organic layers were washed with 20 mL of water, the layers were separated, and the organic layer was dried (K_2CO_3). Removal of the solvent by rotary evaporation generally gave a light yellow oil. Samples of any 2,5-dialkyl(phenyl)pyridine (**6**) formed on decomposition of a 2,5-dialkyl(phenyl)-2,5-dihydropyridine (**2**) and of tetrahydropyridine **4** were collected by preparative GLC. The NMR spectrum of each compound **6** was compared to that of a sample prepared from the reaction of complex **1** and methyl iodide followed by decomposition of the resultant 2,5-dialkyl-(phenyl)-2,5-dihydropyridine (**2**). Each sample of tetrahydropyridine **4** was analyzed for a narrow multiplet near 5.6 ppm which is characteristic of the vinyl protons of these compounds. The NMR spectra of tetrahydropyridines **4b** and **4d** showed more than one absorption in the region near 5.6 ppm, suggesting the presence of stereoisomeric tetrahydropyridines.

General Procedure for Oxidation of Tetrahydropyridines 4a-f. Preparation of 2,3,6-Trialkyl(phenyl)pyridines (5). The crude tetrahydropyridine **4** (~0.4 mol) was refluxed with 0.08 mol (6.5 g) of selenium powder in 35 mL of mesitylene for 36 h. The unreacted selenium was removed by filtration, and the dark brown solution was extracted with four 20-mL portions of 6 M HCl. The combined extracts were cooled to 0 °C, made basic by slow addition of saturated NaOH solution, and extracted with three 30-mL portions of ethyl ether. The combined extracts were dried (K_2CO_3), and the ether was removed by rotary evaporation, leaving a yellow oil which was distilled and analyzed by GLC. Pure samples of trialkyl(phenyl)pyridines were obtained by preparative GLC.

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Registry No. 1a, 77070-58-7; **1b**, 77070-59-8; **1c**, 77070-60-1; **2a**, 66562-51-4; **2b**, 77070-61-2; **2c**, 66562-50-3; **4a**, 77070-62-3; **4b**, 77070-63-4; **4c**, 77070-64-5; **4d**, 77070-65-6; **4e**, 77070-66-7; **4f**, 77070-67-8; **5a**, 38222-84-3; **5b**, 77070-68-9; **5c**, 77070-69-0; **5d**, 77070-70-3; **5e**, 77070-71-4; **5f**, 77070-72-5; **6a**, 56029-43-7; **6c**, 27012-26-6; **6e**, 27012-22-2.

Palladium-Assisted N-Alkylation of Indoles: Attempted Application to Polycyclization

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The palladium(II) complexes of the olefins ethene, propene, and 1-hexene reacted with 1-lithioindole to produce N-alkylated indoles exclusively. Attempts to perform this N-alkylation intramolecularly (to form tricyclic material from 2-allylskatole) failed. Anilines with dienic side chains in the 2-position were subjected to Pd(II)-assisted cyclization conditions in attempts to induce polycyclization. However, only monocyclization was observed.

A variety of heterocyclic systems can be synthesized by using palladium-catalyzed intramolecular functionalization of olefins as the ring-forming step. In this way, *o*-allylphenols were converted to benzofurans,[1] α,β-unsaturated ketoximes to isoxazoles[2] or pyridines,[3] γ,δ-unsaturated alcohols to 2-vinyltetrahydrofurans,[4] 2'-hydroxychalcones to flavones,[5] and penta-2,4-dienoic acids to 2-pyrones.[6] We have recently synthesized isocoumarins from *o*-allylbenzoic acids[7] and indoles from *o*-allylanilines[8] using similar procedures. We have also developed polycyclization processes using sequential, palladium-promoted, cyclization–insertion reactions.[9] A different potential approach to tricyclic systems, particularly to pyrroloindoles, would involve multiple cyclizations of anilines having dienic side chains in the ortho position (eq 1). Since closure of the second ring would necessarily involve the indole nitrogen as the nucleophile, palladium-assisted N-alkylation of indoles was studied concurrently with polycyclization studies.

Indole has been allylated at the 1- or 3-position by allyl acetate, with $Pd(acac)_2$ as a catalyst in refluxing acetic acid.[10] This chemistry probably involves the amination

Table I. Pd(II)-Assisted N-Alkylation of Indole (Eq 2)

R	M	isolation	product	yield, %[a]
H	Li	H_2	1	62
H	Na	H_2	1	9
H	K	H_2	1	trace
H	MgBr	H_2	1	0
H	NBu_4^+	H_2	1	trace
H	Li	β elimination	3	77
H	Li	CO/MeOH	4	40
Me	Li	H_2	1	28
			2	68
n-Bu	Li	H_2	1	66
			2	25
NHAc	Li	H_2		0

[a] Reported yields are based on palladium and are for isolated, purified products.

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(2) K. Maeda, T. Hosokawa, S.-I. Murahashi, and I. Moritani, *Tetrahedron Lett.*, 5075 (1973).
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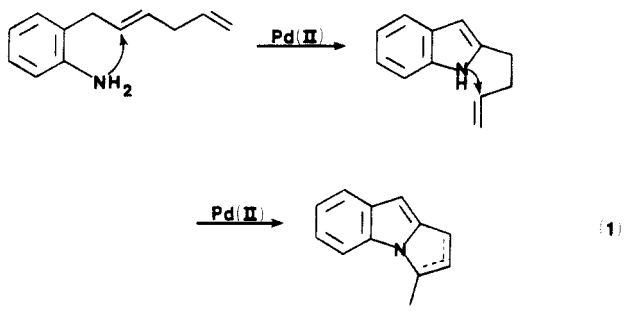
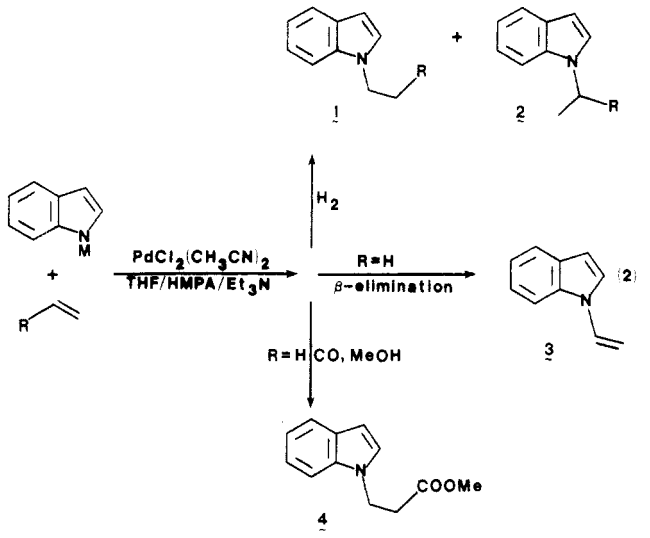


(1)

of a π-allylpalladium complex by indole as the key step. Indole anions are easily alkylated by reactive halides at either the 1- or 3-position, depending on reaction conditions.[11,12]

Results and Discussion

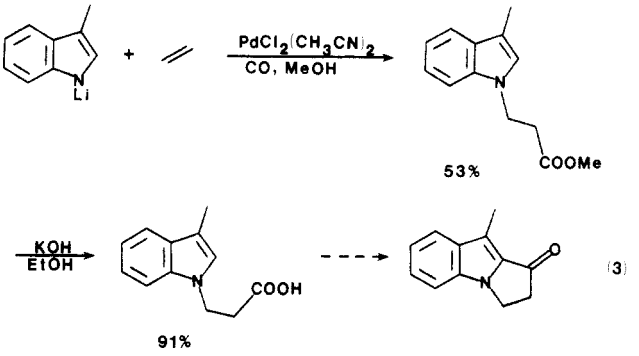
Palladium-Assisted N-Alkylation of Indoles. Palladium(II)–olefin complexes were treated with indolyl anions under the usual[13] conditions (olefin alkylation, THF/HMPA, Et_3N, −78 to +25 °C, reductive (H_2) isolation) as in eq 2. The results are summarized in Table I.



(2)

The lithium salt of indole was by far the most efficient in this reaction, giving moderate to high yields of N-alkylation. Sodium, potassium, and magnesium bromide and tetraalkylammonium salts gave little or no alkylation product. This strong dependence on the nature of the cation stands in contrast to the related palladium-assisted alkylation of olefins by carbanions, for which virtually no effect was noted upon going from lithium to potassium enolates.[13] In all cases only N-alkylation was observed, with no alkylation at the indole 3-position.

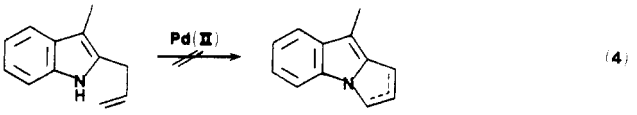
With ethylene, *N*-vinylindole was produced in good yield when β-hydride elimination was effected, whereas CO insertion to give the β-methyl ester went in only modest yield.[9,14,15] With skatole as the indole, this aminoacylation of ethylene proceeded in slightly better yield. The resulting ester was hydrolyzed in excellent yield. The resulting acid has already been cyclized to a pyrroloindole for use in the synthesis of mitosene analogues (eq 3).[16]



(3)

With propene and 1-hexene as substrates the regiochemistry of the reaction with the indole anion paralleled that found for the alkylation of these olefins by nonstabilized carbanions in the presence of Pd(II).[13] Surprisingly, *N*-vinylacetamide, an olefin very reactive in other palladium-assisted reactions with nucleophiles,[13,15] failed to alkylate indole under a variety of conditions.

Polycyclization Attempts. Intramolecular indole alkylation was attempted next. The first system studied was 2-allylskatole, prepared from skatole by mercuration at the 2-position with $Hg(OAc)_2$/NaCl followed by Pd(II)-catalyzed reaction with allyl chloride. Several attempts to cyclize this material (eq 4) failed. Three different approaches were tried. The substrate was treated sequentially with $PdCl_2(CH_3CN)_2$, HMPA, and Et_3N to generate the reactive olefin–palladium complex. Then, lithium diisopropylamide (LDA) was added slowly at −78 °C to form the anion. Under these conditions, only starting material was recovered. Alternatively, the indole anion was preformed and added slowly to a cold solution of $PdCl_2(CH_3CN)_2$, with similar negative results. Finally, the substrate, $PdCl_2(CH_3CN)_2$, and NaH were simply stirred at 25 °C in THF, conditions effective for the cyclization of *o*-allylbenzamide to isocarbostyril.[7] Again, unreacted starting material was recovered.



(4)

Concurrent with these studies, anilines having diene side chains in the ortho position were subjected to cyclization conditions in attempts to form two rings sequentially, as in eq 1. Aniline with a 2,5-hexadienyl side chain (**5**) reacted under both stoichiometric and catalytic conditions to give 2-propylquinoline in 24% yield. It is likely that ring closure occurred to produce a dihydroquinoline and the terminal olefin rearranged into conjugation (eq 5). Under stoichiometric conditions and with a reductive (H_2) isolation procedure there was obtained 2-propyl-1,2,3,4-tetrahydroisoquinoline (**6**), also in 24% yield. This result implies that the rearrangement and aromatization occurs rather slowly, since the quinoline itself is *not* reduced under these conditions.

To preclude six-membered- (quinoline) ring formation, we synthesized aniline with a 1,5-hexadiene side chain (**8**). Under catalytic conditions in DME at reflux, 2-*n*-butyl-

(11) B. Cardillo, G. Casrah, A. Pochini, and A. Ricca, *Tetrahedron*, **33**, 3771 (1967).
(12) M. G. Reinecke, J. F. Sebastian, H. W. Johnson, Jr., and C. Pyun, *J. Org. Chem.*, **37**, 3066 (1972).
(13) L. S. Hegedus, R. E. Williams, M. A. McGuire, and T. Hayashi, *J. Am. Chem. Soc.*, **102**, 4973 (1980).
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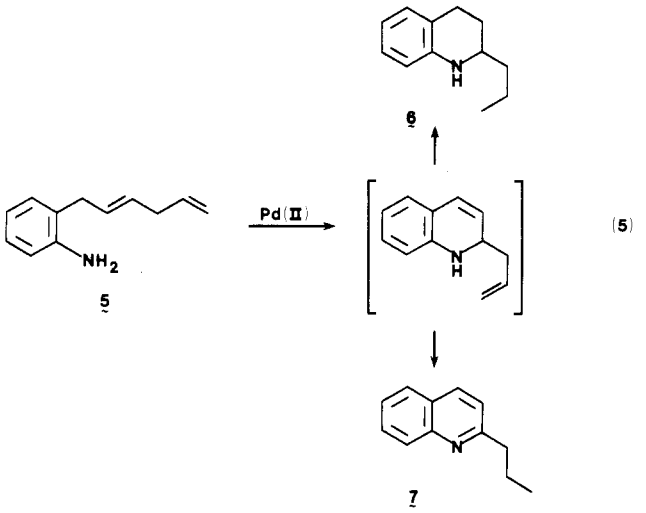
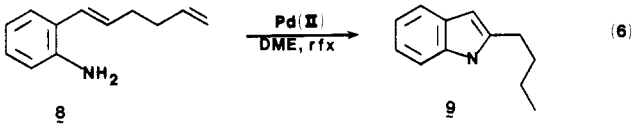
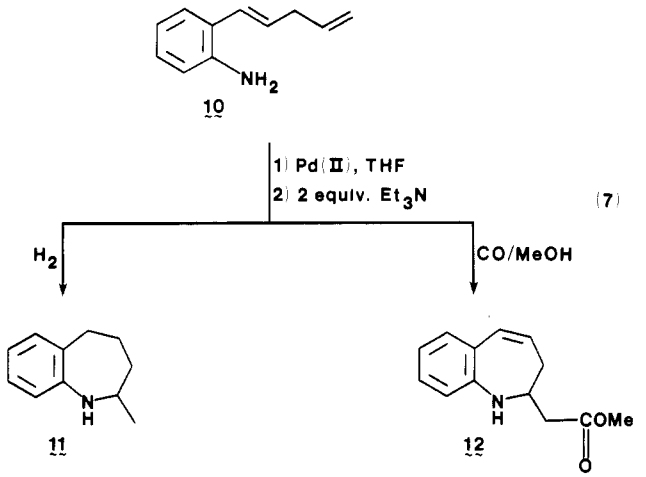


indole was produced in 60% yield (eq 6). Apparently the



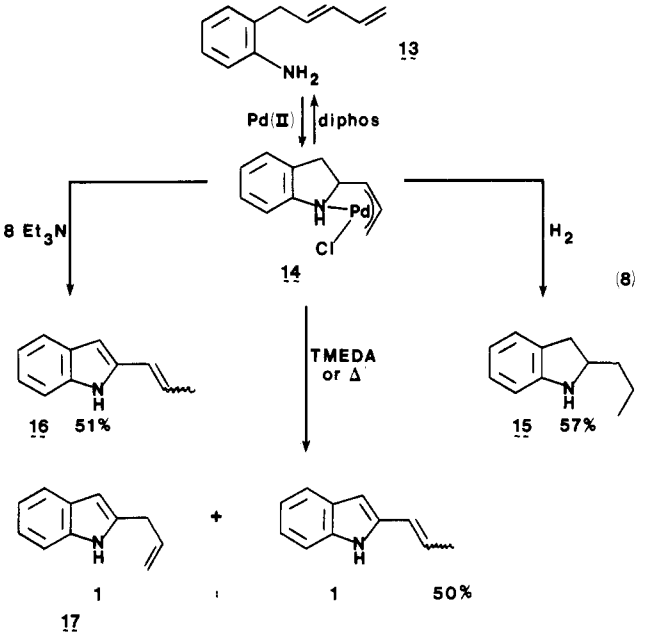
palladium hydride produced in the β-elimination step reduced the terminal double bond. In contrast, under stoichiometric conditions, no cyclization at all was observed. This parallels the observation that 2-aminostyrene cyclizes to indole under catalytic Pd(II) ring-closure conditions but fails to cyclize when stoichiometric amounts of Pd(II) are used.[8]

Still different results were obtained by using aniline with a 1,4-pentadiene side chain (**10**). Under catalytic cyclization conditions a myriad of unidentified compounds was obtained. Under stoichiometric conditions with a reductive isolation, *seven*-membered-ring formation ensued, giving **11** in 35% yield. Exposure of the reaction mixture to carbon monoxide/methanol led to production of the corresponding unsaturated ester **12** (eq 7), also in 35% yield.



In neither case was any indole formation observed. Aniline with 1,3-butadiene as a side chain cyclized exclusively to 2-methylquinoline, with no evidence of seven-membered-ring formation.

The final substrate studied was aniline with a 2,4-pentadiene side chain (**13**). This substrate differs from the others studied in that initial closure to form a five-membered ring should produce a relatively stable π-allylpalladium complex (eq 8). Since the amination of π-allylpalladium complexes has been previously reported,[17-19]



it was felt that formation of the second ring should ensue under similar conditions. This did not prove to be the case. Reaction of **13** with $PdCl_2(CH_3CN)_2$ gave a stable π-allylpalladium complex, **14**, which was isolated and characterized. Reduction of **14** with hydrogen produced 2-propyl-2,3-dihydroindole as expected. All attempts to intramolecularly aminate this π-allylpalladium complex failed. Treatment with diphos, the usual ligand to promote allylic amination, caused complex **14** to revert to starting material. Reaction with excess triethylamine produced diene **16**, a result similar to that recently[19] observed by Heck in his attempted intermolecular amination of π-allylpalladium complexes. Reaction of **14** with tetramethylethylenediamine or simple pyrolysis in the presence or absence of sodium carbonate produced mixtures of 2-allylindole and 2-propenylindole. Thus, strongly coordinative ligands appear to reverse the cyclization reaction, while basic ligands promote a proton abstraction to produce dienes. Appropriate conditions to permit intramolecular amination of this π-allylpalladium complex have not yet been found.

Experimental Section

General Methods. Melting points were taken on a Mel-Temp melting point apparatus. Infrared (IR) spectra were recorded on a Beckman Model 4200 spectrophotometer. Proton NMR spectra were determined on a Varian T-60 or EM360A spectrometer. All the chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. Mass spectra were recorded on an AEI MS 902 spectrometer. Liquid chromatography was carried out at moderate pressures (40–80 psi) with either 15 × 250 mm or 15 × 1000 mm columns of Woelm Type 206 silica gel. Preparative layer chromatography was carried out by using 20 × 20 cm plates coated with EM laboratories 60 PF-254 silica gel. Dry tetrahydrofuran (THF) and diethyl ether were obtained by distillation from sodium. Dry acetonitrile was distilled from P_2O_5. Dimethylformamide (DMF) was distilled over calcium hydride under reduced pressure. Dimethoxyethane (DME) was distilled over lithium aluminum hydride (LAH).

Materials. Indole was recrystallized from petroleum ether before use. THF and HMPA were dried and degassed prior to use. 1-(Trimethylsilyl)indole was prepared by literature methods.[20]

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Indolylsodium[21,22] and indolylmagnesium bromide[22,23] were prepared by the method of Reinecke et al. Indolyl lithium was prepared by the addition of a THF (10 mL) solution of lithium diisopropylamide (0.825 mmol) to a solution of indole (96.5 mg, 0.825 mmol) in THF (5 mL) at −78 °C. This was allowed to warm to 0 °C, HMPA (2 mL) was added to aid solubility, and the mixture was cooled again to −78 °C. Indolyl potassium was prepared by the addition of indole (96.5 mg, 0.825 mmol) to a stirred suspension of KH (33 mg, 0.825 mmol) in THF (5 mL).

General Procedure for the Reaction of Olefins with Indolyl Anions. All reactions were carried out under an argon atmosphere. The bis(chloropalladium)–olefin complexes were prepared by the method previously described.[13] Bis(acetonitrile)palladium(II) chloride (0.13 g, 0.5 mmol) was dissolved in THF (20 mL) and the olefin (1–3 mmol) added. Addition of HMPA (1 mL) followed by cooling to −78 °C and addition of triethylamine (0.139 mL, 1.0 mmol) led to the required intermediate for these reactions.

The indolyl anion in THF (10 mL) and HMPA (2 mL) at −78 °C was added dropwise via a precooled (dry ice) syringe to the solution of the palladium–olefin complex at −60 °C. The reaction was stirred at −55 °C for 45 min. The argon atmosphere was replaced by a hydrogen atmosphere (balloon), and the reaction was allowed to warm slowly to room temperature overnight.

The resultant solution was filtered to remove the precipitated palladium and the solvent removed under reduced pressure. The residue was dissolved in ether (50 mL) and washed with water (3 × 50 mL). The organic phase was dried over magnesium sulfate. The reaction products were separated by preparative layer chromatography.

Reaction of Indolyllithium. (a) With Ethylene and H_2. The reaction was run as above on a 0.5-mmol scale. Purification by preparative layer chromatography (silica gel, 4:1 cyclohexane–ethyl acetate, R_f 0.49) gave 45 mg (62%) of *N*-ethylindole. The spectra and physical properties were identical with those previously reported.[11]

The reactions of the sodium, potassium, and magnesium bromide salts of indole were carried out in an identical fashion.

(b) With Ethylene and β Elimination. The reaction was run as above, but instead of exposure of the mixture to hydrogen gas, it was allowed to stir at 25 °C for 12 h and at 45 °C for 4 h. Purification as above (R_f 0.54) gave 55 mg (77%) of *N*-vinylindole: mp 31 °C (lit.[24] mp 31.5–32 °C); NMR ($CDCl_3$) δ 4.72 (br d, J = 8 Hz, 1, cis $CH{=}CH_2$), 5.15 (br d, J = 16 Hz, 1, trans $CH{=}CH_2$), 6.48–7.60 (m, 7, Ar H, $CH{=}CH_2$).

(c) With Ethylene and CO/MeOH. The reaction was run as above, except that after 45 min at −50 °C, dry methanol (2 mL) was added, the argon atmosphere was replaced by carbon monoxide, and the reaction was allowed to warm slowly to room temperature. After 14 h at 25 °C, the product was purified by preparative layer chromatography (silica gel; 5:4:1 $CHCl_3$/hexane/ethyl acetate, R_f 0.54) and gave 78.6 mg (40% yield by NMR) of the ester, contaminated with small amounts of indole: NMR ($CDCl_3$) δ 2.55 (t, J = 7 Hz, 2, CH_2CO), 3.50 (s, 3, OCH_3), 4.20 (t, J = 7 Hz, 2, NCH_2), 6.33–7.60 (6, Ar H and indole H's); IR (film) 1750 (C=O) cm^{-1}. Indole was removed by saponification of the ester by refluxing the mixture in ethanol (2 mL) containing KOH (180 mg) for 4 h, and then distilling half of the ethanol. The residue was diluted with 5 mL of H_2O, acidified with 2 N HCl, and extracted with ether (3 × 10 mL). The ether extracts were treated with 10 mL of 1 N NaOH, and the alkaline layer was separated, acidified with 2 N HCl, and extracted with ether (3 × 10 mL). Drying over Na_2SO_4 followed by removal of solvent left 40 mg (36%) of pure 1-indolepropionic acid: mp 88–89 °C (lit.[25] mp 89–90 °C); NMR ($CDCl_3$) δ 2.80 (t, J = 7 Hz, 2, CH_2CO_2), 4.38 (t, J = 7 Hz, 2, NCH_2), 6.45 (d, J = 3 Hz, 1, indole 3-H), 7.03–7.70 (m, 5, Ar H), 9.5 (br s, 1, COOH).

(d) With Propene. The reaction was run in the usual fashion. A mixture of the isomeric *N*-propylindoles[11] (29:71 *n*-propyl vs. isopropyl by NMR) was obtained in 95% yield (75.6 mg) by preparative layer chromatography (silica gel; 4:1 cyclohexane–ethyl acetate, R_f 0.53).

(e) With 1-Hexene. The reaction was run in the usual fashion. Isolation by preparative layer chromatography (silica gel; 4:1 cyclohexane/ethyl acetate, R_f 0.63) gave 0.086 g (91%) of *N*-hexylindoles as a 66:25 (by NMR) mixture of normal[11] and secondary hexylindoles. These were separated by GLC (10-ft 5% SE-30, 170 °C, t_R 8.1 and 5.3 min) and were identical to material synthesized by an alternate route.[11]

Reaction of Tetrabutylammonium Indole with Ethylene. Tetrabutylammonium indole was prepared by the addition of *N*-(trimethylsilyl)indole (160 mg, 0.825 mmol) to a THF (7 mL) solution of tetrabutylammonium fluoride (0.520 g, 1.65 mmol) at 0 °C. This was warmed to room temperature and HMPA (2 mL) added. After the mixture was cooled to −60 °C, the indole anion was added to a solution of the palladium–ethylene complex (0.5 mmol) at −60 °C in the usual manner. After the usual reaction and isolation procedures, only a trace of product could be detected in the crude reaction mixture (106.0 mg).

Alternatively, the palladium–olefin complex (0.5 mmol) was formed in the usual manner and *N*-(trimethylsilyl)indole (160 mg, 0.825 mmol) added. To this solution at −70 °C was added tetrabutylammonium fluoride (0.520 g, 1.65 mmol). The reaction was warmed slowly (90 min) to −30 °C, when the argon atmosphere was replaced by hydrogen. After the usual isolation procedure, the crude reaction mixture (72.3 mg) was shown to be indole by NMR spectroscopy.

Preparation of 1-Skatolepropionic Acid. This reaction was run exactly as in part c by using skatole in place of indole. After saponification and purification 49 mg (91%) of the acid was obtained: mp 81 °C (lit.[26] 84–85 °C); NMR ($CDCl_3$) δ 2.28 (s, 3, indole 3-Me), 2.80 (t, J = 7 Hz, 2, CH_2COOH), 4.33 (t, J = 7 Hz, 2, CH_2N), 6.83–7.73 (m, 5, Ar H), 8.7 (br s, 1, COOH).

Preparation of 2-Allylskatole. Skatole (6 g, 45.8 mmol) was dissolved in THF (20 mL). A solution of mercury(II) acetate (16 g, 47 mmol) dissolved in water (60 mL) was then added. This was stirred for 4 h, and the solid 2-[acetoxymercury(II)]skatole was separated by filtration. This solid was then stirred in saturated sodium chloride solution (180 mL) overnight and then heated at 50 °C for 4 h. The 2-[chloromercury(II)]skatole was then separated by filtration and washed with a trace of ethanol to dry it. This yielded 15.1 g (90% from skatole).

2-[Chloromercury(II)]skatole (15 g, 41.0 mmol) was dissolved in THF (350 mL), and the following reactants were added in the following order: lithium chloride (1.89 g, 41.0 mmol), allyl chloride (16.7 mL, 15.7 g, 205 mmol), benzoquinone (4.43 g, 41.0 mmol), bis(benzonitrile)palladium(II) chloride (1.05 g, 4.1 mmol). The mixture was stirred, under argon, for 2 days. The mixture was then washed with saturated sodium chloride (3 × 300 mL). The THF layer was dried over magnesium sulfate and reduced in volume. 2-Allylskatole (0.80 g, 11% from skatole) was obtained from medium-pressure liquid chromatography (silica gel, 3:1 hexane/ether): NMR (CCl_4) δ 2.12 (s, 3, indole 3-CH_3), 3.07 (d, J = 6 Hz, 2, $ArCH_2$), 4.87 (m, 2, $C{=}CH_2$), 5.68 (m, 1, CH=C), 6.67–7.53 (m, 5, Ar H, NH); IR (film) 3420 (NH), 3080 (C=C), 1650 (C=C) cm^{-1}. Anal. $C_{12}H_{13}N$ (C, H, N).

Attempted Ring Closures of 2-Allylskatole. 2-Allylskatole (60 mg, 0.35 mmol) was added to a stirred THF (20 mL) solution of $PdCl_2$·2MeCN (90.6 mg, 0.35 mmol) under argon. The solution was stirred for 10 min, HMPA (1 mL) was added, the mixture was cooled to −78 °C, and triethylamine (0.139 mL) was added. Lithium diisopropylamide (0.35 mmol) was then added dropwise and the solution stirred for 40 min, with the temperature rising to −50 °C. Replacement of the argon atmsophere with hydrogen, followed by the usual workup procedure, gave 2-propylskatole (53.8 mg, 89%) after medium-pressure liquid chromatography (silica gel, 3:1 hexane/ether).

Attempts to close 2-allylskatole by the same procedure as above but by varying the isolation procedure (CO/MeOH, β elimination, and $NaBH_4$/MeOH) also failed.

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[1-(2-Propenyl)-π-allyl]nickel Bromide. This material was prepared by the procedure of Semmelhack[27] from nickel carbonyl (20 mL) and a mixture of 1-bromo-2,5-hexadiene and 3-bromo-1,5-hexadiene (8.0 g) in benzene at 65–70 °C for 1 h. The product was recrystallized from hexane at −78 °C to give 8.3 g (76%) of the desired complex as a red, crystalline, air-sensitive solid.

General Procedure for the Reaction of π-Allylnickel Bromide Complex 1 with Various Substrates. These reactions were carried out by using previously published procedures.[8]

2-(2,5-Hexadienyl)benzamide. The 2-bromobenzamide (3.25 g, 16.2 mmol) dissolved in 10 mL of DMF was treated with 4.2 g (9.5 mmol) of the nickel complex dissolved in 60 mL of DMF, and the mixture was stirred at room temperature for 7 days. The crude product was isolated by following the routine procedure and purified by medium-pressure liquid chromatography (4:1 ether/hexane) to obtain the pure product (2.0 g, 60%) as white crystalline solid: mp 98–100 °C; ^{1}H NMR ($CDCl_3$) δ 2.8 (m, 2, $=CCH_2C=$), 3.6 (m, 2, $ArCH_2$), 4.8–5.2 (m, 2, $=CH_2$), 5.4–6.1 (m, 3, CH=C), 6.5 (br, 2, NH_2), 7.1–7.7 (m, 4, C_6H_4); IR (KBr) 3375 and 3190 (primary amide), 1650, 1620, 1595, 1575, 1490, 1395, 1285, 1135, 970, 910, 770, 750, 680 cm^{-1}. Anal. $C_{13}H_{15}NO$ (C, H, N).

2-(2,5-Hexadienyl)aniline (5). The nickel complex (430 mg, 1.0 mmol) in 15 mL of DMF was treated with 250 mg (1.5 mmol) of 2-bromoaniline dissolved in 2 mL of DMF. The reaction mixture was stirred at room temperature for 5 days. After a standard isolation, the crude brown oil was purified by preparative layer chromatography on silica gel developed with chloroform (R_f 0.54) to give a pale yellow liquid (0.13 g, 51%). Further purification can be done by Kugelrohr distillation at 105 °C (4 mmHg): ^{1}H NMR ($CDCl_3$) δ 2.75 (m, 2, $=CCH_2C=$), 3.15 (m, 2, $ArCH_2$), 3.45 (s, 2, NH_2), 4.75–5.2 (m, 2, $=CH_2$), 5.35–6.2 (m, 3, CH=C), 6.3–7.1 (m, 4, Ar H); IR (neat) 3470 (NH_2), 3390 (NH_2), 3100, 3040, 2900, 2840, 1630, 1590, 1500, 1460, 1435, 1320, 1280, 980, 915, and 750 cm^{-1}. Anal. $C_{12}H_{15}N$ (C, H, N).

1-(2-Nitrophenyl)-1,5-hexadiene. To a stirred suspension of (*o*-nitrobenzyl)triphenylphosphonium bromide[28] (32 g, 67 mmol) in 200 mL of dry benzene kept under an argon atmosphere was added via a syringe 29.1 mL of *n*-butyllithium (2 M solution in hexane). The resulting pink solution was stirred for 2 h, and 4-pentenal[29] (4.7 g, 56.8 mmol) was added via a syringe. The reaction mixture was warmed in an oil bath kept at 40 °C for 7 days. After the reaction mixture was quenched with water, it was extracted with ether several times. The ether extracts were combined, washed with dilute aqueous sodium sulfite solution followed by water, and dried over $MgSO_4$. The solvents were removed under vacuum, and the resulting reddish oil was distilled (Kugelrohr, 80–100 °C, 1 mmHg) to give the title product (47%) along with *o*-nitrotoluene (the hydrolyzed starting material). This crude product was used without purification in the next step.

2-(1,5-Hexadienyl)aniline (8). The crude nitro compound (1.0 g, 2.3 mmol) in a 250-mL, three-necked, round-bottomed flask equipped with a reflux condenser, glass stoppers, and magnetic stirring bar was dissolved in 30 mL of absolute ethanol and 30 mL of glacial acetic acid. The mixture was heated at reflux temperature, and iron dust (1.2 g, 21.5 mmol) was added. After 3.5 h of being stirred, the mixture was cooled to 40 °C, and sodium carbonate was added to make it basic. It was extracted with ether, and the combined ether extracts were dried over $MgSO_4$, filtered, and concentrated to a brown oil. The product was purified by medium-pressure liquid chromatography on silica gel (4:1 hexane/ether) to give a colorless oil: 30% yield; ^{1}H NMR (CCl_4) δ 2.0–2.43 (m, 4, CH_2), 3.5 (s, 2, NH_2), 4.75–5.23 (m, 2, $=CH_2$), 5.24–6.1 (m, 2, CH=), 6.2 (m, 1, α-CH), 6.2–7.2 (m, 4, Ar H); IR (neat) 3380 (NH_2), 3460 (NH_2), 3200, 3075, 3000, 2970, 2920, 2840, 1640, 1615, 1570, 1490, 1455, 1410, 1300, 1280, 1155, 1135, 1030, 990, 970, 910, 845, 750 cm^{-1}. Anal. $C_{12}H_{15}N$ (C, H, N).

1-(*o*-Nitrophenyl)-1,4-pentadiene. To 12 g (30 mmol) of (3-butenyl)triphenylphosphonium bromide (prepared from 4-bromobutene and triphenylphosphine) in a 500-mL, three-necked flask fitted with a stopcock and rubber septum and containing a magnetic stirring bar was added dry benzene (100 mL). The contents were degassed and saturated with argon. The *n*-butyllithium (13 mL, 2 M solution in hexane) was added followed by the addition of 25 mL of THF (cooled to −20 °C and argon saturated). The resulting red solution was stirred at room temperature for 2 h. The *o*-nitrobenzaldehyde (3.5 g, 23.0 mmol) dissolved in 5 mL of argon-saturated THF and cooled to 0 °C was added to the ylide. The contents were slowly warmed to room temperature and stirred for 3 days. After the mixture was quenched with water, the organics were extracted with ether. The ether extracts were washed successively with water and dilute aqueous sodium bisulfite solution, dried over $MgSO_4$, and concentrated to a red syrupy oil. Kugelrohr distillation (75–80 °C, 0.25 mmHg) gave the product as a pale yellow oil: 2.3 g (53%); ^{1}H NMR (CCl_4) δ 2.83 (t, 2, $=CCH_2C=$, J = 6 Hz), 4.83–5.3 (m, 2, $=CH_2$), 5.5–6.43 (m, 3, =CH), 6.8 (d, 1, α-CH=, J = 12 Hz), 7.23–8.1 (m, 4, Ar H); IR (neat) 3080, 3020, 3000, 2980, 2910, 2860, 1970, 1940, 1835, 1635, 1605, 1570, 1520, 1475, 1440, 1410, 1390, 1345, 1300, 1245, 1185, 1165, 1145, 1080, 1040, 995, 960, 910, 860, 810, 790, 760, 740, 705, 670 cm^{-1}. This material was used without further purification.

2-(1,4-Pentadienyl)aniline (10). The nitro compound (1 g, 5.3 mmol) was reduced with iron and glacial acetic acid in absolute ethanol by the procedure above to give the title product in quantitative yield. Purification by medium-pressure liquid chromatography (eluting with 2:1 hexane/ether) gave the pure product as a colorless oil: ^{1}H NMR (CCl_4) δ 2.9 (t, 2, $=CCH_2C=$, J = 6 Hz), 3.56 (s, 2, NH_2), 4.83–5.26 (m, 2, $=CH_2$), 5.5–6.15 (m, 3, =CH), 6.35 (d, 1, α-CH=, J = 12 Hz), 6.5–7.36 (m, 4, Ar H); IR (neat) 3460 (NH_2), 3375 (NH_2), 3200, 3075, 3000, 2975, 2920, 1895, 1820, 1635, 1615, 1570, 1490, 1455, 1430, 1410, 1395, 1300, 1275, 1240, 1205, 1155, 1135, 1055, 1030, 990, 910, 845, 750 cm^{-1}. Anal. $C_{11}H_{13}N$ (C, H, N).

2-(1,3-Butadienyl)aniline. The compound 1-(*o*-nitrophenyl)buta-1,3-diene[30] (5.0 g, 28.6 mmol) was reduced to the title compound with the iron/glacial acetic acid system in the manner described above and purified by medium-pressure liquid chromatography on silica gel (eluting with 1:1 ether/hexane) to obtain 2.5 g (60%) of the pure product as a slightly yellow oil: ^{1}H NMR (CCl_4) δ 3.6 (br, 2, NH_2), 5.0–5.45 (m, 2, $=CH_2$), 6.16–7.4 (m, 7, Ar H, =CH); IR (neat) 3440 (NH_2), 3370 (NH_2), 3215, 3080, 3030, 1800, 1635, 1615, 1570, 1490, 1455, 1305, 1270, 1255, 1155, 1005, 945, 895, 845, 745 cm^{-1}; mass spectrum, m/e 145 (M^+).

5-(*o*-Nitrophenyl)-1,3-pentadiene. To the phosphonium ylide,[31] prepared from allyltriphenylphosphonium bromide (2.8 g, 7.2 mmol) and *n*-butyllithium (2.64 mL, 7.2 mmol, a 2.75 M solution in hexane) by stirring in ether at room temperature for 6 h and cooling to −78 °C, was added via a needle stock an argon-saturated solution of (*o*-nitrophenyl)acetaldehyde[32] (1.2 g, 7.2 mmol) in ether (10 mL) cooled to −40 °C. The reaction flask was slowly warmed to room temperature and stirred overnight. The contents of the flask were filtered, and the residue was washed several times with ether. The combined ether solution was concentrated to obtain 1.2 g (87.3%) of a brown oil containing 71% of the title product and 29% triphenylphosphine oxide. Separation on a preparative layer chromatography (silica gel) using 1:2 ether/hexane as eluent gave the pure product (750 mg, 65%) as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 3.7 (d, 2, CH_2, J = 6 Hz), 5.3 (m, 2, $=CH_2$), 6.26 (m, 3, =CH), 7.53 (m, 4, Ar H); IR (neat) 3060, 3020, 3000, 2950, 2910, 2840, 1600, 1570, 1515, 1470, 1425, 1340, 1180, 1155, 1065, 1000, 945, 900, 850, 780, 735, 720, 695 cm^{-1}.

2-(2,4-Pentadienyl)aniline (13). The above nitro compound (1.53 g, 8.1 mmol) was reduced with iron/glacial acetic acid in absolute ethanol as previously described to give 13 in 75% yield (1.0 g) after purification by medium-pressure liquid chromatography with elution with a mixture of 2:1 hexane/ether on silica gel: ^{1}H NMR ($CDCl_3$) δ 3.25 (d, 2, CH_2, J = 5 Hz), 3.55 (br, 2, NH_2), 5.16 (m, 2, $=CH_2$), 6.03 (m, 3, =CH), 6.8 (m, 4, Ar H); IR (neat) 3440 (NH_2), 3360 (NH_2), 3070, 3010, 2880, 1880, 1615, 1580, 1490, 1450, 1425, 1310, 1270, 1150, 1000, 950, 900, 750 cm^{-1}; mass spectrum, m/e 159 (M^+, parent ion).

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Cyclization Reactions Using $PdCl_2$·(MeCN)$_2$. 3-*n*-Butyl-3,4-dihydrocarbostyril. To a solution of 2-(2,5-hexadienyl)benzamide (100 mg, 0.5 mmol) in THF (40 mL) was added Pd(II) (130 mg, 0.5 mmol), and the mixture was stirred at room temperature for 24 h. To the yellowish orange suspension of the complex in THF was added triethylamine (0.14 mL, 1.0 mmol). After the mixture was stirred at room temperature for 2 h, NaH (0.012 g, 0.5 mmol) was added and the mixture stirred for an additional 32 h. A hydrogen-filled balloon was opened to the reaction flask and the stirring continued for 14 h. Palladium(0) that precipitated was filtered off and the filtrate evaporated to give a slightly yellow oil which was purified by preparative layer chromatography on silica gel with development with 2:1 triethylamine/hexane mixture (R_f 0.58) to yield 66 mg (66%) of a white solid: NMR ($CDCl_3$) δ 0.7–2.05 (m, 9, C_4H_9), 2.34–3.2 (m, 2, $ArCH_2$), 3.4–3.9 (m, 1, C_3 H), 6.76–7.0 (br, 1, NH), 7.05–7.0 (m, 3, C_5, C_6, and C_7 H), 7.95–8.2 (m, C_8 H); IR ($CHCl_3$ evaporated film) 3200 (NH, lactam), 3100, 2940, 2880, 1670 (C=O), 1620, 1590, 1475, 1410, 1350, 1160, 1040, 750 cm^{-1}. Anal. $C_{13}H_{17}NO$ (C, H, N).

2-Propyl-1,2,3,4-tetrahydroquinoline (6). To 100 mg (0.58 mmol) of 2-(2,5-hexadienyl)aniline dissolved in 40 mL of THF was added 150 mg (0.58 mmol) of $PdCl_2$·(MeCN)$_2$, and the mixture was stirred for 4 h at room temperature. To the resulting yellowish orange suspension of the complex in THF was added 1 equiv of triethylamine (0.08 mL). The additions of second and third equivalents of triethylamine followed at 2-h intervals. After 4 h of additional stirring, a hydrogen-filled balloon was attached, and the contents of the flask were stirred for 15 h. The precipitated Pd(0) was filtered and the filtrate concentrated to give a yellow oil. The product was separated and purified by preparative layer chromatography on silica gel developed with chloroform containing 0.75% ethanol (R_f 0.47) to give 24.0 mg (24%) of a slightly yellow oil: ^{1}H NMR ($CDCl_3$) δ 0.8–1.6 (m, 7, C_3H_7), 1.70–2.2 (m, 2, C_3 H), 2.5–2.96 (m, 2, C_4 H), 3.0–3.4 (m, 1, C_2 H), 3.58 (s, 1, NH), 6.35–7.25 (m, 4, Ar H); IR (neat) 3400 (NH), 3060, 3330, 2960, 2920, 2860, 1610, 1590, 1500, 1470, 1380, 1360, 1310, 1280, 1260, 1210, 1180, 1150, 1125, 740 cm^{-1}. Anal. $C_{12}H_{17}N$ (C, H, N).

2-Propylquinoline (7). 2-(2,5-Hexadienyl)aniline (128 mg, 0.74 mmol), $PdCl_2$·(MeCN)$_2$ (20 mg, 0.074 mmol), cupric chloride (200 mg, 1.48 mmol), and lithium chloride (315 mg, 7.43 mmol) were placed in a Teflon-capped combustion tube along with 40 mL of THF and heated in an oil bath at 125 °C. After 21 h, the reaction mixture was cooled to room temperature, treated with 10 mL of water, extracted with ether, washed with saturated sodium chloride solution, dried over $MgSO_4$, and concentrated to give a brown oil. Distillation at 110 °C (4 mmHg), followed by purification by preparative layer chromatography on silica gel developed with a mixture of hexane, ether, and Et_3N (1:1:0.05, respectively, R_f 0.55), gave a slightly yellow oil: 30 mg (24%); mp (picrate) 162.5–163.5 °C (lit.[33] mp 163–164 °C).

2-Butylindole (9). A Telfon-capped combustion tube containing a magnetic stir bar was charged with 151.0 mg (0.87 mmol) of 2-(1,5-hexadienyl)aniline, $PdCl_2$·(MeCN)$_2$ (46.0 mg, 0.17 mmol), benzoquinone (950 mg, 0.87 mmol), and lithium chloride (360 mg, 8.7 mmol). Dry DME (10 mL) was added, and the combustion tube was heated at 105 °C in an oil bath for 68 h. The contents were cooled to room temperature, and water and ether were added. The organic layer was separated, washed with brine, dried over $MgSO_4$, and evaporated to dryness. The resulting solid residue was purified by medium-pressure liquid chromatography with silica gel eluted with 1:1 ethyl acetate/hexane to obtain a tan solid: 61 mg (40%); mp 35–36 °C (lit.[34] mp 36–37 °C); ^{1}H NMR ($CDCl_3$) δ 0.56–2.42 (m, 9, *n*-Bu), 6.2 (s, 1, indole 3-H), 6.9–8.15 (m, 5, Ar H and NH); mass spectrum, *m/e* 173 (M^+); IR ($CDCl_3$) 3470 (NH), 3060, 2960, 2930, 2870, 1605, 1550, 1515, 1455, 1415, 1335, 1325, 1285, 1240, 1150, 1040, 1010, 950 cm^{-1}.

2-Methylbenzazepine (11). The substrate **10** (92 mg, 0.85 mmol) was dissolved in 10 mL of DME. After $PdCl_2$·(MeCN)$_2$ (150 mg, 0.58 mmol) was added, the contents were heated under argon atmosphere in an oil bath kept at 70 °C for 0.75 h. The mixture was then cooled to −30 °C, and 2 equiv of Et_3N was added. The flask was warmed to room temperature and 2 equiv of anhydrous K_2CO_3 was added. After being heated at 70 °C for 16 h, the reaction flask was cooled to room temperature, a hydrogen-filled balloon was opened to the reaction flask, and the mixture was stirred overnight. The contents were diluted with ether, filtered, dried over $MgSO_4$, and concentrated. The crude oil was purified by medium-pressure liquid chromatography on silica gel (1:1:2, EtOAc/CH_2Cl_2/hexane) to obtain 32 mg (34.7%) of a slightly yellow solid: ^{1}H NMR (CCl_4) δ 1.2 (d, 3, CH_3, J = 6 Hz), 1.4–2.0 (m, 4, CH_2), 2.2 (m, 2, $ArCH_2$), 2.2–3.1 (m, 1, =NCH=), 3.25 (s, 1, NH), 6.4–7.0 (m, 4, Ar H); IR (CCl_4) 3360 (NH), 3060, 3020, 2960, 2920, 2852, 1970, 1920, 1885, 1850, 1600, 1585, 1545, 1500, 1475, 1450, 1430, 1375, 1360, 1345, 1305, 1270, 1250, 1155, 1110, 1075, 1053, 1005, 983, 940, 925, 865 cm^{-1}. Anal. $C_{11}H_{15}N$ (C, H, N).

2-[(Carbomethoxy)methyl]-2,3-dihydrobenzazepine (12). The substrate **10** (80 mg, 0.5 mmol) was dissolved in 10 mL of THF, and $PdCl_2$·(MeCN)$_2$ (130 mg, 0.5 mmol) was added to it. After the mixture was stirred at room temperature for 3.5 h, it was cooled to −75 °C, and Et_3N (0.14 mL, 1.0 mmol) was added slowly. It was warmed to −35 °C, and absolute methanol was added immediately followed by opening a CO-filled balloon to the mixture. It was kept at −35 °C for 0.5 h, warmed to room temperature, and stirred overnight. Palladium(0) that precipitated was filtered and washed with ether. The ether solution was washed with water and brine, dried over $MgSO_4$, and evaporated to yield a yellow oil. Separation by medium-pressure liquid chromatography on silica gel eluted with 1:2 ether/hexane yielded 35 mg (34%) of a slightly yellow oil: ^{1}H NMR (CCl_4) δ 2.45 (m, 4, CH_2), 3.66 (s, 3, OCH_3), 3.75 (m, 1, CH), 4.4–4.6 (s, 1, NH), 5.65 (dt, 1, β-CH=, J = 12, 4 Hz), 6.1–7.3 (m, 5, Ar H and β-CH=); IR (neat) 3390 (NH), 3030, 2960, 2910, 1703 (C=O), 1640, 1605, 1580, 1455, 1360, 1325, 1285, 1215, 1165, 1105, 1045, 1010, 970, 935, 845, 695 cm^{-1}. Anal. $C_{13}H_{15}NO_2$ (C, H, N).

2-Propyl-2,3-dihydroindole (15). The substrate **13** (90 mg, 0.57 mmol) and $PdCl_2$·(CH$_3$CN)$_2$ (146.8 mg, 0.57 mmol) were stirred in 15 mL of THF for 4.5 h. A hydrogen-filled balloon was opened to the reaction flask and stirred overnight. Palladium(0) was filtered and the filtrate evaporated to dryness. The resulting solid was taken up in ether and stirred with K_2CO_3 solution. The ether layer was separated, washed with water and brine, dried over $MgSO_4$, and concentrated. The crude product obtained was purified by medium-pressure LC on silica gel (5:1 hexane/ether) to obtain the pure product: 51.6 mg (57%); ^{1}H NMR ($CDCl_3$) δ 0.95 (m, 3, CH_3), 1.4 (m, 4, CH_2), 2.8 (m, 3, =NCH and $ArCH_2$), 3.7 (br, 1, =NH), 7.85 (m, 4, Ar H); IR (neat) 3360 (NH), 3040, 3020, 2940, 2920, 2860, 1605, 1480, 1460, 1400, 1370, 1315, 1260, 1150, 1110, 1090, 1020, 820, 740 cm^{-1}. Anal. $C_{11}H_{15}N$ (C, H, N).

2-(1-Propenyl)indole (16). The substrate **13** (85.3 mg, 0.54 mmol) was dissolved in CH_3CN (10 mL), and $PdCl_2$·(CH$_3$CN)$_2$ (139 mg, 0.52 mmol) was added to the mixture. After this was stirred for 4 h at room temperature, HMPA (1.5 mL) was added. This mixture was added to a refluxing solution of Et_3N (0.59 mL, 4.3 mmol) in CH_3CN (10 mL). After being stirred at reflux temperature for 3.5 h, this mixture was cooled, and the Pd(0) was filtered. The residue was washed with CH_2Cl_2. The CH_2Cl_2 solution was evaporated to dryness, and the resulting oil was redissolved in hexane, washed with water, and dried over $MgSO_4$, and the solvent was removed to give a reddish brown oil. Separation by medium-pressure LC on silica gel (4:1 hexane/ether) gave 43 mg (51%) of a slightly yellow solid: ^{1}H NMR ($CDCl_3$) δ 1.83 (d, 3, CH_3, J = 6 Hz), 5.5–7.8 (series of multiplets, 8, =CH, NH, and Ar H); IR ($CHCl_3$) 3460 (NH), 3050, 3020, 2950, 2920, 2900, 2840, 2200, 1530, 1450, 1410, 1335, 1290, 1230, 1145, 1125, 1010, 950, 800, 770 cm^{-1}.

π-Allyl Complex 14. 2-(2,4-Pentadienyl)aniline (50 mg, 0.31 mmol) and $PdCl_2$·(MeCN)$_2$ (81.5 mg, 0.31 mmol) were stirred in THF at room temperature for 4 h. The solvent was evaporated and the residue washed with dry ether to obtain the title complex as a yellow solid: 100 mg (94.5%); ^{1}H NMR (Me_2SO-d_6) δ 2.9–4.05 (m, 5, C_3 H, C_2 H, π-allyl C_3 H), 4.45 (q, 1, π-allyl C_1 H), 5.65 (q, 1, π-allyl C_2 H), 6.73 (br, 2, $^+NH_2$), 7.33 (s, 4, Ar H).

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Registry No. 1 (R = H), 10604-59-8; 1 (R = M), 16885-94-2; 1 (R = Bu), 42951-62-2; 2 (R = Me), 16885-99-7; 2 (R = Bu), 76916-48-8; 3, 1557-08-0; 4, 76916-49-9; 4 free acid, 6639-06-1; 5, 76916-50-2; 6, 76916-51-3; 7, 1613-32-7; 8, 76916-52-4; 9, 13228-37-0; 10, 76916-53-5; 11, 76916-54-6; 12, 76916-55-7; 13, 76916-56-8; 14, 76927-69-0; 15, 76916-57-9; 16, 76916-58-0; indolyllithium, 18344-49-5; indolylsodium, 16982-67-5; indolylmagnesium bromide, 20356-50-7; indolylpotassium, 31163-74-3; bis(acetonitrile)palladium(II) chloride, 14592-56-4; ethylene, 74-85-1; propene, 115-07-1; 1-hexene, 592-41-6; tetrabutylammonium indole, 76916-59-1; *N*-(trimethylsilyl)indole, 17983-42-5; skatole, 83-34-1; 1-skatolepropionic acid, 57662-47-2; 2-allylskatole, 76916-60-4; 2-[acetoxymercury(II)]skatole, 76916-61-5; 2-[chloromercury(II)]skatole, 76916-62-6; allyl chloride, 107-05-1; 2-propylskatole, 1859-90-1; [1-(2-propenyl)-π-allyl]nickel bromide, 12012-90-7; 2-(2,5-hexadienyl)benzamide, 76916-63-7; 2-bromobenzamide, 4001-73-4; 2-bromoaniline, 615-36-1; 1-(2-nitrophenyl)-1,5-hexadiene, 76916-64-8; (*o*-nitrobenzyl)triphenylphosphonium bromide, 23308-83-0; 4-pentenal, 2100-17-6; 1-(2-nitrophenyl)-1,4-pentadiene, 76916-65-9; (3-butenyl)triphenylphosphonium bromide, 16958-42-2; *o*-nitrobenzaldehyde, 552-89-6; 1-(2-nitrophenyl)buta-1,3-diene, 76916-66-0; 2-(1,3-butadienyl)aniline, 76916-67-1; 5-(2-nitrophenyl)-1,3-pentadiene, 76916-68-2; allyltriphenylphosphonium bromide, 1560-54-9; (*o*-nitrophenyl)acetaldehyde, 1969-73-9; 3-butyl-3,4-dihydrocarbostyril, 76916-69-3.

Bromination and Chlorination of Pyrrole and Some Reactive 1-Substituted Pyrroles[1]

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Monobromination of pyrrole and 1-methyl-, 1-benzyl-, and 1-phenylpyrrole with 1 mol of *N*-bromosuccinimide in tetrahydrofuran results in the regiospecific formation of the 2-bromopyrroles. A little disubstitution is observed. Similarly, brominations with 2, 3, or 4 mol of NBS form primarily the di-, tri-, and tetrabromopyrroles, respectively. The thermodynamically more stable 3-bromopyrroles are the major monobrominated products observed when bromine is used as the brominating agent due to isomerization of the 2-bromopyrroles with hydrogen bromide. These reaction mixtures are further complicated because of disproportionation reactions. Chlorination with *N*-chlorosuccinimide gave results similar to those for the bromination with NBS, but the reaction is not as selective.

The exhaustive bromination or chlorination of pyrrole (1) with bromine or chlorine leads to the corresponding tetrahalopyrroles which are stable.[2] There are no reports of the formation of partially brominated or chlorinated pyrroles by electrophilic halogenation of pyrrole by bromine or chlorine. Other substitution procedures result in the formation of mixtures of partially halogenated pyrroles.[3-6]

Electrophilic bromination of 1-substituted pyrroles, of similar reactivity as 1, such as 1-methylpyrrole (2) and 1-benzylpyrrole (3) with 1 mol of bromine in CCl_4 gives complex reaction mixtures which contain starting material, 2-bromo-, 3-bromo-, di-, tri-, and tetrabromopyrroles.[5,7] Most electrophilic substitutions of pyrrole and its 1-substituted derivatives occur exclusively at the 2-position;[2] however, nitration of 1, 2,[8,9] 3,[1] and 1-phenylpyrrole (4)[10] and nitrosation of 4,[10] also give considerable amounts of 3-substituted pyrroles. Acid-catalyzed proton exchange also occurs at the 2- and 3-positions of pyrrole.[2] Large substituents at the 1-position of pyrrole will cause more substitution to occur at the 3-position.[11,12]

The bromination and chlorination of 1-4 were investigated in order (1) to get a better understanding of why such complex reaction mixtures are obtained when 2, 3, or 4 is brominated in CCl_4, (2) to find out why the increased amount of 3-substitution sometimes occurs, (3) to find conditions under which selectively halogenated pyrroles might be formed, and (4) to determine the regiospecific nature of these halogenations.

Bromination of 2-4 with 1 mol of bromine in CCl_4 was reinvestigated by using procedures similar to those in the literature.[5,7] The results given in Table I are typical percentages because the ratio of products is dependent on experimental conditions such as the rate of addition of bromine, the length of time the reaction mixture is stirred after the addition of bromine is complete, the rate of stirring, etc. Only representative values are reported.

From a combination of GC and mass and ^1H NMR spectrometric techniques it was determined that, under these acidic conditions, some starting material always remains, and varying amounts of 2- and 3-substitution occur. Two dibromopyrroles were observed in the bromination of 2 and 4, and three dibromopyrroles were observed in

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