

Communication

Concise Synthesis of (+)- β - and γ -Apopicropodophyllins, and Dehydrodesoxy podophyllotoxin

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Abstract: Herein, we present an expeditious synthesis of bioactive aryldihydronaphthalene lignans (+)- β - and γ -apopicropodophyllins, and aryl naphthalene lignan dehydrodesoxy podophyllotoxin. The key reaction is regiocontrolled oxidations of stereodivergent aryltetralin lactones, which were easily accessed from a nickel-catalyzed reductive cascade approach developed in our group.

Keywords: aryldihydronaphthalene lignan; aryl naphthalene lignan; oxidation; synthesis

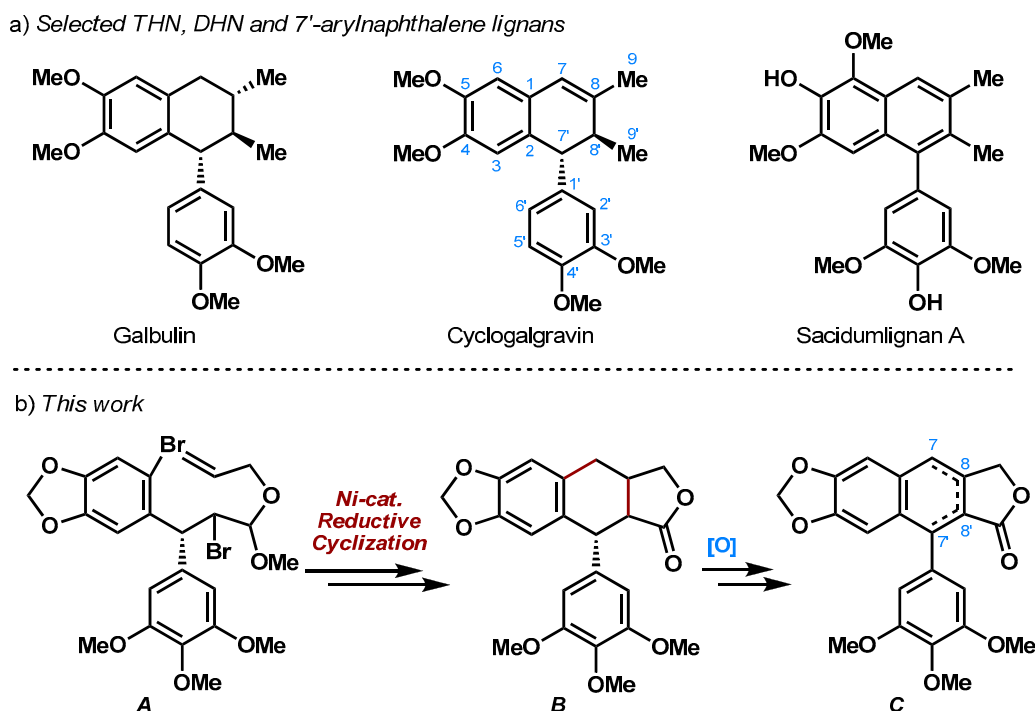
1. Introduction

Lignans are a class of secondary metabolites in various plants, and most of them have demonstrated interesting biological properties [1,2], thus attracting the attention of the synthetic chemists [3,4]. Some of 2,7'-cyclo lignans such as 7,8,8',7'-tetrahydronaphthalene (THN), 7',8'-dihydronaphthalene (DHN) and 7'-arylnaphthalene types are exemplified in Scheme 1a. Hong and co-workers used organocatalytic domino Michael–Michael–aldol reactions to construct THN skeleton of galbulin and realized its first enantioselective synthesis [5]. Barker and co-workers completed the first asymmetric synthesis of (–)-cyclogalgravin based on a key construction of C2–C7' bond from in situ generated quinoid intermediate [6]. Notably, the other two structurally distinct class of lignans could also be obtained from a common precursor in their syntheses. Ramana et al. proposed a dehydrative cyclization of an aldehyde intermediate to build the DHN unit of sacidumlignan B, whose subsequent aromatization led to the synthesis of sacidumlignan A [7]. We were also involved in this fascinating field and achieved the synthesis of these three molecules through Ueno–Stork radical cyclization and Friedel–Crafts reaction [8,9]. However, almost all of the above syntheses applied stepwise strategies (i.e., a sequence of C2–C7', C8–C8', then C1–C7 bonds formation in our previous routes) for construction of the central core [10].

2. Results and Discussion

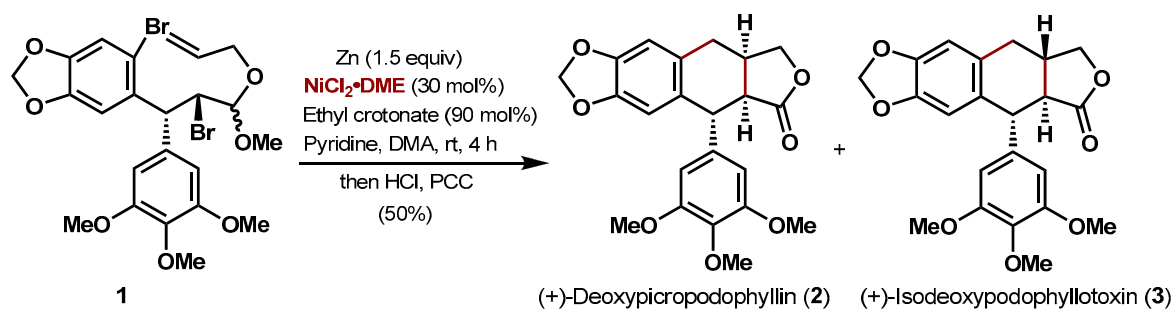
Recently, we completed a new synthesis of podophyllotoxin [11,12], an aryltetralin lignan used as building block for the chemotherapeutic drugs etoposide and teniposide. The key reaction is a Ni-catalyzed reductive tandem coupling [13–19] of dibromide A that led to the simultaneous construction of C8–C8' and C1–C7 bonds in THN framework of B (Scheme 1b). We envision that this

aryltetralin lactone could serve as an advanced intermediate for the unified synthesis of the titled arylnaphthalene, DHN and THN lignans *C*, by means of the regioselective late-stage oxidation. Herein, we disclosed the preliminary results.



Scheme 1. (a) Several arylnaphthalene lignans and their DHN and THN derivatives; (b) Our synthetic logic.

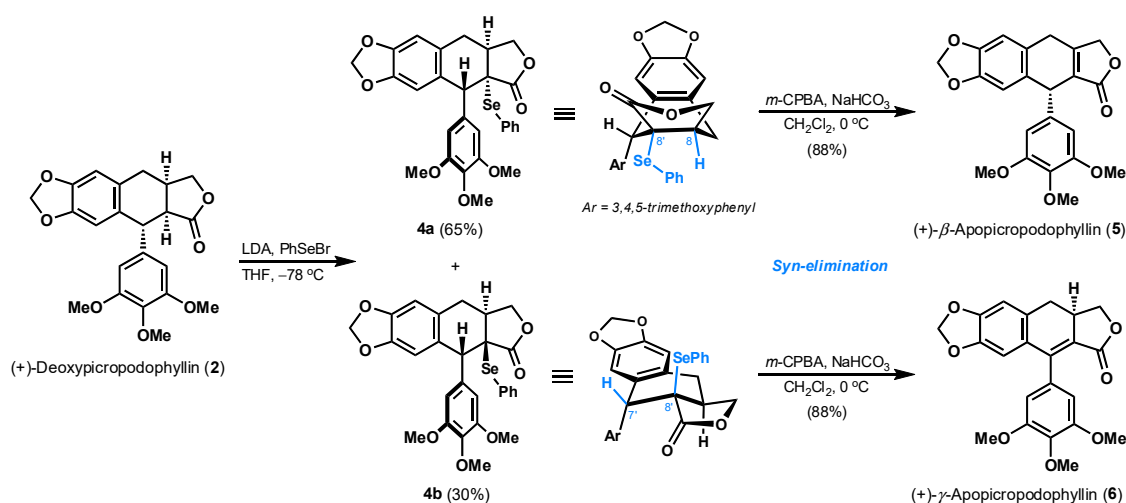
Starting from the commercially available 6-bromopiperonal and 3,4,5-trimethoxyphenyl bromide, the chiral β -bromo acetal **1** was straightforwardly prepared as in gram-scale according to a known route [11]. Under a fully intramolecular reductive nickel-catalysis ligated by ethyl crotonate (Scheme 2), diastereodivergent (+)-deoxypicropodophyllin (**2**) and (+)-isodeoxypodophyllotoxin (**3**) were obtained in 50% overall yield after a conversion of acetal moiety to the corresponding lactone. With aryltetralin lactones **2** and **3** in hand, the designed regiocontrolled oxidation in central aliphatic ring could be executed (*vide infra*).



Scheme 2. Reductive tandem cyclization for tetralin lactones.

First of all, the increase of an unsaturation degree at either C8–C8' or C7'–C8' location was pursued in order to get (+)- β -apopicropodophyllin (**5**) and (+)- γ -apopicropodophyllin (**6**) quickly. As shown in Scheme 3, the introduction of a phenylselenenyl group at C8' position of (+)-deoxypicropodophyllin (**2**) was done by an initial enolization and subsequent quench with phenylselenenyl bromide (PhSeBr) at -78°C . The generated products as two diastereoisomers (**4a** and **4b**) were separated by column

chromatography on silica gel in 95% overall yield. The α -phenylselenide **4a** is supposed to adopt a pseudo-boat conformation, where the hydrogen atom at C8 is arranged *cis* to the -SePh. The requisite *syn*-elimination of phenylselenoxide in situ generated from oxidation of **4a** [20], eventually provided (+)- β -apopicropodophyllin (**5**) with in vivo insecticidal activity against the fifth-instar larvae of *Brontispa longissima* [21]. Its ^1H NMR spectral data (Table S2) and optical rotation were in agreement with the reported data by Toste and Meyers [22,23]. The structure was later unambiguously confirmed by its single-crystal analysis (Figure 1) [24]. In contrast, the hydrogen atom at C7' is oriented at *cis*-position of C8'-PhSe in the favored half-chair conformer of β -phenylselenide **4b**. Thus, a double bond within C7'-C8' was formed upon the subjection of **4b** to *m*-CPBA, therefore affording to (+)- γ -apopicropodophyllin (**6**) in 88% yield. As shown in Table S3, ^1H NMR spectra of the synthetic **6** was accord with the literature [25].



Scheme 3. Regiodivergent oxidation of (+)-deoxypicropodophyllin (**2**).

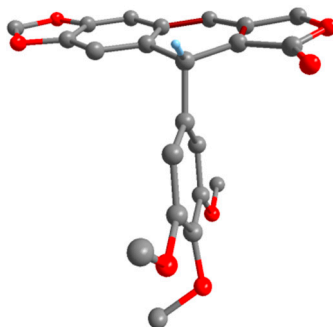
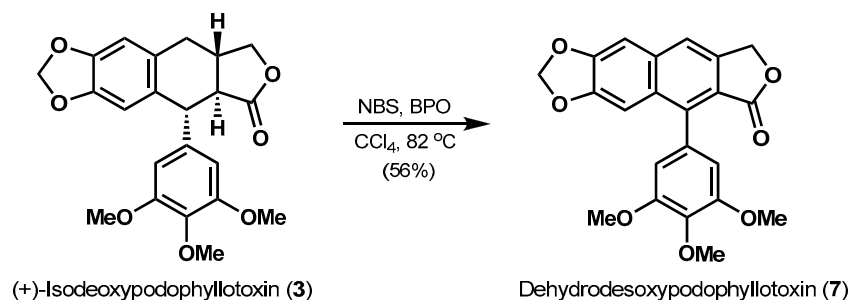


Figure 1. X-ray crystal structure of (+)- β -apopicropodophyllin (**5**), selected H atoms have been omitted for clarity.

Next, the potential aromatization within tetralin lactone was investigated. As shown in Scheme 4, one-step conversion of (+)-isodeoxypodophyllotoxin (**3**) to dehydridesoxypodophyllotoxin (**7**) was realized in 56% yield promoted by a mixture of *N*-bromosuccinimide (NBS) and dibenzoyl peroxide (BPO) in refluxing CCl_4 . The plausible mechanism of this tandem reaction would be radical bromination [26] catalyzed by BPO occurs firstly, and a fast elimination of the resulting labile benzylbromide followed by further oxidation, providing the central benzene ring in **7**. ^1H NMR spectra data (Table S4) of synthetic dehydridesoxypodophyllotoxin was consistent with previous report [27].



Scheme 4. One-step conversion of tetralin to aryl naphthalene skeleton.

3. Materials and Methods

3.1. General Procedure

For product purification by flash column chromatography, SiliaFlash P60 (particle size: 40–63 μm , pore size 60A) and petroleum ether (bp. 60–90 $^{\circ}\text{C}$) were used. All solvents were purified and dried by standard techniques and distilled prior to use. All of experiments were conducted under an argon or nitrogen atmosphere in oven-dried or flame-dried glassware with magnetic stirring, unless otherwise specified. Organic extracts were dried over Na_2SO_4 or MgSO_4 , unless otherwise noted. ^1H and ^{13}C -NMR spectra were taken on a Bruker AM-400, AM-600 and Varian mercury 300 MHz spectrometer with TMS as an internal standard and CDCl_3 as solvent unless otherwise noted. HRMS were determined on a Bruker Daltonics APEXII 47e FT-ICR spectrometer with ESI positive ion mode. The X-ray diffraction studies were carried out on a Bruker SMART Apex CCD area detector diffractometer equipped with graphite-monochromated Cu-K α radiation source. Melting points were measured on Kofler hot stage and are uncorrected.

3.2. Synthesis of C9a-PhSe-Deoxy podophyllin (4a and 4b)

A solution of **2** [11] (100 mg, 0.25 mmol) in THF (8 mL) under argon was cooled to -78°C , followed by the addition of freshly prepared LDA (0.5 mmol, 2.0 equiv). The stirred solution was maintained at this temperature for 20 min, and a solution of PhSeBr (118 mg, 0.5 mmol, 2.0 equiv) in THF (3 mL) was then added. The resulting mixture was stirred for 20 min at -78°C , and then quenched by water (1 mL). The mixture was extracted with EtOAc (2×30 mL). The combined organic layers were washed with water (2×8 mL) and brine (8 mL) respectively, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/EtOAc = 4:1 \rightarrow petroleum ether/EtOAc = 2:1) on silica gel to afford **4a** (90 mg, 65% yield) as a white solid and **4b** (42 mg, 30% yield) as a white solid. Characterization data for **4a**: R_f = 0.42 (petroleum ether/EtOAc = 1:1); ^1H -NMR (400 MHz, CDCl_3): δ = 7.48 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 7.2 Hz, 1H), 7.28 (t, J = 7.2 Hz, 2H), 6.68 (s, 1H), 6.61 (s, 2H), 6.56 (s, 1H), 5.88 (d, J = 1.2 Hz, 1H), 5.87 (d, J = 1.2 Hz, 1H), 4.49 (s, 1H), 4.10 (dd, J = 9.2, 7.6 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 6H), 3.75 (dd, J = 5.2, 4.0 Hz, 1H), 3.48 (dd, J = 16.4, 8.4 Hz, 1H), 3.32–3.27 (m, 1H), 2.62 (d, J = 16.4 Hz, 1H) ppm; ^{13}C -NMR (100 MHz, CDCl_3): δ = 176.7, 152.9 (2C), 147.2, 146.9, 137.7 (2C), 137.3, 134.6, 131.8, 129.9, 129.1 (2C), 126.1, 126.0, 109.3, 108.8, 106.8 (2C), 101.0, 73.3, 60.9, 56.2 (2C), 53.9, 51.3, 41.5, 35.0 ppm; HRMS (ESI): calcd. for $\text{C}_{28}\text{H}_{30}\text{NO}_7\text{Se}^+$ [$\text{M} + \text{NH}_4$] $^+$: 572.1182, found: 572.1186.

3.3. Synthesis of (+)- β -Apopicropodophyllin (5)

To a stirred solution of **4a** (90 mg, 0.076 mmol) in CH_2Cl_2 (4 mL) was added *m*-CPBA (77%, 34.0 mg, 0.15 mmol, 2.0 equiv) at 0°C followed by the addition of NaHCO_3 (12.6 mg, 0.15 mmol, 2.0 equiv). After stirring for 15 min, the reaction mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with saturated aqueous NaHCO_3 (4×5 mL), water (5 mL) and brine (5 mL) respectively, then dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (petroleum ether/EtOAc = 3:1 \rightarrow petroleum

ether/EtOAc = 1:1) on silica gel to afford (+)- β -apopicropodophyllin (**5**) (56 mg, 88% yield) as a white solid. R_f = 0.37 (petroleum ether/EtOAc = 1:1); $[\alpha]_D^{20}$ = +92.04 (c = 1.00, CHCl₃), $[\alpha]_D^{23}$ = +65.1 (c = 2.72, CHCl₃) [23]; m.p. 188–190 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 6.72 (s, 1H), 6.63 (s, 1H), 6.37 (s, 2H), 5.954 (s, 1H), 5.947 (s, 1H), 4.90 (d, J = 17.4 Hz, 1H), 4.82 (d, J = 17.4 Hz, 1H), 4.81 (s, 1H), 3.86 (dd, J = 22.2, 3.9 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 6H), 3.65 (dd, J = 22.2, 3.6 Hz, 1H) ppm; ¹³C-NMR (100 MHz, CDCl₃): δ = 172.2, 157.2, 153.2 (2C), 147.3, 147.0, 138.3, 137.1, 129.7, 128.2, 123.8, 109.6, 107.7, 105.6 (2C), 101.3, 71.0, 60.8, 56.2 (2C), 42.8, 29.2 ppm.

This product (5 mg) was dissolved in EtOAc (1 mL) and hexane (2 mL). After three days, colorless single crystals were obtained by slow evaporation of solvents at room temperature.

3.4. Synthesis of (+)- γ -Apopicropodophyllin (**6**)

To a stirred solution of **4b** (42 mg, 0.16 mmol) in CH₂Cl₂ (3 mL) was added *m*-CPBA (77%, 72.0 mg, 0.32 mmol, 2.0 equiv) at 0 °C followed by the addition of NaHCO₃ (26.9 mg, 0.32 mmol, 2.0 equiv). After stirring for 15 min, the reaction mixture was extracted with CH₂Cl₂ (3 × 20 mL). The combined organic layers were washed with saturated aqueous NaHCO₃ (4 × 5 mL), water (5 mL) and brine (5 mL) respectively, then dried over Na₂SO₄, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (petroleum ether/EtOAc = 3:1 → petroleum ether/EtOAc = 1:1) on silica gel to afford (+)- γ -apopicropodophyllin (**6**) (26 mg, 88% yield) as a white solid. R_f = 0.23 (petroleum ether/EtOAc = 1:1); $[\alpha]_D^{20}$ = +27.03 (c = 1.00, CHCl₃), $[\alpha]_D^{19}$ = +25.0 (c = 1, CHCl₃) [28]; m.p. 206–208 °C; ¹H-NMR (300 MHz, CDCl₃): δ = 6.77 (s, 1H), 6.52 (brs, 3H), 5.97 (s, 2H), 4.70 (t, J = 8.7 Hz, 1H), 4.01 (t, J = 8.7 Hz, 1H), 3.92 (s, 3H), 3.83 (s, 6H), 3.39 (td, J = 15.9, 8.7 Hz, 1H), 2.94 (dd, J = 15.0, 6.9 Hz, 1H), 2.79 (dd, J = 15.6, 15.3 Hz, 1H) ppm; ¹³C-NMR (150 MHz, CDCl₃): δ = 168.1, 152.7, 148.7 (2C), 147.3, 146.8, 138.1, 130.7 (2C), 129.9, 129.6, 119.9, 109.5, 108.6, 101.6 (2C), 70.9, 61.0, 56.2 (2C), 35.8, 33.3 ppm.

3.5. Synthesis of Dehydrodesoxypodophyllotoxin (**7**)

An oven-dried 10 mL round-bottom flask was charged with NBS (17.8 mg, 0.1 mmol, 1.0 equiv) and BPO (2.4 mg, 0.01 mmol, 0.1 equiv) at room temperature under argon, followed by the addition of a solution of **3** (40.0 mg, 0.1 mmol) in CCl₄ (3 mL). The reaction mixture was stirred for 2 h at 82 °C. The reaction solvent was then evaporated in vacuo. The resulting residue was purified by flash column chromatography (petroleum ether/EtOAc = 5:1 → petroleum ether/EtOAc = 2:1) on silica gel to afford dehydrodesoxypodophyllotoxin (**7**) (22.2 mg, 56% yield) as a white solid. R_f = 0.45 (petroleum ether/EtOAc = 1:1); m.p. 271–273 °C; ¹H-NMR (400 MHz, CDCl₃): δ = 7.70 (s, 1H), 7.21 (s, 1H), 7.12 (s, 1H), 6.55 (s, 2H), 6.09 (s, 2H), 5.38 (s, 2H), 3.97 (s, 3H), 3.84 (s, 6H) ppm; ¹³C-NMR (150 MHz, CDCl₃): δ = 169.6, 153.0 (2C), 150.0, 148.7, 140.5, 139.8, 137.8, 134.6, 130.34, 130.30, 119.1, 118.7, 107.3 (2C), 103.8, 103.6, 101.8, 68.0, 61.0, 56.1 (2C) ppm.

4. Conclusions

In summary, a two-phase strategy was developed for the unified synthesis of (+)- β -apopicropodophyllin (**5**), (+)- γ -apopicropodophyllin (**6**), and dehydrodesoxypodophyllotoxin (**7**). In phase I, their tetrahydronaphthalene (THN) backbone was constructed by a Ni-catalyzed reductive cascade. In phase II, regioselective oxidation of stereodivergent tetralin lactone (**2** and **3**) gave aryl-naphthalene lignan **7** and its dihydronaphthalene (DHN) congeners (**5** and **6**) efficiently.

Supplementary Materials: The following are available online. Copies of ¹H-, ¹³C-NMR, and crystallographic information files (CIFs) for **5**.

Author Contributions: Y.P. conceived and designed the experiments; J.X. performed the experiments; J.X., G.N., Y.-W.W., and Y.P. analyzed the data; Y.-W.W. and Y.P. wrote the paper.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. Ayres, D.C.; Loike, J.D. *Lignans, Chemical, Biological and Clinical Properties*; Cambridge University Press: Cambridge, UK, 1990.
2. Shi, J. *Lignans Chemistry*, 1st ed.; Chemical Industrial Press: Beijing, China, 2010; pp. 1–395, ISBN 978-7-122-06559-9.
3. Peng, Y. Lignans, lignins, and resveratrols. In *From Biosynthesis to Total Synthesis: Strategies and Tactics for Natural Products*; Zografos, A.L., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2016; pp. 331–379.
4. Sellars, J.D.; Steel, P.G. Advances in the synthesis of aryltetralin lignan lactones. *Eur. J. Org. Chem.* **2007**, *2007*, 3815–3828. [[CrossRef](#)]
5. Hong, B.C.; Hsu, C.S.; Lee, G.H. Enantioselective total synthesis of (+)-galbulin via organocatalytic domino Michael-Michael-aldol condensation. *Chem. Commun.* **2012**, *48*, 2385–2387. [[CrossRef](#)] [[PubMed](#)]
6. Rye, C.E.; Barker, D. Asymmetric synthesis of (+)-galbelgin, (–)-kadangustin J, (–)-cyclogalgravin and (–)-pycnanthuligenes A and B, three structurally distinct lignan classes, using a common chiral precursor. *J. Org. Chem.* **2011**, *76*, 6636–6648. [[CrossRef](#)] [[PubMed](#)]
7. Route, J.K.; Ramana, C.V. Total synthesis of (–)-sacidumignans B and D. *J. Org. Chem.* **2012**, *77*, 1566–1571. [[CrossRef](#)] [[PubMed](#)]
8. Zhang, J.J.; Yan, C.S.; Peng, Y.; Luo, Z.B.; Xu, X.B.; Wang, Y.W. Total synthesis of (±)-sacidumignans D and A through Ueno-Stork radical cyclization reaction. *Org. Biomol. Chem.* **2013**, *11*, 2498–2513. [[CrossRef](#)] [[PubMed](#)]
9. Peng, Y.; Luo, Z.B.; Zhang, J.J.; Luo, L.; Wang, Y.W. Collective synthesis of several 2,7'-cycloignans and their correlation by chemical transformations. *Org. Biomol. Chem.* **2013**, *11*, 7574–7586. [[CrossRef](#)] [[PubMed](#)]
10. Kocsis, L.S.; Brummond, K.M. Intramolecular Dehydro-Diels–Alder Reaction Affords Selective Entry to Arylnaphthalene or Aryldihydronaphthalene Lignans. *Org. Lett.* **2014**, *16*, 4158–4161. [[CrossRef](#)] [[PubMed](#)]
11. Xiao, J.; Cong, X.W.; Yang, G.Z.; Wang, Y.W.; Peng, Y. Divergent asymmetric syntheses of podophyllotoxin and related family members via stereoselective reductive Ni-catalysis. *Org. Lett.* **2018**, *20*, 1651–1654. [[CrossRef](#)] [[PubMed](#)]
12. Xiao, J.; Cong, X.W.; Yang, G.Z.; Wang, Y.W.; Peng, Y. Stereoselective synthesis of *podophyllum* lignans core by intramolecular reductive nickel-catalysis. *Chem. Commun.* **2018**, *54*, 2040–2043. [[CrossRef](#)] [[PubMed](#)]
13. Yan, C.S.; Peng, Y.; Xu, X.B.; Wang, Y.W. Nickel-mediated inter- and intramolecular reductive cross-coupling of unactivated alkyl bromides and aryl iodides at room temperature. *Chem. Eur. J.* **2012**, *18*, 6039–6048. [[CrossRef](#)] [[PubMed](#)]
14. Xu, X.B.; Liu, J.; Zhang, J.J.; Wang, Y.W.; Peng, Y. Nickel-mediated inter- and intramolecular C-S coupling of thiols and thioacetates with aryl iodides at room temperature. *Org. Lett.* **2013**, *15*, 550–553. [[CrossRef](#)] [[PubMed](#)]
15. Peng, Y.; Luo, L.; Yan, C.S.; Zhang, J.J.; Wang, Y.W. Ni-catalyzed reductive homocoupling of unactivated alkyl bromides at room temperature and its synthetic application. *J. Org. Chem.* **2013**, *78*, 10960–10967. [[CrossRef](#)] [[PubMed](#)]
16. Peng, Y.; Xu, X.B.; Xiao, J.; Wang, Y.W. Nickel-mediated stereocontrolled synthesis of spiroketals via tandem cyclization-coupling of β-bromo ketals and aryl iodides. *Chem. Commun.* **2014**, *50*, 472–474. [[CrossRef](#)] [[PubMed](#)]
17. Luo, L.; Zhang, J.J.; Ling, W.J.; Shao, Y.L.; Wang, Y.W.; Peng, Y. Unified synthesis of (–)-folicanthine and (–)-ditryptophenaline enabled by a nickel-mediated reductive dimerization at room temperature. *Synthesis* **2014**, *46*, 1908–1916. [[CrossRef](#)]
18. Peng, Y.; Xiao, J.; Xu, X.B.; Duan, S.M.; Ren, L.; Shao, Y.L.; Wang, Y.W. Stereospecific synthesis of tetrahydronaphtho[2,3-*b*]furans enabled by a nickel-promoted tandem reductive cyclization. *Org. Lett.* **2016**, *18*, 5170–5173. [[CrossRef](#)] [[PubMed](#)]
19. Xiao, J.; Wang, Y.W.; Peng, Y. Nickel-promoted reductive cyclization cascade: A short synthesis of a new aromatic strigolactone analogue. *Synthesis* **2017**, *49*, 3576–3581.
20. Uchiyama, M.; Kimura, Y.; Ohta, A. Stereoselective total syntheses of (±)-arthrinone and related natural compounds. *Tetrahedron Lett.* **2000**, *41*, 10013–10017. [[CrossRef](#)]
21. Zhang, J.; Liu, Y.Q.; Yang, L.; Feng, G. Podophyllotoxin derivatives show activity against *Brontispa longissima* larvae. *Nat. Prod. Commun.* **2010**, *5*, 1247–1250. [[PubMed](#)]

22. Kennedy-Smith, J.J.; Young, L.A.; Toste, F.D. Rhenium-catalyzed aromatic propargylation. *Org. Lett.* **2004**, *6*, 1325–1327. [[CrossRef](#)] [[PubMed](#)]
23. Andrews, R.C.; Teague, S.J.; Meyers, A.I. Asymmetric total synthesis of (–)-podophyllotoxin. *J. Am. Chem. Soc.* **1988**, *110*, 7854–7858. [[CrossRef](#)]
24. CCDC-1875746 (5) Contain the Supplementary Crystallographic Data for This Paper. These Data Can Be Obtained Free of Charge. Available online: <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (accessed on 28 October 2018).
25. Kashima, T.; Tanoguchi, M.; Arimoto, M.; Yamaguchi, H. Studies on the constituents of the seeds of *Hernandia ovigera* L. VIII. Synthesis of (±)-desoxypodophyllotoxin and (±)-β-peltatin-A methyl ether. *Chem. Pharm. Bull.* **1991**, *39*, 192–194. [[CrossRef](#)]
26. Yamaguchi, H.; Arimoto, M.; Nakajima, S.; Tanoguchi, M.; Fukada, Y. Studies on the constituents of the seeds of *Hernandia ovigera* L. V. Syntheses of epipodophyllotoxin and podophyllotoxin from desoxypodophyllotoxin. *Chem. Pharm. Bull.* **1986**, *34*, 2056–2060. [[CrossRef](#)]
27. Nishii, Y.; Yoshida, T.; Asano, H.; Wakasugi, K.; Morita, J.-I.; Aso, Y.; Yoshida, E.; Motoyoshiya, J.; Aoyama, H.; Tanabe, Y. Regiocontrolled benzannulation of diaryl(*gem*-dichlorocyclopropyl)methanols for the synthesis of unsymmetrically substituted α-arylnaphthalenes: Application to total synthesis of natural lignan lactones. *J. Org. Chem.* **2005**, *70*, 2667–2678. [[CrossRef](#)] [[PubMed](#)]
28. Schrecker, A.W.; Hartwell, J.L. Components of podophyllin. IX. The structure of apopicropodophyllins. *J. Am. Chem. Soc.* **1952**, *74*, 5676–5683. [[CrossRef](#)]

Sample Availability: Samples of the compounds are not available from the authors.



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