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Aza-Achmatowicz rearrangement coupled with intermolecular aza-Friedel–Crafts enables total syntheses of uleine and aspidosperma alkaloids†

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Aspidosperma and uleine alkaloids belong to the large family of monoterpene indole alkaloids with diverse biological activities and thus have attracted extensive synthetic interest. Reported is the development of a new synthetic strategy that allows direct C3–C2′ linkage of indoles with functionalized 2-hydroxypiperidines to construct the core common to all aspidoserma and uleine alkaloids. Such indole-piperidine linkage is enabled by coupling aza-Achmatowicz rearrangement (AAR) with indoles *via* an intermolecular aza-Friedel–Crafts (iAFC) reaction. This AAR-iAFC reaction proceeds under mild acidic conditions with wide tolerance of functional groups (33 examples). The synthetic application of the AAR-iAFC method was demonstrated with collective total syntheses of 3 uleine-type and 6 aspidosperma alkaloids: (+)-3-*epi*-*N*-nor-dasycarpidone, (+)-3-*epi*-dasycarpidone, (+)-3-*epi*-uleine, 1,2-didehydropseudoaspidospermidine, 1,2-dehydroaspidospermidine, vincadifformine, winchinine B, aspidospermidine, and *N*-acetylaspidospermidine. We expect that this AAR-iAFC strategy is applicable to other monoterpene indole alkaloids with the C3–C2′ linkage of indoles and piperidines.

Introduction

The aspidosperma and uleine alkaloids (Scheme 1a and b) belong to the large family of monoterpenoid indole alkaloids (*ca.* 3000 members) with diverse biological activities and intricate skeletal diversity.[1–7] They continue to influence the research fields of natural products, drug discovery, biochemistry, and especially organic chemistry (total synthesis and methodology development).[8,9] Structurally, the direct covalent C3–C2′ linkage of indole (in blue) with piperidine (in red) characterizes this subclass of alkaloids and thus has sparked great interest from generations of organic chemists in developing novel and efficient synthetic strategies[10–40] (Scheme 1c). For example, many innovative synthetic strategies for aspidosperma alkaloids have been developed, most of which can be classified into three categories: (i) intermolecular or intramolecular indolization of anilines with piperidine derivatives,[41–50] (ii) late-stage piperidine formation from 1,2,3,4-tetrahydrocarbazoles,[51–62] and (iii) intramolecular (or transannular) Mannich reaction of indoles with tethered piperidinium.[63–72] It was interestingly noted that the intermolecular reaction of indoles with piperidine derivatives was first reported in 1955 but rarely explored for the total synthesis of aspidosperma (and uleine) alkaloids,[73–75] probably due to the instability and unavailability of functionalized 2-hydroxypiperidines. In this article, we report the development of an intermolecular aza-Friedel-Crafts (iAFC) reaction[76–78] of indoles with functionalized 2-hydroxypiperidines, which can be readily available from aza-Achmatowicz rearrangement and thus enables collective total synthesis of aspidosperma and uleine alkaloids (Scheme 1c(iv)).

Aza-Achmatowicz rearrangement (AAR) represents one of the most facile entries into functionalized piperidines,[79] and our research group has great interest in exploiting AAR for total syntheses of bioactive alkaloids.[80–82] To extend the synthetic utility of rather unstable AAR products in total synthesis, we envisioned that the freshly prepared AAR products (functionalized 2-hydroxypiperidines) might react with indoles to enable a direct C3–C2′ coupling (iAFC) for aspidosperma and uleine alkaloids (Scheme 1e). We noticed that Qi *et al.*[83,84] had reported an intramolecular reaction of indoles with AAR products (C2–C2′ coupling) to construct the indole-fused azabicyclo[3.3.1] nonane core and accomplished elegantly the total synthesis of alstofolinine A and sarpagine alkaloids (Scheme 1d). The challenge of this intramolecular reaction was well recognized by the authors due to limited substrates and oxidants ("upon exposure to oxidizing conditions (*m*-CPBA), the primary amine and the indole were preferentially oxidized to *N*-oxide and oxindole, respectively, prior to the oxidation of the furan"),[83] which represents a significant limitation in synthetic applications. We

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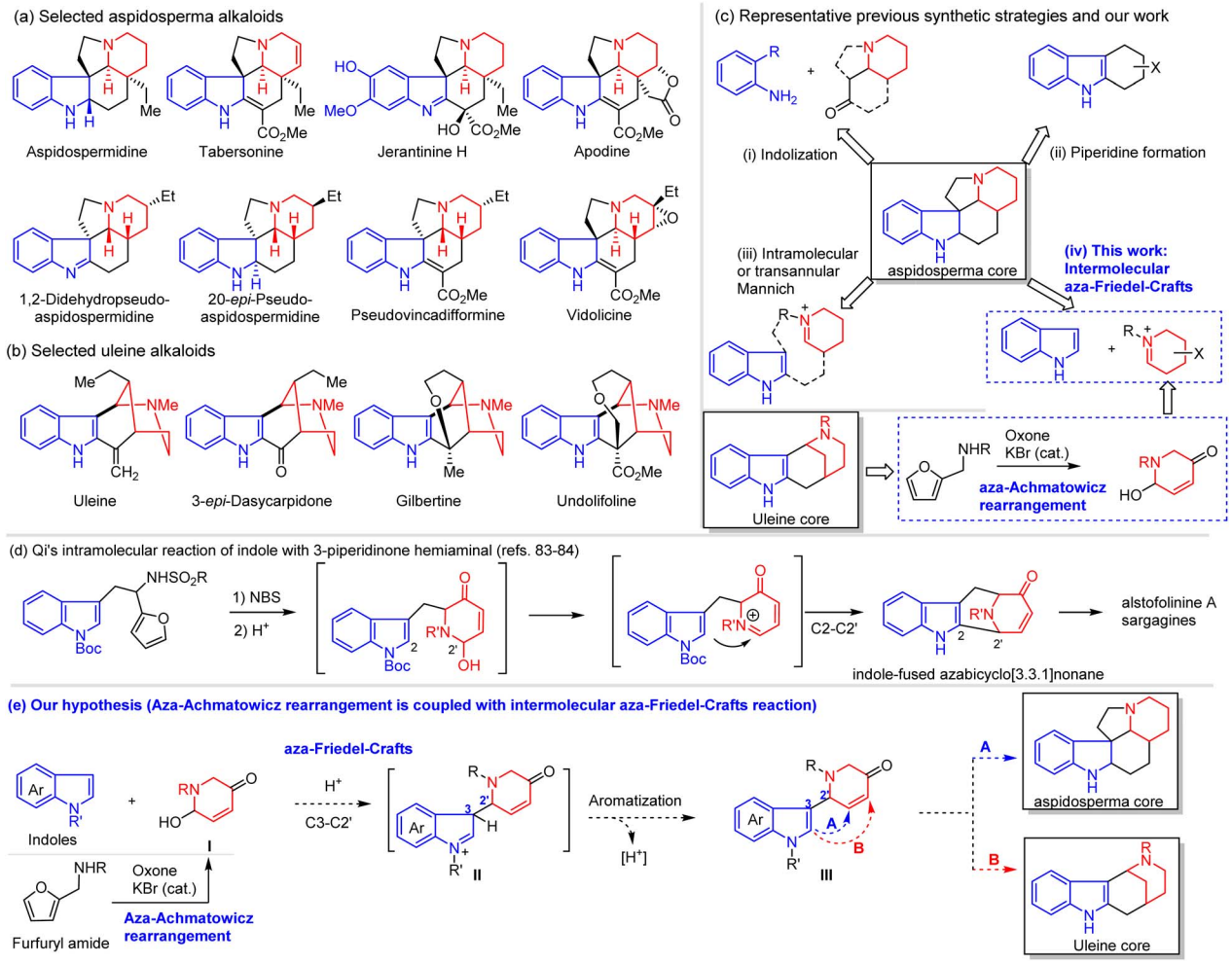


Scheme 1 Representative members of aspidosperma and uleine alkaloids, selected synthetic strategies, and our hypothesis.

believed that an intermolecular coupling version of indoles with AAR products could significantly expand the synthetic utility with the highest flexibility. Additionally, the restriction on NBS oxidation for aza-Achmatowicz rearrangement could be largely relaxed to use our green oxidation protocol (Oxone/KBr).[85–87] If our hypothesis works, the coupling product **III** with C3–C2′ linkage could be used for the total synthesis of aspidosperma (path A) and uleine-type alkaloids (cyclization *via* path B, Scheme 1e).

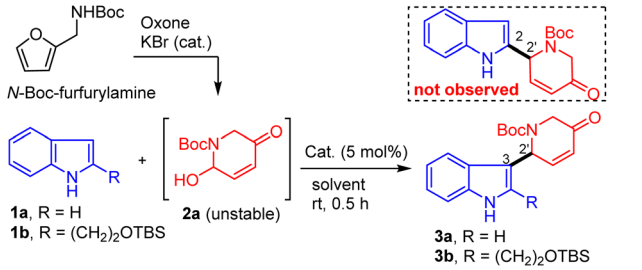
Results and discussion

Methodology development: aza-Achmatowicz rearrangement is coupled with intermolecular aza-Friedel–Crafts (iAFC) reaction

We began our study with aza-Achmatowicz rearrangement of *N*-Boc-furfurylamine under our oxone/KBr (cat.) conditions[85–87] to provide functionalized 2-hydroxypiperidine (**2a**, AAR product), which was unstable for storage and should be used immediately for the subsequent reaction with indoles (Table 1). Two indoles, **1a** and **1b**, were chosen to evaluate the reaction efficiency and functional group tolerance. Trifluoroacetic acid (TFA) was used first as the catalyst (5 mol%) for the iAFC reaction of indole[88] (**1a**) and AAR product **2a** under various solvents and the results were excellent with 78% to 88% yields of **3a** derived from selective C3–C2′ coupling (entries 1–7). Notably, the C2–C2′ coupling product was not observed. It was noteworthy that the widely used Lewis acid BF_3–Et_2O gave a lower yield of **3a** (60%, entry 8) while the unusual organic Brønsted acid pentacarbomethoxycyclopentadiene (PCCP)[89–91] in toluene delivered slightly higher yield (90%, entry 9). Surprisingly, the iAFC reaction of indole **1b** with AAR product **2a** under various acidic conditions gave consistently lower yields of **3b** (0–58%, entries 10–18), which might be due to the steric hindrance exerted by the C2-alkyl substituent. It was noted that the *tert*-butyldimethylsilyl (TBS) ether survived under these conditions and usually indole **1b** was not fully consumed, which suggested that the decomposition of **2a** occurred under acidic conditions with prolonged reaction time. Extensive experiments revealed that PCCP was the optimal protic acid as the catalyst with high reproducibility and best efficiency at 0.05–0.2 M concentration (58% yield of **3a**, entry 18).

Under the optimal conditions (PCCP or TFA in toluene), the scope of the iAFC reaction of indoles (**1**) with AAR products (**2**)

Table 1 Optimization of the reaction conditions of iAFC[a]



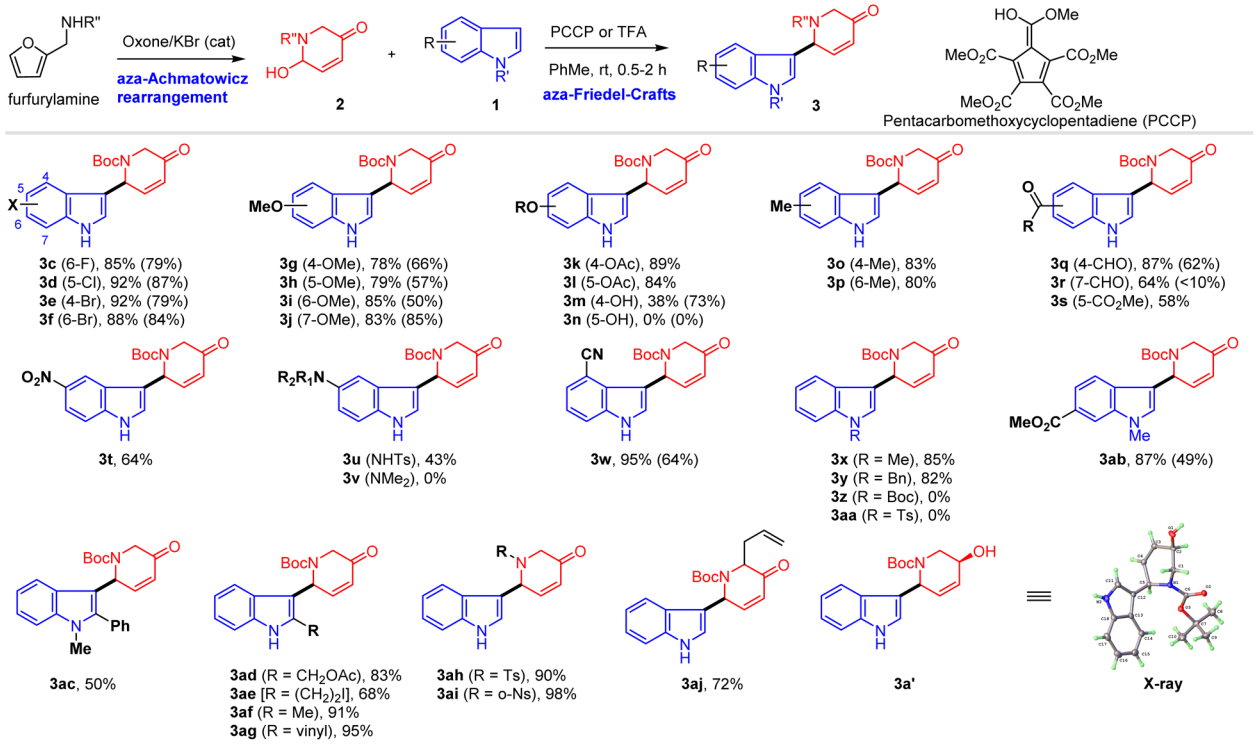
Entry	1a/1b	Catalyst	Solvent	Yield (%)
1	**1a**	TFA	DCM	82
2	**1a**	TFA	PhMe	88
3	**1a**	TFA	MeOH	78
4	**1a**	TFA	DCE	85
5	**1a**	TFA	THF	81
6	**1a**	TFA	EtOAc	86
7	**1a**	TFA	$CHCl_3$	88
8	**1a**	BF_3–Et_2O	DCM	60
9	**1a**	PCCP	PhMe	90
10	**1b**	TFA	DCM	35
11	**1b**	(−)-CSA	DCM	37
12	**1b**	F_2CHCO_2H	DCM	42
13	**1b**	*p*TSA·H_2O	DCM	40
14	**1b**	$ClCH_2CO_2H$	DCM	Trace
15	**1b**	Cl_2CHCO_2H	DCM	40
16	**1b**	Cl_3CCO_2H	DCM	24
17	**1b**	—	HFIP	10
18	**1b**	PCCP	DCM	58

[a] Conditions: **1a**/**1b** (0.1 mmol), **2a** (0.12 mmol), acid (0.005 mmol), solvent (0.05–0.2 M), room temperature, 0.5–12 h. Yield was determined by ^{1}H NMR analysis using dibromomethane as the internal standard. PCCP: pentacarbomethoxycyclopentadiene.

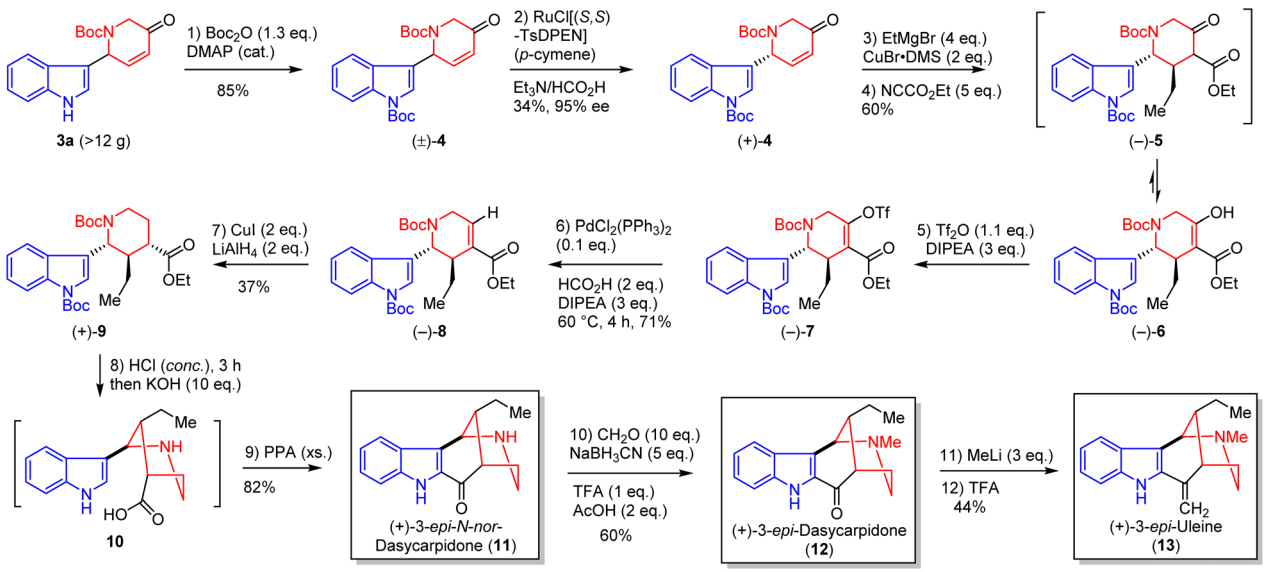
was evaluated and the results are presented in Table 2. Generally, a wide variety of functionalized indoles could be employed for this iAFC with AAR products **2** in good to excellent yield and with excellent regioselectivity (C3–C2′ linkage). For example, substituents at the benzene moiety of indoles including halide (6-F, 5-Cl, 4-Br, and 6-Br) (**3c–3f**), methoxy (4-OMe, 5-OMe, 6-OMe, and 7-OMe) (**3g–3j**), acetoxyl (4-OAc and 5-OAc) (**3k** and **3l**), alkyl (4-Me and 6-Me) (**3o** and **3p**), and carbonyl (4-CHO, 7-CHO, and 5-CO_2Me) (**3q–3s**) were well tolerated in the reaction. The only substituent that could not be tolerated was 5-OH on the indole (**3n**), while 4-hydroxylindole (4-OH) was a suitable substrate using TFA as the catalyst to provide **3m** in 73% yield. We further examined indoles with nitrogen-containing substituents such as NO_2 (**3t**), NHTs (**3u**), NMe_2 (**3v**), and CN (**3w**) at C5 or C4 and found that only NMe_2 at C5 was not able to deliver the desired coupling product (**3v**) which might be attributed to the basicity of the NMe_2 group to form the ammonium salt with the protic acid catalyst, preventing the formation of the requisite cyclic iminium ion for iAFC. It was noted that the electron-withdrawing group (EWG) on the indole nitrogen such as *N*-Boc (**3z**) and *N*-Ts (**3aa**) deactivated the nucleophilicity of indole and thus iAFC did not occur, which was in contrast to the electron-donating group (EDG) such as *N*–Me (**3x** and **3ab** 85% and 87%, respectively) and *N*-Bn (**3y**, 82%). Substitution at C2 indole was found to be possible for iAFC as exemplified by **1b** in Table 1. To further understand such substitution effect, C2-Ph (**3ac**), C2-alkyl (**3ad–3af**), and C2-alkenyl (**3ag**) were employed for the iAFC with **2a** and they proved efficient with 50–95% yield. The compatibility of C2 substitution was significant in terms of its potential application in total synthesis. Variation of AAR products for iAFC was also briefly examined and different EWG groups (*N*-Ts and *N*-Ns) on AAR products (**3ah** and **3ai**) as well as C6′-allyl (**3aj**) were well tolerated in the iAFC reaction, yielding products in good to excellent yields. Finally, iAFC product **3a** was reduced and then confirmed by X-ray diffraction analysis (**3a′**) (CCDC 2299125).

Total syntheses of uleine and aspidosperma alkaloids. The iAFC reaction of indoles with AAR products not only greatly expanded the synthetic utility of AAR but also allowed access to the structural skeleton that could not be constructed by the intramolecular AFC reaction.[83,84] To demonstrate such advantage of iAFC as compared to the intramolecular version, we undertook the total syntheses of uleine and aspidosperma alkaloids (Schemes 2 and 3). Our first synthetic targets were 3-*epi*-*N*-nor-dasycarpidone, 3-*epi*-dasycarpidone, and 3-*epi*-uleine. As depicted in Scheme 2, iAFC product **3a** was obtained in >12 grams (90% yield) and used as the starting material for the synthesis of these three alkaloids. Protection of indole nitrogen with Boc_2O provided compound **4** (85%), which was investigated for the kinetic resolution. While Corey–Bakshi–Shibata (CBS)[92,93] reduction of enone **4** using (*S*)-(−)-2-methyl-CBS-oxazaborolidine and BH_3·THF was not effective (<10% ee), Noyori asymmetric transfer hydrogenation[94] with RuCl[(*S*,*S*)-TsDPEN](*p*-cymene) and HCO_2H/Et_3N could reduce the undesired enantiomer and the unreacted desired (+)-**4** was obtained in 34% yield with 95% ee. Copper-mediated conjugate addition of ethyl Grignard to (+)-**4** followed by acylation with ethyl cyanoformate delivered 1,3-dicarbonyl (−)-**5** (60% for two steps) which was in equilibrium (tautomerization) with its enol form (−)-**6**. The enol (−)-**6** was treated with triflate anhydride (Tf_2O) and reduced with palladium catalysis to provide α,β-unsaturated ester (−)-**8** in 71% yield. Palladium-catalyzed hydrogenation of the alkene was unexpectedly difficult, and we found that the conjugate reduction could be achieved by $LiAlH_4$/CuI[95] to generate (+)-**9** in 37% yield (62% brsm). Removal of both *N*-Boc groups of (+)-**9** with HCl and then KOH-promoted hydrolysis of ester gave carboxylic acid **10**, which was subjected to polyphosphoric acid (PPA) for an intramolecular Friedel–Crafts reaction,[96] furnishing (+)-3-*epi*-*N*-nor-dasycarpidone (**11**) (82%, two steps). However, the NMR data of our synthetic sample (**11**) were not in good agreement with those reported for natural product 3-*epi*-*N*-nor-dasycarpidone,[97] which suggested that the structure of 3-*epi*-*N*-nor-dasycarpidone might be wrongly assigned. Reductive amination of **11** accomplished the synthesis of (+)-3-*epi*-dasycarpidone (**12**) in 60% yield, whose spectroscopic data were in well agreement with those of previously synthesized 3-*epi*-dasycarpidone.[98–100] Finally, the synthesis of (+)-3-*epi*-uleine (**13**) was achieved in 44% yield by following Zhu's procedure.[101]

Table 2 Aza-Friedel–Crafts reaction of indoles (**1**) with AAR products (**2**)[a]

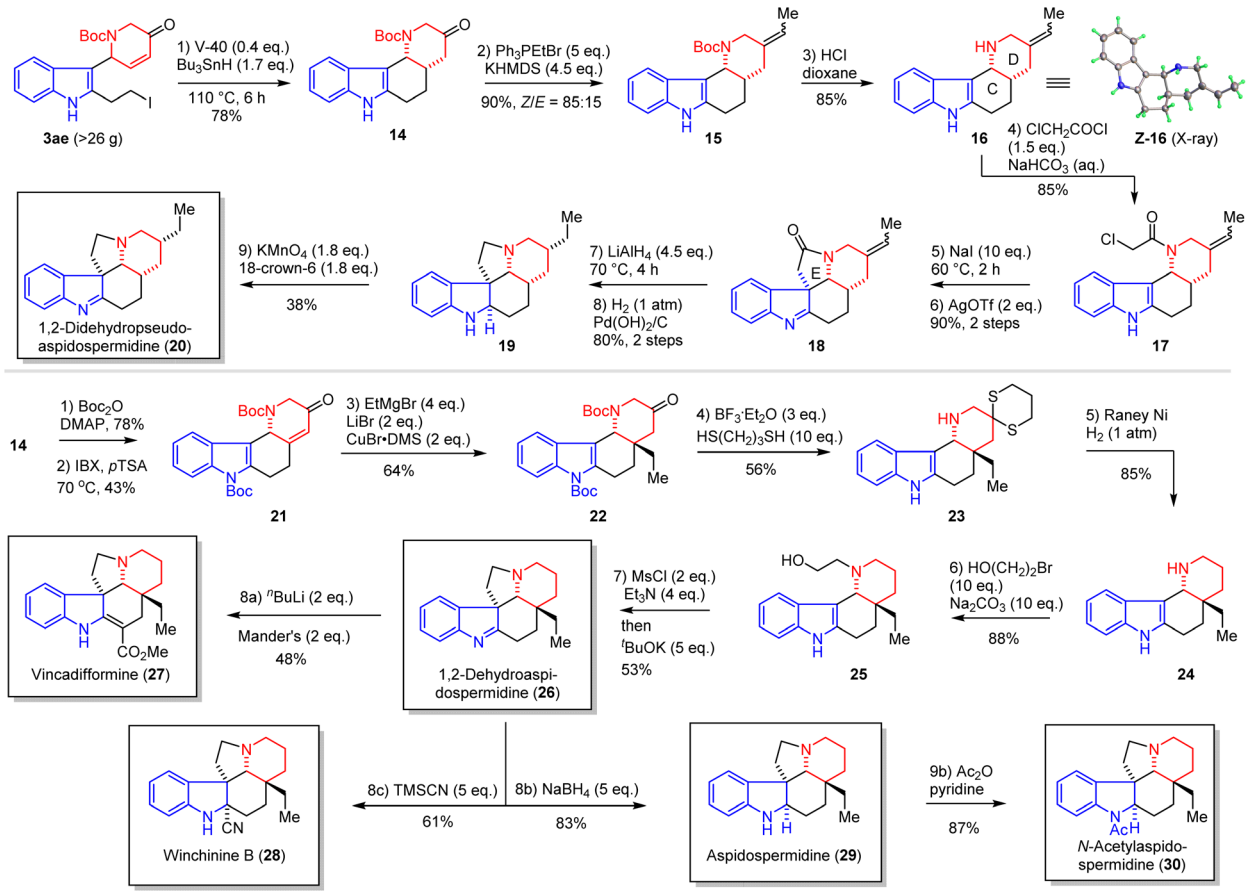


[a] Conditions**1**(0.2 mmol), **2**(0.24 mmol), PCCP (0.01 mmol), toluene (1 mL), room temperature, 0.5–2 h. Yields in parentheses were obtained using TFA (15 mol%) as the catalyst.



Scheme 2 Total syntheses of uleine-type alkaloids.

Next, we focused our efforts on the total synthesis of aspidosperma alkaloids by exploiting iAFC of indoles with AAR products. As depicted in Scheme 3, the iAFC product **3ae** (Table 2) was obtained in >26 g from **3b** and used as the starting material for the synthesis of all aspidosperma alkaloids. The 6-*exo-trig* cyclization of **3ae** failed to occur with samarium iodide (SmI_2)[102–104] or palladium catalysis (Heck) but could be realized *via* a radical mechanism by treatment with 1,1′-azobis(cyclohexane-1-carbonitrile) (V-40) and tributyltin hydride[105] under refluxed toluene to provide the tetracyclic core



Scheme 3 Total syntheses of aspidosperma alkaloids.

14 (78% yield), which was common to all aspidosperma alkaloids. Wittig olefination of **14** gave a *Z*/*E* mixture of **15** (90%, *Z*/*E* = 85 : 15). Removal of *N*-Boc of **15** with HCl in dioxane afforded compound **16** (85%), in which the *Z*-isomer was suitable for single crystal X-ray diffraction analysis (CCDC 2299184) and thus confirmed the *cis*-fused CD ring. The E ring of 1,2-didehydropseudoaspidospermidine (**20**) was constructed by *N*-acylation of **16** with 2-chloroacetyl chloride (**17**, 85% yield) and then intramolecular S_N2 substitution with assistance of AgOTf (90% yield). $LiAlH_4$ reduction of indolenine **18** and palladium-catalyzed hydrogenation provided pseudoaspidospermidine (**19**, 80% yield), which was then oxidized by $KMnO_4$ to furnish 1,2-didehydropseudoaspidospermidine (**20**) in 38% yield.[106] Next, we employed **14** for the synthesis of other aspidosperma alkaloids. Protection of indole nitrogen of **14** as *N*-Boc was performed (78% yield), followed by direct desaturation of the tetracyclic ketone with 2-iodoxybenzoic acid[107] (IBX, 43% yield), and conjugate addition of ethyl Grignard to **21** was facilitated with copper bromide and lithium bromide to provide **22** (64% yield) with the correct quaternary carbon center.

Deoxygenation of the ketone group of **22** was investigated with three approaches (Wolff–Kishner–Huang reduction, Bamford–Stevens reduction, and thioketalization/desulfurization) and thioketalization/desulfurizaiton was the most effective to give **24** in 48% yield over 2 steps. A well-developed 2-step sequence, *N*-alkylation and intramolecular S_N2 substitution, was performed to furnish 1,2-dehydroaspidospermidine (**26**),[14] which could serve as a common precursor to vincadifformine (**27**, 48% yield), winchinine B (**28**, 61% yield), aspidospermidine (**29**, 83% yield), and *N*-acetylaspidospermidine (**30**) (87%) in a single or two steps. All spectroscopic data of our 6 synthetic aspidosperma alkaloids were in good agreement with those reported for the natural alkaloids (see ESI†).

Conclusion

In summary, we have developed an efficient synthetic methodology to couple indoles and functionalized piperidines with C3–C2′ linkage for the synthesis of uleine and aspidosperma alkaloids. The coupling reaction is effectively promoted by Brønsted acid [H^+: trifluoroacetic acid or 1,2,3,4,5-pentacarbomethoxycyclopentadiene (PCCP)] at room temperature with broad substrate scope (33 examples) and diverse functional group tolerance. As compared to previous intramolecular coupling (C2–C2′ linkage with bridged nitrogen), this intermolecular aza-Friedel–Crafts (iAFC) reaction greatly expands the synthetic utility of aza-Achmatowicz rearrangement (AAR) with high skeletal diversity, permitting access to different types of indole alkaloids. We demonstrated such advantage by using the AAR-iAFC coupling products as starting materials to accomplish

the efficient total synthesis (7–12 steps) of 9 indole alkaloids consisting of two subclasses: uleine and aspidosperma, namely (+)-3-*epi*-*N*-nor-dasycarpidone, (+)-3-*epi*-dasycarpidone, (+)-3-*epi*-uleine, 1,2-didehydropseudoaspidospermidine, 1,2-dehydroaspidospermidine, vincadifformine, winchinine B, aspidospermidine, and *N*-acetylaspidospermidine. We expect that such high efficient coupling reaction (AAR-iAFC) will find wide application in total synthesis of other indole alkaloids and pave the way for medicinal chemistry and drug discovery.

Data availability

Synthetic procedures and complete characterization data for all new compounds can be found in the ESI.†

Author contributions

F. M., Y. L., K. A., H. Q. and Y. T. C. performed the synthetic experiments. Z. G. provided some suggestions on the work. R. T. conceptualized and directed the project and drafted the manuscript with assistance from all co-authors.

Conflicts of interest

The authors declare no competing interests.

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Notes and references

1 A. E. Mohammed, Z. H. Abdul-Hameed, M. O. Alotaibi, N. O. Bawakid, T. R. Sobahi, A. Abdel-Lateff and W. M. Alarif, *Molecules*, 2021, **26**, 488.
2 D. Williams and V. De Luca, *Phytochem. Rev.*, 2023, **22**, 309–338.
3 M.-J. U. Ferreira and A. Paterna, *Phytochem. Rev.*, 2019, **18**, 971–987.
4 F. Omar, A. M. Tareq, A. M. Alqahtani, K. Dhama, M. A. Sayeed, T. B. Emran and J. Simal-Gandara, *Molecules*, 2021, **26**, 2297.
5 S.-F. Teng, F.-R. Li, Q.-M. Cui, A. Khan, T. He, X.-D. Luo, Y.-P. Liu and G.-G. Cheng, *Phytochem. Rev.*, 2023, DOI: 10.1007/s11101-023-09871-2.
6 J. Song, B. Zhang, M. Li and J. Zhang, *Fitoterapia*, 2023, **165**, 105430.
7 L. Wang, S. Chen, X. Gao, X. Liang, W. Lv, D. Zhang and X. Jin, *J. Enzyme Inhib. Med. Chem.*, 2023, **38**, 2155639.
8 S. Zhao, G. Sirasani and R. B. Andrade, *Alkaloids: Chem. Biol.*, 2021, **86**, 1–143.
9 V. L. de Almeida, C. G. Silva, A. F. Silva, P. R. V. Campana, K. Foubert, J. C. D. Lopes and L. Pieters, *J. Ethnopharmacol.*, 2019, **231**, 125–140.
10 J. M. Lopchuk, in *Prog. Heterocycl. Chem.*, ed. G. W. Gribble and J. A. Joule, Elsevier, 2011, vol. 23, pp. 1–25.
11 N. Wang, X. Xiao, C.-X. Liu, H. Yao, N. Huang and K. Zou, *Adv. Synth. Catal.*, 2022, **364**, 2479–2501.
12 R. Tanifuji, A. Minami, H. Oguri and H. Oikawa, *Nat. Prod. Rep.*, 2020, **37**, 1098–1121.
13 L. McMurray, E. M. Beck and M. J. Gaunt, *Angew. Chem., Int. Ed.*, 2012, **51**, 9288–9291.
14 S. A. Kozmin, T. Iwama, Y. Huang and V. H. Rawal, *J. Am. Chem. Soc.*, 2002, **124**, 4628–4641.
15 E. L. Campbell, A. M. Zuhl, C. M. Liu and D. L. Boger, *J. Am. Chem. Soc.*, 2010, **132**, 3009–3012.
16 J. M. Saya, E. Ruijter and R. V. A. Orru, *Chem.–Eur. J.*, 2019, **25**, 8916–8935.
17 J. E. Saxton, in *Alkaloids Chem. Biol.*, ed. G. A. Cordell, Academic Press, 1998, vol. 50, pp. 343–376.
18 H. Ohno and S. Inuki, *Org. Biomol. Chem.*, 2021, **19**, 3551–3568.
19 X. Zeng, V. Shukla and D. L. Boger, *J. Org. Chem.*, 2020, **85**, 14817–14826.
20 O. Wagnières, Z. Xu, Q. Wang and J. Zhu, *J. Am. Chem. Soc.*, 2014, **136**, 15102–15108.
21 L.-P. Zhao, P.-J. Li, L. Wang and Y. Tang, *Angew. Chem., Int. Ed.*, 2022, **61**, e202207360.
22 B. Horst, D. S. Verdoorn, S. Hennig, G. van der Heijden and E. Ruijter, *Angew. Chem., Int. Ed.*, 2022, **61**, e202210592.
23 Z. Xu, Q. Wang and J. Zhu, *Chem. Soc. Rev.*, 2018, **47**, 7882–7898.
24 S. B. Jones, B. Simmons, A. Mastracchio and D. W. C. MacMillan, *Nature*, 2011, **475**, 183–188.
25 L. Pan, C.-W. Zheng, G.-S. Fang, H.-R. Hong, J. Liu, L.-H. Yu and G. Zhao, *Chem.–Eur. J.*, 2019, **25**, 6306–6310.
26 H. Mizoguchi, H. Oikawa and H. Oguri, *Nat. Chem.*, 2014, **6**, 57–64.
27 C. Zheng and S.-L. You, *Nat. Prod. Rep.*, 2019, **36**, 1589–1605.
28 B. Qin, Y. Wang, X. Wang and Y. Jia, *Org. Chem. Front.*, 2021, **8**, 369–383.
29 B. Qin, Z. Lu and Y. Jia, *Angew. Chem., Int. Ed.*, 2022, **61**, e202201712.
30 M. Amat, M. Pérez, N. Llor, C. Escolano, F. J. Luque, E. Molins and J. Bosch, *J. Org. Chem.*, 2004, **69**, 8681–8693.
31 M. Amat, M. Pérez, N. Llor, M. Martinelli, E. Molins and J. Bosch, *Chem. Commun.*, 2004, 1602–1603.
32 M. Amat, C. Escolano, A. Gómez-Esqué, O. Lozano, N. Llor, R. Griera, E. Molins and J. Bosch, *Tetrahedron: Asymmetry*, 2006, **17**, 1581–1588.
33 V. Semak, C. Escolano, C. Arróniz, J. Bosch and M. Amat, *Tetrahedron: Asymmetry*, 2010, **21**, 2542–2549.
34 E. A. Peterson and E. N. Jacobsen, *Angew. Chem., Int. Ed.*, 2009, **48**, 6328–6331.
35 Y. Zhang, Z.-J. Yi, A.-M. Yang, J.-M. Guo, X. Li and B.-G. Wei, *Org. Biomol. Chem.*, 2023, **21**, 1303–1315.
36 J. Song, Z.-J. Zhang and L.-Z. Gong, *Angew. Chem., Int. Ed.*, 2017, **56**, 5212–5216.
37 B. K. Corkey, S. T. Heller, Y.-M. Wang and F. D. Toste, *Tetrahedron*, 2013, **69**, 5640–5646.

38 M. Amat, B. Checa, N. Llor, M. Pérez and J. Bosch, *Eur. J. Org Chem.*, 2011, 898–907.
39 C. L. Martin, L. E. Overman and J. M. Rohde, *J. Am. Chem. Soc.*, 2010, **132**, 4894–4906.
40 E. Wenkert and T. Hudlicky, *J. Org. Chem.*, 1988, **53**, 1953–1957.
41 N. Wang and X. Jiang, *Chem. Rec.*, 2021, **21**, 295–314.
42 N. Wang, S. Du, D. Li and X. Jiang, *Org. Lett.*, 2017, **19**, 3167–3170.
43 G. Martin, P. Angyal, O. Egyed, S. Varga and T. Soós, *Org. Lett.*, 2020, **22**, 4675–4679.
44 R. Iyengar, K. Schildknegt, M. Morton and J. Aubé, *J. Org. Chem.*, 2005, **70**, 10645–10652.
45 S. Katahara, Y. Sugiyama, M. Yamane, Y. Komiya, T. Sato and N. Chida, *Org. Lett.*, 2021, **23**, 3058–3063.
46 J.-Y. Kim, C.-H. Suhl, J.-H. Lee and C.-G. Cho, *Org. Lett.*, 2017, **19**, 6168–6171.
47 M. M. Heravi, S. Rohani, V. Zadsirjan and N. Zahedi, *RSC Adv.*, 2017, **7**, 52852–52887.
48 F. Reuß and P. Heretsch, *Org. Lett.*, 2020, **22**, 3956–3959.
49 S. Varga, P. Angyal, G. Martin, O. Egyed, T. Holczbauer and T. Soós, *Angew. Chem., Int. Ed.*, 2020, **59**, 13547–13551.
50 B. Delayre, C. Piemontesi, Q. Wang and J. Zhu, *Angew. Chem., Int. Ed.*, 2020, **59**, 13990–13997.
51 R. Yang and F. G. Qiu, *Angew. Chem., Int. Ed.*, 2013, **52**, 6015–6018.
52 X.-L. Shen, R.-R. Zhao, M.-J. Mo, F.-Z. Peng, H.-B. Zhang and Z.-H. Shao, *J. Org. Chem.*, 2014, **79**, 2473–2480.
53 S. Zhao and R. B. Andrade, *J. Am. Chem. Soc.*, 2013, **135**, 13334–13337.
54 Z. Liu, X. Ju, S. Ma, C. Du, W. Zhang, H. Li, X. Wang, X. Xie and X. She, *J. Org. Chem.*, 2019, **84**, 14994–15000.
55 D. L. Cain, N. A. Anderson, D. B. Cordes, A. M. Z. Slawin and A. J. B. Watson, *J. Org. Chem.*, 2022, **87**, 15559–15563.
56 H. Ma, X. Xie, P. Jing, W. Zhang and X. She, *Org. Biomol. Chem.*, 2015, **13**, 5255–5259.
57 W. Chen, X.-D. Yang, W.-Y. Tan, X.-Y. Zhang, X.-L. Liao and H. Zhang, *Angew. Chem., Int. Ed.*, 2017, **56**, 12327–12331.
58 L. Yang, S. Huang, R. Huang, A. Hou, S. Zhang, H. Su, X. Ding, B. Lin, M. Cheng and Y. Liu, *Org. Lett.*, 2021, **23**, 6471–6476.
59 J.-Y. Du, C. Zeng, X.-J. Han, H. Qu, X.-H. Zhao, X.-T. An and C.-A. Fan, *J. Am. Chem. Soc.*, 2015, **137**, 4267–4273.
60 H. Xu, H. Huang, C. Zhao, C. Song and J. Chang, *Org. Lett.*, 2019, **21**, 6457–6460.
61 Z. Li, S. Zhang, S. Wu, X. Shen, L. Zou, F. Wang, X. Li, F. Peng, H. Zhang and Z. Shao, *Angew. Chem., Int. Ed.*, 2013, **52**, 4117–4121.
62 D. Jiang, P. Tang, H. Xiong, S. Lei, Y. Zhang, C. Zhang, L. He, H. Qiu and M. Zhang, *Angew. Chem., Int. Ed.*, 2023, **62**, e202307286.
63 M. Mewald, J. W. Medley and M. Movassaghi, *Angew. Chem., Int. Ed.*, 2014, **53**, 11634–11639.
64 T. Sato, M. Yoritate, H. Tajima and N. Chida, *Org. Biomol. Chem.*, 2018, **16**, 3864–3875.
65 F. De Simone, J. Gertsch and J. Waser, *Angew. Chem., Int. Ed.*, 2010, **49**, 5767–5770.
66 K. Yoshida, K. Okada, H. Ueda and H. Tokuyama, *Angew. Chem., Int. Ed.*, 2020, **59**, 23089–23093.
67 T. Kang, K. L. White, T. J. Mann, A. H. Hoveyda and M. Movassaghi, *Angew. Chem., Int. Ed.*, 2017, **56**, 13857–13860.
68 I.-S. Myeong, N. H. Avci and M. Movassaghi, *Org. Lett.*, 2021, **23**, 9118–9122.
69 P. W. Tan, J. Seayad and D. J. Dixon, *Angew. Chem., Int. Ed.*, 2016, **55**, 13436–13440.
70 M. V. Mijangos and L. D. Miranda, *Org. Biomol. Chem.*, 2018, **16**, 9409–9419.
71 M. A. Toczko and C. H. Heathcock, *J. Org. Chem.*, 2000, **65**, 2642–2645.
72 Y. Han-ya, H. Tokuyama and T. Fukuyama, *Angew. Chem., Int. Ed.*, 2011, **50**, 4884–4887.
73 E. E. van Tamelen and G. G. Knapp, *J. Am. Chem. Soc.*, 1955, **77**, 1860–1862.
74 E. Wenkert, K. G. Dave, F. Haglid, R. G. Lewis, T. Oishi, R. V. Stevens and M. Terashima, *J. Org. Chem.*, 1968, **33**, 747–753.
75 E. Wenkert and T. Hudlicky, *J. Org. Chem.*, 1988, **53**, 1953–1957.
76 A. Hadj Mohamed and N. Masurier, *Org. Chem. Front.*, 2023, **10**, 1847–1866.
77 S. Brunen, B. Mitschke, M. Leutzsch and B. List, *J. Am. Chem. Soc.*, 2023, **145**, 15708–15713.
78 Y.-S. Cheng, S.-H. Chan, G. A. Rao, R. Gurubrahamam and K. Chen, *Adv. Synth. Catal.*, 2021, **363**, 3502–3506.
79 F. van der Pijl, F. L. van Delft and F. P. J. T. Rutjes, *Eur. J. Org Chem.*, 2015, **2015**, 4811–4829.
80 F. Ma, C. He, E. Wang and R. Tong, *Org. Lett.*, 2021, **23**, 6583–6588.
81 W. F. Cheng, S. Ma, Y. T. Lai, Y. T. Cheung, K. Akkarasereenon, Y. Zhou and R. Tong, *Angew. Chem., Int. Ed.*, 2023, **62**, e202311671.
82 L. Liang, L.-D. Guo and R. Tong, *Acc. Chem. Res.*, 2022, **55**, 2326–2340.
83 L. Zhang, Y. Zhang, W. Li and X. Qi, *Angew. Chem., Int. Ed.*, 2019, **58**, 4988–4991.
84 Y. Zhang, L. Zhang and X. Qi, *Angew. Chem., Int. Ed.*, 2023, **62**, e202304435.
85 Z. Li and R. Tong, *J. Org. Chem.*, 2016, **81**, 4847–4855.
86 G. Zhao and R. Tong, *Green Chem.*, 2019, **21**, 64–68.
87 G. Zhao and R. Tong, *Tetrahedron*, 2019, **75**, 1669–1675.
88 T. Ahmad, S. Khan and N. Ullah, *ACS Omega*, 2022, **7**, 35446–35485.
89 I. E. Mikhailov, G. A. Dushenko and V. I. Minkin, *Russ. J. Org. Chem.*, 2021, **57**, 1757–1808.
90 C. Yuan, J. Li and P. Li, *ACS Omega*, 2018, **3**, 6820–6826.
91 C. D. Gheewala, B. E. Collins and T. H. Lambert, *Science*, 2016, **351**, 961–965.
92 E. J. Corey, R. K. Bakshi and S. Shibata, *J. Am. Chem. Soc.*, 1987, **109**, 5551–5553.
93 E. J. Corey, R. K. Bakshi, S. Shibata, C. P. Chen and V. K. Singh, *J. Am. Chem. Soc.*, 1987, **109**, 7925–7926.
94 R. Noyori and S. Hashiguchi, *Acc. Chem. Res.*, 1997, **30**, 97–102.

95 E. C. Ashby, J. J. Lin and R. Kovar, *J. Org. Chem.*, 1976, **41**, 1939–1943.
96 M. Amat, S. Hadida, N. Llor, S. Sathyanarayana and J. Bosch, *J. Org. Chem.*, 1996, **61**, 3878–3882.
97 Z. E. Dos Santos Torres, E. R. Silveira, L. F. Rocha e Silva, E. S. Lima, M. C. De Vasconcellos, D. E. De Andrade Uchoa, R. B. Filho and A. M. Pohlit, *Molecules*, 2013, **18**, 6281–6297.
98 T. Kametani and T. Suzuki, *J. Org. Chem.*, 1971, **36**, 1291–1293.
99 M. L. Bennasar, T. Roca and D. García-Díaz, *J. Org. Chem.*, 2008, **73**, 9033–9039.
100 P. Forns, A. Diez, M. Rubiralta, X. Solans and M. Font-Bardia, *Tetrahedron*, 1996, **52**, 3563–3574.
101 B. Delayre, C. Fung, Q. Wang and J. Zhu, *Helv. Chim. Acta*, 2021, **104**, e2100088.
102 D. J. Edmonds, D. Johnston and D. J. Procter, *Chem. Rev.*, 2004, **104**, 3371–3404.
103 M. M. Heravi and A. Nazari, *RSC Adv.*, 2022, **12**, 9944–9994.
104 M. Szostak, N. J. Fazakerley, D. Parmar and D. J. Procter, *Chem. Rev.*, 2014, **114**, 5959–6039.
105 K. Hagiwara, T. Tabuchi, D. Urabe and M. Inoue, *Chem. Sci.*, 2016, **7**, 4372–4378.
106 E. Wenkert, B. Porter, D. P. Simmons, J. Ardisson, N. Kunesch and J. Poisson, *J. Org. Chem.*, 1984, **49**, 3733–3742.
107 K. C. Nicolaou, T. Montagnon, P. S. Baran and Y. L. Zhong, *J. Am. Chem. Soc.*, 2002, **124**, 2245–2258.