for the preparation of **21**, a solution of **27** (119 mg, 0.473 mmol) in 3:1:1 AcOH/THF/H_2O (8 mL) was treated with Zn dust (420 mg, 6.42 mmol) at 60 °C for 2.5 h. Workup and purification of the crude product by column chromatography on silica gel ($CHCl_3$/10% methanolic NH_3 (40:1)) gave **27** (113 mg, 94%): a pale yellow oil; $[\alpha]^{20}_D$ -14.5° (*C* 1.13, $CHCl_3$); IR (neat) 3263, 3005, 2927, 1652, 1456, 1377, 1338, 1286, 1118, 1061, 933, 888, 824, 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (3 H, d, J = 6.5 Hz), 0.94 (3 H, t, J = 7.5 Hz), 1.08 (2 H, dt, J = 8.5, 2.7 Hz), 1.28–1.46 (6 H, m), 1.50–1.82 (7 H, m), 1.95–2.04 (4 H, m), 2.23 (1 H, ddd, J = 9.9, 6.5, 2.4 Hz), 2.45–2.55 (1 H, m), 3.50–3.62 (2 H, m), 5.26–5.39 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 14.4, 18.6, 20.6, 26.1, 27.2, 29.4, 32.7, 33.2, 34.0, 34.8, 36.6, 56.9, 62.4, 63.0, 128.9, 132.1; MS *m/z* (rel intensity) 253 (M^+, 5), 252 (3), 194 (74), 182 (26), 169 (9), 156 (100), 138 (28); HRMS calcd for $C_{16}H_{31}NO$ (M^+) 253.2405, found 253.2398.

(5*R*,8*R*,8a*S*)-8-Methyl-5-[4(*Z*)-heptenyl]octahydroindolidine [(-)-Indolizidine 235B] (4). In a manner similar to that described for the cyclization of **21**, a mixture of **28** (110 mg, 0.434 mmol), CBr_4 (180 mg, 0.543 mmol), and CH_2Cl_2 (2 mL) was treated, successively, with PPh_3 (170 mg, 0.648 mmol) and Et_3N (0.8 mL). Workup and purification of the crude product by column chromatography on silica gel ($CHCl_3$/10% methanolic NH_3 (200:1)) gave **4** (72 mg, 71%): a pale yellow oil; $[\alpha]^{28}_D$-85.4° (*c* 0.79, MeOH); IR (neat) 3005, 2962, 2932, 2873, 2777, 2701, 1457, 1375, 1332, 1243, 1221, 1163, 1134, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (3 H, d, J = 6.5 Hz), 0.95 (3 H, t, J = 7.5 Hz), 1.17–1.52 (8 H, m), 1.56–1.79 (5 H, m), 1.79–2.09 (7 H, m), 3.25 (1 H, dt, J = 8.7, 1.8 Hz), 5.27–5.39 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 14.5, 19.0, 20.5, 20.6, 26.1, 27.5, 29.2, 31.4, 33.9, 34.4, 36.7, 52.0, 63.6, 71.5, 129.1, 131.9; MS *m/z* (rel intensity) 235 (M^+, 3), 234 (2), 164 (10), 151 (8), 138 (100), 96 (10), 70 (8); HRMS calcd for $C_{16}H_{29}N$ (M^+) 235.2299, found 235.2311.

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Supplementary Material Available: ^1H and ^{13}C NMR spectra of compounds 1–4, 11–13, 15, 21, 23–26, and 28 (28 pages). Ordering information is given on any current masthead page.

Synthesis of 2-Arylbenzoxazoles via the Palladium-Catalyzed Carbonylation and Condensation of Aromatic Halides and *o*-Aminophenols

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A new synthetic method is reported in which 2-arylbenzoxazoles can be prepared by the palladium-catalyzed condensation of aryl halides with *o*-aminophenols followed by dehydrative cyclization. This method is tolerant of a wide variety of functional groups on either aromatic ring and gives good to excellent yields of products. An aliphatic vicinal amino alcohol gave a bis-acylated product as well as a chlorine-containing product with only a small amount of the desired 2-aryloxazole being formed. Methyl iodide and benzyl bromide gave only alkylated products.

Introduction

As part of an effort to explore the synthetic utility of aromatic halides, we initiated a study of the palladium-catalyzed carbonylation of aryl iodides and bromides and their reactions with various nucleophiles. These "Heck" carbonylation reactions have been well documented for the formation of amides[1] and esters,[2] as well as α-keto amides,[3] α-keto esters,[3e,4] α-keto acids,[5] α-hydroxy acids,[6] anhydrides,[7] acid fluorides,[8] acids,[9] lactams,[10] lactones,[11] aldehydes,[12] and imides.[13] During the course of our investigation, we became aware that the use of *o*-aminophenols could lead to *N*-(2-hydroxyphenyl)amides **1**, which are precursors to the benzoxazole ring system **2** (eq 1).

Arylbenzoxazoles are commonly made by the condensation of an aromatic carboxylic acid (derivative) with an *o*-aminophenol (eq 1, path b). Initial reaction between these two compounds results in the formation of a 2-hydroxy amide intermediate **1**, which is the same as that obtained through carbonylation reaction (eq 1, path a).

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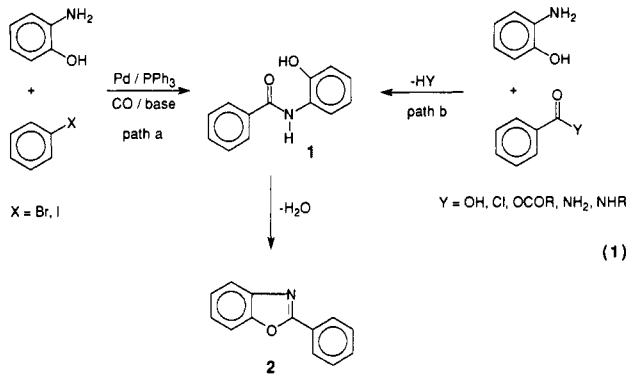
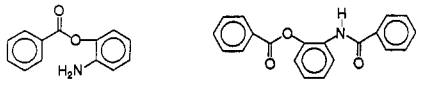


This intermediate is then subjected to dehydrative cyclization to give **2**.[14] One limitation of the conventional method is the unavailability of certain aryl carboxylic acid reagents. Use of the corresponding nitrile,[14] selenoamide,[15] or *N*-(ethoxycarbonyl)thioamide[16] provides alternate routes to the desired product but suffers from long syntheses and/or toxic byproducts. Haloaromatic compounds are generally more available than the corresponding carboxylic acid derivatives and the requirements of the Heck carbonylation reaction are such that a wide variety of functional groups can be tolerated. This route offers an alternative to the traditional synthesis of benzoxazoles. We report the results of our study on the palladium-catalyzed carbonylation and condensation of aryl halides and *o*-aminophenols to form 2-arylbenzoxazoles.

Results and Discussion

The reaction between iodobenzene and *o*-aminophenol (eq 1, path a, X = I) was first examined as the model reaction for this system. An equimolar solution of iodobenzene and *o*-aminophenol in DMAc was treated with 3% $PdCl_2L_2$ (L = PPh_3), 6% PPh_3, and 1.2 equiv of DBU and 90 psig carbon monoxide (CO) at 120 °C. Analysis of the reaction mixture by gas chromatography (GC) after 0.5 h indicated a single product peak and the absence of the two starting reagents.

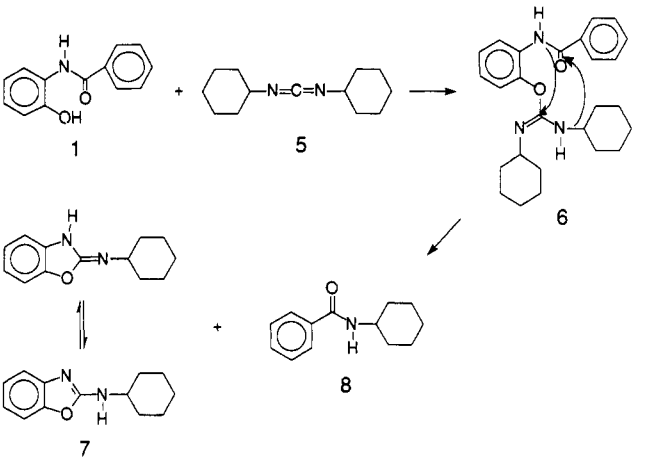
It was assumed that the product was hydroxy amide **1**, but the bifunctional nature of the aminophenol did not preclude the formation of amino ester **3**. The production of **1** was confirmed by isolation of the reaction product and analysis of the infrared bands at 1645 (amide I), 1545 (amide II), and 1285 cm^{-1}, all indicative of an amide functional group. No ester bands were observed in the 1735-cm^{-1} region. In addition, there was no evidence for the formation of amide–ester **4**, an authentic sample of which was made and characterized by GC/MS.



3 4

With the nature of the intermediate established, a suitable cyclization method needed to be found. We wished to have a one-pot synthetic procedure that afforded cyclized product without the isolation of the intermediate amide phenol. Thermal cyclization methods are commonly employed on poly(amide phenols),[17] but continued heating of the reaction mixture at 120 °C for 6 h resulted in less than 5% product formation. Replacement of the DMAc solvent with *N*-cyclohexylpyrrolidinone (CHP) and heating to 200 °C for 18 h still was not sufficient to induce cyclization.

Scheme I



Dicyclohexylcarbodiimide (DCC) **5** has been used as a dehydrative coupling agent in peptide syntheses,[18] but in this instance use of the carbodiimide resulted in the formation of two major products, neither of which was the expected cyclized one. One compound was tentatively identified as *N*-cyclohexylbenzamide **8**; an independent synthesis of this substance confirmed its identity. The formation of **8** could occur as outlined in Scheme I. Attack of the free phenolic group in **1** on DCC would give rise to amide–urea **6**. Intramolecular transamidation could then form the observed cyclohexylbenzamide **8** and the tautomer of 2-(cyclohexylamino)benzoxazole, **7**. The identity of **7** was also verified by the synthesis and isolation of an authentic sample.

We next turned to acid catalysts to enhance the dehydrative cyclization. Boric acid,[19] in refluxing DMAc, afforded only a 40% yield of **2** after 24 h. With dibutyltin oxide,[20] all the intermediate amidol **1** had been consumed and only the cyclized product was detected by GC after 4 h, but workup of the reaction mixture gave only a 10% yield. Likewise, introduction of *p*-toluenesulfonic acid into the DMAc reaction mixture failed to effect the desired ring closure. Addition of several drops of concentrated HCl to the reaction mixture at 120 °C resulted in very slow cyclization (22 h) to the product **2**. However, increasing the reaction temperature to 165 °C (refluxing DMAc) with HCl resulted in a much faster rate of ring closure. Using this latter method, all the intermediate **1** had cyclized to **2** in 3 h as determined by GC. The use of triphenylmethane as an internal standard indicated that a GC yield of 71% was achieved. Product isolation was achieved by concentrating the reaction mixture in vacuo and then extracting the residue with ether. Evaporation of the solvent and chromatography on silica gel gave a 63% yield of product.

A variety of benzoxazoles were made by this method (Table I, method A). Electron-rich *p*-iodoanisole **10c** gave only 19% product and 50% of the intermediate uncyclized material **9c**. When the bromo analogue was used, a 24% yield of **11c** was isolated along with a substantial amount of **9c**. Complete cyclization was not achieved even after

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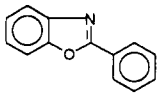
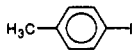
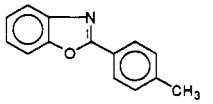
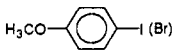
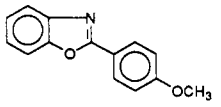
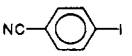
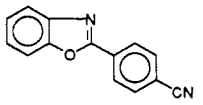
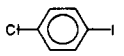
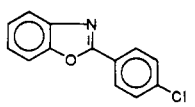
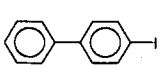
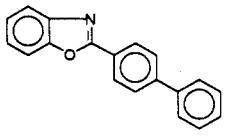
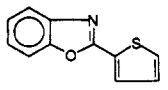
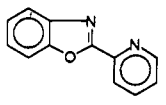
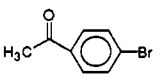
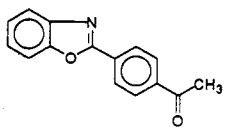
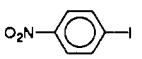
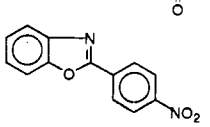
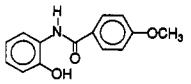
Table I. Benzoxazoles from Aryl Halides and *o*-Aminophenol

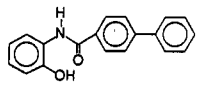
entry	aryl halide (10)	product (11)	yield (%)[a] method A	yield (%)[a] method B
a			63	86
b			80	
c			19 (24)[b]	82
d			56	
e			54	
f			11[c]	97
g			51	
h			33	82
i			54	86
j				74

[a] Yield of isolated, purified material. [b] A 19% yield was obtained from iodoanisole with 50% uncyclized intermediate recovered; a 24% yield of product was obtained from the bromo analogue. [c] 41% uncyclized intermediate was also recovered.

4 days in refluxing DMAc with HCl. Electron-withdrawing substituents on the aromatic ring, such as cyano **10d** and chloro **10e**, gave good yields of benzoxazoles. Biphenyl amide **9f** cyclized very slowly and only a small amount (11%) of the desired product **10f** was isolated.



9c



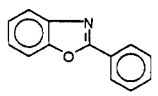
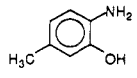
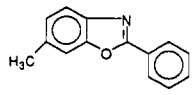
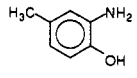
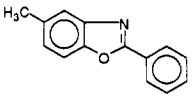
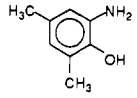
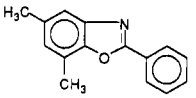
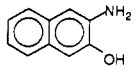
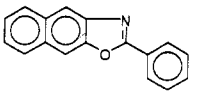
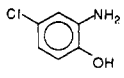
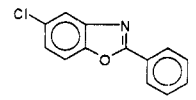
9f

This reaction was not limited to the use of aromatic iodides. Bromoarenes also worked as seen by the reaction of *p*-bromoacetophenone **10i** with *o*-aminophenol. A 54% yield of the acetoxy-substituted phenylbenzoxazole **11i** was obtained. Heterocyclic rings were also tolerated as shown by examples **11g** and **11h**.

While some cyclizations occurred readily with HCl, several did not. To make this procedure more synthetically useful, an alternate procedure was developed. The initial amide forming reaction was run in *toluene*, and after carbonylation and coupling were complete, methanesulfonic or *p*-toluenesulfonic acid was added and the solution refluxed to remove water (method B). This resulted in much cleaner and faster reactions from which high yields of the benzoxazole products could be easily isolated. Isolation consisted of neutralization with NH_4OH, digestion with hot toluene then concentration of the toluene fractions, and chromatography through a short column of silica gel. In most of these reactions small amounts of the amide–esters were formed as determined by GC/MS. These were easily removed when the crude product was passed through a short column or plug of silica gel. This procedure also removed PPh_3 and any DBU remaining. Most of the DBU salts that formed from the amidation reaction were left behind as a sludge after the hot toluene extraction.

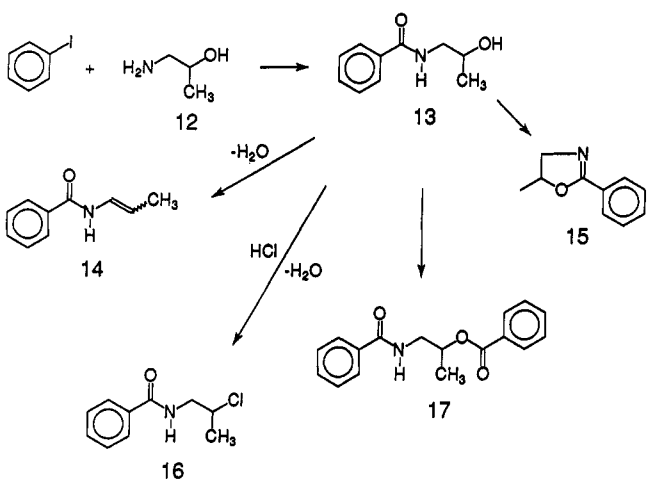
As shown in Table I, method B improved the yield of parent benzoxazole, **11a**, to 86%, as compared to 63% using HCl. The problems with incomplete ring closure seen in method A were overcome as shown by high yields of the *p*-methoxy and biphenylyl derivatives **11c** and **11f**. Increased yields were also exhibited by the pyridyl, **11h**, and acetyl, **11i**, compounds. Even the nitro group survived the reaction conditions to afford 74% of the *p*-nitro de-

Table II. Benzoxazoles from Iodobenzene and *o*-Aminophenols

entry	aminophenol	product (11)	yield (%)[a]
a			86
k			89
l			85
m			82
n			91
o			79

[a] Yield of isolated, purified material made by method B.

Scheme II

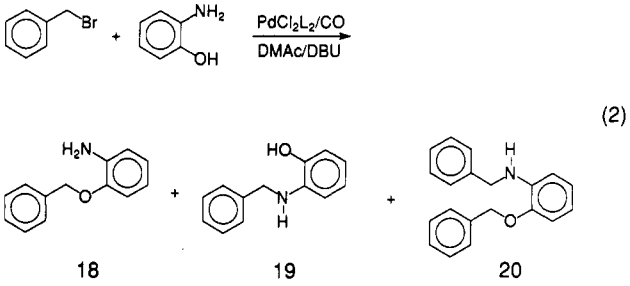


rivative **11j**. Using a variety of aminophenols, high yields of substituted 2-phenylbenzoxazoles were also isolated (Table II).

In an attempt to extend this chemistry to nonfused oxazoles such as **15** (Scheme II), an initial experiment using aliphatic amino alcohol **12** as the nucleophile was performed. This resulted in the formation of several products, none of which were expected. The two major products were the chlorinated amide **16** and the amide–ester **17**. The latter arose from reaction of both nucleophilic ends of **12** with the palladium acyl species derived from iodobenzene.

The formation of **16** can be explained by the nucleophilic attack of chloride ion on the protonated alcohol of **13**. Amidol **13** was also subject to dehydration and the presence of **14** was seen by GC and confirmed by MS. Only very small amounts of the desired 5-methyl-2-phenyloxazole (**15**) were detected by GC/MS.

Palladium-mediated carbonylations of aliphatic compounds have also been reported.[21] When benzyl bromide was allowed to react with *o*-aminophenol in the presence of $PdCl_2L_2$, DBU, and CO, none of the expected 2-benzylbenzoxazole was formed (eq 2). Rather, nucleophilic



displacement of the bromide by both the phenol and the amine function resulted in the formation of the benzyl ether **18** and amine **19** and the dibenzylated product **20**, as determined by GC/MS. Similar results were obtained with methyl iodide and *o*-aminophenol. No carbonylated products were detected by GC/MS analysis of the reaction mixture. Instead, mono- and bis-methylated aminophenols were observed.

Conclusions

The amidation reaction and subsequent cyclization to benzoxazoles occurs readily with commercially available starting materials in the form of iodo- or bromo-substituted aromatic or heterocyclic compounds and common *o*-aminophenols. Good to excellent yields of products containing electron-donating or -withdrawing groups may be produced by this method. This synthetic procedure nicely compliments those derived from benzoic acid intermediates where such compounds are unavailable or synthetically difficult to obtain.

Unlike the aryl halides, benzyl and methyl halides are more prone to undergo simple alkylation chemistry rather than the carbonylation reactions desired. In addition, competition between the alkyl hydroxy group and the amino group in alkylhydroxyamines gives rise to the bis-acylated product seen in Scheme II. If this reaction is to be useful for aliphatic systems, then conditions must be found that will promote a single nucleophilic attack at the acyl complex, as well as suppress the elimination reactions common to saturated alcohols.

Experimental Section

General Procedures. The initial amide forming reaction was performed in a 100-mL pressure reaction vessel (containing a stir bar) fitted with a pressure gauge, a pressure-release valve, a gas inlet, and a straight ball valve for degassing and sample withdrawal. All reactions were run at 0.33 M in *N,N*-dimethylacetamide (DMAc) at 120 °C under 90 psig of CO using 3% $PdCl_2L_2$ and 6% PPh_3 as the catalyst system, unless otherwise noted. Dehydrative cyclizations were accomplished by transferring the contents of the pressure reactor to a 3-neck, round-bottom flask equipped with a stir bar, a Dean–Stark trap, a condenser, and a gas inlet for argon and then adding the appropriate reagent as described later.

All reactions were monitored by chromatography as previously reported.[13] Proton NMR and ^{13}C NMR spectra were acquired on a 300-MHz spectrometer using $CDCl_3$ as both solvent and reference. Fourier transform infrared spectra were recorded as KBr pellets. Chromatography was performed on a radial layer chromatographic device, using 4-mm PF-254 silica gel plates.

Iodobenzene, 4-iodotoluene, 4-iodoanisole, 4-iodobenzonitrile, 4-iodobenzoic acid, 2-iodothiophene, 2-bromopyridine, 4′-bromoacetophenone, 4-bromobiphenyl, cyclohexylamine, benzoyl chloride, 2-chlorobenzoxazole, triethylamine, 1-amino-2-propanol, *p*-toluenesulfonic acid, toluene (all Kodak), 1-chloro-4-iodobenzene, *N*-cyclohexyl-2-pyrrolidinone, anhydrous DMAC, DCC, 6-amino-*m*-cresol, 6-amino-*p*-cresol, 6-amino-2,5-dimethylphenol, 3-amino-2-naphthol, 2-amino-4-chlorophenol, bis(triphenyl-

(21) Heck, R. F. In *Palladium Reagents in Organic Syntheses*; Academic Press: New York, 1985; pp 365–369.

phosphine)palladium(II) chloride ($PdCl_2L_2$) (all Aldrich), anhydrous diethyl ether (Baker, reagent), and CO (Air Products, UPC grade) were all used as received. Triphenylphosphine (Kodak) was recrystallized from hexanes, 4-iodobiphenyl and *o*-aminophenol (both Kodak) were recrystallized from ethanol, and DBU (Aldrich) was fractionally distilled under reduced pressure.

2-(Cyclohexylamino)benzoxazole, (7). Cyclohexylamine (2.12 mL, 17.5 mmol) and triethylamine (Et_3N, 2.9 mL, 21 mmol) were dissolved in diethyl ether (Et_2O, 20 mL) and added dropwise over 30 min to a solution of 2-chlorobenzoxazole (2.0 mL, 17.5 mmol) and Et_2O (130 mL) at room temperature under argon. After stirring for 18 h, the solid was removed by filtration, and the ethereal filtrate was washed with water (1 × 50 mL), 0.1 N HCl (3 × 50 mL), and then water (1 × 50 mL) again. The organic layer was dried over $MgSO_4$, concentrated in vacuo, and purified by chromatography with 3:1 hexanes–ethyl acetate to give 380 mg (10%) product as a colorless oil, which solidified on standing: mp 106.5–108.5 °C; ^1H NMR ($CDCl_3$) δ 7.34 (d, J = 7.2 Hz, 1), 7.24 (d, J = 7.8 Hz, 1), 7.15 (t, J = 7.1 Hz, 1), 7.00 (t, J = 7.6 Hz, 1), 6.18 (br s, 1), 3.75 (br s, 1), 2.13 (m, 2), 1.76 (m, 2), 1.63 (m, 1), 1.36 (m, 5); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 161.7, 148.2, 142.9, 123.7, 120.3, 115.7, 108.5, 51.9, 33.4, 25.4, 24.7.

Preparation of Benzoxazoles. For these preparative-scale reactions, two methods were employed. A representative example is given for each method below. Analytical data for newly reported compounds is also reported below. Isolation and characterization data for previously reported benzoxazoles can be found in the supplementary material.

Preparation of 2-Phenylbenzoxazole (11a). Method A. A pressure reaction vessel was charged with *o*-aminophenol (540 mg, 4.95 mmol), iodobenzene (540 μL, 4.95 mmol), $PdCl_2L_2$ (35 mg, 0.05 mmol), PPh_3 (26 mg, 0.10 mmol), and DMAc (15 mL). The contents were deoxygenated with argon then placed under 20 psig of CO and stirred at 120 °C until all reagents had dissolved. The pressure was released, and DBU (890 μL, 5.94 mmol) was added by syringe. The reactor was charged to 90 psig of CO and stirred for 0.5 h, after which time a small aliquot was removed. GC analysis indicated no iodobenzene or aminophenol remained, but a single peak for the amidephenol 1 was present: ^1H NMR ($CDCl_3$) δ 8.63 (br s, 1), 8.15 (br s, 1), 7.92 (d, J = 7.0 Hz, 2), 7.61 (m, 1), 7.53 (m, 1), 7.20 (m, 3), 7.09 (d, J = 7.8 Hz, 1), 6.93 (t, J = 7.0 Hz, 1); IR ($CDCl_3$) 3415, 3060, 1645, 1610, 1590, 1575, 1545, 1455, 1440, 1365, 1285, 1240, 750, 700 cm^{-1}. The contents of the vessel were transferred to a flask and diluted with 10 mL of DMAc, and 5 drops of concentrated HCl was added. The solution was brought to reflux and allowed to react for 16 h. The contents of the flask were concentrated in vacuo, diluted with ether (100 mL), and washed with water (3 × 50 mL). The ether layer was dried over $MgSO_4$, concentrated in vacuo, and purified by chromatography using 3:1 hexanes–ethyl acetate to give 604 mg (63%) product as white crystalline solid: mp 101–103 °C [lit. mp 102–104 °C (Aldrich)]; ^1H NMR ($CDCl_3$) δ 8.28 (m, 2), 7.81 (m, 1), 7.61 (m, 1), 7.55 (m, 3), 7.37 (m, 2); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 163.0, 150.8, 142.0, 131.4, 128.8, 127.5, 127.0, 125.0, 124.5, 119.9, 110.5; IR (KBr) 3070, 1625, 1555, 1460, 1245, 1060, 750, 705, 690 cm^{-1}.

2-Phenylbenzoxazole (11a). Method B. A pressure vessel was charged with *o*-aminophenol (976 mg, 8.94 mmol), iodobenzene (1.00 mL, 8.94 mmol), $PdCl_2L_2$ (94 mg, 0.13 mmol), and toluene (27 mL) and treated as in method A. DBU (1.60 mL, 10.7 mmol) was added, the reactor was charged to 90 psig of CO, and the reaction was allowed to proceed for 75 min. The reaction mixture was transferred to a round-bottom flask, diluted with more toluene, treated with methanesulfonic acid (3 mL), and refluxed. A Dean–Stark trap collected the water of dehydration. After 2 h, the amide had completely cyclized. The reaction mixture was neutralized with NH_4OH (4 mL). The organic solution was decanted and the residue extracted with hot toluene (2 × 30 mL). The toluene extracts were combined, concentrated in vacuo, and filtered through a plug of silica gel (eluting with toluene). A pale yellow solid was isolated and was further purified by sublimation at 80 °C (1.7 Torr) to give 1.44 g of product (86%).

2-(4-Acetylphenyl)benzoxazole (11i). Method B. As described above, *o*-aminophenol (873 mg, 8.00 mmol), 4-bromoacetophenone (1.592 g, 8.00 mmol), $PdCl_2L_2$ (84 mg, 0.12 mmol), PPh_3 (63 mg, 0.25 mmol), toluene (25 mL), and DBU (1.44 mL, 9.60 mmol) were allowed to react together for 3 h under psig of CO and then transferred to a flask, diluted with toluene, and heated to reflux in the presence of *p*-toluenesulfonic acid (*p*-TSA, 6.0 g) for 2 h. After extraction with hot toluene, the toluene fractions were combined and concentrated in vacuo, and the solid was recrystallized from toluene to give 1.63 g of product (86%): mp 168–170 °C; ^1H NMR ($CDCl_3$) δ 8.42 (d, J = 8.4 Hz, 2), 8.17 (d, J = 8.4 Hz, 2), 7.87 (m, 1), 7.67 (m, 1), 7.46 (m, 1), 2.74 (s, 3); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 197.2, 161.6, 150.9, 141.9, 138.8, 131.0, 128.7, 125.7, 124.8, 120.3, 110.7, 26.7; IR (KBr) 3060, 2940, 1680, 1620, 1600, 1555, 1450, 1410, 1360, 1260, 1055, 845, 750 cm^{-1}. Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90. Found: C, 76.14; H, 4.75; N, 6.01.

5,7-Dimethyl-2-phenylbenzoxazole (11m). Method B. As described above, 2-amino-4,6-dimethylphenol (1.226 g, 8.94 mmol), iodobenzene (1.00 mL, 8.94 mmol), $PdCl_2L_2$ (94 mg, 0.13 mmol), toluene (27 mL), and DBU (1.60 mL, 10.07 mmol) were allowed to react for 2 h under 95 psig of CO, transferred to a flask, diluted with toluene, and heated to reflux in the presence of *p*-toluenesulfonic acid (*p*-TSA, 6.0 g) for 2 h. After extracting with hot toluene, the organic solution was concentrated and cooled. The solid was washed with cold toluene and dried to give 438 mg (22%) of pure product. The liquors were subjected to the usual workup and gave 1.17 g of product (59%). Chromatographic purification (3:1, hexane–EtOAc) gave product with mp 98.5–100 °C: ^1H NMR ($CDCl_3$) δ 8.25 (m, 2), 7.50 (m, 3), 7.38 (s, 1), 6.94 (s, 1), 2.53 (s, 3), 2.44 (s, 3); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 162.6, 148.1, 141.8, 134.1, 131.1, 128.7, 127.4, 127.3, 120.3, 117.1, 21.4, 15.1; IR (KBr) 3055, 2920, 2860, 1555, 1480, 1450, 1335, 1190, 1100, 1055, 1020, 820, 795, 700, 690 cm^{-1}. Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.61; H, 5.89; N, 6.16.

1-Benzamido-2-benzoxypropane (14). A solution of Et_3N (7.0 mL, 50.5 mmol) and 1-amino-2-propanol (1.5 mL, 19.4 mmol) in Et_2O (20 mL) was added dropwise to a solution of benzoyl chloride (5.63 mL, 48.6 mmol) in Et_2O (130 mL) at room temperature over 30 min. The reaction mixture was allowed to react for 18 h then filtered, and the filtrate was washed with water (1 × 50 mL), dried over $MgSO_4$, concentrated in vacuo, and purified on a Chromatotron with 3:1 hexanes–ethyl acetate to give 675 mg (12%) of product as a colorless oil: ^1H NMR ($CDCl_3$) δ 7.99 (d, J = 7.6 Hz, 2), 7.74 (d, J = 7.4 Hz, 2), 7.43 (m, 2), 7.33 (m, 5), 5.32 (m, 1), 3.67 (m, 2), 1.34 (d, J = 6.4 Hz, 3); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 167.6, 166.3, 134.0, 132.8, 131.1, 129.8, 129.3, 128.1, 128.0, 126.8, 70.5, 44.5, 17.6.

Acknowledgment. We would like to thank J. Lugert for obtaining and P. Keogh for intrepreting GC/MS information for us and J. Guilment and D. Margevich for FTIR spectra.

Registry No. 1, 3743-70-2; 2, 833-50-1; 7, 10450-11-0; 8, 1759-68-8; **9c**, 114331-87-2; **11a**, 833-50-1; **11b**, 835-71-2; **11c**, 838-34-6; **11d**, 838-33-5; **11e**, 1141-35-1; **11f**, 17064-45-8; **11g**, 23999-63-5; **11h**, 32959-62-9; **11i**, 37069-08-2; **11j**, 840-58-4; **11k**, 14016-00-3; **11l**, 7420-86-2; **11m**, 139976-25-3; **11n**, 88741-38-2; **11o**, 1019-90-5; **14**, 69775-41-3; $Pd_2Cl_2L_2$, 13965-03-2; cyclohexylamine, 108-91-8; 2-chlorobenzoxazole, 615-18-9; benzoyl chloride, 98-88-4; *o*-aminophenol, 95-55-6; 6-amino-*m*-cresol, 2835-98-5; 2-amino-*p*-cresol, 95-84-1; 2-amino-4,6-dimethylphenol, 41458-65-5; 3-amino-2-naphthol, 5417-63-0; 5-chloro-2-aminophenol, 28443-50-7; iodobenzene, 591-50-4; 4-iodotoluene, 624-31-7; 4-bromoanisole, 104-92-7; 4-iodoanisole, 696-62-8; 4-iodobenzonitrile, 3058-39-7; 4-chloroiodobenzene, 637-87-6; 4-iodobiphenyl, 1591-31-7; 2-iodothiophene, 3437-95-4; 2-bromopyridine, 109-04-6; 4-bromoacetophenone, 99-90-1; 4-nitroiodobenzene, 636-98-6; 1-amino-2-propanol, 78-96-6.

Supplementary Material Available: Experimental procedures and physical and spectral properties of all benzoxazoles synthesized (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.