0.578358
H	-2.261458	-1.898324	1.110485

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

H	-2.974823	1.110855	1.113595
H	-2.992326	1.661548	-0.568247
C	3.914671	0.372213	-0.118938
H	4.912073	-0.080638	-0.143615
H	3.788258	0.975083	-1.024872
H	3.865981	1.050204	0.739979
H	-1.163988	3.135513	0.089839

C-da

C	-1.450296	-0.754032	0.086059
C	-0.925456	-0.232728	1.409506
C	0.455090	0.963145	0.022116
C	-0.820246	1.390080	-0.795092
C	-3.174114	0.515788	-1.119511
C	-3.847237	-0.478082	-0.156977
C	-2.762151	-1.549212	0.083518
H	-4.769151	-0.897337	-0.568972
H	-4.091909	0.027262	0.784693
C	1.424927	2.164746	0.043324
H	0.817712	3.068160	-0.069457
H	2.048782	2.127185	-0.854666
N	0.020139	0.621097	1.399464
N	-1.772004	0.446934	-0.706744
O	-1.452620	-0.741615	2.542350
O	-0.944168	2.448801	-1.426657
H	-3.539754	1.541978	-1.027582
H	-3.278521	0.202572	-2.166402
H	-2.744292	-2.265233	-0.746060
H	-2.907310	-2.107036	1.010749
C	2.284374	2.347740	1.300740
H	2.961649	3.198472	1.156026
H	1.655567	2.557462	2.170798
C	-0.218801	-1.417223	-0.569319
C	0.932363	-0.371826	-0.731561
H	0.079545	-2.264124	0.053788
H	-0.517374	-1.818235	-1.542280
H	0.976474	-0.086230	-1.790817
C	2.333231	-1.015110	-0.428599
C	2.511995	-1.403192	1.052249
H	1.759783	-2.130768	1.378159
H	3.497594	-1.862633	1.199382
H	2.434966	-0.536005	1.711502
C	3.504195	-0.107079	-0.869327
H	4.441597	-0.675454	-0.828968
H	3.369163	0.236969	-1.902625
C	2.451904	-2.297775	-1.294587
H	2.309180	-2.069249	-2.358796
H	3.451810	-2.732263	-1.176652
H	1.728927	-3.070090	-1.015172
H	-0.974912	-0.353027	3.300734
H	3.634349	0.767121	-0.232949
H	2.894813	1.475366	1.545743

A-diene

C	1.273205	0.584487	-0.050275
C	0.365246	1.713667	0.068476
C	-1.427628	0.037132	0.312985
C	-0.519739	-0.984700	0.153963
C	1.898467	-1.666185	-0.185545
C	3.171097	-0.832527	0.037620
C	2.747271	0.625837	-0.259207
H	-1.619382	2.083882	0.375932
H	3.984632	-1.170674	-0.605821
H	3.493561	-0.921533	1.078619
C	-2.899407	-0.183212	0.501185
H	-3.260424	0.501135	1.278258
H	-3.048110	-1.201468	0.868833
N	-0.955900	1.319720	0.261036
N	0.808973	-0.653739	-0.001666
O	0.710674	2.893764	0.015348
O	-0.819659	-2.301345	0.246761
H	-1.137615	-2.658840	-0.602165
H	1.747711	-2.477404	0.525471
H	1.800324	-2.055714	-1.202801
H	2.951173	0.924445	-1.297196
H	3.222439	1.368293	0.387768
C	-3.696022	0.031809	-0.803267
H	-4.760819	-0.127423	-0.607056
H	-3.568337	1.049082	-1.188750
H	-3.379734	-0.672847	-1.579158

A-da

C	-1.475330	-0.776402	0.156119
C	-1.000086	-0.332783	1.552993
C	0.469053	0.932841	0.064252

C	-0.811252	1.320030	-0.712770
C	-3.161069	0.511656	-1.118985
C	-3.868349	-0.481466	-0.185434
C	-2.795720	-1.550300	0.116538
H	0.440116	0.961802	2.233308
H	-4.761088	-0.904188	-0.651299
H	-4.169101	0.028477	0.735780
C	1.427504	2.147833	0.115246
H	0.823413	3.063518	0.128386
H	2.005095	2.159599	-0.812186
N	0.006687	0.564485	1.409404
N	-1.778383	0.470393	-0.602500
O	-1.437833	-0.755122	2.617811
O	-0.980079	2.370416	-1.479216
H	-0.208129	2.966755	-1.480270
H	-3.537762	1.534738	-1.074239
H	-3.150432	0.173753	-2.160343
H	-2.757871	-2.296282	-0.683325
H	-2.969406	-2.065057	1.063275
C	2.361744	2.275241	1.330108
H	3.072867	3.083935	1.136407
H	1.810205	2.550296	2.235670
H	3.631828	0.741112	-0.300834
C	-0.245506	-1.423068	-0.522724
C	0.914798	-0.392291	-0.720336
H	0.060108	-2.262550	0.104484
H	-0.554018	-1.834749	-1.486571
H	0.924178	-0.096882	-1.777393
C	2.321304	-1.041661	-0.464091
C	2.543425	-1.453535	1.004191
H	1.781500	-2.157754	1.355344
H	3.515880	-1.950305	1.100280
H	2.540108	-0.599733	1.685330
C	3.474951	-0.128823	-0.937516
H	4.412108	-0.697007	-0.929659
H	3.308629	0.220401	-1.964028
H	2.935616	1.372026	1.538470
C	2.394832	-2.314640	-1.349200
H	2.209908	-2.075729	-2.403952
H	3.397021	-2.751203	-1.274997
H	1.682608	-3.087256	-1.045067

3-methyl-1-butene

C	-2.212566	0.077741	-0.000078
C	-1.010395	0.665684	-0.000207
H	-2.337041	-1.002399	0.000078
H	-3.125666	0.668920	-0.000094
H	-0.968759	1.757956	-0.000331
C	0.352574	-0.001456	-0.000029
C	0.262628	-1.536058	-0.000026
H	-0.263352	-1.906263	-0.888259
H	1.269113	-1.971496	0.000296
H	-0.263915	-1.906268	0.887871
C	1.119675	0.467915	1.258812
H	2.135666	0.052953	1.264337
H	1.201690	1.561732	1.288428
H	0.610600	0.139884	2.173159
C	1.120093	0.467908	-1.258546
H	1.202115	1.561732	-1.288192
H	2.136100	0.052978	-1.263734
H	0.611395	0.139874	-2.173115

guanidine

C	0.000922	-0.000537	0.000097
N	-0.415471	1.270239	0.002568
N	-0.894232	-0.994166	0.002852
N	1.309596	-0.276691	-0.005893
H	1.650258	-1.223588	0.092219
H	-1.885627	-0.808595	0.072280
H	-1.395630	1.502928	-0.081270
H	-0.612851	-1.960851	-0.087267
H	2.002899	0.457386	-0.059460
H	0.236171	2.040266	0.066220

epoxy-SSR

C	1.653352	1.052397	-0.390609
C	2.367162	-0.161065	-0.500066
C	3.758050	-0.209713	-0.346589
C	4.398752	1.009355	-0.015189
C	3.698973	2.211624	0.124752
C	2.310509	2.233485	-0.070181
C	0.232545	0.754341	-0.705086
C	0.175526	-0.695172	-0.953921
H	4.247726	3.113727	0.375920
H	1.761499	3.166797	0.023069

N	1.484062	-1.226074	-0.718161
H	1.784506	-2.050874	-1.222930
O	0.077651	0.218375	-2.080729
C	4.586905	-1.396984	-0.518098
C	5.871831	-1.378729	-0.128058
H	4.161072	-2.284251	-0.979896
H	6.519368	-2.242944	-0.251076
C	6.453968	-0.163571	0.561837
C	6.291203	-0.276591	2.085475
H	6.706121	0.610881	2.577066
H	5.232530	-0.367423	2.351013
H	6.817166	-1.163561	2.455821
C	7.913623	0.063226	0.172779
H	8.011417	0.166379	-0.912846
H	8.294703	0.972050	0.650267
H	8.524278	-0.784687	0.500659
O	5.759917	1.049898	0.116277
C	-1.049917	-1.549115	-0.673515
C	-0.941042	1.563298	-0.228462
H	-0.674593	2.099990	0.688571
H	-1.165267	2.328950	-0.976920
C	-2.306322	-0.617891	-0.798645
H	-2.358964	-0.326494	-1.851183
C	-2.214443	0.735526	0.009567
C	-1.159949	-2.652038	-1.749254
H	-0.283494	-3.310197	-1.725598
H	-2.041810	-3.278620	-1.578562
H	-1.235997	-2.216940	-2.751857
C	-0.864701	-2.198814	0.716453
H	-1.775755	-2.701104	1.052849
H	-0.071696	-2.950908	0.671486
H	-0.579866	-1.467987	1.476803
C	-3.641089	-1.317798	-0.405490
H	-4.276205	-1.458211	-1.284583
H	-3.481232	-2.304665	0.034829
N	-2.381380	0.412314	1.442287
C	-3.495813	-0.252148	1.828044
H	-1.654391	0.615331	2.118546
O	-3.726464	-0.659296	2.968937
C	-3.481291	1.553514	-0.401673
O	-3.463581	2.626852	-1.015059
N	-4.584334	0.896375	-0.012618
C	-4.414206	-0.436959	0.609387
C	-5.849591	-0.875043	0.911608
H	-5.966786	-1.959492	0.837631
H	-6.111216	-0.576911	1.932118
C	-6.699897	-0.104661	-0.120830
H	-6.694303	-0.626392	-1.084458
H	-7.740172	0.008018	0.195505
C	-5.984999	1.250481	-0.258674
H	-6.325326	1.971609	0.494970
H	-6.086771	1.707268	-1.246553

int1-SSR

C	-1.236674	-0.016499	-0.999478
C	-1.940491	-0.311859	0.189177
C	-3.320144	-0.543941	0.187404
C	-3.957420	-0.534761	-1.077540
C	-3.261809	-0.290411	-2.267902
C	-1.886961	-0.022971	-2.227656
C	0.141212	0.363501	-0.605019
C	0.194781	0.210862	0.857530
H	-3.807573	-0.298641	-3.205739
H	-1.346749	0.198300	-3.144062
N	-1.064251	-0.307475	1.277579
H	-1.390303	-0.171553	2.225522
O	0.131166	1.569446	0.290288
C	-4.145987	-0.724849	1.374417
C	-5.425198	-1.110640	1.246555
H	-3.724631	-0.519368	2.354921
H	-6.072029	-1.239349	2.110347
C	-6.003449	-1.449317	-0.109815
C	-5.831481	-2.945122	-0.411610
H	-6.249195	-3.182159	-1.396640
H	-4.770495	-3.216486	-0.399474
H	-6.349362	-3.544703	0.345094
C	-7.463584	-1.016982	-0.225365
H	-7.564687	0.055716	-0.030840
H	-7.841968	-1.232321	-1.229979
H	-8.073186	-1.563883	0.501529
O	-5.309429	-0.692357	-1.161014
C	1.459469	-0.108985	1.632903
C	1.350789	0.293913	-1.490938
H	1.192313	-0.454101	-2.275005
H	1.466121	1.253463	-2.002996
C	2.673570	0.408948	0.782898
H	2.596635	1.499814	0.785824

C	2.654657	-0.012420	-0.738248
C	1.444027	0.666342	2.968708
H	0.596202	0.359133	3.591822
H	2.356482	0.470728	3.541464
H	1.371370	1.745623	2.795793
C	1.465565	-1.627717	1.918475
H	2.402102	-1.943274	2.385735
H	0.655830	-1.878093	2.609956
H	1.321722	-2.219801	1.012404
C	4.059794	0.005905	1.369437
H	4.591385	0.887100	1.739259
H	3.973797	-0.689823	2.206929
N	2.986282	-1.450067	-0.805830
C	4.151689	-1.868735	-0.257749
H	2.347843	-2.123610	-1.213508
O	4.521219	-3.041612	-0.175810
C	3.851470	0.745686	-1.398853
O	3.742107	1.616759	-2.269205
N	5.002534	0.323192	-0.855862
C	4.927182	-0.646585	0.261664
C	6.394746	-0.891203	0.621829
H	6.522637	-1.088994	1.689400
H	6.760024	-1.764530	0.071775
C	7.114795	0.392147	0.156349
H	7.019176	1.179525	0.912514
H	8.179934	0.229380	-0.027625
C	6.361965	0.802558	-1.121013
H	6.764721	0.304440	-2.011732
H	6.349817	1.880483	-1.301666
H	-1.761006	2.730657	-1.038922
C	-3.190069	2.821795	0.392875
N	-2.749010	2.885422	-0.876720
N	-4.501258	2.871353	0.644365
N	-2.297104	2.769053	1.384315
H	-2.592213	2.764694	2.351336
H	-5.173991	3.018779	-0.095780
H	-3.353611	2.570836	-1.625815
H	-4.864820	2.733154	1.577168
H	-1.347796	2.458689	1.167774

TS-C2O-SSR

C	-1.331052	-0.038640	-1.007116
C	-2.047049	-0.404060	0.142523
C	-3.430961	-0.551019	0.167935
C	-4.090252	-0.355465	-1.073768
C	-3.395667	-0.018794	-2.238226
C	-2.001852	0.147511	-2.206526
C	0.092908	0.226838	-0.575142
C	0.116614	-0.245869	0.820451
H	-3.955669	0.123310	-3.157036
H	-1.466861	0.434586	-3.107403
N	-1.131874	-0.542107	1.219746
H	-1.406863	-0.668270	2.185472
O	0.224429	1.501395	0.069990
C	-4.242480	-0.828234	1.346590
C	-5.542044	-1.129345	1.200718
H	-3.793533	-0.767319	2.334540
H	-6.178007	-1.333214	2.057982
C	-6.166604	-1.261363	-0.171273
C	-6.092988	-2.715771	-0.659107
H	-6.545529	-2.802775	-1.653202
H	-5.051064	-3.049141	-0.712169
H	-6.630783	-3.373534	0.032395
C	-7.600019	-0.734329	-0.189347
H	-7.630971	0.308501	0.142552
H	-8.011078	-0.796075	-1.202223
H	-8.227029	-1.334273	0.478525
O	-5.451192	-0.419380	-1.139043
C	1.377973	-0.554560	1.575446
C	1.243447	-0.128452	-1.492181
H	1.013546	-1.066067	-2.009285
H	1.321696	0.651117	-2.256091
C	2.569681	0.077641	0.789064
H	2.416419	1.155618	0.855580
C	2.596848	-0.241308	-0.759607
C	1.341151	0.043072	2.998110
H	0.494249	-0.345249	3.574414
H	2.251604	-0.221617	3.544436
H	1.264586	1.134488	2.958696
C	1.430118	-2.106004	1.663677
H	2.363498	-2.429884	2.131390
H	0.605058	-2.476436	2.279405
H	1.359701	-2.579220	0.681584
C	3.969799	-0.254793	1.377091
H	4.356691	0.595720	1.945163
H	3.952869	-1.112437	2.055148
N	3.175948	-1.589763	-0.940731

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

C	4.417002	-1.837967	-0.459152
H	2.686808	-2.309437	-1.460142
O	5.007757	-2.917428	-0.531252
C	3.643482	0.768637	-1.331242
O	3.392875	1.667262	-2.141278
N	4.842051	0.528730	-0.775542
C	4.950177	-0.566007	0.217825
C	6.436879	-0.574211	0.581345
H	6.597539	-0.864949	1.622999
H	6.959119	-1.296328	-0.054527
C	6.904849	0.864934	0.277580
H	6.657242	1.530749	1.112173
H	7.982540	0.926212	0.105198
C	6.093518	1.266655	-0.965714
H	6.580742	0.944317	-1.894565
H	5.888697	2.338163	-1.034466
H	-1.159848	2.654076	-0.655666
C	-2.642475	2.984708	0.659939
N	-2.071801	3.111697	-0.547084
N	-3.931874	3.296786	0.846895
N	-1.878530	2.568416	1.675705
H	-2.270553	2.407733	2.592789
H	-4.465632	3.751403	0.118557
H	-2.654547	3.184142	-1.370770
H	-4.343296	3.280862	1.770271
H	-0.985764	2.131284	1.428657

TS-C3O-SSR

C	-1.221618	-0.214198	-0.984427
C	-1.959609	-0.328474	0.235465
C	-3.343428	-0.545218	0.229712
C	-3.948186	-0.698392	-1.038689
C	-3.228131	-0.601963	-2.252202
C	-1.866132	-0.350486	-2.226271
C	0.110059	0.141141	-0.636900
C	0.161964	0.364675	0.822084
H	-3.767573	-0.725052	-3.185089
H	-1.305181	-0.255848	-3.151377
N	-1.116318	-0.153822	1.303934
H	-1.446584	0.031969	2.240789
O	0.107792	1.716059	0.409360
C	-4.203911	-0.525277	1.405725
C	-5.491072	-0.888001	1.299760
H	-3.801832	-0.175469	2.352803
H	-6.165878	-0.856836	2.150740
C	-6.047981	-1.415098	-0.002618
C	-5.939143	-2.944362	-0.064224
H	-6.334317	-3.314609	-1.016732
H	-4.894400	-3.257274	0.035049
H	-6.513455	-3.392044	0.754144
C	-7.478254	-0.938925	-0.243637
H	-7.530377	0.154238	-0.218954
H	-7.834401	-1.289654	-1.217662
H	-8.137758	-1.339330	0.533279
O	-5.281756	-0.874929	-1.144874
C	1.404593	-0.042832	1.617951
C	1.325250	0.223072	-1.490608
H	1.225493	-0.455832	-2.344975
H	1.400096	1.226470	-1.920214
C	2.641429	0.411747	0.770963
H	2.587199	1.503208	0.729409
C	2.626928	-0.065922	-0.731880
C	1.421981	0.725597	2.954015
H	0.552952	0.462849	3.568723
H	2.316079	0.478194	3.535775
H	1.409229	1.807582	2.784983
C	1.336655	-1.561695	1.885199
H	2.282990	-1.949160	2.272309
H	0.564949	-1.776397	2.630094
H	1.086798	-2.126780	0.983115
C	4.012852	-0.000386	1.382607
H	4.544635	0.876552	1.762186
H	3.904459	-0.695599	2.218956
N	2.956397	-1.504845	-0.757498
C	4.125375	-1.904178	-0.201631
H	2.322419	-2.192380	-1.148737
O	4.501445	-3.072635	-0.093406
C	3.819254	0.673940	-1.413581
O	3.705371	1.515093	-2.312612
N	4.968942	0.278468	-0.847856
C	4.892364	-0.666092	0.292049
C	6.359289	-0.893814	0.664904
H	6.482391	-1.068959	1.736976
H	6.733689	-1.775359	0.134460
C	7.072920	0.384730	0.177222
H	6.964836	1.187606	0.915220
H	8.140767	0.226800	0.005178

C	6.326969	0.761196	-1.114706
H	6.739735	0.246241	-1.991095
H	6.308735	1.834818	-1.319165
H	-1.290868	2.479691	-0.861523
C	-2.955142	2.960517	0.165553
N	-2.243597	2.830456	-0.966669
N	-4.277353	3.161638	0.116740
N	-2.303947	2.921138	1.330906
H	-2.797407	2.989201	2.210178
H	-4.752632	3.307779	-0.763452
H	-2.719050	2.597792	-1.828903
H	-4.816600	3.304066	0.959676
H	-1.342464	2.563776	1.318187

int2-SSR

C	-1.447703	0.279024	-0.661023
C	-2.122714	-0.581898	0.207373
C	-3.500510	-0.777047	0.207989
C	-4.210283	-0.048097	-0.781917
C	-3.563784	0.819013	-1.665493
C	-2.171722	0.992199	-1.604520
C	0.014473	0.344086	-0.223941
C	0.061797	-0.766462	0.802545
H	-4.161206	1.357424	-2.394545
H	-1.679081	1.679099	-2.285918
N	-1.152025	-1.176915	1.078596
H	-1.386580	-1.825881	1.823722
O	0.263320	1.438834	0.603643
C	-4.261553	-1.605512	1.134943
C	-5.556454	-1.855355	0.885857
H	-3.783066	-1.996590	2.028309
H	-6.155252	-2.464260	1.557845
C	-6.225544	-1.354037	-0.375357
C	-6.123123	-2.403760	-1.491695
H	-6.611665	-2.035271	-2.400577
H	-5.073623	-2.622833	-1.715414
H	-6.611101	-3.333996	-1.180986
C	-7.674451	-0.944661	-0.118949
H	-7.727088	-0.183733	0.666331
H	-8.118071	-0.540266	-1.034506
H	-8.258432	-1.815534	0.196343
O	-5.570721	-0.124833	-0.840893
C	1.340713	-1.299357	1.371334
C	1.064981	0.137786	-1.317480
H	0.748742	-0.682326	-1.972478
H	1.107925	1.048106	-1.922698
C	2.497638	-0.401938	0.826029
H	2.327152	0.580884	1.267096
C	2.462626	-0.153957	-0.735215
C	1.334338	-1.236846	2.916958
H	0.508720	-1.820043	3.338647
H	2.265665	-1.657447	3.308234
H	1.243920	-0.202583	3.262655
C	1.419634	-2.786168	0.914977
H	2.372343	-3.221693	1.226145
H	0.620814	-3.369239	1.383889
H	1.332989	-2.893579	-0.168264
C	3.922939	-0.877159	1.215624
H	4.311336	-0.279791	2.045321
H	3.953481	-1.923819	1.531345
N	3.071378	-1.325032	-1.403245
C	4.341505	-1.669747	-1.082678
H	2.592558	-1.814089	-2.150723
O	4.965530	-2.618978	-1.561175
C	3.453839	1.031418	-0.957292
O	3.155656	2.133095	-1.429225
N	4.676984	0.667868	-0.534717
C	4.862053	-0.704322	-0.005253
C	6.363495	-0.777652	0.285978
H	6.576294	-1.404605	1.156055
H	6.877158	-1.213605	-0.576954
C	6.780010	0.694823	0.486358
H	6.551765	1.020771	1.507603
H	7.847014	0.854903	0.310898
C	5.903524	1.468332	-0.512348
H	6.351747	1.497591	-1.513737
H	5.676660	2.491878	-0.203232
H	-0.309620	3.017606	-0.076892
C	-2.012214	3.642787	0.804516
N	-0.997122	3.791861	-0.053384
N	-3.084338	4.454848	0.759676
N	-1.922734	2.667235	1.715277
H	-2.721821	2.416970	2.280987
H	-3.070634	5.284961	0.182400
H	-1.057799	4.443171	-0.823716
H	-3.756987	4.449855	1.514814
H	-1.160598	1.981010	1.553855

int3-SSR

C	1.142723	-0.653660	1.051287
C	2.021165	-0.117572	0.009468
C	3.359007	-0.548194	-0.109217
C	3.774428	-1.525417	0.802555
C	2.931352	-2.056942	1.846895
C	1.642156	-1.637584	1.970288
C	-0.064705	-0.031207	0.941346
C	-0.043593	1.007011	-0.175912
H	3.361842	-2.802581	2.506498
H	0.994305	-2.036538	2.744074
N	1.354266	0.777783	-0.711937
H	1.761835	1.359831	-1.431546
O	-0.195995	2.255060	0.326533
C	4.341989	-0.000334	-1.035210
C	5.550254	-0.571280	-1.143061
H	4.098834	0.894046	-1.601854
H	6.315653	-0.168019	-1.799756
C	5.894896	-1.840440	-0.401513
C	5.658511	-3.073074	-1.281116
H	5.894254	-3.987147	-0.725409
H	4.615428	-3.112497	-1.611464
H	6.300703	-3.023134	-2.167046
C	7.309944	-1.805765	0.169124
H	7.442527	-0.936843	0.821149
H	7.509032	-2.716434	0.742945
H	8.034558	-1.744045	-0.649465
O	5.017628	-2.005547	0.790668
C	-1.123546	0.613588	-1.259215
C	-1.320170	-0.174849	1.706595
H	-1.285503	-0.982107	2.443813
H	-1.484337	0.761264	2.255579
C	-2.485409	0.602543	-0.489265
H	-2.601578	1.616432	-0.094715
C	-2.524443	-0.342511	0.767000
C	-1.177298	1.718214	-2.330058
H	-0.211922	1.814966	-2.841252
H	-1.923714	1.479458	-3.095800
H	-1.430656	2.685869	-1.887961
C	-0.769562	-0.726977	-1.937688
H	-1.598020	-1.098135	-2.548428
H	0.089993	-0.594839	-2.601627
H	-0.514509	-1.512572	-1.222209
C	-3.722680	0.257839	-1.368838
H	-4.332927	1.148376	-1.544118
H	-3.439756	-0.136542	-2.348647
N	-2.654578	-1.736508	0.303522
C	-3.717719	-2.051586	-0.474967
H	-1.970726	-2.445561	0.542300
O	-3.931433	-3.155302	-0.979422
C	-3.846129	0.005129	1.511250
O	-3.909483	0.502339	2.641174
N	-4.886380	-0.287394	0.715839
C	-4.597196	-0.800498	-0.645656
C	-5.987950	-1.035435	-1.240486
H	-6.001921	-0.856954	-2.318999
H	-6.285040	-2.074812	-1.067003
C	-6.899092	-0.065531	-0.458329
H	-6.836686	0.942422	-0.883796
H	-7.947650	-0.374069	-0.473023
C	-6.313458	-0.066653	0.963889
H	-6.717690	-0.885379	1.572200
H	-6.458107	0.872385	1.504345
H	1.225375	2.785156	1.275983
C	2.370601	4.111404	0.276122
N	2.078695	3.373947	1.351402
N	3.508812	4.826198	0.211649
N	1.509744	4.091449	-0.748132
H	1.585297	4.746382	-1.513759
H	4.069216	4.970660	1.040827
H	2.764544	3.209089	2.074821
H	3.672168	5.462558	-0.556837
H	0.661056	3.507271	-0.619568

epoxy-RRR

C	1.567540	1.196447	-0.455802
C	2.221023	-0.040944	-0.640102
C	3.588385	-0.194185	-0.380363
C	4.264779	0.940884	0.128956
C	3.622060	2.164063	0.342813
C	2.258207	2.293234	0.043609
C	0.164422	1.023557	-0.909294
C	0.048278	-0.391364	-1.317155
H	4.195389	2.998637	0.733682
H	1.754159	3.243738	0.197457

N	1.304789	-1.019905	-1.041565
H	1.603629	-1.804134	-1.608470
O	0.092976	0.640017	-2.340074
C	4.358893	-1.410983	-0.605779
C	5.604099	-1.515648	-0.113759
H	3.922685	-2.220605	-1.185500
H	6.207888	-2.405892	-0.269499
C	6.194304	-0.413884	0.740588
C	5.896500	-0.664616	2.226955
H	6.320751	0.139943	2.838582
H	4.815396	-0.708152	2.397004
H	6.334485	-1.617530	2.544114
C	7.692077	-0.247176	0.491544
H	7.886442	-0.048842	-0.567542
H	8.083625	0.585448	1.085322
H	8.222622	-1.160764	0.780275
O	5.610491	0.880291	0.370219
C	-1.237146	-1.207452	-1.258197
C	-1.002014	1.854719	-0.444342
H	-0.746681	2.371115	0.484859
H	-1.198172	2.614015	-1.210014
C	-2.429113	-0.187991	-1.233807
H	-2.441234	0.290283	-2.217280
C	-2.262426	1.012832	-0.222746
C	-1.358583	-2.055673	-2.542762
H	-0.536162	-2.776779	-2.615541
H	-2.294482	-2.625226	-2.542663
H	-1.341172	-1.421511	-3.435525
C	-1.167160	-2.147700	-0.034351
H	-2.099329	-2.704520	0.092992
H	-0.367538	-2.880496	-0.175835
H	-0.955724	-1.609553	0.891812
C	-3.822131	-0.832894	-0.981161
H	-4.475767	-0.712867	-1.850398
H	-3.752577	-1.904468	-0.782526
C	-4.487276	-0.159085	0.248185
C	-2.341882	0.440713	1.216422
C	-4.678090	1.317281	-0.137753
N	-3.462375	1.861784	-0.381133
N	-3.517203	-0.191625	1.370215
H	-3.382896	2.836874	-0.647252
O	-5.759000	1.900511	-0.240583
O	-1.452477	0.536056	2.070127
C	-5.719277	-0.865671	0.820636
C	-4.005059	-0.927053	2.538839
C	-5.151989	-1.759951	1.943238
H	-4.361695	-0.225976	3.304119
H	-3.196521	-1.526457	2.965666
H	-5.905052	-2.021085	2.691220
H	-6.407491	-0.117812	1.227641
H	-6.253592	-1.431934	0.053039
H	-4.753912	-2.690981	1.523636

int1-RRR

C	-1.156240	0.057548	-1.044097
C	-1.794183	-0.180461	0.193422
C	-3.142628	-0.545386	0.267294
C	-3.809893	-0.739610	-0.966683
C	-3.173672	-0.558529	-2.200736
C	-1.833963	-0.150146	-2.239453
C	0.184135	0.613845	-0.741865
C	0.293095	0.617449	0.730037
H	-3.738589	-0.724901	-3.112158
H	-1.343250	0.021216	-3.193627
N	-0.894797	0.022098	1.240893
H	-1.200096	0.194421	2.189352
O	0.073168	1.895456	0.032349
C	-3.913581	-0.674013	1.496921
C	-5.147158	-1.201731	1.459863
H	-3.491438	-0.313289	2.431586
H	-5.755261	-1.296938	2.355492
C	-5.720743	-1.745561	0.169387
C	-5.398208	-3.239444	0.020049
H	-5.811612	-3.623162	-0.919528
H	-4.314572	-3.398241	0.022980
H	-5.831614	-3.803769	0.853031
C	-7.221316	-1.480973	0.063947
H	-7.430406	-0.409739	0.150720
H	-7.601119	-1.838618	-0.898695
H	-7.751121	-2.007356	0.864855
O	-5.140327	-1.039394	-0.981761
C	1.597930	0.526542	1.506415
C	1.372660	0.586190	-1.662562
H	1.235259	-0.188613	-2.421390
H	1.422505	1.554391	-2.172781
C	2.743561	0.971128	0.531645
H	2.596752	2.040652	0.356794

C	2.682876	0.331043	-0.910198
C	1.549944	1.524333	2.683870
H	0.748825	1.264580	3.385601
H	2.492045	1.507892	3.242206
H	1.378723	2.545590	2.327472
C	1.735906	-0.909078	2.060945
H	2.692432	-1.044780	2.571883
H	0.947875	-1.100937	2.794982
H	1.647957	-1.668395	1.281396
C	4.180267	0.755338	1.087705
H	4.693803	1.710474	1.232620
H	4.177950	0.246444	2.053888
C	4.994258	-0.111961	0.090165
H	-1.941263	2.712463	-1.363827
C	-3.358504	2.806731	0.080288
N	-2.936294	2.806044	-1.196901
N	-4.665205	2.747693	0.351694
N	-2.457408	2.934172	1.058675
H	-2.747549	2.936968	2.027263
H	-5.356341	2.717331	-0.385301
H	-3.524653	2.398991	-1.913396
H	-5.001281	2.663902	1.301191
H	-1.483652	2.701455	0.853478
C	2.993243	-1.182222	-0.773816
C	5.070003	0.706892	-1.209379
N	3.811725	0.905752	-1.670142
N	4.202644	-1.330534	-0.208734
H	3.657122	1.433775	-2.521746
O	6.099827	1.139897	-1.728774
O	2.230545	-2.095122	-1.111123
C	6.323728	-0.667466	0.608699
C	4.886700	-2.572678	0.157818
C	5.966438	-2.074388	1.132616
H	5.322779	-3.039819	-0.734210
H	4.174785	-3.271800	0.604296
H	6.832407	-2.740545	1.165787
H	7.036090	-0.729560	-0.220253
H	6.758230	-0.023555	1.378007
H	5.549985	-2.010151	2.144346

TS-C2O-RRR

C	-1.263549	0.086602	-1.072199
C	-1.881339	-0.234403	0.143805
C	-3.219094	-0.602761	0.253508
C	-3.931515	-0.684115	-0.971365
C	-3.330984	-0.395273	-2.199366
C	-1.984605	-0.001632	-2.253722
C	0.113951	0.622776	-0.748515
C	0.247109	0.341623	0.700076
H	-3.928606	-0.470888	-3.102264
H	-1.526552	0.242985	-3.208042
N	-0.926957	-0.080068	1.185559
H	-1.151681	-0.126758	2.171717
O	0.069772	1.985960	-0.315282
C	-3.943054	-0.853978	1.493285
C	-5.176208	-1.381296	1.445247
H	-3.487825	-0.592835	2.444825
H	-5.747585	-1.573109	2.349508
C	-5.802572	-1.793009	0.130629
C	-5.496426	-3.267021	-0.173021
H	-5.952647	-3.557200	-1.126065
H	-4.414847	-3.428666	-0.232030
H	-5.898555	-3.906835	0.620146
C	-7.304448	-1.515819	0.111158
H	-7.503801	-0.457876	0.309961
H	-7.721646	-1.777771	-0.866564
H	-7.805616	-2.117569	0.876482
O	-5.263021	-0.979422	-0.966553
C	1.533225	0.428717	1.475632
C	1.275989	0.320370	-1.680552
H	1.085851	-0.593285	-2.249610
H	1.327203	1.157281	-2.385520
C	2.654374	0.883000	0.478376
H	2.447209	1.931518	0.257623
C	2.610445	0.174962	-0.933362
C	1.423495	1.481441	2.602963
H	0.618451	1.232165	3.302901
H	2.357084	1.516046	3.174037
H	1.230114	2.473931	2.186566
C	1.751296	-0.969361	2.121192
H	2.701043	-0.997965	2.659878
H	0.961216	-1.170331	2.851112
H	1.741332	-1.778590	1.389170
C	4.100914	0.763499	1.035742
H	4.562377	1.749962	1.139310
H	4.131654	0.294362	2.021231
C	4.954400	-0.098903	0.067665

H	-1.491684	2.799939	-1.091691
C	-2.949512	3.108999	0.256639
N	-2.455636	3.140523	-0.989554
N	-4.261309	3.269185	0.480883
N	-2.089747	2.942609	1.267902
H	-2.412029	2.854080	2.221300
H	-4.882823	3.551837	-0.264898
H	-3.077865	3.020182	-1.777904
H	-4.622395	3.339543	1.422758
H	-1.154933	2.602856	1.018871
C	3.003587	-1.312662	-0.718486
C	4.974949	0.664385	-1.266541
N	3.705649	0.769822	-1.726461
N	4.226904	-1.369209	-0.167632
H	3.516451	1.260581	-2.592912
O	5.975932	1.132251	-1.811824
O	2.282809	-2.283008	-0.980094
C	6.315828	-0.557609	0.596771
C	4.975934	-2.555195	0.254845
C	6.038060	-1.954804	1.190772
H	5.426419	-3.045081	-0.617518
H	4.304443	-3.265327	0.744506
H	6.938060	-2.572787	1.244011
H	7.023274	-0.621338	-0.236226
H	6.721886	0.144573	1.329819
H	5.629238	-1.865106	2.203618

TS-C3O-RRR

C	-1.136877	-0.103692	-1.012101
C	-1.826531	-0.203702	0.236920
C	-3.180090	-0.558383	0.293573
C	-3.797187	-0.872374	-0.938441
C	-3.122574	-0.795322	-2.179568
C	-1.795684	-0.400408	-2.218537
C	0.161635	0.397661	-0.734503
C	0.234988	0.723799	0.708159
H	-3.668993	-1.048226	-3.081779
H	-1.270688	-0.321911	-3.166031
N	-0.977797	0.125519	1.261703
H	-1.296940	0.333211	2.197693
O	0.042598	2.034732	0.213546
C	-4.006474	-0.536208	1.493490
C	-5.248349	-1.042647	1.459829
H	-3.619297	-0.072388	2.396776
H	-5.901564	-1.015892	2.327613
C	-5.773268	-1.731604	0.221129
C	-5.484411	-3.237741	0.270890
H	-5.855308	-3.724597	-0.637913
H	-4.407654	-3.416761	0.358734
H	-5.980941	-3.684729	1.138998
C	-7.255684	-1.446117	-0.005047
H	-7.435860	-0.368107	-0.066597
H	-7.593885	-1.916904	-0.933732
H	-7.841888	-1.853105	0.825424
O	-5.106128	-1.197432	-0.984565
C	1.528334	0.500605	1.504284
C	1.338766	0.552900	-1.635014
H	1.250752	-0.136521	-2.479409
H	1.334386	1.571544	-2.036560
C	2.700307	0.928853	0.558752
H	2.573726	2.002000	0.390113
C	2.654012	0.305429	-0.889724
C	1.527202	1.432683	2.732295
H	0.704570	1.183875	3.413285
H	2.458902	1.328473	3.298417
H	1.420571	2.479914	2.431236
C	1.589820	-0.970207	1.967331
H	2.564505	-1.211583	2.400033
H	0.836350	-1.152482	2.738834
H	1.397515	-1.669566	1.150132
C	4.124322	0.680852	1.134141
H	4.633312	1.625305	1.348530
H	4.097607	0.111787	2.066561
C	4.961906	-0.130442	0.110019
H	-1.422190	2.595320	-1.089358
C	-3.118380	2.988517	-0.075385
N	-2.398155	2.871375	-1.202306
N	-4.453657	3.078048	-0.126865
N	-2.464893	3.046262	1.088629
H	-2.964082	3.059602	1.967405
H	-4.934502	3.168075	-1.011719
H	-2.853657	2.603792	-2.064780
H	-4.994050	3.271207	0.705514
H	-1.476397	2.769103	1.078234
C	2.982934	-1.206106	-0.790434
C	5.030989	0.732217	-1.162342
N	3.774327	0.908844	-1.638384

N	4.194585	-1.353445	-0.232541
H	3.614284	1.479423	-2.461193
O	6.055301	1.210492	-1.651580
O	2.229980	-2.116857	-1.155223
C	6.298389	-0.678810	0.618171
C	4.895891	-2.594581	0.103714
C	5.963370	-2.107169	1.097496
H	5.343054	-3.030333	-0.798591
H	4.192363	-3.316150	0.527150
H	6.840640	-2.759002	1.113867
H	7.015752	-0.703339	-0.208489
H	6.718178	-0.051394	1.408911
H	5.542404	-2.081366	2.109024

int2-RRR

C	-1.756539	0.644665	-0.273231
C	-2.449226	-0.330196	0.444561
C	-3.826760	-0.523637	0.387773
C	-4.516576	0.348472	-0.493975
C	-3.852811	1.338970	-1.221983
C	-2.461806	1.495416	-1.111647
C	-0.283705	0.597397	0.129286
C	-0.270845	-0.650010	1.009286
H	-4.436045	1.981506	-1.874170
H	-1.953856	2.267606	-1.682524
N	-1.491082	-1.068265	1.214799
H	-1.743862	-1.833213	1.834739
O	0.065488	1.629148	0.988033
C	-4.604312	-1.491161	1.152129
C	-5.890895	-1.701993	0.833159
H	-4.145526	-2.019582	1.983259
H	-6.500642	-2.414058	1.382695
C	-6.534553	-1.005338	-0.345954
C	-6.404059	-1.862493	-1.613533
H	-6.873394	-1.352125	-2.461973
H	-5.349353	-2.043916	-1.846102
H	-6.896485	-2.830100	-1.467303
C	-7.990210	-0.643345	-0.059023
H	-8.062641	-0.017996	0.836596
H	-8.415197	-0.097646	-0.907627
H	-8.577561	-1.553755	0.099545
O	-5.875287	0.283010	-0.593245
C	0.990147	-1.288891	1.514962
C	0.688042	0.382935	-1.046045
H	0.280917	-0.359852	-1.739291
H	0.761129	1.326729	-1.597564
C	2.168655	-0.432870	0.958469
H	2.058178	0.541403	1.434081
C	2.078278	-0.096383	-0.587015
C	1.030710	-1.257244	3.063030
H	0.189983	-1.810243	3.493946
H	1.954440	-1.729035	3.412489
H	0.999208	-0.228033	3.432510
C	0.993499	-2.764006	1.026715
H	1.933217	-3.245631	1.309239
H	0.184457	-3.328537	1.500351
H	0.877762	-2.841416	-0.056830
C	3.593808	-0.955295	1.274330
H	4.043444	-0.388281	2.094693
H	3.602093	-2.009468	1.563704
C	4.469171	-0.821252	-0.000505
H	1.459349	2.721023	0.775489
C	0.911138	4.586598	0.258348
N	1.841537	3.642664	0.492558
N	1.266990	5.859864	0.032780
N	-0.366716	4.208039	0.241590
H	-1.109424	4.847167	-0.004354
H	2.238958	6.123920	-0.051015
H	2.769794	3.911505	0.791741
H	0.576695	6.568165	-0.175885
H	-0.557867	3.219647	0.498839
C	2.557774	-1.337383	-1.400104
C	4.388250	0.649766	-0.445260
N	3.113751	0.936381	-0.808090
N	3.817538	-1.637481	-1.050107
H	2.851752	1.893694	-1.020620
O	5.327702	1.447487	-0.447736
O	1.874750	-1.957384	-2.223593
C	5.876634	-1.416835	0.093405
C	4.643983	-2.754368	-1.516444
C	5.704175	-2.866335	-0.408005
H	5.090601	-2.507964	-2.487812
H	4.028073	-3.649615	-1.634000
H	6.640162	-3.296025	-0.774056
H	6.551004	-0.855267	-0.561270
H	6.272918	-1.361647	1.110661
H	5.330588	-3.506569	0.399071

int3-RRR

C	-1.032784	-0.533833	-1.143078
C	-1.902411	-0.079308	-0.056887
C	-3.198792	-0.609068	0.110153
C	-3.575863	-1.609197	-0.793235
C	-2.737997	-2.068905	-1.875195
C	-1.492055	-1.548375	-2.048742
C	0.126731	0.177454	-1.075705
C	0.076262	1.195178	0.060673
H	-3.135049	-2.844810	-2.520740
H	-0.844341	-1.894112	-2.847524
N	-1.274123	0.853949	0.651159
H	-1.692966	1.395141	1.395786
O	0.108810	2.457017	-0.432275
C	-4.182935	-0.138879	1.076704
C	-5.340158	-0.799066	1.227476
H	-3.985764	0.771444	1.636161
H	-6.109479	-0.455440	1.912945
C	-5.613386	-2.090697	0.494159
C	-5.240931	-3.301867	1.356551
H	-5.424453	-4.231019	0.806110
H	-4.185190	-3.256671	1.643035
H	-5.847932	-3.306024	2.268355
C	-7.049591	-2.169575	-0.015463
H	-7.279515	-1.313329	-0.657107
H	-7.199055	-3.092429	-0.584837
H	-7.740944	-2.167779	0.833482
O	-4.778239	-2.181524	-0.735302
C	1.230108	0.878156	1.094314
C	1.354357	0.144364	-1.903427
H	1.332464	-0.645679	-2.657140
H	1.418748	1.118333	-2.408557
C	2.544935	0.949691	0.256268
H	2.563665	1.956273	-0.172577
C	2.589465	0.001993	-1.000020
C	1.261003	1.988805	2.159050
H	0.314589	2.025915	2.711970
H	2.053328	1.799402	2.891839
H	1.434341	2.969240	1.706913
C	1.006227	-0.480023	1.790955
H	1.890131	-0.781158	2.362204
H	0.172133	-0.409503	2.495457
H	0.778041	-1.285205	1.088422
C	3.859159	0.730919	1.059589
H	4.409221	1.668955	1.179624
H	3.667227	0.336126	2.060563
C	4.748580	-0.302583	0.319630
H	-1.417639	2.902979	-1.267039
C	-2.569192	4.129928	-0.155500
N	-2.308070	3.438528	-1.269621
N	-3.745238	4.760951	0.010670
N	-1.633032	4.150426	0.800197
H	-1.695346	4.781475	1.586566
H	-4.385479	4.867357	-0.764591
H	-3.038186	3.227403	-1.935411
H	-3.904393	5.354668	0.813538
H	-0.758590	3.628508	0.594656
C	2.803924	-1.464711	-0.544428
C	4.998803	0.265012	-1.089981
N	3.814030	0.361068	-1.742921
N	3.944432	-1.538820	0.158641
H	3.770207	0.776515	-2.666924
O	6.093580	0.603017	-1.542416
O	2.037604	-2.401972	-0.794344
C	5.990993	-0.781756	1.076144
C	4.533852	-2.706662	0.816921
C	5.521716	-2.060233	1.802116
H	5.044989	-3.336818	0.077928
H	3.750455	-3.298591	1.297363
H	6.350775	-2.726977	2.053058
H	6.785164	-1.010773	0.358194
H	6.367540	-0.016802	1.760360
H	5.001154	-1.802218	2.731506

TS-C2O-nr

C	2.575077	0.828762	-1.901912
C	3.075206	1.155679	-0.638638
C	2.477299	0.676163	0.554668
C	1.345112	-0.116604	0.383529
C	0.823319	-0.456850	-0.867793
C	1.440147	0.012755	-2.021329
N	0.557786	-0.737523	1.373210
C	-0.445185	-1.477553	0.842453
C	-0.323681	-1.429674	-0.647914
C	-1.439817	-1.395590	-1.691415

C	-2.374402	-0.160732	-1.763006
N	-1.719947	1.073504	-1.313848
C	-2.353236	2.202083	-0.924092
C	-3.867508	2.103984	-0.879070
N	-4.330270	0.734289	-0.611265
C	-3.705329	-0.382103	-1.014580
O	-4.178454	-1.514678	-0.852113
O	-1.756862	3.248276	-0.645844
C	-4.561162	2.923830	0.214764
C	-5.912705	2.201264	0.363213
C	-5.570566	0.710645	0.182108
C	-1.475976	-2.101201	1.768216
C	-2.480151	-1.035218	2.205339
C	-2.404387	0.290402	2.065958
O	4.217678	1.896141	-0.578131
C	3.111493	1.001493	1.825830
C	4.078902	1.930970	1.864082
C	4.471317	2.703577	0.623510
C	-2.241838	-3.273859	1.116549
C	-0.778508	-2.652968	3.044222
C	5.971765	2.985931	0.586152
C	3.649088	3.995654	0.511505
H	3.083718	1.211150	-2.780967
H	1.062768	-0.247394	-3.006360
H	0.832167	-0.796064	2.344247
H	-0.932883	-1.505870	-2.656776
H	-2.067990	-2.277697	-1.574248
H	-4.659201	3.975374	-0.062449
H	-3.980384	2.866705	1.141556
H	-6.391143	2.395708	1.326675
H	-6.599159	2.527397	-0.426366
H	-6.348040	0.147412	-0.342069
H	-5.367958	0.206731	1.133925
H	-3.345167	-1.460862	2.714685
H	-3.195247	0.926959	2.452496
H	-1.579011	0.793274	1.571743
H	2.807948	0.477113	2.727959
H	4.578041	2.193706	2.792870
H	-2.952256	-3.672536	1.849357
H	-1.549552	-4.066552	0.828387
H	-2.811000	-2.953338	0.245400
H	-0.027986	-3.404720	2.776117
H	-0.307751	-1.869418	3.647454
H	-1.528649	-3.131046	3.681777
H	6.252178	3.628887	1.426993
H	6.541313	2.053296	0.652351
H	6.235175	3.496503	-0.345775
H	3.824763	4.630537	1.386758
H	3.936965	4.548854	-0.389522
H	2.579557	3.765477	0.461313
H	-0.717413	1.157559	-1.447851
H	-2.665676	-0.046708	-2.818379
H	-4.230985	2.424740	-1.869328
O	0.180155	-2.743485	-0.376223
C	3.398580	-3.036153	-0.873213
N	2.924387	-3.031211	0.379019
N	4.705067	-2.864554	-1.117702
N	2.534100	-3.251503	-1.873602
H	2.813415	-3.097581	-2.833024
H	5.373968	-2.812985	-0.361406
H	3.511499	-2.755760	1.154424
H	5.081178	-3.001125	-2.046255
H	1.539131	-3.161724	-1.639492
H	1.908552	-2.945151	0.476752

int2-nr

C	2.832331	0.476180	-1.670919
C	3.020692	1.201778	-0.492164
C	2.218541	0.983443	0.657985
C	1.224882	0.020627	0.505243
C	0.997610	-0.704616	-0.661095
C	1.812040	-0.483742	-1.763669
N	0.270174	-0.410591	1.466882
C	-0.569300	-1.311777	1.007629
C	-0.155302	-1.694804	-0.428726
C	-1.214465	-1.650976	-1.562352
C	-2.066944	-0.377918	-1.815915
N	-1.381277	0.851100	-1.395904
C	-1.969166	2.037674	-1.114771
C	-3.485170	2.026949	-1.124360
N	-4.042419	0.696062	-0.848135
C	-3.472424	-0.470081	-1.188457
O	-4.044049	-1.560228	-1.047976
O	-1.325910	3.068284	-0.890037
C	-4.176136	2.911860	-0.080849
C	-5.582928	2.289191	-0.002966
C	-5.348044	0.774746	-0.169205

C	-1.564263	-1.959486	1.946111
C	-2.568150	-0.930578	2.464179
C	-2.651108	0.376891	2.206808
O	4.050254	2.092574	-0.445129
C	2.516823	1.745870	1.863861
C	3.351292	2.794539	1.788113
C	3.935006	3.240267	0.465140
C	-2.346731	-3.117844	1.286764
C	-0.786742	-2.543178	3.166103
C	5.365223	3.751464	0.621981
C	3.027722	4.287942	-0.196712
H	3.486147	0.676128	-2.513901
H	1.668448	-1.033217	-2.688950
H	0.283945	-0.105803	2.435858
H	-0.642718	-1.874263	-2.469663
H	-1.900274	-2.485567	-1.417709
H	-4.183379	3.962972	-0.375858
H	-3.653604	2.827836	0.878035
H	-6.092888	2.520885	0.935755
H	-6.202587	2.665969	-0.824378
H	-6.119348	0.281577	-0.768162
H	-5.273590	0.250677	0.789416
H	-3.303815	-1.382501	3.129864
H	-3.436359	0.975010	2.660091
H	-1.966601	0.903801	1.549338
H	2.074555	1.455997	2.812794
H	3.596433	3.387009	2.665510
H	-2.992848	-3.575219	2.043763
H	-1.653333	-3.869512	0.905583
H	-2.979316	-2.764450	0.472929
H	-0.064247	-3.291042	2.825166
H	-0.260386	-1.774821	3.741045
H	-1.499204	-3.028353	3.840898
H	5.375749	4.642066	1.258793
H	6.001488	2.986131	1.077897
H	5.777380	4.017905	-0.356582
H	2.931222	5.165697	0.451457
H	3.454968	4.602423	-1.155410
H	2.027946	3.875991	-0.370230
H	-0.378957	0.895478	-1.546032
H	-2.250785	-0.330155	-2.900020
H	-3.787924	2.345423	-2.135598
O	0.318255	-2.982450	-0.226574
C	3.405628	-3.578313	-0.693571
N	2.947115	-3.245572	0.517334
N	4.726598	-3.655553	-0.939804
N	2.507708	-3.837520	-1.650587
H	2.793169	-3.991850	-2.607545
H	5.388063	-3.626534	-0.175480
H	3.573970	-2.917915	1.238923
H	5.062561	-4.061441	-1.802938

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english

Reference

(1) Sato, M.; Yagishita, F.; Mino, T.; Uchiyama, N.; Patel, A.; Chooi, Y.-H.; Goda, Y.; Xu, W.; Noguchi, H.; Yamamoto, T.; et al. Involvement of Lipocalin-like CghA in Decalin-Forming Stereoselective Intramolecular [4+2] Cycloaddition. *ChemBioChem* **2015**, *16* (16), 2294-2298. DOI: https://doi.org/10.1002/cbic.201500386.

(2) Szewczyk, E.; Nayak, T.; Oakley, C. E.; Edgerton, H.; Xiong, Y.; Taheri-Talesh, N.; Osmani, S. A.; Oakley, B. R. Fusion PCR and gene targeting in Aspergillus nidulans. *Nat. Protocols* **2007**, *1* (6), 3111-3120, DOI: 10.1038/nprot.2006.405.

(3) Chooi, Y.-H.; Cacho, R.; Tang, Y. Identification of the viridicatumtoxin and griseofulvin gene clusters from Penicillium aethiopicum. *Chem. Biol.* **2010**, *17* (7), 483-494. DOI: 10.1016/j.chembiol.2010.03.015.

(4) Xu, W.; Raetz, L. B.; Wang, P.; Tang, Y. An ATP-dependent ligase catalyzes the fourth ring cyclization in tetracycline biosynthesis. *Tetrahedron* **2015**, *72* (25), 3599-3604. DOI: 10.1016/j.tet.2015.09.029.

(5) Sheldrick, G. M.; Schneider, T. R. SHELXL: high-resolution refinement. *Methods Enzymol.* **1997**, *277*, 319-343.

(6) *Gaussian 09 Rev. D.01*; Wallingford, CT, 2009.

(7) Hehre, W. J.; Ditchfield, R.; Pople, J. A. Self-consistent molecular orbital methods. XII. Further extensions of Gaussian-type basis sets for use in molecular orbital studies of organic molecules. *J. Chem. Phys.* **1972**, *56* (5), 2257-2261. DOI: 10.1063/1.1677527.

(8) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. Self-consistent molecular orbital methods. XX. A basis set for correlated wave functions. *J. Chem. Phys.* **1980**, *72* (1), 650-654. DOI: 10.1063/1.438955. Frisch, M. J.; Pople, J. A.; Binkley, J. S. Self-consistent molecular orbital methods. 25. Supplementary functions for Gaussian basis sets. *J. Chem. Phys.* **1984**, *80* (7), 3265-3269. DOI: 10.1063/1.447079. Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R. Efficient diffuse function-augmented basis sets for anion calculations. III. The 3-21 + G basis set for first-row elements, lithium to fluorine. *J. Comput. Chem.* **1983**, *4* (3), 294-301. DOI: 10.1002/jcc.540040303.

(9) Legault, C. Y. CYLview20. *Université de Sherbrooke* **2020** (http://www.cylview.org).

(10) Lu, T.; Chen, F. Multiwfn: A multifunctional wavefunction analyzer. *J. Comput. Chem.* **2012**, *33* (5), 580-592, 10.1002/jcc.22885. DOI: 10.1002/jcc.22885. Humphrey, W.; Dalke, A.; Schulten, K. VDM: visual molecular dynamics. *J. Mol. Graphics* **1996**, *14* (1), 33-38, plates, 27-28. DOI: 10.1016/0263-7855(96)00018-5.

(11) Kato, H.; Yoshida, T.; Tokue, T.; Nojiri, Y.; Hirota, H.; Ohta, T.; Williams, R. M.; Tsukamoto, S. Notoamides A-D: prenylated indole alkaloids isolated from a marine-derived fungus, Aspergillus sp. *Angew. Chem., Int. Ed.* **2007**, *46* (13), 2254-2256. DOI: 10.1002/anie.200604381.

(12) Cai, S.; Luan, Y.; Kong, X.; Zhu, T.; Gu, Q.; Li, D. Isolation and Photoinduced Conversion of 6-epi-Stephacidins from Aspergillus taichungensis. *Org. Lett.* **2013**, *15* (9), 2168-2171. DOI: 10.1021/ol400694h.

(13) Tsukamoto, S.; Kato, H.; Greshock, T. J.; Hirota, H.; Ohta, T.; Williams, R. M. Isolation of notoamide E, a key precursor in the biosynthesis of prenylated indole alkaloids in a marine-derived fungus, Aspergillus sp. *J. Am. Chem. Soc.* **2009**, *131* (11), 3834-3835. DOI: 10.1021/ja810029b.

(14) Tsukamoto, S.; Kawabata, T.; Kato, H.; Greshock, T. J.; Hirota, H.; Ohta, T.; Williams, R. M. Isolation of antipodal (-)-versicolamide B and notoamides L-N from a marine-derived Aspergillus sp.

Org. Lett. **2009**, *11* (6), 1297-1300. DOI: 10.1021/ol900071c.
(15) Tsukamoto, S.; Umaoka, H.; Yoshikawa, K.; Ikeda, T.; Hirota, H. Notoamide O, a structurally unprecedented prenylated indole alkaloid, and notoamides P-R from a marine-derived fungus, Aspergillus sp. *J. Nat. Prod.* **2010**, *73* (8), 1438-1440. DOI: 10.1021/np1002498.
(16) Chang, Y.-W.; Yuan, C.-M.; Zhang, J.; Liu, S.; Cao, P.; Hua, H.-M.; Di, Y.-T.; Hao, X.-J. Speramides A-B, two new prenylated indole alkaloids from the freshwater-derived fungus Aspergillus ochraceus KM007. *Tetrahedron Lett.* **2016**, *57* (45), 4952-4955. DOI: 10.1016/j.tetlet.2016.09.071.
(17) Greshock, T. J.; Grubbs, A. W.; Jiao, P.; Wicklow, D. T.; Gloer, J. B.; Williams, R. M. Isolation, structure elucidation, and biomimetic total synthesis of versicolamide B, and the isolation of antipodal (-)-stephacidin A and (+)-notoamide B from Aspergillus versicolor NRRL 35600. *Angew. Chem., Int. Ed.* **2008**, *47* (19), 3573-3577. DOI: 10.1002/anie.200800106.
(18) Greshock, T. J.; Grubbs, A. W.; Tsukamoto, S.; Williams, R. M. A concise, biomimetic total synthesis of stephacidin A and notoamide B. *Angew. Chem., Int. Ed.* **2007**, *46* (13), 2262-2265. DOI: 10.1002/anie.200604378.
(19) Miller, K. A.; Tsukamoto, S.; Williams, R. M. Asymmetric total syntheses of (+)- and (−)-versicolamide B and biosynthetic implications. *Nat. Chem.* **2009**, *1*, 63-68, DOI: 10.1038/nchem.110.
(20) Chen, M.; Shao, C.-L.; Fu, X.-M.; Xu, R.-F.; Zheng, J.-J.; Zhao, D.-L.; She, Z.-G.; Wang, C.-Y. Bioactive indole alkaloids and phenyl ether derivatives from a marine-derived Aspergillus sp. fungus. *J. Nat. Prod.* **2013**, *76* (4), 547-553. DOI: 10.1021/np300707x.
(21) Kato, H.; Nakahara, T.; Sugimoto, K.; Matsuo, K.; Kagiyama, I.; Frisvad, J. C.; Sherman, D. H.; Williams, R. M.; Tsukamoto, S. Isolation of Notoamide S and Enantiomeric 6-epi-Stephacidin A from the Fungus Aspergillus amoenus: Biogenetic Implications. *Org. Lett.* **2015**, 700-703. DOI: 10.1021/ol5037198. Li, S.; Finefield, J. M.; Sunderhaus, J. D.; McAfoos, T. J.; Williams, R. M.; Sherman, D. H. Biochemical Characterization of NotB as an FAD-Dependent Oxidase in the Biosynthesis of Notoamide Indole Alkaloids. *J. Am. Chem. Soc.* **2012**, *134* (2), 788-791. DOI: 10.1021/ja2093212.

https://engine.scichina.com/doi/10.1007/s11426-024-2134-0
http://chem.scichina.com/english