

## Summary

The reactions of  $O_2^-$  as well as other species can be readily investigated by the use of rare gas filled vacuum-UV lamps in combination with a stopped-flow spectrophotometer or ESR spectrometer. The best lamp design is that shown in Figure 1. A lamp of this type filled with 7.5 Torr Xe produces only moderate yields of  $O_2^-$  but is advantageous because almost no peroxide is formed at short photolysis times. The medium-pressure (30–200 Torr) Xe lamp is recommended where large yields of  $O_2^-$  are desired. The argon-filled lamps are more intense when first prepared but may change with time since the output depends upon impurity lines.

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# Palladium-Assisted Intramolecular Amination of Olefins. Synthesis of Nitrogen Heterocycles

Louis S. Hegedus,\* Gary F. Allen, Joseph J. Bozell, and Edward L. Waterman

Contribution from the Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523. Received March 2, 1978

**Abstract:** 2-Bromoanilines were converted to 2-allylanilines by treatment with  $\pi$ -allylnickel halide complexes. These were cyclized to 2-methylindoles or to quinolines by treatment with palladium chloride under both stoichiometric and catalytic conditions. 2-Aminostyrene was converted to indole. The cyclization is thought to proceed by a palladium-assisted nucleophilic attack on the olefin of the allyl group.

## Introduction

In recent years, organometallic reagents have been used in the synthesis of a variety of heterocyclic ring system. Indoles, benzofurans, and phthalides were prepared from *o*-iodoanilines, *o*-halophenols, or *o*-halocarboxylic acids, respectively, by treatment with copper acetylides.<sup>1</sup> Intramolecular oxymercuration of 2-allylcyclohexanols led to both cyclohexane fused pyrans and furans after reduction.<sup>2</sup> The cyclization of  $\gamma,\delta$ -unsaturated alcohols was also studied.<sup>3</sup> A similar oxymercuration was used to convert 2'-hydroxychalcones to aurones using mercury(II) acetate in  $Me_2SO$ .<sup>4</sup> The same procedure converted *o*-allylphenols to 2-methyl-2,3-dihydrofurans.<sup>5</sup> Ring closure by mercury was also used to form the heteroyohimbane  $\epsilon$  ring.<sup>6</sup> Chromanocoumarans were synthesized by the reaction of 2-*H*-chromenes with *o*-chloromercuriphenols.<sup>7</sup>

Indoles were prepared from 2-chloro-*N*-methyl-*N*-allylaniline,<sup>8</sup> and oxindoles from 2-chloro-*N*-alkyl-*N*-acrylanilide<sup>9</sup> by treatment with tetrakis(triphenylphosphine)nickel. Indoles and isoquinolines were prepared from similar substrates using a palladium catalyst<sup>10</sup> (Heck arylation conditions<sup>11</sup>). Acrylic acid diallylamides were cyclized to a mixture of pyrrolidones and *N*-acetylpyrroles by treatment with  $PdCl_2$  or  $RhCl_3$ .<sup>12</sup>  $\pi$ -Allylpalladium complexes were intermediates in the palladium-catalyzed cyclization of amino olefins to alkaloid ring systems such as ibogamine, mesembrine, and actinobolamine.<sup>13</sup> Divinylpiperadines were synthesized by the Pd(II)-catalyzed reaction of butadiene with imines,<sup>14</sup> while imidazolones, dihydroxyoxadiazinones, and tetrahydrotriazinones were synthesized by the  $PdCl_2$ -catalyzed reactions of isonitriles with  $\alpha$ -amino acid esters,  $\alpha$ -hydroxy acid hydrazides, and  $\alpha$ -amino acid hydrazides.<sup>15</sup>

**Table I.** Reaction of  $\pi$ -Allylnickel Bromide Complexes with 2-Bromoanilines<sup>a</sup>

substrate	nickel complex	time, days	temp, °C	product	yield, % <sup>b</sup>
2-bromoaniline	$\pi$ -allylnickel bromide	2	50	2-(2-propenyl) aniline ( <b>1</b> )	62 (75)
2-bromo-4-methylaniline	$\pi$ -allylnickel bromide	2	25	2-(2-propenyl)-4-methylaniline ( <b>2</b> )	75 (99)
2-bromo-4-carbomethoxyaniline	$\pi$ -allylnickel bromide	4	50	2-(2-propenyl)-4-carbomethoxyaniline ( <b>3</b> )	94
2-bromo-4-methoxyaniline	$\pi$ -allylnickel bromide	2	50	2-(2-propenyl)-4-methoxyaniline ( <b>4</b> )	92
2-bromo-5-methoxyaniline	$\pi$ -allylnickel bromide	3	50	2-(2-propenyl)-5-methoxyaniline ( <b>5</b> )	79 (99)
2-bromo-4,5-dimethoxyaniline	$\pi$ -allylnickel bromide	4	50	2-(2-propenyl)-4,5-dimethoxyaniline ( <b>6</b> )	69 (80)
2-bromoaniline	$\pi$ -2-methylallylnickel bromide	1	50	2-(2-methyl-2-propenyl)aniline ( <b>7</b> )	69
2-bromoaniline	$\pi$ -crotylnickel bromide	4	25	2-(2-butenyl)aniline ( <b>8</b> )	72 (92)
2-bromoaniline	$\pi$ -(1,1-dimethylallyl)nickel bromide	2	50	2-(3-methyl-2-butenyl)aniline ( <b>9</b> )	56 (82)
2-bromoaniline	$\pi$ -cyclohexenylnickel bromide	2	50	2-(2-cyclohexenyl)aniline ( <b>10</b> )	49 (84)
2-bromo- <i>N</i> -methylaniline	$\pi$ -allylnickel bromide	4	50	2-(2-propenyl)- <i>N</i> -methylaniline ( <b>11</b> )	95
2-bromoacetamide	$\pi$ -allylnickel bromide	4	50	2-(2-propenyl)acetamide ( <b>12</b> )	39 (50) <sup>c</sup>

<sup>a</sup> All reactions were run in DMF solution using 1–5 mol of nickel complex/mol substrate. <sup>b</sup> Yields are of isolated, purified products. Yields in parentheses are based on consumed substrate. <sup>c</sup> Much better yields (86%) are obtained by acetylating allylaniline.

Intramolecular nucleophilic attack on palladium complexed olefins has accounted for several heterocyclic syntheses. Thus,  $\alpha,\beta$ -unsaturated ketoximes were converted to isoxazoles,<sup>16</sup> 2'-hydroxychalcones to flavones,<sup>17</sup> penta-2,4-dienoic acids to 2-pyrones,<sup>18</sup> *o*-allylphenols to benzofurans,<sup>19</sup> unsaturated ketoximes to pyridines,<sup>20</sup>  $\gamma,\delta$ -unsaturated alcohols to 2-vinyltetrahydrofurans,<sup>21</sup> and *o*-allylbenzoic acids to isocoumarins<sup>22</sup> by treatment with palladium(II) salts. *endo*-Brevicomin was synthesized by palladium(II)-catalyzed cyclization of a terminal olefin with a suitably located vicinal diol.<sup>23</sup>

We<sup>24</sup> had previously reported the palladium-assisted intramolecular amination of olefins to produce indoles, quinolines, and isoquinolines. We now report the full experimental details of these studies, as well as those of the subsequently developed catalytic cyclizations of this type.

## Results and Discussion.

**Preparation of 2-Allylanilines.** Literature methods for the synthesis of 2-allylanilines are characterized by low yields and intolerance toward functional groups. The best method to date appears to be the acid-promoted rearrangement of *N*-allylanilines.<sup>25</sup> While adequate for the preparation of simple compounds such as 2-allyl- (53%) and 2-crotylaniline (40%), the rearrangement conditions (e.g., 2 N H<sub>2</sub>SO<sub>4</sub>, reflux 18 h) are too severe to tolerate many functional groups. The well-known reaction of  $\pi$ -allylnickel halides with aromatic halides to introduce an allyl group<sup>26</sup> offered a more general approach to a variety of 2-allylanilines (eq 1).

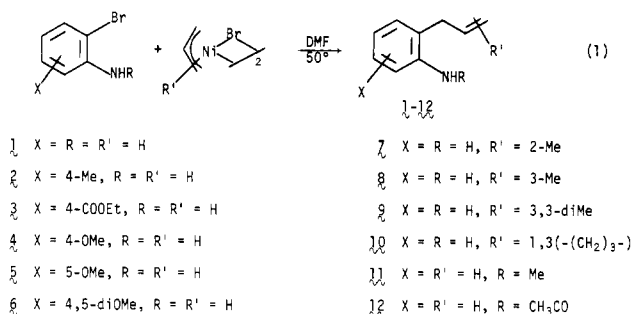
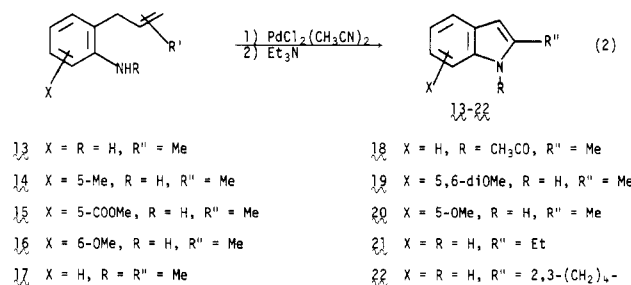


Table I summarizes our use of this approach. Several features of the reaction merit comment. Both commercial and synthetic 2-bromoanilines are frequently contaminated with small amounts of nitro aromatics. Since the reactions of  $\pi$ -allylnickel halides with aromatic halides are radical chain processes,<sup>27</sup> nitro aromatics completely inhibit the reactions, and care must be taken to free substrates of these impurities. Even with purified substrates the reaction is sluggish, and takes 2–4 days at 50 °C to go to completion. At higher temperatures thermolysis of the nickel complex is the major reaction. The

reactions of  $\pi$ -cyclohexenylnickel bromide and  $\pi$ -(1,1-dimethylallyl)nickel bromide with 2-bromoaniline were particularly sensitive, and on occasion gave very low yields and a great deal of reduction of bromoaniline to aniline for no apparent reason. Upon repeating, normal behavior was observed. This anomalous reduction has also been observed with 2-bromobenzoic acids,<sup>22</sup> and is under investigation in these laboratories. In addition the solvent DMF must be distilled from CaH<sub>2</sub> prior to use for best results. In spite of these difficulties, under the conditions of Table I a variety of both ring and side chain substituted 2-allylanilines were prepared in fair to excellent yield. The reaction also proceeded well with 2-bromo-*N*-methylaniline and 2-bromobenzylamine, while 2-bromoacetamide reacted only slowly and incompletely. For this substrate, much higher yields were obtained by acetylating 2-allylaniline. The ease of preparing a wide variety of  $\pi$ -allylnickel bromide complexes directly from the corresponding allylic bromide, and the tolerance of the reaction of these complexes with organic halides to the presence of a wide variety of functional groups both on the aromatic ring and the allylic chain, make this a versatile procedure for the synthesis of 2-allylanilines and benzylamines.

**Stoichiometric Cyclization.** Addition of the 2-allylanilines in Table I to a suspension of PdCl<sub>2</sub>(CH<sub>3</sub>CN)<sub>2</sub> in THF produced a homogeneous, coffee-brown solution, which began to deposit a yellow precipitate after 30–60 min. Treatment of either the solution or the suspension with triethylamine immediately produced a deep cherry red, homogeneous solution which deposited metallic palladium over the course of 2 h. Filtration followed by evaporation gave the crude indole, often as the sole organic product by NMR. Without addition of triethylamine, no indole formed. The results are summarized in Table II and eq 2.



With substrates having the simple allyl side chain, 2-methylindoles were obtained in excellent yield. The stoichiometric cyclization reaction tolerated methyl and carbomethoxy groups in the aniline 4 position (para to NH<sub>2</sub>), and methoxy in the 5 position, as well as the *N*-methyl group. (While the *N*-acetyl substrate cyclized only in low yields under these

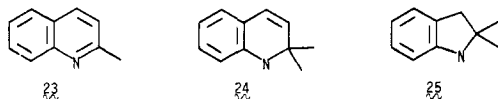
**Table II.** Cyclization of 2-Allylanilines

substrate	product	yield, % <sup>a</sup> stoichio- cata- metric <sup>b</sup> lytic <sup>c</sup>	
1	2-methylindole (13)	85	86
2	2,5-dimethylindole (14)	82	
3	2-methyl-5-carbomethoxyindole (15)	74	
5	2-methyl-6-methoxyindole (16)	82	
11	1,2-dimethylindole (17)	69	89
12	<i>N</i> -acetyl-2-methylindole (18)	27	71
6	2-methyl-5,6-dimethoxyindole (19)	46	48 <sup>d</sup>
4	2-methyl-5-methoxyindole (20)	17	32 <sup>d</sup>
8	2-ethylindole (21)	10 <sup>e</sup>	79 <sup>f</sup>
8	2-methylquinoline (23)	38	58 <sup>g</sup>
10	tetrahydrocarbazole (22)	46	<i>h</i>
9	2,2-dimethyl-1,2-dihydroquinoline (24)	52	54
7	2,2-dimethylindoline (25)	31	<i>h</i>
2-vinyl- aniline	indole	<i>i</i>	74

<sup>a</sup> Yields of isolated product, purified by recrystallization or chromatography. <sup>b</sup> Reactions run using 1 equiv of Pd/quiv substrate. <sup>c</sup> Reactions run using 1–10 mol % Pd(II) with either Cu<sup>2+</sup> or benzoquinone as reoxidant, in refluxing THF. <sup>d</sup> Reaction was run at 25 °C. <sup>e</sup> Reaction was run at 0 °C. <sup>f</sup> Reaction was run in the presence of added LiCl (10 equiv). <sup>g</sup> Varying amounts of the tetrahydroquinoline were also obtained. <sup>h</sup> Substrate was consumed producing a number of unidentified products. <sup>i</sup> Insoluble material which gave 2-ethyl-aniline upon reduction was obtained.

conditions, catalytic cyclization (vide infra) produced a much better yield of this material. Acetylation of 2-methylindole leads to a considerable amount of acylation in the 3 position.<sup>28</sup> Methoxy substitution in the 4 position of the allylaniline posed a special problem. Both the starting materials and the product indoles (19, 20) were rather unstable, and difficult to purify. Upon short exposure to air, purified materials rapidly darkened. Both recrystallization and layer chromatography led to extensive decomposition of the products, and the low yields of 19 and 20 are, at least in part, due to problems with purification rather than problems attributable to the cyclization process.

In all cases with the simple allyl side chain, cyclization produced only indoles from attack at the secondary carbon of the olefin. No quinolines, from attack at the terminal (primary) carbon of the olefin, were observed. For allylanilines containing alkyl groups on the double bond (7–10) several changes in the cyclization reaction were noted. Most noticeable was the considerably lower yields of cyclization products 21–25 ob-

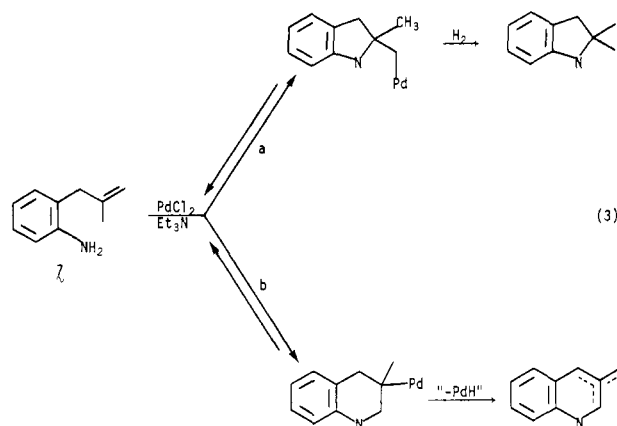


tained from these substrates. Several factors contribute to this lowering of yields. The stability of olefin–palladium(II) complexes decreases as substitution on the olefin increases.<sup>29</sup> Hence, with compounds 7–10 the olefin would be less firmly bound to palladium, and displacement of the olefin from palladium by added by triethylamine producing unreactive bisaminopalladium complexes would become competitive with the displacement of the aniline required for cyclization (see below). That this is a factor is shown by the following experiment. 2-(2-Cyclohexenyl)aniline (10) was treated with 1 equiv of palladium chloride followed by 2 equiv of triethylamine. Upon isolation, tetrahydrocarbazole (22) was obtained in 46% yield as the sole organic product, along with a mixture of Pd metal and a yellow, insoluble palladium complex. Exposure of this mixture of palladium species to hydrogen for several hours produced a 45% yield of reduced starting material, 2-cyclohexylaniline, giving a 91% material balance. This indi-

cates that the low yields obtained in these systems were not due to destruction of starting materials, but rather to loss of olefin activation capabilities by the palladium. An additional factor which may contribute to this problem is the slowing of the ring closure step owing to steric repulsions involved in attacking substituted olefins, thereby making olefin displacement a more competitive reaction.

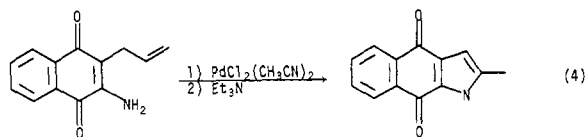
A second difference caused by substitution on the olefin is a change in ring size. While 2-(2-cyclohexenyl)aniline (10) closes to form tetrahydrocarbazole (22) (a five-membered ring) both 2-(2-butenyl)aniline (8) and 2-(3-methyl-2-butenyl)aniline (9) close to give quinolines 23 and 24, respectively. The quinoline is the expected product from 9, since attack (amination) usually occurs at the most substituted (in this case tertiary) terminus of the olefin.<sup>30</sup> With 8, the formation of the six-membered ring quinaldine rather than the five-membered ring indole must reflect ring size preference, since both closures would involve attack on a secondary carbon. Additionally, the initially formed dihydroquinoline undergoes further oxidation to the quinoline under the conditions of cyclization. It is likely that this dehydrogenation is effected by the palladium metal generated, although palladium chloride is also capable of this type of oxidation.<sup>31</sup> Interestingly, when this cyclization was run at 0 °C rather than 25 °C, no quinaldine was formed, while a low yield of 2-ethylindole was instead obtained. The remainder of the starting material appeared to be in the form of intractable palladium complexes.

Two substrates which failed to cyclize in appreciable yields under standard stoichiometric conditions were *o*-(2-methyl)aniline (7) and 2-vinylaniline. If closure to form a five-membered ring were to occur with 7,  $\beta$ -elimination is not possible (eq 3). The resulting complex could only revert to



starting material. If closure to a six-membered ring were to occur,  $\beta$ -elimination to form the 3-methyldihydroquinoline should result. When 7 was reacted under standard stoichiometric conditions, an intractable and uncharacterized mixture of Pd-containing organic materials was obtained. Exposure of this material to an atmosphere of H<sub>2</sub> produced 2,2-dimethylindoline (26) and 2-isopropylaniline in equal amounts. Hence, five-membered ring closure was strongly favored over six (or attack at a tertiary center over attack at a primary center) even though  $\beta$ -elimination was not possible for the favored path. When 2-vinylaniline was reacted under standard stoichiometric conditions, intractable material was again obtained. However, exposure of this mixture to hydrogen produced only 2-ethylaniline, and no indole. Hence, ring closure did not occur with this substrate. Since indole was formed from this substrate under catalytic conditions (vide infra), and since 2-vinylbenzoic acid cyclized to isocoumarin under similar conditions, this lack of cyclization is not due to intrinsic lack of reactivity of styryl systems. Finally, in relation to an ongoing synthetic problem, 2-(2-propenyl)-3-aminonaphthoquinone

was cyclized to the 2-methylindole under the standard stoichiometric conditions (eq 4) indicating the tolerance of the



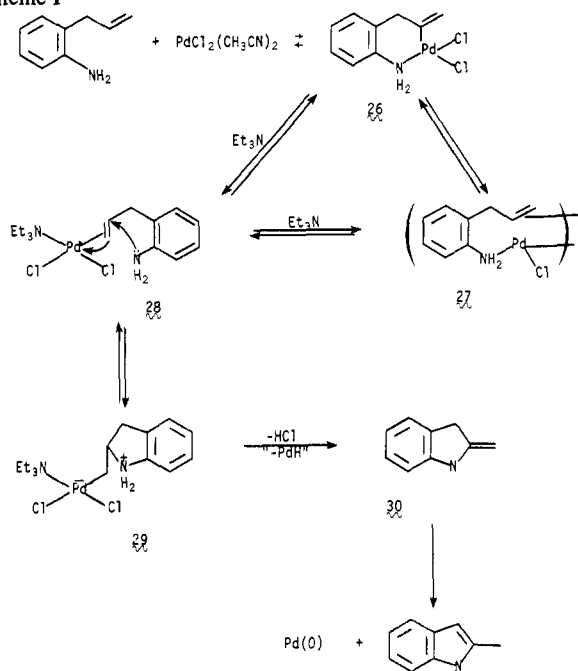
quinone functional group to the cyclization reaction conditions.

**Course of the Reaction.** The probable course of the stoichiometric cyclization reaction is outlined in Scheme I. The *o*-allylaniline reacts with  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  to produce **26**, in which both the amine and olefin groups are coordinated in chelating fashion.<sup>32</sup> With allylaniline itself, a heavy yellow precipitate, insoluble in common organic solvents, rapidly forms, while with 2-methallylaniline the solution remains homogeneous for at least 1 h. It is likely that monomeric complex **26** converts to polymeric complex **27**, with the allylamine group bridging two palladium centers. The infrared spectra of both **26** and **27** indicate that both the amine and olefin groups are coordinated. Thus the NH stretching bands shift from 3470 and 3380  $\text{cm}^{-1}$  in allylaniline to 3190 and 3140  $\text{cm}^{-1}$  in the complexes. The 1630- $\text{cm}^{-1}$  N-H bending band (which covers the C=C stretch of the olefin at 1630  $\text{cm}^{-1}$ ) of the free amine disappears upon complexation, while a weak band at 1520  $\text{cm}^{-1}$  attributed to coordinated olefin<sup>33</sup> appears. Similarly in the  $^1\text{H}$  NMR spectrum of free *o*-2-methallylaniline the signals due to the  $\text{CH}_2=\text{CH}(\text{CH}_3)\text{CH}_2$  group appear at  $\delta$  1.80 ( $\text{CH}_3\text{C}=\text{C}$ ), 3.20 ( $\text{CH}_2\text{C}=\text{C}$ ), and 4.80 ( $=\text{CH}_2$ ) and shift to  $\delta$  2.20, 3.80, and 5.20, respectively, upon coordination. In the  $^{13}\text{C}$  NMR spectrum the  $=\text{CH}_2$  carbon shifts from 110.7 ppm in the free ligand to 84.2 ppm upon coordination. Attempts to follow this reaction further by the use of NMR proved impossible. Addition of triethylamine to either the allyl- or methallylaniline complex produced a deep red, homogeneous solution. With the allylaniline complex (**27**), palladium metal immediately began to precipitate, making NMR measurements impossible. With the methallylaniline system, which cannot  $\beta$ -eliminate to produce palladium metal, addition of triethylamine produced an NMR spectrum consisting of a forest of unassignable peaks, indicating equilibration of many different intermediates.

In the absence of added triethylamine, complex **27** is very stable. Since the amino group is coordinated it cannot attack the olefin. Addition of triethylamine leads to displacement of the weakly basic aromatic amine generating **28**, in which the aromatic amine can achieve the trans stereochemistry required for amination of coordinated olefin.<sup>34</sup> Attack of the coordinated olefin by the aromatic amine results in the  $\sigma$ -alkylpalladium complex **29**, which upon loss of HCl and  $\beta$ -elimination of "Pd-H" gives **30**. This spontaneously rearranges to the indole. Evidence for the intermediacy of **29** was obtained by trapping it with carbon monoxide in methanol to produce an indoline acetic acid ester.<sup>35,36</sup>

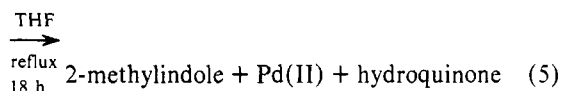
**Catalytic Cyclizations.** While the chemistry presented above provides a simple high-yield synthesis of indoles under very mild conditions, it suffers from requiring the use of a stoichiometric amount of palladium chloride. Although the palladium is not consumed in the reaction, it is reduced to metallic Pd, and recycling requires either tedious reoxidation or costly "trading in" for new  $\text{PdCl}_2$ . For this reason the development of a catalytic cycle to carry out this chemistry was desirable. The problem was to find a method to reoxidize  $\text{Pd}(0)$  to  $\text{Pd}(\text{II})$  in the presence of both *o*-allylanilines and indoles, both of which are very readily oxidized themselves. (Methoxyindoles **19** and **20** discolor within minutes upon exposure to air.) In addition, the oxidizing agent should not complex strongly to substrate or to palladium(II), since this would interfere with

Scheme I



the cyclization process. While in principle neither anhydrous  $\text{CuCl}_2$  or benzoquinone meet all these criteria, in practice both are efficient oxidizing agents for catalytic cyclizations. Copper salts complicated the purification of indole products, while hydroquinone was easily separated. Hence most of the catalytic cyclizations in Table II were carried out using benzoquinone as oxidant (eq 5).

2-(2-propenyl)aniline + 1-10%  $\text{Pd}(\text{II})$  + benzoquinone



The source of  $\text{Pd}(\text{II})$  used was  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ . Neither lithium chloropalladate nor palladium acetate was as effective as a catalyst. Under the conditions of eq 5, 2-methylindole (**13**), 1,2-dimethylindole (**17**), and 2,2-dimethyl-1,2-dihydroquinoline (**24**) were formed in higher yield under catalytic conditions than under stoichiometric conditions, while *N*-acetyl-2-methylindole (**18**) was formed in considerably higher yield. Indoles with methoxy substituents in the 5 position are particularly sensitive to oxidation, and provide a good test for the tolerance of sensitive indole products to the reoxidation conditions. Both 2-methoxy-5,6-dimethoxyindole (**19**) and 2-methyl-5-methoxyindole (**20**) were formed in fair yield<sup>37</sup> under catalytic conditions at 25  $^\circ\text{C}$ . (Higher temperatures led to lower yields.) Thus, even sensitive reactants and products are compatible with conditions of eq 5.

Catalytic cyclization of 2-crotylaniline (**8**) under the standard conditions resulted in exclusive formation of six-membered ring product, 2-methylquinoline (**23**). In addition, varying amounts of the corresponding tetrahydroquinoline were also obtained, indicating that disproportionation of the initially formed dihydroquinoline had occurred, in addition to quinone- or palladium-catalyzed oxidation. In an attempt to suppress this disproportionation, the reaction was run using a 1 equiv excess of benzoquinone. Surprisingly, the sole product of this reaction was 2-ethylindole rather than 2-methylquinoline, excess quinone having favored five-membered ring formation. An even better yield of 2-ethylindole (79%) was obtained by addition of excess lithium chloride to the standard catalytic system. It is likely that both chloride and benzoqui-

**Table III.** Purification and Characterization of 2-Allylanilines<sup>a</sup>

product	purification	characterization
1	A, 6:1:1 PhH/hexane/ Et <sub>2</sub> O <i>R<sub>f</sub></i> 0.5	C, <sup>25</sup> D mp 123–123.5 °C (lit. 123–124 °C) <sup>49</sup>
2	B, 6:1 PhH/Et <sub>2</sub> O	Anal. C <sub>10</sub> H <sub>13</sub> N) C, H, N
3	E	E, IR, NMR
4	A, 3:1 PhH/Et <sub>2</sub> O <i>R<sub>f</sub></i> 0.3	E, IR, NMR
5	A, 4:4:1 PhH/hexane/ Et <sub>2</sub> O <i>R<sub>f</sub></i> 0.3	Anal. Calcd for C <sub>10</sub> H <sub>13</sub> N: NO: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.16; H, 7.53; N, 8.55.
6	A, 3:1 PhH/Et <sub>2</sub> O <i>R<sub>f</sub></i> 0.3	exact mass calcd C <sub>11</sub> H <sub>15</sub> NO <sub>2</sub> , 193.1102; found, 193.1100.
7	A, 6:1:1 benzene/hexane/ Et <sub>2</sub> O <i>R<sub>f</sub></i> 0.6	E, IR, NMR
8	B, 6:1 hexane/Et <sub>2</sub> O	C <sup>25</sup>
9	A, 6:1 benzene/hexane <i>R<sub>f</sub></i> 0.5	C <sup>25</sup>
10	A, 6:1 benzene/hexane <i>R<sub>f</sub></i> 0.4	E
11		C <sup>25</sup>
12	A, 10:1 chloroform/acetone <i>R<sub>f</sub></i> 0.3 recrystallize from PhCH <sub>3</sub>	C <sup>46</sup>

<sup>a</sup> A, silica gel preparative layer chromatography; B, silica gel medium pressure liquid chromatography; C, identical in all respects with material prepared by an alternate procedure; D, *N*-benzoyl derivatives; E, 95% pure used without further purification; F, unstable.

none coordinate to palladium during the cyclization, changing the metal center environment sufficiently to alter the regiochemistry of the ring closure in this case. A similar alteration of regioselectivity of palladium(II)-induced cyclization of allylphenols upon addition of sodium acetate has been reported.<sup>38</sup> However, excess quinone or lithium chloride had no effect on the catalytic cyclization of 2-(3-methyl-2-butenyl)-aniline.

Finally, the catalytic cyclization of 2-vinylaniline to indole itself proceeded cleanly in high yield. This is in direct contrast to the stoichiometric system in which no cyclization of this substrate was observed.

Two substrates failed to cyclize under catalytic conditions. They were 2-(2-methyl-2-propenyl)aniline (**7**) and 2-(2-cyclohexenyl)aniline (**10**). As previously discussed, closure of **7** to form a five-membered ring would product a  $\sigma$ -alkylpalladium complex which could not  $\beta$ -eliminate (eq 3a), disrupting the catalytic cycle, while closure to form a six-membered ring (eq 3b) should proceed catalytically. Since closure to form the five-membered ring is strongly preferred, the catalytic cyclization failed. Starting material was consumed, producing a number of unidentified products but none of the desired material. Similar observations were made with substrate **10**. The reason for this failure is not clear since  $\beta$ -elimination is possible, and since stoichiometric cyclization proceeded routinely.

## Summary

The chemistry presented here offers an attractive method for the synthesis of a wide variety of indoles. The required 2-bromoaniline starting materials are readily available by classical methods. The introduction of the allyl group using  $\pi$ -allylnickel halide chemistry proceeds under very mild conditions and tolerates a range of functionality in both the aromatic ring and the allyl group. The nickel chemistry is *not* compatible with nitro aromatic compounds, however (nitro aromatics suppress the coupling reaction<sup>27</sup>), and is somewhat slow. In addition, 2-allylanilines are available by a variety of other methods as well. The catalytic cyclizations proceed well with

most allyl as well as styryl systems under mild, neutral conditions. A variety of functional groups are tolerated. The cyclization is regiospecific, and in some cases the regiospecificity can be altered by changing reaction conditions. Easily oxidized starting materials and products survive catalytic cyclization conditions sufficiently to allow isolation of acceptable yields. Gram-scale reactions can be carried out easily using \$0.10 to \$0.20 worth of palladium chloride. This cyclization should find application in the synthesis of natural products containing structural features intolerant of the conditions required for other indole syntheses.

## Experimental Section

**General.** All melting points are uncorrected. Infrared spectra were recorded on a Beckman Acculab 3 spectrophotometer and are reported in cm<sup>-1</sup>. <sup>1</sup>H NMR were measured with either Varian Model A60-A, T-60, EM360, or JEOL MA100 using Me<sub>4</sub>Si as internal standard and are reported in  $\delta$ . <sup>13</sup>C NMR were recorded on a Bruker 90 instrument. LC was performed at moderate pressures (40–60 psi) using 25  $\times$  250 mm column packed with Woelm type 206 silica gel. Analytical and preparative TLC was performed using Brinkmann 60F254 silica gel. Products were visualized by UV light. Analyses were performed by Midwest Microanalytical Labs, Indianapolis, Ind.

**Materials.** All solvents were freshly distilled and stored under an argon atmosphere. Immediately before use they were degassed and saturated with argon. DMF (Mallinckrodt, reagent grade) was distilled from calcium hydride at 15–20 mmHg. THF (Fisher, reagent grade) was refluxed over LiAlH<sub>4</sub> and distilled at atmospheric pressure. Benzene (Fisher, reagent grade, thiophene-free) used in preparation of the nickel complexes was distilled and stored over Type 4A sieves prior to its use. Nickel carbonyl was purchased from Matheson. 2-Methyl-3-bromopropene and 2-methyl-4-bromo-2-butene were prepared by the method of Osbond.<sup>39</sup> Allyl bromide and crotyl bromide were purchased from Aldrich and were used without further purification. 3-Bromocyclohexene was prepared by the method of Vogel.<sup>40</sup> The  $\pi$ -allylnickel bromide complexes were prepared by the method of Semmelhack and Helquist.<sup>41</sup> All manipulations of the nickel complexes were carried out under an argon atmosphere. *o*-Bromoaniline, 2-bromo-4-methylaniline, *N*-methylaniline, and aniline are commercially available. 2-Bromo-4-carboethoxyaniline,<sup>42</sup> 2-bromo-4-methoxyaniline,<sup>43</sup> 2-bromo-5-methoxyaniline,<sup>43</sup> 2-bromo-4,5-dimethoxyaniline,<sup>44</sup> *N*-methyl-2-bromoaniline,<sup>45</sup> and *N*-acetyl-2-bromoaniline<sup>46</sup> were all standard literature preparations. 2-Bromobenzylamine was prepared by the diborane reduction of the corresponding nitrile.<sup>47</sup> 2-Vinylaniline was prepared from a Fe/HOAc reduction of the corresponding nitro compound which was in turn prepared from 2-nitrobenzyl bromide and formaldehyde.<sup>48</sup> All substituted anilines prepared by reduction of nitro compounds were further purified by acid-base extraction to remove all traces of nitro compounds which interfere with the nickel reaction.

### General Procedure for the Preparation of 2-(2-Propenyl)anilines.

All reactions between the substituted anilines and the various allylic nickel complexes follow the same procedure. In a nitrogen-filled glovebag the specific nickel complex (1 mmol) was transferred to a 50-mL two-neck flask fitted with a stopcock, a rubber serum cap, and a stirring bar. The flask was removed from the glovebag and alternately evacuated and filled with argon on a vacuum line, and 20 mL of degassed DMF was added via syringe. The substituted aniline (1 mmol) was placed in a second flask fitted as the first. The flask was degassed on the vacuum line and 15 mL of degassed DMF was added via syringe. After the solution was stirred until the contents of both flasks were homogeneous, the substituted bromoaniline was added via syringe to the nickel complex. The reaction flask was placed in an oil bath at 50 °C with constant stirring for 2–6 days depending upon the specific substrate (Table I). Upon completion the reaction mixture contained a considerable amount of nickel metal and the solution was green. The reaction mixture was quenched with 50 mL of 1 M HCl and extracted with 3  $\times$  50 mL of ethyl ether. The aqueous layer was made basic with Na<sub>2</sub>CO<sub>3</sub> and extracted twice more with ether. The combined ether extracts were washed three times with 50-mL portions of a saturated NaCl solution to remove the DMF. The ether phase was dried over MgSO<sub>4</sub> and the solvent removed on a rotary evaporator. Products were separated by preparative TLC or LC using SiO<sub>2</sub> and eluting with benzene–hexane mixtures.

**Spectral Data. 2-(2-Propenyl)-4-methylaniline (2):** NMR ( $\text{CDCl}_3$ )  $\delta$  2.24 (s, 3,  $\text{ArCH}_3$ ), 3.24 (d,  $J = 6$  Hz, 2,  $=\text{CCH}_2$ ), 3.48 (s, 2,  $\text{NH}_2$ ), 5.0 (d of m, 1), 5.2 (m, 1), 5.6–6.4 (m, 1,  $(-\text{CH}=\text{CH}_2)$ ), 6.4–7 (m, 3,  $\text{ArH}$ ); IR (neat) 3460 (m), 3380 (s), 3240 (w,  $\text{NH}_2$ ), 3090 (w), 3010 (s), 2980 (m), 2920 (s), 2875 (m), 1640 (vs), 1630 (vs), 1525 (vs), 1280 (s), 1160 (m), 1000 (s), 915 (s), 815  $\text{cm}^{-1}$  (vs).

**2-(2-Propenyl)-4-carboethoxyaniline (3):** 100-MHz NMR ( $\text{CDCl}_3$ )  $\delta$  1.24 (t,  $J = 6$  Hz, 3,  $\text{CH}_3$ ), 3.2 (d,  $J = 3$  Hz, 2,  $\text{PhCH}_2\text{C}=\text{C}$ ), 4.18 (q,  $J = 6$  Hz, 2,  $\text{CH}_2\text{O}-$ ), 4.90 (d,  $J = 6$  Hz, 1), 5.02 (s, 1), 5.8 (m, 1,  $(-\text{CH}=\text{CH}_2)$ ), 6.42 (d,  $J = 4$  Hz, 1, aromatic), 7.58 (m, 2, aromatic); IR (neat) 3480 (m), 3380 (s), 3250 (w,  $-\text{NH}_2$ ), 2980 (s), 2940 (m), 1700 (vs,  $\text{C}=\text{O}$ ), 1630 (vs), 1610 (vs), 1580 (m), 1510 (s), 1370 (s), 1270 (vs), 1190 (s), 1150 (s), 1105 (vs), 911 (s), 770  $\text{cm}^{-1}$  (s).

**2-(2-Propenyl)-4-methoxyaniline (4):** NMR ( $\text{CDCl}_3$ )  $\delta$  3.24 (d,  $J = 6$  Hz, 2,  $\text{PhCH}_2\text{C}=\text{C}$ ), 3.25 (s, 2,  $\text{NH}_2$ ), 3.65 (s, 3,  $\text{OMe}$ ), 4.85 (m, 1), 5.2 (m, 1), 5.8 (m, 1,  $(-\text{CH}=\text{CH}_2)$ ), 6.6 (s, 3,  $\text{ArH}$ ); IR (neat) 3440 (m), 3360 (s,  $\text{NH}$ ), 3010 (m), 2950 (s), 2850 (m), 1680 (m), 1640 (s), 1610 (s), 1510 (vs), 1470 (s), 1440 (s), 1290 (s), 1250 (vs), 1160 (s), 1040 (vs), 920 (m), 816  $\text{cm}^{-1}$  (m).

**2-(2-Propenyl)-5-methoxyaniline (5):** NMR ( $\text{CDCl}_3$ )  $\delta$  3.23 (d, 2,  $\text{PhCH}_2\text{C}=\text{C}$ ), 3.6 (br s, 2,  $\text{NH}_2$ ), 3.74 (s, 3,  $\text{OMe}$ ), 5.0 (m, 1), 5.20 (m, 1), 6.0 (m, 1,  $(-\text{CH}=\text{CH}_2)$ ), 6.24 (s), 6.4 (d), 6.95 (d, 3, aromatic); IR (neat) 3450 (m), 3370 (m,  $\text{NH}_2$ ), 3070 (w), 3000 (m), 2970–2900 (m), 2830 (m), 1614 (vs), 1580 (s), 1505 (vs), 1290 (s), 1210 (vs), 1170 (s), 1030 (m), 915 (m), 840  $\text{cm}^{-1}$  (m).

**2-(2-Propenyl)-4,5-dimethoxyaniline (6):** NMR ( $\text{CDCl}_3$ )  $\delta$  3.20 (d,  $J = 6$  Hz, 2,  $\text{PhCH}_2\text{C}=\text{C}$ ), 3.54 (s, 2,  $\text{NH}_2$ ), 3.78, 3.80 (s, 6,  $\text{OMe}$ ), 5.0 (m, 1), 5.20 (m, 1), 6.0 (m, 1,  $(-\text{CH}=\text{CH}_2)$ ), 6.29 (s, 1, aromatic), 6.58 (s, 1, aromatic); IR (neat) 3460 (m), 3380 (m), 3250 (w,  $\text{NH}_2$ ), 3080 (w), 3010 (m), 2950 (m), 2850 (m), 1640 (m), 1530 (vs), 1475 (s), 1460 (s), 1420 (m), 1300 (m), 1240 (vs), 1215 (vs), 1135 (s), 1035 (m), 1010 (s), 920  $\text{cm}^{-1}$  (m).

**2-(2-Methyl-2-propenyl)aniline (7):** NMR ( $\text{CDCl}_3$ )  $\delta$  1.8 (s, 3,  $=\text{CCH}_3$ ), 3.3 (s, 2,  $\text{PhCH}_2\text{C}=\text{C}$ ), 3.7 (br s, 2,  $-\text{NH}_2$ ), 4.9 (d,  $J = 7$  Hz,  $=\text{CH}_2$ ), 6.4–7.2 (m, 4, aromatic); IR (neat) 3430 (s,  $-\text{NH}_2$ ), 3360 (s,  $-\text{NH}_2$ ), 3057 (m), 3010 (m), 2960 (m), 2900 (m), 1630 (s), 1615 (m), 1490 (s), 1450 (s), 1370 (m), 1305 (m), 1270 (m), 885 (s), 737  $\text{cm}^{-1}$  (s).

**2-(2-Cyclohexenyl)aniline (10):** NMR ( $\text{CDCl}_3$ )  $\delta$  1.80, 2.10 (br m, 6,  $-\text{CH}_2-$ ), 3.41 (m, 1,  $\text{PhCHCH}=\text{C}$ ), 3.94 (s, 2,  $-\text{NH}_2$ ), 5.83 (m, 2,  $\text{CH}=\text{CH}$ ), 6.5–7.4 (m, 4, aromatic); IR (neat) 3460 (s,  $-\text{NH}_2$ ), 3370 (s,  $-\text{NH}_2$ ), 3020 (s), 2960 (s), 2940 (s), 1635 (s), 1585 (s), 1500 (s), 1460 (s), 1300 (s), 1280 (s), 1160 (m), 1135 (m), 1060 (m), 985 (m), 880 (m), 750  $\text{cm}^{-1}$  (s).

**2-(2-Propenyl)-N-methylaniline (11):** NMR ( $\text{CDCl}_3$ )  $\delta$  2.80 (s, 3,  $\text{N-Me}$ ), 3.3 (d,  $J = 6$  Hz, 2,  $\text{PhCH}_2\text{C}=\text{C}$ ), 3.8 (s, 1,  $\text{NH}$ ), 5.0 (m, 1), 5.25 (m, 1), 5.6–6.5 (m, 1,  $\text{CH}=\text{CH}_2$ ), 6.5–7.4 (m, 4, aromatic); IR (neat) 3440 (s,  $\text{NH}$ ), 3080 (m), 3060 (m), 3020 (m), 2980 (s), 2900 (s), 2820 (s), 1640 (m,  $\text{C}=\text{C}$ ), 1610 (vs), 1590 (vs), 1520 (vs), 1470 (vs), 1430 (m), 1320 (vs), 1270 (s), 920 (vs), 750  $\text{cm}^{-1}$  (vs).

**General Procedure for the Reaction of  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  with Alkylanilines under Stoichiometric Conditions.** The  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (1 equiv) was transferred to a 50-mL side arm flask fitted with a stopcock, stir bar, and serum cap. The flask was alternately evacuated and filled with argon on the vacuum line. THF (14 mL/mmol complex) was added to the complex via syringe and allowed to stir for 5–10 min. The substrate (1 equiv) was taken up in THF (3.5 mL/mmol of substrate) and added to the slurry of complex via syringe. The mixture was stirred for 1.5–2 h. To this solution was added  $\text{Et}_3\text{N}$  (139  $\mu\text{L}$ /mmol). After an additional 1.5 h, a second equivalent of  $\text{Et}_3\text{N}$  was added. Finally, a third equivalent of  $\text{Et}_3\text{N}$  was added after an additional 1 h of stirring. The mixture was then allowed to stir for an additional 2–3 h and was then filtered. The resulting solution was concentrated on the rotary evaporator. Products were isolated by preparative layer chromatography using a variety of solvent systems.

**Spectral Data. 2-Methyl-5-carboethoxyindole (15):** NMR ( $\text{CDCl}_3$ )  $\delta$  1.40 (t,  $J = 8$  Hz, 3,  $\text{CH}_3\text{CH}_2$ ), 2.50 (s, 3,  $\text{CH}_3-$ ), 4.44 (q,  $J = 8$  Hz, 2,  $\text{OCH}_2\text{CH}_3$ ), 6.35 (s, 1, indole-3-H), 7.24 (d,  $J = 9$  Hz, 1, aromatic), 7.90 (d of d, 1,  $J = 9$ , 2 Hz,  $\text{ArH}$ ), 8.35 (d,  $J = 2$  Hz, 1,  $\text{ArH}$ ); IR (KBr) 3320 (s), 3010 (w), 2920 (w), 1680 (vs,  $\text{C}=\text{O}$ ), 1620 (vs), 1490 (w), 1460 (m), 1420 (m), 1390 (m), 1370 (m), 1350 (s), 1290 (vs), 1240 (s), 1215 (s), 1030 (s), 945 (m), 910 (m), 800 (vs), 770  $\text{cm}^{-1}$  (vs).

**2-Methyl-6-methoxyindole (16):** NMR ( $\text{CDCl}_3$ )  $\delta$  2.30 (s, 3,  $\text{CH}_3-$ ), 3.80 (s, 3,  $\text{OCH}_3$ ), 6.13 (s, 1, indole-3-H), 6.70, 6.83, 7.32, 7.48 (3, aromatic), 7.6 (1,  $\text{NH}$ ); IR (neat) 3480 (s,  $\text{NH}$ ), 3010 (w), 2940 (s),

**Table IV.** Purification and Characterization of Cyclization Products<sup>a</sup>

product	purification	characterization
13	A, 4:4:1 PhH/hexane/ $\text{Et}_2\text{O}$ $R_f$ 0.5	B <sup>50</sup>
14	recrystallized from hexane	B <sup>51,52</sup>
15	A, $\text{CHCl}_3$ $R_f$ 0.7	mp 138–139 °C (lit. 140–141 °C) <sup>53</sup>
16	recrystallized from heptane	mp 103–104 °C (lit. 103 °C) <sup>54</sup>
17	A, 6:1 benzene/hexane $R_f$ 0.5	mp 54–55 °C (lit. 56 °C) <sup>55</sup>
18	A, 10:1 $\text{CHCl}_3$ /acetone $R_f$ 0.5	Anal. ( $\text{C}_{11}\text{H}_{11}\text{NO}$ ) C, H, N mp 39.5–41.5 °C
19	B, PhH, recrystallized from hexane	mp 88–88.5 °C (lit. 90 °C) <sup>56</sup>
20	C, PhH, recrystallized from hexane	mp 89–90 °C (lit. 89–90 °C) <sup>57</sup>
21	A, 9:1 PhH/acetone	B <sup>58</sup>
23	A, 95:5 PhH/ $\text{CH}_3\text{OH}$ $R_f$ 0.4	B <sup>59</sup>
22	A, 20:1 PhH/ $\text{Et}_2\text{O}$ $R_f$ 0.6	B <sup>60</sup>
24	A, 1:1 PhH/ $\text{Et}_2\text{O}$ $R_f$ 0.8	D <sup>25</sup>
25	A, 3:1 petroleum ether/ $\text{Et}_2\text{O}$ $R_f$ 0.5	E <sup>61</sup>

<sup>a</sup> A, silica gel preparative layer chromatography; B, identical in all respects with authentic material; C, Woelm activity 5 neutral alumina, Ph elution; D, identical with material prepared by an alternate procedure; E, infrared identical with that reported for authentic material.

2840 (w), 1630 (s), 1565 (w), 1500 (s), 1460 (s), 1390 (s), 1345 (m), 1312 (s), 1303 (s), 1245 (s), 1220 (m), 1200 (m), 1160 (s), 816  $\text{cm}^{-1}$  (s).

**1,2-Dimethylindole (17):** NMR ( $\text{CDCl}_3$ )  $\delta$  2.40 (s, 3,  $\text{CH}_3$ ), 3.6 (s, 3,  $\text{NCH}_3$ ), 6.3 (s, 1, indole-3-H), 7.0–7.7 (m, 4, aromatic); IR (neat) 3050 (w), 3020 (w), 2970 (m), 1610 (w), 1400 (s), 1340 (m), 1240 (m), 930, 910 (w), 780 (m), 750 (m), 730  $\text{cm}^{-1}$  (s).

**N-Acetyl-2-methylindole (18):** NMR ( $\text{CDCl}_3$ )  $\delta$  2.60 (s, 3,  $\text{CH}_3$ ), 2.70 (s, 3,  $\text{CH}_3\text{CO}$ ), 6.40 (s, 1, indole-3-H), 7.2–8.0 (m, 4, aromatic); IR (KBr) 3080 (w), 3050 (w), 3020 (w), 2970 (w), 2930 (w), 2870 (w), 1705 (vs,  $\text{CH}_3\text{CON}$ ), 1590 (m), 1570 (m), 1460 (s), 1450 (s), 1370 (vs), 1310 (vs), 1210 (m), 1200 (m), 800 (m), 750  $\text{cm}^{-1}$  (s).

**2-Methyl-5,6-dimethoxyindole (19):** NMR ( $\text{CDCl}_3$ )  $\delta$  2.40 (s, 3,  $\text{CH}_3-$ ), 3.90 (s, 3,  $\text{OCH}_3$ ), 3.93 (s, 3,  $\text{OCH}_3$ ), 6.15 (s, 1, indole-3-H), 6.82 (s, 1, aromatic), 7.04 (s, 1, aromatic), 7.9 (1,  $\text{NH}$ ); IR (neat) 3400 (vs,  $\text{NH}$ ), 3360 (s), 3000 (w), 2970 (w), 2950 (w), 2920 (w), 2840 (w), 1630 (w), 1610 (w), 1490 (vs), 1480 (w), 1450 (w), 1400 (w), 1335 (vs), 1205 (vs), 1180 (w), 1155 (m), 1125 (s), 1010 (m), 850 (m), 750  $\text{cm}^{-1}$  (m).

**2-Methyl-5-methoxyindole (20):** NMR ( $\text{CDCl}_3$ )  $\delta$  2.30 (s, 3,  $\text{CH}_3$ ), 3.70 (s, 3,  $\text{OCH}_3$ ), 6.10 (s, 1, indole-3-H), 6.5–7.3 (m, 3, aromatic).

**2,2-Dimethylindoline (25).** 2-(2-Methyl-2-propenyl)aniline (90 mg, 0.61 mmol) and  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (159 mg, 0.61 mmol) were reacted in the normal fashion. After 1 h of stirring, 3 equiv of  $\text{Et}_3\text{N}$  (85  $\mu\text{L}$  equiv) was added at 1-h intervals (1 equiv/h). Following the addition of the third equivalent, the mixture was stirred for 2.5 h, at which time the system was opened to a hydrogen balloon and allowed to stir overnight. Typical isolation and preparative layer chromatography (3:1 petroleum ether/ether,  $R_f$  0.5) yielded 28 mg (31%) of 2,2-dimethylindoline as a light yellow oil. The IR was identical with that of authentic material.<sup>64</sup> NMR ( $\text{CDCl}_3$ ):  $\delta$  1.34 (s, 6,  $\text{CH}_3$ ), 2.86 (s, 2,  $\text{PhCH}_2$ ), 6.50–7.17 (m, 4, aromatic). Also recovered was 77 mg of 2-(2-isopropyl)aniline from reduction of the starting amine.

**Attempted Preparation of Indole.** 2-(2-Ethenyl)aniline (119 mg, 1 mmol) and  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (260 mg, 1 mmol) were combined as usual. A heavy yellow precipitate formed after 10 min.  $\text{Et}_3\text{N}$  (139  $\mu\text{L}$  in 5 mL of THF) was added over 20 min using a constant addition funnel. A second and third equivalent of  $\text{Et}_3\text{N}$  were added in the same manner 4 and 5.5 h after the start of the reaction. The chocolate brown mixture was then filtered and the solid material taken up in THF and stirred under  $\text{H}_2$  overnight. Filtration and removal of solvent yielded a dark brown oil which by NMR contained primarily 2-ethylaniline. No indole was formed.



**Preparation of 2-(2-Propenyl)-3-aminonaphthoquinone and Cyclization to 2-Methylbenzof[*h*]indole-4,9-dione (eq 4).**  $\pi$ -Allylnickel bromide (0.33 g, 0.92 mmol) in 10 mL of DMF was added to 2-aminonaphthoquinone (0.30 g, 1.84 mmol) in 10 mL of DMF at  $-50^{\circ}\text{C}$  under an argon atmosphere. The resulting mixture was stirred at  $-50^{\circ}\text{C}$  for 3 h, and allowed to warm slowly to  $25^{\circ}\text{C}$  and to stir at this temperature for 18 h. The resulting solution was partitioned between water and ether. (A few drops of 2 N HCl was added to disperse the emulsion which formed.) The aqueous phase was washed with ether until the ether was colorless. The combined ether phases were washed with water three times and dried over anhydrous  $\text{MgSO}_4$  and solvent was removed under vacuum leaving an orange solid (0.364 g, 92%): NMR ( $\text{Me}_2\text{SO}-d_6$ )  $\delta$  2.82 (d, 2,  $J = 10$  Hz,  $-\text{CH}_2\text{C}=\text{CH}_2$ ), 4.4–5.6 (m, 3,  $-\text{CH}=\text{CH}_2$ ), 5.40 (s, 1,  $=\text{CHC}=\text{O}$ ), 6.95 (br s, 2,  $\text{NH}_2$ ), 7.3–8.0 (m, 4, aromatic). This product is the allylquinol from allylation of the carbonyl adjacent to the  $\text{NH}_2$ . The material was placed on a silica gel preparative TLC plate ( $\text{CH}_3\text{OH}$ ) and eluted twice with ether. The  $R_f$  0.62 band contained the desired 2-(2-propenyl)-3-aminonaphthoquinone: IR ( $\text{CHCl}_3$ ) 3450 (NH), 1680 (CO), 1624, 1605, 1585, 1565  $\text{cm}^{-1}$  (aromatic) NMR ( $\text{CDCl}_3$ )  $\delta$  3.3 (d, 2,  $J = 12$  Hz,  $\text{CH}_2\text{C}=\text{C}$ ), 5.2 (m, 2,  $\text{C}=\text{CH}_2$ ), 5.8 (m, 1,  $\text{C}=\text{CH}$ ), 7.22 (s, 2,  $\text{NH}_2$ ), 7.7–8.1 (m, 4, aromatic). This material was used without further purification by adding 97 mg (0.455 mmol) of it in 5 mL of THF to  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (119 mg, 0.455 mmol) in THF under an argon atmosphere. Triethylamine (128  $\mu\text{L}$ ,  $\sim 1$  mmol) was added in two equal portions after 1 and 2 h, respectively. Palladium metal began to precipitate upon addition of triethylamine. After stirring for 18 h at  $25^{\circ}\text{C}$ , the mixture was filtered and the crude material purified by preparative TLC (silica gel, ether eluent). The product (30 mg, 30%) was contained in the  $R_f$  0.75 band. It had identical IR and NMR spectra and melting point with those reported for 2-methylbenzof[*h*]indole-4,9-dione.<sup>62</sup>

**Isolation of Intermediate  $\text{PdCl}_2$  Complexes.** *o*-(Methallyl)aniline (60 mg, 0.41 mmol) in 5 mL of THF was added to a stirred slurry of  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (107 mg, 0.41 mmol) in 5 mL of THF. After 30 min the solvent was removed and the residue was subjected to 0.1 mm vacuum for 2 h, giving 154 mg of golden brown platlets. The compound was unstable in the solid state at room temperature in air, forming a dark, oily solid insoluble in THF and acetone: IR (KBr) 3500 (m), 3200 (s), 3100 (vs), 2990 (s), 2960 (s), 2890 (s), 1620 (m), 1585 (s), 1530 (m), 1505 (s), 1490 (s), 1470 (s), 1450 (s), 1440 (s), 1390 (m), 1380 (m), 1150 (m), 1100 (m), 1050 (s), 1030 (s), 960 (m), 760  $\text{cm}^{-1}$  (m); NMR (acetone- $d_6$ )  $\delta$  2.25 (s, 3,  $\text{CH}_3$ ), 3.79 (s, 2,  $\text{CH}_2$ ), 5.1 (s, 1, olefin), 6.0 (s, 2,  $\text{NH}_2$ ), 7.2–7.8 (m, 4, aromatic) (peak at 6.0 disappeared with exposure to  $\text{D}_2\text{O}$ );  $^{13}\text{C}$  NMR (acetone- $d_6$ ) ppm 27.1 ( $=\text{CCH}_3$ ), 42.4 ( $\text{PhCH}_2\text{C}=\text{CH}_2$ ), 84.2 (coord  $=\text{CH}_2$ ), 122.6, 127.8, 129.8, 131.6, 144.5, 144.7. For comparison 2-(2-propenyl)aniline  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) ppm 21.387 ( $=\text{CCH}_3$ ), 40.262 ( $\text{PhCH}_2\text{C}=\text{CH}_2$ ), 110.7 ( $=\text{CH}_2$ ), 115.1 (aromatic C-5), 117.9 (aromatic C-4), 123.1 (aromatic C-2), 126.6 (aromatic C-5), 130.1 (aromatic C-3), 142.8, 144.4 (aromatic C-1 and disubstituted olefinic carbon).

2-(2-Propenyl)aniline (133 mg, 1 mmol) was added to  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (260 mg, 1 mmol) in 10 mL of THF. After 2 h of stirring solvent was siphoned off. The gray-green solid was washed twice with THF and dried at room temperature (0.3 mmHg): IR (KBr pellet under  $\text{N}_2$  atmosphere) 3200 (vs), 3160 (vs), 3100 (vs), 2375 (s), 1615 (w), 1570 (m), 1525 (m), 1500 (s), 1460 (s), 1445 (m), 1390 (m), 1160 (s), 1105 (m), 1005 (m), 985 (s), 767 (vs), 730  $\text{cm}^{-1}$  (m).

**General Procedure for the Catalytic Cyclization of 2-Allylanilines.** In a one-neck flask were placed  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (10 mol %), benzoquinone (1 equiv), and LiCl (10 equiv). THF (14 mL/mmol substrate) was then added, and was stirred for 3–5 min. The substrate in THF (3–4 mL/mmol substrate) was added to the flask via syringe and the solution was refluxed for 18 h. The THF was removed on the rotary evaporator and the residue was taken up in approximately 20 mL of ether and stirred for 20 min with a small amount of decolorizing charcoal. The solution was filtered and the residue purified by preparative layer chromatography.

**A. Large-Scale Preparation of 2-Methylindole (13).** 2-(2-Propenyl)aniline (1.0 g, 7.52 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (0.195 g, 0.75 mmol), benzoquinone (0.812 g, 7.52 mmol), and LiCl (3.158 g, 75.2 mmol) were combined as usual in 95 mL of THF. After 5 h at reflux, the solvent was removed and the residue was stirred with ether and decolorizing charcoal for approximately 20 min and filtered. The filtrate was washed five times with 50-mL portions of 1 M NaOH. The solvent was removed on the rotary evaporator and the residue was

placed on a silica gel column and eluted with 3:1 petroleum ether/ether. 2-Methylindole (0.818 g, 86%) was collected as a white, crystalline solid, identical with authentic material.<sup>45</sup>

**B. *N*-Acetyl-2-methylindole (18).** *N*-Acetyl-2-(2-propenyl)aniline (105 mg, 0.6 mmol) in 10 mL of THF was slowly added over 36 h to a refluxing slurry of 15 mg of  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ ,  $\text{Cu}(\text{OAc})_2$  (240 mg, 1.2 mmol), and  $\text{Na}_2\text{CO}_3$  (61 mg, 0.6 mmol) in 10 mL of THF. After an additional 1 day at reflux, 50 mL of ether was added and the crude reaction mixture was filtered through a short  $\text{SiO}_2$  plug. The solvent was removed giving 150 mg of a yellow semisolid. Starting material (40 mg) was recovered and the indole product (72 mg, 71%) was isolated by TLC and was identical with the product prepared above.

**C. 2-Methyl-5,6-dimethoxyindole (19).** 3,4-Dimethoxy-2-(2-propenyl)aniline (194 mg, 1 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (25 mg, 0.1 mmol), benzoquinone (108 mg, 1 mmol), and LiCl (420 mg, 10 mmol) were combined as usual. The mixture was then stirred for 18 h at room temperature. The usual isolation followed by preparative layer chromatography (1:1 petroleum ether/ether,  $R_f$  0.20) yielded 93 mg (48%) of 2-methyl-5,6-dimethoxyindole as a yellow solid which quickly darkened. The product was identical with that prepared above.

**D. 2-Methyl-5-methoxyindole (20).** 4-Methoxy-2-(2-propenyl)aniline (105 mg, 0.53 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (17 mg, 0.06 mmol), benzoquinone (60 mg, 0.64 mmol), and LiCl (269 mg, 6.4 mmol) were reacted as usual at  $25^{\circ}\text{C}$ . Normal isolation, including decolorizing charcoal, followed by preparative layer chromatography (1:1 petroleum ether/ether,  $R_f$  0.43) yielded 33 mg (32%) of 2-methyl-5-methoxyindole as a yellow solid, identical with the same material prepared previously.

**E. 2-Ethylindole (21).** 2-(3-Methyl-2-propenyl)aniline (147 mg, 1 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (26 mg, 0.1 mmol), benzoquinone (108 mg, 1 mmol), and LiCl (420 mg, 10 mmol) were reacted in the normal manner. Usual isolation, followed by preparative layer chromatography (3:1 petroleum ether/ether,  $R_f$  0.48) yielded 103 mg (79%) of 2-ethylindole as light tan crystals, identical in all respects with authentic material.<sup>53</sup>

**F. 2-Methylquinoline (23).** 2-(3-Methyl-2-propenyl)aniline (147 mg, 1 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (26 mg, 0.1 mmol), and benzoquinone (108 mg, 1 mmol) were reacted in the usual manner. Normal isolation and preparative layer chromatography (3:1 petroleum ether/ether,  $R_f$  0.17) yielded 84 mg (58%) of 2-methylquinoline as a light yellow oil, identical with authentic material.<sup>48</sup>

**G. Attempted Preparation of Tetrahydrocarbazole.** 2-(2-Cyclohexenyl)aniline (148 mg, 0.86 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (22 mg, 0.09 mmol), and benzoquinone (186 mg, 1.72 mmol) were combined as usual. Typical isolation and preparative layer chromatography (1:1 petroleum ether/ether) failed to give any identifiable products. The reaction also failed when  $\text{Cu}(\text{OAc})_2$  was used as the oxidant.

**H. 2,2-Dimethyl-1,2-dihydroquinoline (24).** 2-(3-Methyl-2-butenyl)aniline (143 mg, 0.89 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (23 mg, 0.09 mmol), and benzoquinone (96 mg, 0.89 mmol) were combined as usual. Normal isolation and preparative layer chromatography (1:1 petroleum ether/ether,  $R_f$  0.60) yielded 77 mg (54%) of 2,2-dimethyl-1,2-dihydroquinoline as a yellow oil, identical in all respects with material prepared above.

**I. Attempted Preparation of 3-Methyl-1,2,3,4-tetrahydroisoquinoline.** 2-(2-Propenyl)benzylamine (134 mg, 0.81 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (24 mg, 0.09 mmol), benzoquinone (98 mg, 0.91 mmol), and LiCl (383 mg, 9.1 mmol) were combined as usual. Typical workup and preparative layer chromatography (1:1 petroleum ether/ether) failed to yield any identifiable products. The reaction also failed when  $\text{Cu}(\text{OAc})_2$  was used as the oxidant.

**J. Attempted Preparation of 2,2-Dimethylindoline.** 2-(2-Methyl-2-propenyl)aniline (131 mg, 0.89 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (23 mg, 0.09 mmol), benzoquinone (96 mg, 0.89 mmol), and LiCl (374 mg, 8.9 mmol) were combined as previously described. Typical workup followed by preparative layer chromatography (1:1 petroleum ether/ether) failed to yield any identifiable products.

**K. Preparation of Indole.** 2-(2-Ethenyl)aniline (55 mg, 0.46 mmol),  $\text{PdCl}_2(\text{CH}_3\text{CN})_2$  (24 mg, 0.09 mmol), benzoquinone (50 mg, 0.46 mmol), and LiCl (193 mg, 4.6 mmol) were reacted as usual. The THF was removed on the rotary evaporator after 18 h of reflux. The residue was slurried in  $\text{CCl}_4$  and stirred for 20 min with decolorizing charcoal. The solution was filtered and the solvent level was reduced on the rotary evaporator. Preparative layer chromatography (1:1 petroleum ether/ether,  $R_f$  0.55) yielded 40 mg (74%) of indole as a white solid,

identical with authentic material.<sup>63</sup>

**L. Preparation of 1,2,3,4-Tetrahydro-2-methylquinoline.** *o*-Crotylaniline (147 mg, 1 mmol), PdCl<sub>2</sub>(CH<sub>3</sub>CN)<sub>2</sub> (26 mg, 0.1 mmol), and benzoquinone (108 mg, 1 mmol) were reacted in the standard fashion. Normal isolation and preparative layer chromatography (1:1 petroleum ether/ether, *R<sub>f</sub>* 0.54) yielded 42 mg (29%) of 1,2,3,4-tetrahydro-2-methylquinoline as a yellow oil. The NMR spectrum was identical with that of authentic material.<sup>64</sup> IR (neat 3420 (m), 2980 (m), 2950 (m), 1620 (m), 1590 (m), 1500 (s), 1320 (m), 915 (ms), 900 (m), 845 (s), 745 cm<sup>-1</sup> (s).

**M. Large-Scale Preparation of 2-Ethylindole (21).** 2-(3-Methyl-2-propenyl)aniline (1.0 g, 6.8 mmol), PdCl<sub>2</sub>(CH<sub>3</sub>CN)<sub>2</sub> (177 mg, 0.68 mmol), benzoquinone (734 mg, 6.8 mmol), and LiCl (2856 mg, 68 mmol) were combined as usual in 85 mL of THF. After 18 h, the solvent was removed on the rotary evaporator. The residue was taken up in ether and stirred with decolorizing charcoal for approximately 30 min. The solution was filtered and the ether filtrate was extracted three times with 50-mL portions of 1 M NaOH. The organic layer was dried over MgSO<sub>4</sub> and filtered and the solvent was removed on the rotary evaporator. The residue was placed on a silica gel column and eluted with 5:1 petroleum ether/ether to give 497 mg (50%) of 2-ethylindole as a light yellow solid. Recrystallization from dilute ethanol gave white plates, mp 39–41 °C (lit. 40–41 °C).<sup>58</sup> The spectra were identical with that of authentic material. Also isolated was 180 mg (18%) of 2-methylquinoline with spectra identical with that of authentic material. The reaction corresponds to 68% total closure.

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