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(15) Samples (1–5 mg) were heated at 110 °C in a sealed tube for 16 h with 6 N hydrochloric acid. Liberated thymine was quantitated by TLC and UV spectral analysis.
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(25) II, III, pyridinium 3′-*O*-acetyl-N^6-benzoyl-2′-deoxyadenosine-5′-phosphate, and pyridinium 3′-*O*-acetyl-N^2-isobutyryl-2′-deoxyguanosine-5′-phosphate were the four protected mononucleotides used.

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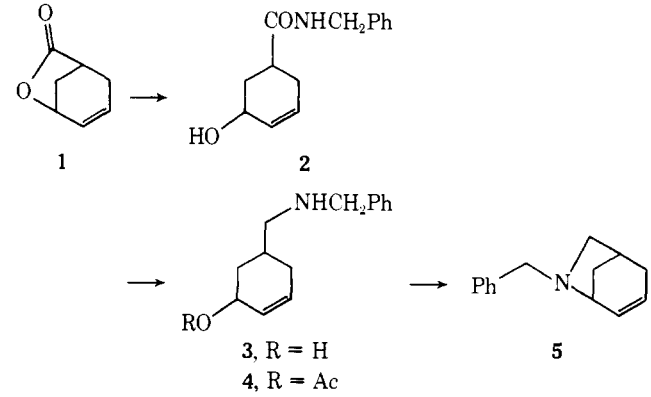
Palladium Catalyzed Cyclizations to Alkaloid Skeletons. Facile Synthesis of Desethylibogamine

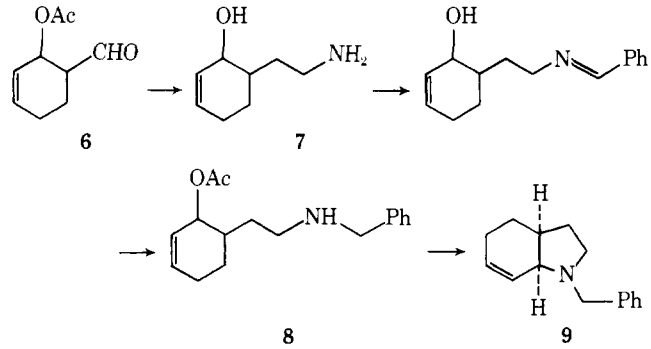
Sir:

Difficulties in alkaloid syntheses stem in large part from the high reactivity of the nitrogen. The chemospecificity demonstrated by palladium catalyzed reactions suggested their applicability to this important class of natural products without the need to protect the nitrogen, e.g., as an amide. We have now determined that, in the palladium catalyzed allylations of amines,[1] the allylic position is substituted with predominant *retention of configuration*[2] and such a reaction can be accomplished in an intramolecular sense (i.e., cyclization). This finding allows one to make use of the endo selectivity in the Diels–Alder reaction to generate facile approaches to the ring skeletons of many alkaloids. We have synthesized the basic ring system of three different classes of alkaloids, representatives of which are actinobolamine,[3] ibogamine,[4] and mesembrine.[5] We have further illustrated the utility of this approach by a short regiocontrolled total synthesis of desethylibogamine.[6]

Scheme I. Synthesis of 6-Azabicyclo[3.2.1]oct-3-ene System



Scheme II. Synthesis of 2,3,3a,4,5,7a-Hexahydro-1*H*-indole System



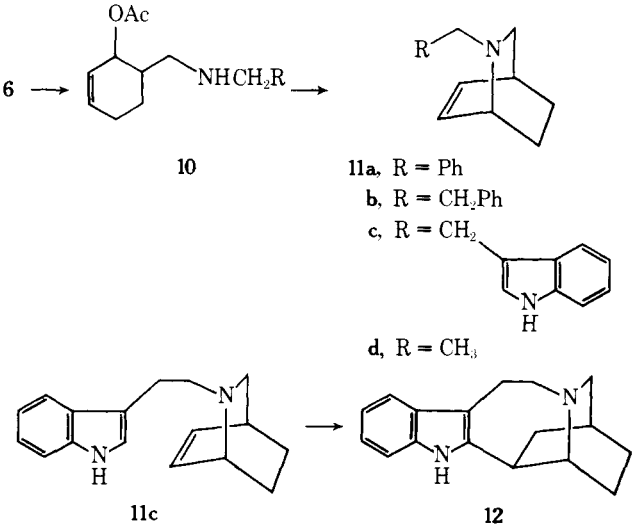
A second key step in the latter sequence employs a palladium catalyzed intramolecular alkylation of an olefin.

Scheme I outlines the synthesis of 6-benzyl-6-azabicylo[3.2.1]oct-2-ene. The lactone **1**,[7] readily available from the Diels–Alder adduct of butadiene and acrylic acid, was opened with benzylamine (neat, 120–125 °C, 89%) to give amide **2**, mp 123–124 °C, and the resulting amide subsequently reduced with lithium aluminum hydride (THF, reflux, 98%) to give amino alcohol **3**. Acetylation at oxygen to give **4**[8] required complete protonation of the amine and careful workup to avoid O to N acetyl migration (1.1 equiv of $HClO_4$, Ac_2O, CH_2Cl_2, O → 25 °C). Treatment of the allylic acetate **4** with a catalytic quantity of tetrakistriphenylphosphinepalladium[9] in the presence of additional triphenylphosphine and triethylamine at 55 °C for 8.5 h gave the desired product **5**[8,10] in 67% distilled yield (bp 78–85 °C at 0.1 mm).

A mesembrine skeleton is available from the Diels–Alder adduct **6** of acrolein and 1-acetoxy-1,3-butadiene as outlined in Scheme II. Reduction ($NaBH_4$, methanol, 0 °C, 100%), tosylation (TsCl, pyridine, 0 °C, 72%), cyanide displacement (NaCN, Me_2SO, 70 °C, 90%, bp 100–105 °C at 0.1 mm), and reduction (LAH, ether, room temperature, 94%) gave the desired amino alcohol **7**. Imine formation (PhCHO, PhH, Dean–Stark trap, 64%), reduction ($NaBH_4$, methanol, room temperature, 100%), and acetylation (70% yield) as previously described gave the crucial allylic acetate **8**.[8] Cyclization to **9**[8] was achieved at 70 °C in acetonitrile in the presence of a catalytic amount of the Pd^0 complex and triethylamine (>50% yield). The stereohomogeneity of **9** was established chromatographically and spectroscopically.[11] The cis stereochemistry was confirmed by the J = 7 Hz coupling constant for the protons on C(3a) and C(7a) and the low field absorption (δ 2.88, td, J = 8.7, 2.4 Hz) for one proton on C(2).[12]

The same adduct **6** serves as a precursor to the isoquinuclidine[13] skeleton as illustrated in Scheme III. In particular, reductive amination by forming the Schiff's base ($PhCH_3$, $MgSO_4$, −25 to 0 °C) followed by sodium borohydride workup (add CH_3OH, −15 to 0 °C) gave the desired amino acetates

Scheme III. Synthesis of Isoquinuclidine System. Synthesis of Desethylibogamine



10a and **b**.[8] Cyclization (catalytic amount of $(Ph_3P)_4Pd$, $(C_2H_5)_3N$, CH_3CN, 70 °C, 1.5 h) gave the desired isoquinuclidines **11a** and **b**[8] in 65 and 56% yields, respectively. The structures were confirmed spectroscopically and by elemental composition. The NMR spectra match that reported for the *N*-methyl derivative **10d**[14] indicating the syn relationship of the N-alkyl substituent and the double bond. Such a stereochemistry is necessary for the synthesis of the iboga system and led to a facile approach to desethylibogamine. The success of this net S_N2' cyclization suggests the intermediacy of the π-allyl complexes and that ring strain determines the regiochemistry.

Repetition of the above reductive amination utilizing tryptamine gave in 68% yield the desired amino acetate **10c** as a viscous oil which upon cyclization in the standard way gave isoquinuclidine **11c**[8,11] (mp 118–120 °C from acetonitrile) in 60% yield. Again, the similarity of the NMR spectrum for the isoquinuclidine nucleus to those of **10 a–c** confirms the syn relationship of the tryptyl unit and the double bond. The final cyclization was also envisioned to utilize palladium catalysis to achieve chemospecificity in the presence of the basic nitrogen. Treatment of the lithio derivative with mercuric chloride followed by palladium chloride in THF and quenching with sodium borohydride gave desethylibogamine, mp 182–184 °C, identical by NMR, MS, and TLC with an authentic sample.[6] This cyclization, modeled after the Heck arylation reaction,[15] is envisioned to involve the cis addition of an organopalladium intermediate to the double bond followed by reductive cleavage of the C-Pd bond. These results demonstrate the feasibility and potential utility in organic synthesis of palladium catalyzed cyclizations[16] that proceed by S_N2 or S_N2' substitution with net retention of configuration.

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Opto-Galvanic Detection of Species in Flames

Sir:

An electrical signal, resulting directly from discreet optical absorptions in atomic vapors,[1-6] has been observed in atmospheric pressure analytical flames. Specifically, if the current from a constant voltage source is passed through the flame, the current is found to change when the flame is irradiated by intense monochromatic radiation (laser) corresponding to an absorption of a species present in the flame. This change in current is easily detected by standard electrical measurement techniques and can be used for spectroscopy, analytical determinations, and combustion research. In many respects, the technique corresponds to the generation of fluorescence excitation spectra with the important difference that no optical measurements are necessary to detect the absorption process. Consequently, problems associated with the measurement of weak optical signals, such as collection efficiency and scattered excitation light, are no longer important. As an example of the analytical application of this technique, the quantitative analysis of sodium in a flame is described.

The apparatus used for the detection of sodium in an air–C_2H_2 flame is shown in Figure 1. The flame was irradiated by a commercial, CW tunable dye laser chopped at 2 kHz. The bandwidth of the laser was approximately 0.003 nm and the wavelength could be fine-tuned over a range of 0.05 nm by tilting a 0.5-mm thick etalon placed in the laser cavity. The