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Total Synthesis of Pteridic Acids A and B†

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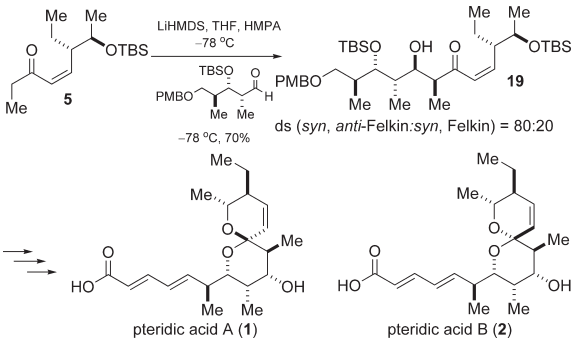

The total synthesis of pteridic acids A and B is reported. The convergent asymmetric synthesis involved the use of a diastereoselective ethyl ketone aldol reaction followed by an efficient spiroketalization and provided pteridic acids A and B in 2.9% and 2.8% overall yield, respectively.

Introduction

Pteridic acids A and B (**1** and **2**) are spirocyclic polyketides isolated in minor amounts by Igarashi and co-workers[1] from the fermentation broth of *Streptomyces hygroscopicus* TP-A0451 (Figure 1). These compounds exhibit potent plant growth promoter properties with auxin-like activity, inducing the formation of adventitious roots in kidney beans at 1 nM concentrations. The structures of pteridic acids have been suggested by spectroscopic studies including HMBC and NOESY experiments, and the absolute configuration has been determined by total synthesis.[2] Their complex molecular architecture comprises a highly substituted [6,6]-spiroketal motif, which bears seven stereocenters, an unsaturated side chain appended at C7 that incorporates another stereocenter, and a terminal carboxylic acid.[2,3] In a recent paper, Paterson et al.[2c] showed that the spiroketal unit of pteridic acid A presents a double anomeric effect, which is counterbalanced by pseudoaxial ethyl and methyl groups at C14 and C15, respectively. On the other hand, pteridic acid B displays only a single anomeric effect with pseudoequatorial alkyl substituents at C14 and C15.[2c] Applying molecular modeling (Macro Model, MM2), these authors found that the global minima of **1** and **2** are of similar energies, accounting for the existence of both as secondary metabolites.[2c]

As limited amounts of pteridic acids A and B are available from nature, we initiated a project directed toward their total synthesis. In addition, attracted by their promising anticancer activities, we intend to provide material for more extensive biological studies, along with access to novel analogues.

Results and Discussion

Our synthetic planning revealed that the unsaturated side chain at C7 could be undertaken via a Horner−Wadsworth−Emmons reaction with triethyl-4-phosphonocrotonate (Scheme 1).[4] Further dissection provides the possibility

†Dedicated to Prof. Vítor Francisco Ferreira (Universidade Federal Fluminense - RJ) for his outstanding contributions to the field of synthetic organic chemistry in Brazil.

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(4) The numbering of pteridic acids A and B as well as of each intermediate follows that suggested in ref 1.

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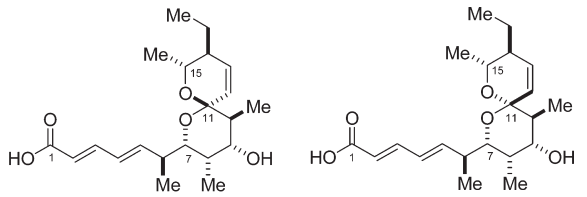


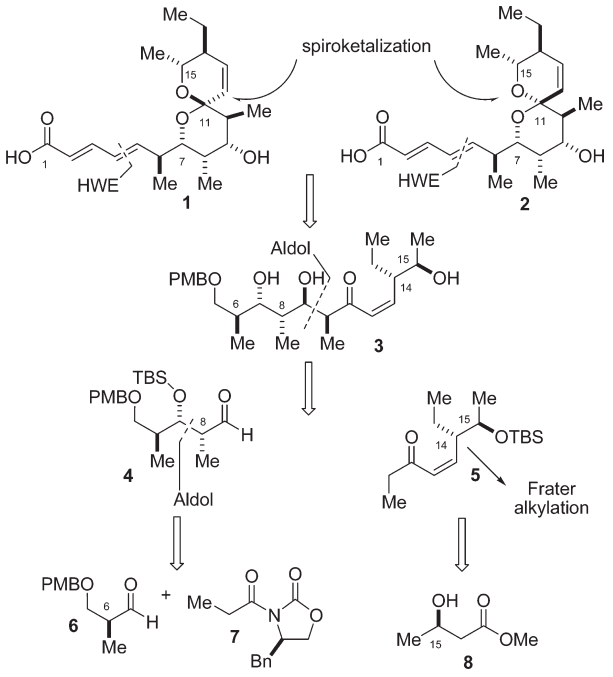
FIGURE 1. Pteridic acids A and B.

of spiroketalization of **3** preceded by late-stage aldol addition of aldehyde **4** with ethyl ketone **5** in a convergent route. Aldehyde **4** may be obtained by exploiting the Evans asymmetric aldol reaction between aldehyde **6** and *N*-propionyloxazolidinone **7**. By employing an asymmetric Frater alkylation on commercially available (*R*)-methyl-3-hydroxybutanoate **8**, we planned to establish the stereocenter at C14 in ethyl ketone **5**. We anticipated the aldol reaction between the (*Z*)-metal enolate derived from ethyl ketone **5** and aldehyde **4** to proceed with an *anti*-Felkin addition.[5]

The synthesis commenced with an asymmetric aldol addition of the boron enolate derived from oxazolidinone (*R*)-**7** with aldehyde **6** to give aldol adduct **9**[8] in 75% yield, exhibiting excellent diastereoselectivity (ds >95:5) (Scheme 2).[6−8] Removal of the oxazolidinone auxiliary in the *syn*-aldol **9** with *N,O*-dimethylhydroxylamine generated the Weinreb amide **10** (85% yield).[9] The oxazolidinone chiral auxiliary was recovered by crystallization from the reaction mixture. Protection of the OH function as its TBS ether cleanly provided Weinreb amide **11**[8] (89% yield), which was smoothly reduced to the aldehyde **4**[8] (used in the next step without further purification), corresponding to the C(5)−C(9) fragment, on treatment with diisobutylaluminum hydride in THF at −78 °C, in 90% yield (Scheme 2).[8,10]

We next moved to the preparation of ethylketone **5**, corresponding to the C(10)−C(16) fragment, necessary to couple with fragment C(5)−C(9) (Scheme 3). As shown in Scheme 3, the synthesis of the C(10)−C(16) fragment began from commercially available hydroxyester **8**. Frater alkylation[11] of hydroxyester **8** provided the 1,2-*anti* ester **12**[12] in 89% yield (95:5 diastereoselectivity).[12] Protection of the OH function as its TBS ether (87% yield), followed by DIBAL-H

SCHEME 1. Retrosynthetic Analysis



reduction of ester **13**,[12] gave primary alcohol **14**[12] in 86% yield.[12] Exposure of alcohol **14** to the Swern[13] oxidation protocol provided aldehyde **15**[12] which was treated with ketophosphonate **16** under Ando's[14] conditions to give (*Z*)-α,β-unsaturated ester **17** (*Z*/*E* = 95:5) in 79% yield over the two-step sequence. Ester **17** was converted to the Weinreb amide **18**, which was followed by treatment of **18** with EtMgBr to give the (*Z*)-α,β-unsaturated ketone **5** in excellent yields for the two-step sequence.[15]

With the successful synthesis of fragments C(5)−C(9) and C(10)−C(16) (**4** and **5**, respectively) in hand, we proceeded to assemble both the segments (Scheme 4). After considerable experimentation, this was accomplished by an aldol reaction of **5** with aldehyde **4** in 70% yield and 80:20 diastereoselectivity favoring the 1,2-*syn anti*-Felkin adduct **19** (Scheme 4).[5] The optimized conditions involved treatment of ethyl ketone **5** with LiHMDS in THF/HMPA followed by slow addition of aldehyde **4**. The 80:20 ratio was determined after separation of the diastereoisomers by flash column chromatography, which afforded 56% isolated yield of pure **19**. The relative stereochemistry for the major 1,2-*syn anti*-Felkin aldol adduct **19** was determined initially by vicinal coupling constant analysis as showed in Figure 2.[16] The ^{1}H NMR spectra (250 MHz, in $CDCl_3$) exhibit Hb at 2.64 ppm as a quartet of doublets with coupling constants 1.6 Hz (J_{Hb-Ha}) and 7.3 Hz (J_{Hb-Me}). Hydrogen Ha appears at 4.0 ppm as a doublet of doublets with coupling constants 1.6 Hz (J_{Hb-Ha}) and 7.2 Hz (J_{Ha-Hc}). This assignment was subsequently

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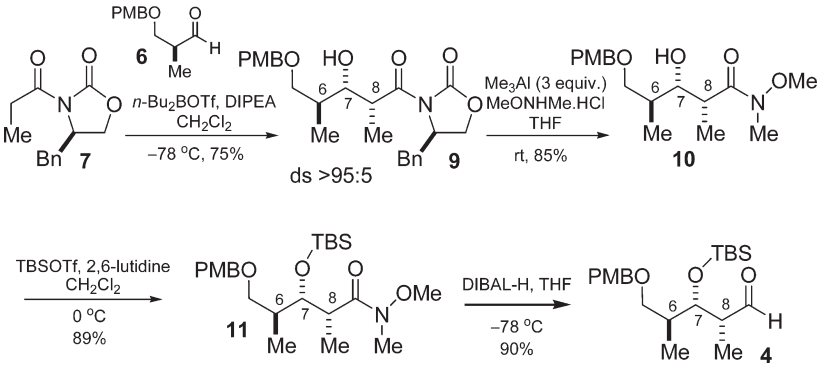
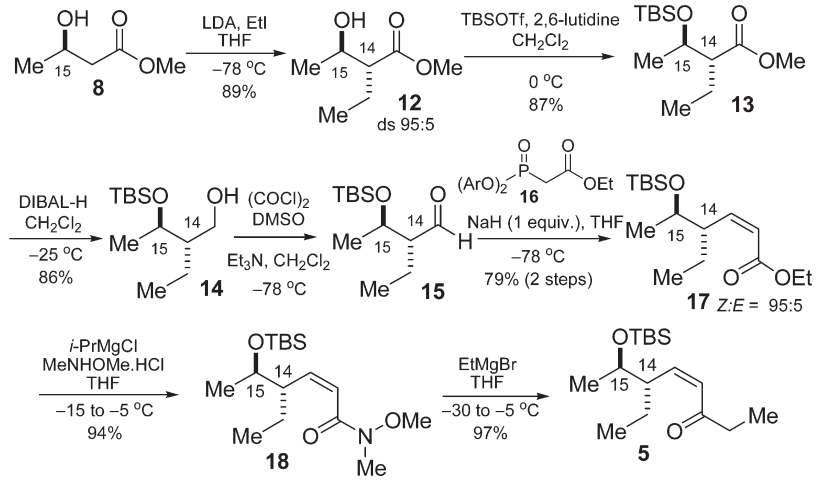
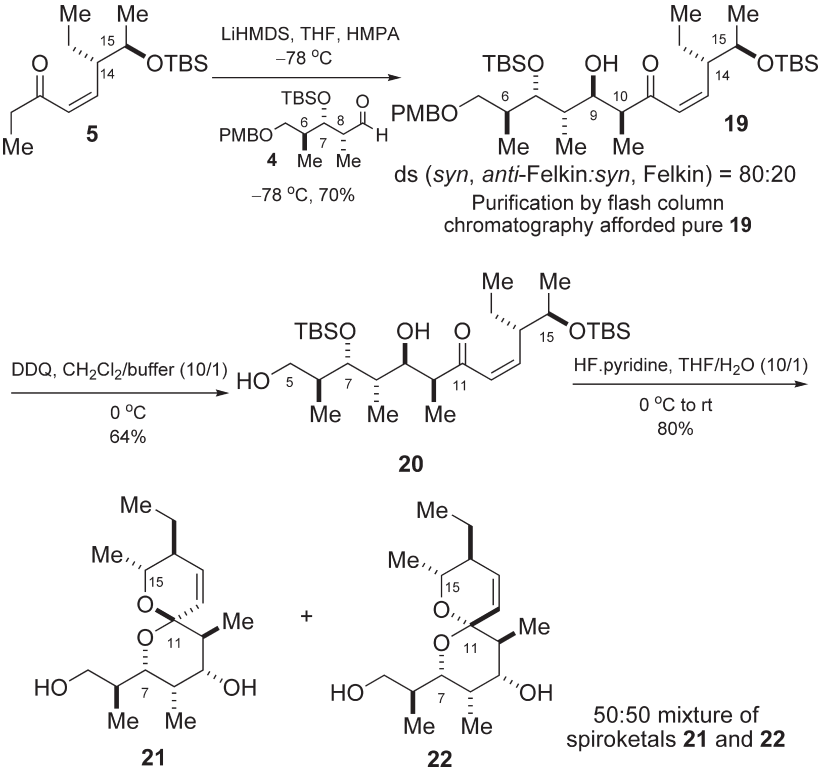
SCHEME 2. Preparation of Aldehyde 4



SCHEME 3. Preparation of (*Z*)-α,*β*-Unsaturated Ethylketone 5



SCHEME 4. Synthesis of Spiroketals 21 and 22



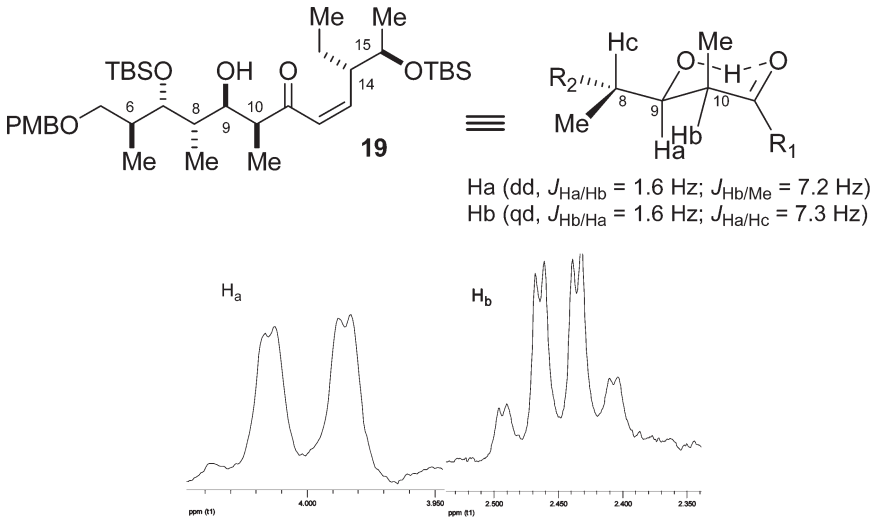
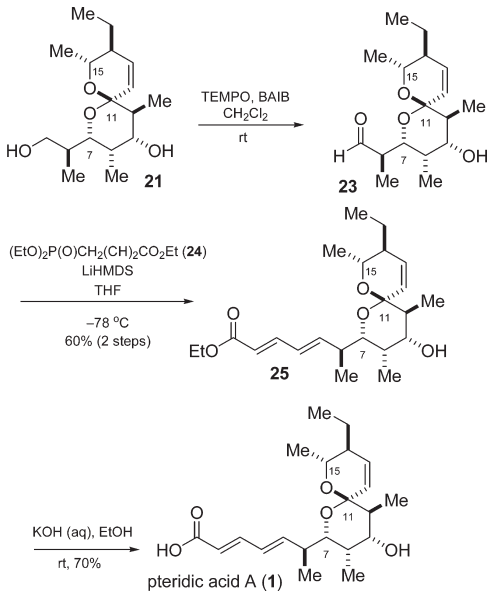
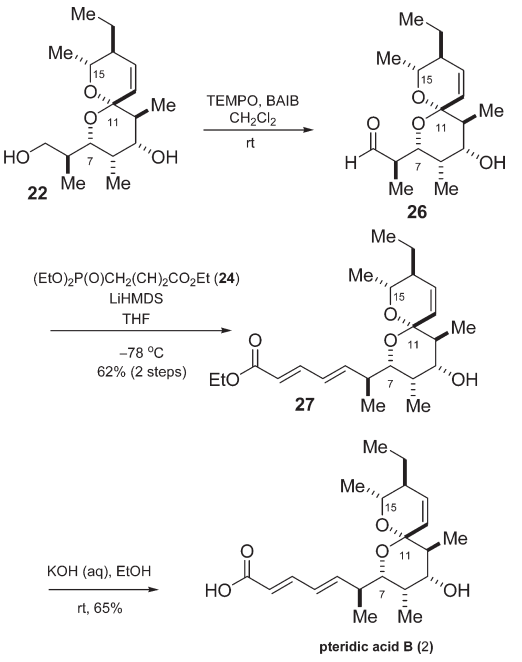


FIGURE 2. Assignment of the relative stereochemistry for aldol adduct **19**.

SCHEME 5. Total Synthesis of Pteridic Acid A



SCHEME 6. Total Synthesis of Pteridic Acid B



confirmed by correlation with the spectroscopic data of esters **25** and **27**, as well as pteridic acids A and B, known in the literature.[1,2]

Treatment of pure **19** with DDQ in CH_2Cl_2 at 0 °C provided primary alcohol **20**, a key synthetic intermediate, in 64% yield. Subsequent efficient removal of the TBS protecting groups positioned at C7 and C15 with concomitant spiroketalization was achieved upon treatment of **20** with HF−pyr in THF/H_2O (10/1) to give a 50:50 mixture of spiroketals **21** and **22** in 80% isolated yield, which were separated by careful silica gel column chromatography (Scheme 4).[18]

As illustrated in Scheme 5, spiroketal **21** was converted to pteridic acid A (**1**). Oxidation of the primary alcohol **21** to aldehyde **23** was accomplished with TEMPO and BAIB in CH_2Cl_2 at rt.[18] At this stage, Horner−Wadsworth−Emmons homologation of aldehyde **23** with ketophosphonate **24** occurred readily to give the corresponding α,β-unsaturated ester **25** in 60% overall yield (two steps).[2c] Conclusion of the synthesis required hydrolysis of ester **25** with aqueous KOH in EtOH at rt to provide pteridic acid A in 70% yield. The spectroscopic and physical data [^{1}H and ^{13}C NMR, IR, $[\alpha]_D$, R_f] were identical in all respects with the published data for both natural and synthetic pteridic acid A (see the Supporting Information for comparison of natural and our synthetic pteridic acid A).[1,2] The 13-step sequence (longest linear sequence) starting from **8** proceeded in 2.9% overall yield and is amenable to a gram scale-up.

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The same sequence applied to spiroketal **22** provided pteridic acid B (**2**) in 2.8% overall yield for the 13-step linear sequence (Scheme 6). The spectroscopic and physical data [^{1}H and ^{13}C NMR, IR, $[\alpha]_D$, R_f] were identical in all respects with the published data for both natural and synthetic pteridic acid B (see the Supporting Information for comparison of natural and our synthetic pteridic acid B).[1,2]

Conclusions

In summary, we have achieved the total synthesis of pteridic acids A and B. Notable features of this approach include convergence, a lithium enolate-mediated aldol reaction to set up the desired C9 and C10 stereocenters, and a spiroketalization reaction. This approach compares very well with previously published routes and, in principle, is readily applicable for the preparation of additional novel structural analogues. Further optimization of the synthesis as well as application of this strategy to the synthesis of pteridic acid analogues is underway and the results will be described in due course.[19]

Experimental Section

(5*R*,6*S*,10*S*,11*R*,12*S*,13*S*,*Z*)-6-Ethyl-11-hydroxy-13-((*S*)-1-(4-methoxybenzyloxy)propan-2-yl)-2,2,3,3,5,10,12,15,15,-16,16-undecamethyl-4,14-dioxa-3,15-disilaheptadec-7-en-9-one (19). To a solution of LHMDS (0.94 mL, 0.94 mmol, 1 M in THF/ethylbenzene, 1.2 equiv) in THF (6.5 mL) at −78 °C was added a solution of ethyl ketone 5 (0.221 g, 0.78 mmol) and HMPA (0.42 mL, 2.37 mmol, 3 equiv) in THF (16 mL). The reaction mixture was stirred at −78 °C for 2 h before a solution of aldehyde **4** (0.296 g, 0.78 mmol, 1 equiv) in THF (2.9 mL) was added dropwise. The solution was stirred at −78 °C for 2 h, quenched with saturated NH_4Cl (50 mL), and warmed to room temperature. The aqueous layer was extracted with Et_2O/EtOAc (1:1, 3×15 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash chromatography (10% hexanes/EtOAc) to afford 0.293 g (0.44 mmol) of aldol **19** as a colorless oil (56% yield), together with a second diastereoisomer tentatively assigned as the corresponding *syn* aldol with Felkin addition (0.073 g, 0.11 mmol, 14% yield). **Aldol 19:** R_f 0.45 (10% EtOAc in hexane); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.25 (br d, *J* 8.6 Hz, 2H), 6.86 (br d, *J* 8.7 Hz, 2H), 6.32 (br d, *J* 11.7 Hz, 1H), 6.14 (ap t, *J* 10.5 Hz, 1H), 4.41 (br s, 2H), 4,00 (dd, *J* 7.2, 1.5 Hz, 1H), 3.82−3.92 (m, 2H), 3.80 (s, 3H), 3.58 (dd, *J* 8.9, 4.3 Hz, 1H), 3.35−3.15 (m, 3H), 2.64 (qd, *J* 7.3, 1.6 Hz, 1H), 1.91−2.01 (m, 1H), 1.62−1.19 (m, 3H), 1.08 (d + m, *J* 7.2 Hz, 3H + 1H), 1.04 (d, *J* 6.3 Hz, 3H), 0.96 (d, *J* 6.8 Hz, 3H), 0.88 (s, 9H), 0.86 (s + t, 12H), 0.77 (d, *J* 6.9 Hz, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (62.5 MHz, C_6D_6) δ −4.7, −4.1, −3.9, −3.7, 8.3, 9.8, 12.1, 14.7, 18.3, 18.8, 22.3, 25.0, 26.1, 26.5, 38.4, 39.3, 47.2, 47.8, 54.7, 70.6, 71.1, 72.5, 73.1, 73.3, 114.0, 129.4, 131.4, 151.0, 159.6, 207.6; IR ν_{max} (film) 3472, 3053, 2959, 2932, 2856, 1674, 1612, 1514, 1462, 1265, 1036, 837; $[\alpha]^{23}_D$ +21.0 (*c* 1.4, CH_2Cl_2); HRMS (ESI TOF-MS) calcd for $C_{37}H_{69}O_6Si_2$ 665.4633, found 665.4546.

Spiroketals 21 and 22. To a solution of aldol **20** (42 mg, 0.08 mmol) in THF/H_2O (10:1, 9.3 mL) in a polypropylene vessel at 0 °C was added HF−pyridine (1.70 mL). After 8 h at rt, the reaction mixture was partitioned between saturated aqueous $NaHCO_3$ (20 mL) and CH_2Cl_2 (10 mL). The phases were separated, and the aqueous phase was washed with CH_2Cl_2 (3 × 10 mL). The combined organic phases were then dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (40% EtOAc/Hex) afforded spiroketals **21** (9 mg, 0.03 mmol, 40%) and **22** (9 g, 0.03 mmol, 40%) as colorless oils.

Spiroketal (21):. R_f 0.31 (40% EtOAc in hexane); ^{1}H NMR (500 MHz, C_6D_6) δ 5.62 (dd, *J* 10.2, 5.5 Hz, 1H), 5.33 (dd, *J* 10.2, 1.3 Hz, 1H), 3.85−3.90 (q, *J* 7.1 Hz, 1H + dd, *J* 10.1, 2.2 Hz, 1H), 3.77 (dd, *J* 11.0, 4.8 Hz, 1H), 3.72 (dd, *J* 10.7, 7.8 Hz, 1H), 3.57 (dd, *J* 10.7, 3.8 Hz, 1H), 1.90−2.00 (m, 2H), 1.70−1.79 (m, 2H), 1.52−1.61 (m, 2H), 1.38 (d, *J* 6.8 Hz, 3H), 0.98 (d, *J* 6.7 Hz, 3H), 0.92 (d, *J* 6.9 Hz, 3H), 0.74 (t, *J* 7.4 Hz, 3H), 0.56 (d, *J* 6.9 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 4.9, 11.8, 12.9, 13.0, 21.6, 26.4, 37.01, 37.02, 40.7, 41.0, 68.3, 71.7, 71.9, 77.1, 97.2, 128.3, 130.4; $[\alpha]^{23}_D$ +2.8 (*c* 0.4, CH_2Cl_2); HRMS (ESI TOF-MS) calcd for $C_{17}H_{31}O_4$ 299.2222, found 299.2192.

Spiroketal (22):. R_f 0.20 (40% EtOAc in hexane); ^{1}H NMR (500 MHz, C_6D_6) δ 5.73 (ap t, *J* 11.6 Hz, 1H + d, *J* 11.9 Hz, 1H), 3.96 (dq, *J* 9.8, 6.1 Hz, 1H), 3.72 (ap t, *J* 11.1, 10.8 Hz, 1H), 3.61 (dd, *J* 10.6, 6.8 Hz, 1H), 3.25 (dd, *J* 11.4, 4.7 Hz, 1H), 3.18 (dd, *J* 9.8, 2.0 Hz, 1H), 2.01−1.85 (m, 2H), 1.70−1.60 (m, 2H), 1.32−1.17 (m, 2H), 1.12 (d, *J* 6.2 Hz, 3H), 1.02 (d, *J* 6.7 Hz, 3H), 0.91 (d, *J* 6.9 Hz, 3H), 0.76 (t, *J* 7.5 Hz, 3H), 0.56 (d, *J* 6.9 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 5.0, 10.2, 11.9, 12.8, 19.5, 23.5, 36.85, 36.92, 41.0, 42.7, 68.4, 69.0, 73.7, 77.9, 98.6, 124.0, 133.7; $[\alpha]^{23}_D$ −2.0 (*c* 0.3, CH_2Cl_2); HRMS (ESI TOF-MS) calcd for $C_{17}H_{31}O_4$ 299.2222, found 299.2198.

Ester 25. To a solution of triethyl 4-phosphonocrotonate (31 mg; 0.123 mmol) in THF (0.5 mL) at −78 °C was added LiHMDS (0.12 mL, 1 M in THF/ethylbenzene, 0.120 mmol) and the resultant solution stirred for 10 min. A solution of aldehyde **23** (0.050 mmol) in THF (0.25 mL) was then added slowly and the reaction mixture allowed to warm to −25 °C and stirred for 1.5 h. The reaction was then allowed to warm to rt and quenched by the addition of saturated aqueous NH_4Cl (1 mL). The aqueous phase was extracted with Et_2O (3×5 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (20% EtOAc/Hex) afforded ester **25** (12 mg, 0.031 mmol, 60% for two steps) as a colorless oil: R_f 0.30 (30% EtOAc/40−60 petroleum ether); ^{1}H NMR (400 MHz, C_6D_6) δ 7.53 (dd, *J* 15.4, 10.3 Hz, 1H), 6.06 (dd, *J* 15.4, 7.5, 1H), 5.97 (dd, *J* 15.4, 10.4 Hz, 1H), 5.90 (d, *J* 15.6 Hz, 1H), 5.65 (ddd, *J* 10.3, 5.6, 1.1 Hz, 1H), 5.42 (dd, *J* 10.3, 0.8 Hz, 1H), 4.06 (q, *J* 7.0, 2H), 3.85 (br q, *J* 6.9, 1H), 3.78 (dt, *J* 10.9, 4.7, 1H), 3.66 (dd, *J* 9.8, 2.2 Hz, 1H), 2.38−2.27 (m, 1H), 1.79−1.72 (m, 1H), 1.61−1.53 (m, 1H), 1.39−1.27 (m, 3H), 1.21 (d, *J* 6.9 Hz, 3H), 1.01 (d, *J* 6.4 Hz, 3H), 0.99 (t, *J* 7.3 Hz, 3H), 0.93 (d, *J* 6.7 Hz, 3H), 0.77 (t, *J* 7.5 Hz, 3H), 0.71 (d, *J* 6.9 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 4.8, 11.9, 12.9, 14.4, 15.1, 23.1, 26.7, 36.8, 38.8, 40.7, 41.1, 59.9, 71.7, 72.2, 74.7, 97.0, 120.0, 127.3, 127.8−128.8 (obs), 129.6, 145.3, 148.7, 166.8; IR ν_{max} (film) 3454, 2964, 2928, 1713, 1641, 1618, 1460, 1421, 1265, 1144, 1030, 1003; $[\alpha]^{23}_D$ +20.5 (*c* 0.14, MeOH); HRMS (ESI TOF-MS) calcd for $C_{23}H_{37}O_5$ 393.2641, found 393.2593.

Ester 27. To a solution of triethyl-4-phosphonocrotonate (9.3 g, 0.037 mmol) in THF (0.3 mL) at −78 °C was added LiHMDS (0.035 mL, 1 M in THF/ethylbenzene, 0.035 mmol) and the resultant solution stirred for 10 min. A solution of aldehyde **26** (0.015 mmol) in THF (0.1 mL) was then added slowly and the reaction mixture allowed to warm to −25 °C and stirred for 1.5 h. The reaction was then allowed to warm to rt and quenched by the addition of saturated aqueous NH_4Cl (0.5 mL). The aqueous phase was extracted with Et_2O (3×5 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (20% EtOAc/Hex) afforded ester **27** (3,5 g; 0.009 mmol, 62% for two steps) as a colorless oil: R_f 0.20 (30% EtOAc/40−60 petroleum ether); ^{1}H NMR (400 MHz, C_6D6) δ 7.54 (dd, *J* 15.4, 10.6 Hz, 1H), 6.05 (dd, *J* 15.4,

(19) New compounds and the isolatable intermediates gave satisfactory ^{1}H and ^{13}C NMR, IR, HRMS, and analytical data. Yields refer to chromatographically and spectroscopically homogeneous materials.

10.6 Hz, 1H), 5.96 (d, *J* 15.2 Hz, 1H), 5.91 (dd, *J* 14.5, 6.2 Hz, 1H), 5.67 (br d, *J* 10.3 Hz, 1H), 5.65 (ddd, *J* 10.3, 5.6, 1.1 Hz, 1H), 4.13 (dd *J* 9.8, 6.1 Hz, 1H), 4.07 (q, *J* 7.0 Hz, 2H), 3.29 (dt, *J* 11.2, 5.0, 1H), 2.97 (dd, *J* 9.8, 2.2 Hz, 1H), 2.36−2.26 (m, 1H), 1.78−1.63 (m, 3H), 1.32−1.23 (m, 1H), 1.15−1.09 (obs, 1H), 1.14 (d, *J* 6.2 Hz, 3H), 1.05 (d, *J* 6.7 Hz, 3H), 0.99 (t, *J* 7.0 Hz, 3H), 0.92 (d, *J* 6.9 Hz, 3H), 0.82 (t, *J* 7.5 Hz, 3H), 0.76 (d, *J* 6.2 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 4.9, 10.1, 11.8, 14.3, 15.3, 19.6, 23.6, 36.7, 38.7, 41.0, 42.6, 60.0, 68.0, 73.9, 75.7, 98.1, 119.9, 124.6, 128.5, 133.8, 145.6, 148.2, 166.9; $[\alpha]^{23}_D$ −18.7 (*c* 0.12, MeOH); HRMS (ESI TOF-MS) calcd for $C_{23}H_{37}O_5$ 393.2641, found 393.2598.

Pteridic Acid B. To a solution of ester **27** (12.5 mg, 0.031 mmol) in EtOH/H_2O (2:1, 1.5 mL) at rt was added aqueous KOH (10%, 0.12 mL) dropwise. After 24 h at rt, the reaction mixture was partitioned between pH 4 buffer (1 mL) and CH_2Cl_2 (3 mL). The phases were separated, and the aqueous phase was washed with CH_2Cl_2 (5×4 mL). The combined organic phases were then dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (8% MeOH/ CH_2Cl_2) afforded pteridic acid B (7.5 mg, 0.020 mmol, 65%) as a white solid: R_f 0.52 (8% MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (1H, obscured), 6.23 (dd, *J* 15.2, 10.5 Hz, 1H), 6.14 (dd, *J* 15.3, 7.1 Hz, 1H), 5.92 (dd, *J* 10.5, 1.8 Hz, 1H), 5.89 (br d, *J* 11.1 Hz, 1H), 5.76 (d, *J* 15.3 Hz, 1H), 3.89 (dq, *J* 10.0, 6.1 Hz, 1H), 3.69 (dd *J* 11.2, 4.8 Hz, 1H), 3.26 (dd, *J* 10.0, 1.8 Hz, 1H), 2.53 (m, 1H), 2.05 (m, 1H), 1.85 (m, 1H), 1.76 (m, 1H), 1.48 (m, 1H), 1.21 (d, *J* 6.1 Hz, 3H), 1.20 (m, 1H), 0.96 (d, *J* 6.9 Hz, 6H), 0.92 (d, *J* 6.7 Hz, 3H), 0.87 (t, *J* 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.9, 10.0, 11.5, 15.3, 19.6, 23.4, 36.3, 38.4, 40.8, 42.3, 68.1, 74.3, 75.6, 97.9, 118.1, 123.5, 127.4, 134.0, 147.5, 149.4, 171.3; $[\alpha]^{23}_D$ −20.0 (*c* 0.10, $CHCl_3$); HRMS (ESI TOF-MS) calcd for $C_{21}H_{33}O_5$ 365.2328, found 365.2295. For ^{1}H and ^{13}C NMR analysis of pteridic acids A and B, deuterated $CDCl_3$ has been passed through a plug of basic alumina and stored in K_2CO_3 just before use.

Pteridic Acid A. To a solution of ester **25** (10 mg, 0.025 mmol) in EtOH/H_2O (2:1, 1.2 mL) at rt was added aqueous KOH (10%, 0.10 mL) dropwise. After 24 h at rt, the reaction mixture was partitioned between pH 4 buffer (1 mL) and CH_2Cl_2 (3 mL). The phases were separated and the aqueous phase washed with CH_2Cl_2 (5 × 4 mL). The combined organic phases were then dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (8% MeOH/CH_2Cl_2) afforded pteridic acid A (6.6 mg, 0.018 mmol, 70%) as a white solid: R_f 0.54 (8% MeOH/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (dd, *J* 15.1, 10.3 Hz, 1H), 6.24 (dd, *J* 15.2, 6.6 Hz, 1H), 6.17 (dd, *J* 15.4, 10.0 Hz, 1H), 5.95 (dd, *J* 10.3, 5.6 Hz, 1H), 5.77 (d, *J* 15.1 Hz, 1H), 5.50 (dd, *J* 10.3, 1.2 Hz, 1H), 3.90 (q, *J* 6.6 Hz, 1H), 3.83 (dd *J* 10.9, 4.9 Hz, 1H), 3.74 (dd, *J* 10.0, 2.2 Hz, 1H), 2.50 (m, 1H), 2.05 (m, 1H), 1.63 (q, *J* 6.7 Hz, 1H), 1.60 (dq, *J* 11.0, 6.4 Hz, 1H), 1.44 (quint, *J* 7.6 Hz, 2H), 1.23 (d, *J* 7.0 Hz, 3H), 0.99 (d, *J* 6.8 Hz, 3H), 0.92 (t, *J* 7.4 Hz, 3H), 0.91 (d, *J* 6.8 Hz, 3H), 0.90 (d, *J* 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.5, 11.9, 12.5, 15.2, 22.8, 26.2, 36.3, 38.5, 40.4, 40.9, 71.6, 72.4, 74.5, 96.8, 118.2, 126.8, 127.5, 130.2, 147.4, 150.1, 171.5; $[\alpha]^{23}_D$ + 19.1 (*c* 0.10, $CHCl_3$); HRMS (ESI TOF-MS) calcd for $C_{21}H_{33}O_5$ 365.2328, found 365.2291.

For ^{1}H and ^{13}C NMR analysis of pteridic acids A and B, deuterated $CDCl_3$ has been passed through a plug of basic alumina and stored in K_2CO_3 just before use.

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Supporting Information Available: Experimental procedures and spectral data for the prepared compounds. This material is available free of charge via the Internet at http://pubs.acs.org.