and ^{15}N NMR data for **5**, including ^{1}H–^{13}C and ^{1}H–^{15}N HMBC data, CD spectra for **1**–**7**, and Corbett/Valeriote assay data for **2** (10 pages). Ordering information is given on any current masthead page.

Total Syntheses of (+)-Paspalicine and (+)-Paspalinine

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Recently we reported a second-generation synthesis of (−)-paspaline (**1**),[1a,b] the simplest member of a family of architecturally novel indole diterpenes. Central to the former was the development of a unified strategy, designed to encompass this entire class of fungal metabolites which now include (+)-paspalicine (**2**), (+)-paspalinine (**3**), and (+)-paxilline (**4**)[2] (Scheme I). The cornerstone of the approach comprised a stereocontrolled, nine-step construction of tricyclic ketone (−)-**5** [9.4% overall yield from (+)-Wieland–Miescher ketone], a prospective common intermediate containing the critical C(12b,12c) vicinal quaternary centers.[1a] In this communication we demonstrate the viability of this unified strategy with the first total syntheses of (+)-paspalicine (**2**) and (+)-paspalinine (**3**). Importantly, the potent tremorgen (+)-paspalinine represents the first biologically active indole diterpene to yield to total synthesis.

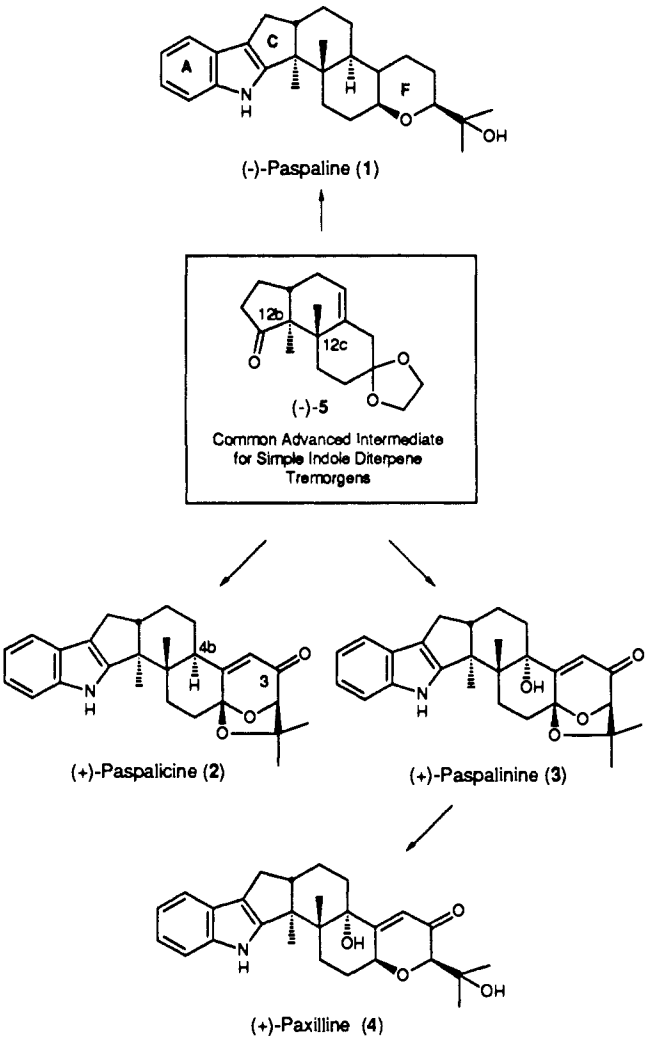
In contrast with the paspaline venture, wherein the indole nucleus was incorporated late in the synthesis, our point of departure for paspalicine and paspalinine entailed the conversion of common intermediate (−)-**5** to (+)-**7**[3] via the Gassman indole protocol[4] (46% overall yield; Scheme II). With the ABCDE-ring system of the simple tremorgens in hand, we envisioned installation of rings F and G via alkylation of the thermodynamic enolate derived from (+)-**7** with epoxide (−)-**17**; acid-promoted cyclization, oxidation of the C(3) hydroxyl, and migration of the C(4a,4b) olefin into conjugation would then complete the synthesis of paspalicine (**2**). Further oxidation at C(4b) would in turn furnish paspalinine (**3**).

Epoxide (−)-**17**, required for rings F and G, was prepared in six steps as outlined in Scheme III. Key transformations included a Sharpless asymmetric epoxidation,[5] protection of the resultant epoxy alcohol as the *p*-nitrobenzoate ester (95% ee after one recrystallization),[5] and a highly diastereoselective methylenation[6] of aldehyde (+)-**16** (>95% de).

Coupling of enone (+)-**7** and epoxide (−)-**17** (Scheme II) proceeded in 50% yield via the Stork metalloenamine protocol[7] [i.e., conversion of (+)-**7** to the corresponding dimethylhydrazone, deprotonation [LDA (1.9 equiv), THF, 65 °C, 15 h], and alkylation with (−)-**17**]. Best results required rigorous exclusion of oxygen. Workup with benzoic acid effected migration of the β,γ-olefinic bond into conjugation to provide (+)-**8**. Acetylation of the secondary hydroxyl, hydrazone hydrolysis [(i) MeI (10 equiv), MeCN, room temperature; (ii) HCO_2Na (20 equiv), $MeO(CH_2)_2OH$, 110 °C, 20 h], and acid-promoted deketalization [70% $HClO_4$ (1 equiv), CH_2Cl_2, 0 °C, 1 h] with concomitant cyclization then afforded (+)-**10**, an advanced intermediate well suited for conversion to paspalicine and paspalinine.

Toward this end, acetate removal and Moffatt oxidation[8] provided the corresponding β,γ-unsaturated enone (+)-**12**, along with a minor amount of (+)-paspalicine (**2**) (ca. 5:1). Initial attempts to isomerize (+)-**12** to (+)-**2** employing either acidic or basic conditions did not signficantly alter this ratio. Fortunately, the Clive modification of Grieco's rhodium chloride protocol [$RhCl_3$ (0.66 equiv), absolute EtOH–benzene (1:4), at reflux, 17 h][9] effected complete conversion to (+)-paspalicine. Synthetic (+)-**2** was identical in all respects (500-MHz ^{1}H NMR, 125-MHz ^{13}C NMR, IR, MS, X-ray, mp, mmp, and specific rotation) with an authentic sample kindly provided by Professor Arigoni.[10]

Scheme I



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(3) The structure assigned to each new compound was in accord with its infrared, 500-MHz ^{1}H NMR, and 125-MHz ^{13}C NMR spectra, as well as appropriate parent ion identification by HRMS.

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(10) We thank Professor D. Arigoni of the Eidgenossische Technische Hochschule, Zurich, for providing generous samples of both (+)-paspalicine and (+)-paspalinine.

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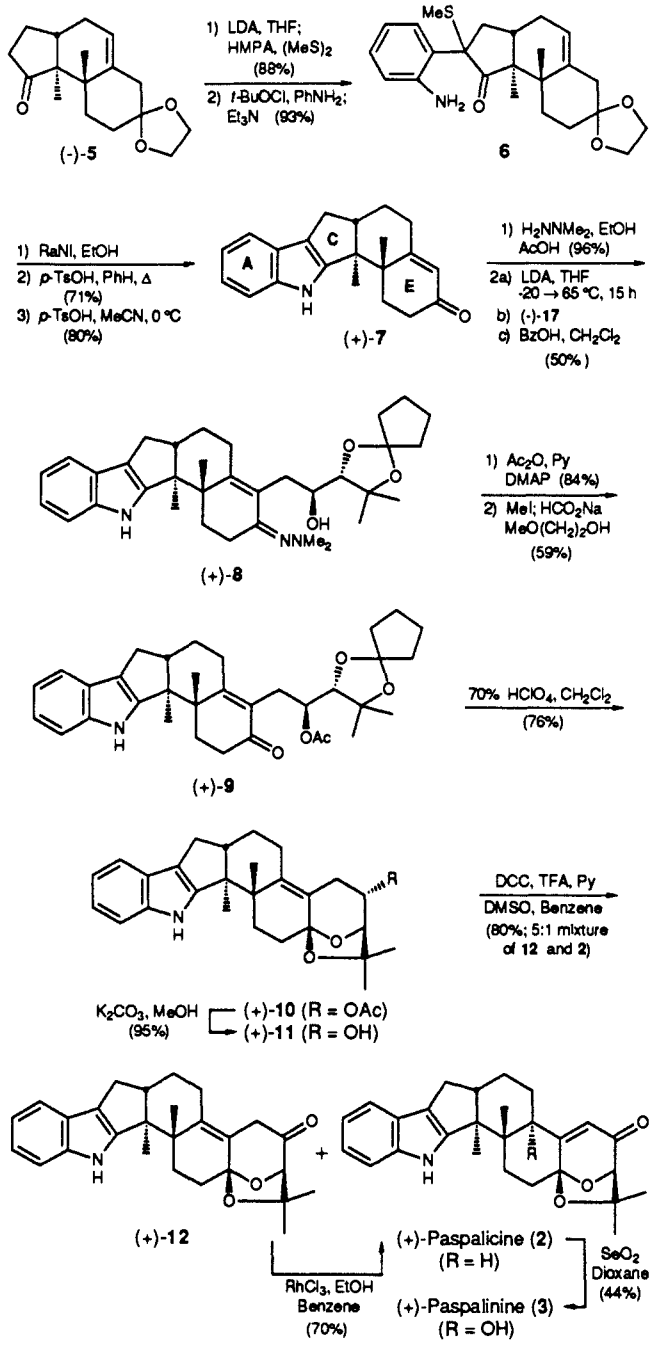
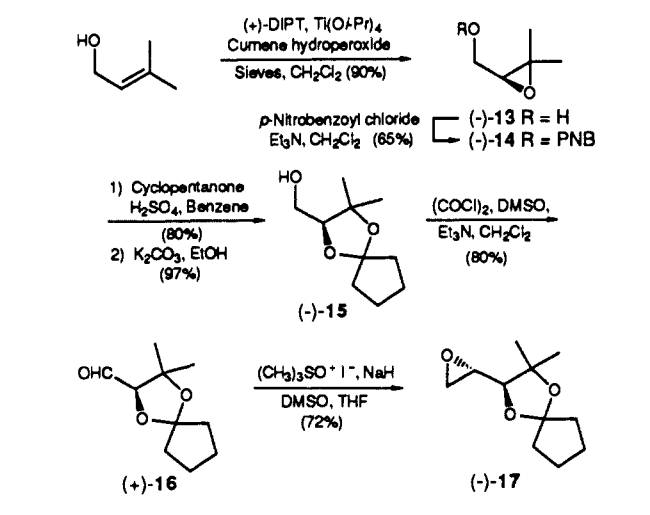
Scheme II



Scheme III



Oxidation of (+)-**2** with selenium dioxide[11] then provided (+)-paspalinine (**3**) in 44% yield, along with an as-yet-unidentified byproduct. Detailed analysis again established the identity of synthetic (+)-**3** with the natural material.[10] Given the importance of the C(4b) tertiary hydroxyl group for tremorgenic activity,[2c] the latter transformation should prove useful for elaboration of other significant structures.

In summary, the first total syntheses of (+)-paspalicine (**2**) and (+)-paspalinine (**3**) have been achieved in 22 and 23 steps, respectively, exploiting a unified strategy which earlier afforded (-)-paspaline (**1**). Progress toward construction of the remaining members of this class, as well as the design and synthesis of biologically active congeners, will be reported in due course.

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Supplementary Material Available: Spectroscopic and analytical data for (+)-**2**, (+)-**3**, (+)-**7**, (+)-**8**, (+)-**11**, (+)-**16**, and (-)-**17** (2 pages). Ordering information is given on any current masthead page.

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Solution Chemistry and Derivatives of Centered Zirconium Chloride Cluster Phases

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The diverse chemistry of centered zirconium analogues of the traditional $(Nb,Ta)_6Cl_{12}^{n+}$ clusters that has been broadly developed via high-temperature solid-state reactions[1-8] has now been extended to a surprisingly versatile solution chemistry of some of the same clusters. Solid phases of general compositions $M^i_x[Zr_6(Z)Cl^i_{12}]Cl^a_n$ with five different interstitial atoms Z = H, Be, B, C, and Fe have been dissolved in acetonitrile and solid derivatives isolated. Fifteen products have been structurally characterized.[9] Reactants with $n < 6$ exhibit intercluster bridging by shared chlorine atoms, increasing in number with decreasing n. Therefore, excision of soluble cluster units from such solids requires that additional ligands open up these Zr–Cl^a–Zr linkages or, alternatively, displace the bridging chlorides. The inner Cl^i atoms are not disturbed. In practice, we find that the phases with $n = 3$, 4, or 6 often react with either $n - 6$ chloride anions or 6 neutral ligands L (NH_2R, PR_3) to afford new $(Zr_6Cl_{12}Z)Cl_6^{m-}$ or $Zr_6Cl_{12}Z{\cdot}L_6$ products.

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