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Carbonylative Synthesis of Phthalimides and Benzoxazinones by Using Phenyl Formate as a Carbon Monoxide Source

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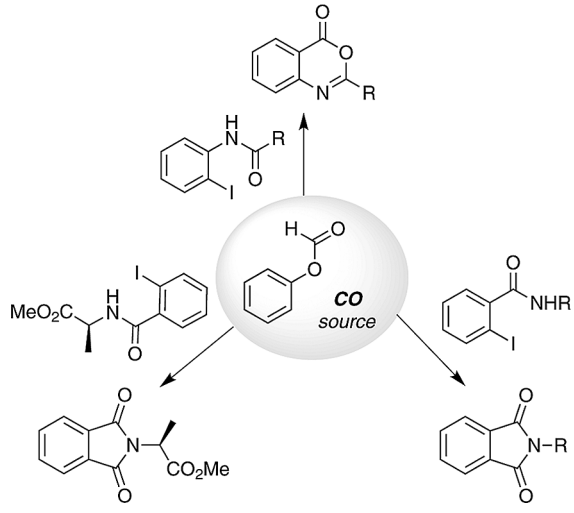
A simple and efficient palladium-catalyzed carbonylative cyclization of *N*-substituted 2-iodobenzamides and 2-iodoanilides was investigated for the synthesis of phthalimides and benzoxazinones, respectively, by using phenyl formate as a CO source. The present catalytic protocol circumvents the use of an expensive phosphine ligand as well as solvent in the case of the phthalimide synthesis. Moreover, mild reaction conditions and a tolerance of various functional groups enhance the general applicability of this method.

Introduction

Annulated heterocycles such as phthalimides and benzoxazinones are important motifs that are present in the numerous biologically active molecules.[1] Hence, the development of environmentally benign protocols for the synthesis of annulated heterocycles has always been a key area of interest among organic chemists. The classical approach to synthesize phthalimides involves the condensation of a phthalic anhydride with a primary amine.[2] Benzoxazinones are typically synthesized by the cyclization of anthranilic acids, *N*-acylanthranilic acids, or isatonic anhydrides.[3]

In recent years, transition-metal-catalyzed direct carbonylation reactions have served as a prime method for the synthesis of various heterocycles by using carbon monoxide gas as C1 source.[4] In this regard, there are only few reports of transition-metal-catalyzed carbonylative syntheses of phthalimides[5] and benzoxazinones,[6] which use CO gas as a C1 source. Indeed, CO gas is most widely used as a C1 source, but it is highly lethal, and there are concerns involving its handling, storage, transport, and need for a specially designed high-pressure reactor, which restricts its common use among academic researchers. Hence, the development of new methodology that involves the use of simple, easy-to-handle, and less toxic CO surrogates is highly desirable.[7] In recent years, much development has been made in this direction, and various inorganic[8] and organic[9] carbon monoxide alternatives have been intensively examined. Ilhyong Ryu and co-workers developed a two chamber technique and continuous microflow tube-in-tube reactor system for an aminocarbonylation by using a Morgan reaction to generate CO.[10] Recently, two groups independently reported the use of aryl formate as a CO source for the esterification of aryl halides.[11] Yasushi Tsuji and co-workers reported the hydroesterification of alkynes and alkenes by using aryl formate as the CO source.[12] Later, Yian Shi and co-workers synthesized a variety of lactones by employing the hydroesterification of alkenylphenols using phenyl formate as the CO source.[13] Very recently, Beller and co-workers reported the use of aryl formate as a bifunctional reagent, that is, a pseudohalide, as well as a CO source for various carbonylation reactions.[14]

In continuation with our ongoing research of simple, less toxic, atom efficient and carbon monoxide free protocols for carbonylation reactions,[15] we herein report the synthesis of *N*-substituted phthalimides and benzoxazinones by using phenyl formate as a simple and efficient carbon monoxide source. Moreover, the methodology has also been suc-



Scheme 1. Carbon monoxide free synthesis of phthalimide and benzoxazinone.

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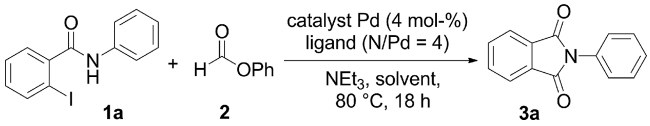
cessfully applied to the synthesis of amino acid derived phthalimides (Scheme 1).

Results and Discussion

We started our initial investigation by employing 2-iodo-*N*-phenylbenzamide (**1a**) as a model substrate, phenyl formate (**2**) as a CO source, and NEt_3 as a base in the presence of a palladium catalyst at 80 °C (Table 1). We then screened different bidentate nitrogen ligands such as 1,10-phenanthroline, 2,2′-bipyridine, and bathophenanthroline (Table 1, Entries 2–4) and found that 2,2′-bipyridine provided *N*-phenylphthalimide (**3a**) in 60% yield (Table 1, Entry 2). A significant improvement in the yield of **3a** was observed by switching from an aromatic to an aliphatic bidentate ligand (Table 1, Entry 5). Subsequently, we screened various palladium catalysts (Table 1, Entries 6–9). Among them, $PdCl_2(PhCN)_2$ gave **3a** in 93% yield (Table 1, Entry 7), However, the reaction did not proceed in the absence of the catalyst (Table 1, Entry 10). We also studied the effect of various solvents and determined that polar solvents are more effective for this transformation (Table 1, Entries 11–13). Surprisingly, the reaction also worked very well under solvent-free conditions, which furnished **3a** in 92% yield (Table 1, Entry 14).

Table 1. Optimization of the reaction conditions.[a]

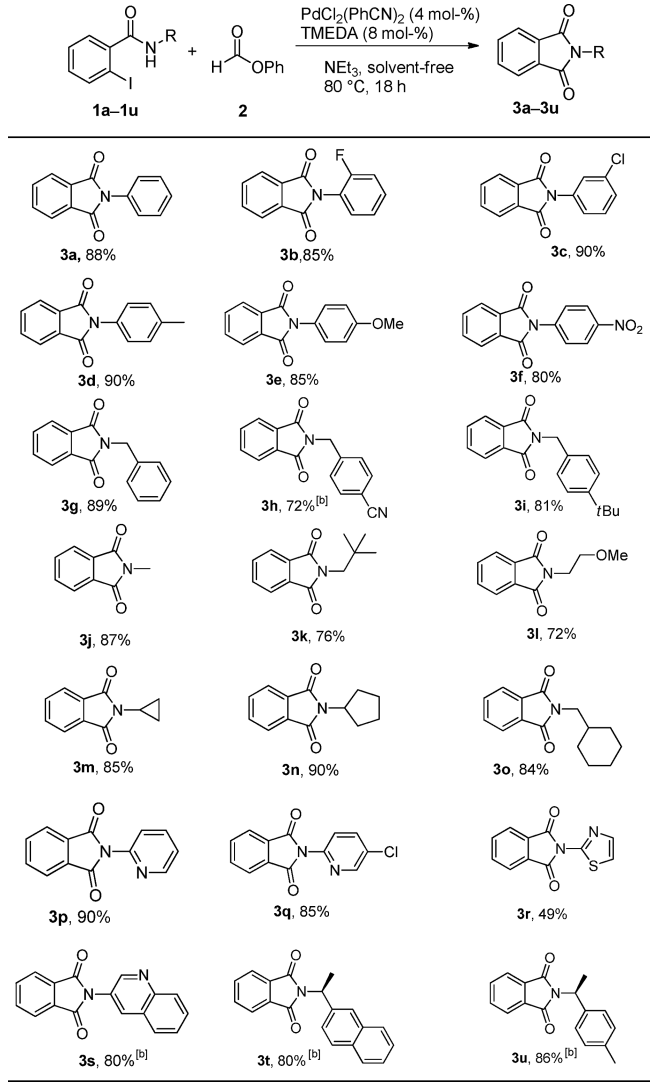


Entry	Catalyst	Ligand	Solvent	Yield [%][b]
1	$Pd(OAc)_2$	–	DMF[c]	10
2	$Pd(OAc)_2$	2,2′-bipyridine	DMF	60
3	$Pd(OAc)_2$	1,10-phenanthroline	DMF	38
4	$Pd(OAc)_2$	bathophenanthroline	DMF	45
5	$Pd(OAc)_2$	TMEDA[c]	DMF	88
6	$PdCl_2(PPh_3)_2$	TMEDA	DMF	70
7	$PdCl_2(PhCN)_2$	TMEDA	DMF	93
8	$Pd(PPh_3)_4$	TMEDA	DMF	69
9	$Pd(dba)_2$[c]	TMEDA	DMF	70
10	–	TMEDA	DMF	00
11	$PdCl_2(PhCN)_2$	TMEDA	THF[c]	64
12	$PdCl_2(PhCN)_2$	TMEDA	toluene	45
13	$PdCl_2(PhCN)_2$	TMEDA	ACN[c]	81
14[d]	$PdCl_2(PhCN)_2$	TMEDA	–	92

[a] Reagents and conditions: **1a** (0.5 mmol), **2** (1 mmol), catalyst (4 mol-%), ligand (8 mol-%), and NEt_3 (1 mmol) in solvent (1 mL). The reaction mixture was stirred at 80 °C for 18 h. [b] GC yields. [c] dba = dibenzylideneacetone, TMEDA = *N*,*N*,*N*′,*N*′-tetramethyl-1,2-ethylenediamine, DMF = *N*,*N*-dimethylformamide, THF = tetrahydrofuran, ACN = acetonitrile. [d] NEt_3 (2 mmol) was used.

To evaluate the scope and limitations of the developed protocol, we applied the optimized reaction parameters to various *N*-substituted 2-iodobenzamides, which were converted into the corresponding phthalimides in good to excellent yields (Table 2). Notably, various substituents on the *N*-phenyl ring, which include halo groups such as –F and –Cl, electron-donating groups such as $–CH_3$ and –OMe, and electron-withdrawing groups such as the nitro group were also well-tolerated to provide the corresponding products **3b**–**3f** in excellent yields. *N*-benzyl and *N*-benzyl groups with either a cyano or *tert*-butyl substituent were also sustainable under the optimized reaction conditions (i.e., **3g**–**3i**). Various simple aliphatic as well as cyclic *N*-substituted 2-iodobenzamides also worked well and furnished the corresponding phthalimides **3j**–**3o** in good yields. Moreover, 2-iodobenzamides with an *N*-heterocyclic substituent such as a pyridine, substituted pyridine, thiazole, or quinolone group were also compatible under the present catalytic system (i.e., **3p**–**3s**). Chiral *N*-substituted 2-iodobenzamides were also successful under the present reaction conditions to furnish the corresponding phthalimides **3t** and **3u** in good yields.

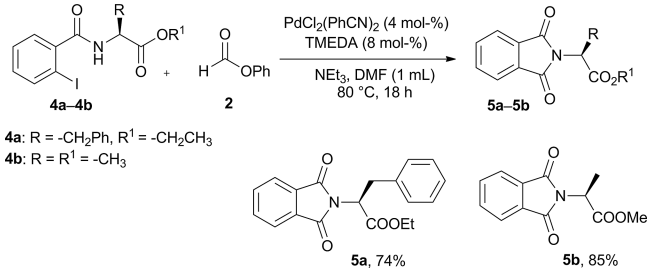
Table 2. Substrate scope for phthalimide synthesis.[a]



[a] Reagents and conditions: **1a**–**1u** (0.5 mmol), **2** (1 mmol), catalyst (4 mol-%), ligand (8 mol-%), and NEt_3 (2 mmol). The reaction mixture was then stirred at 80 °C for 18 h. [b] DMF (1 mL) was used as the solvent.

To our delight, chiral amino acid derived 2-iodobenzamides were tested under the optimized reaction conditions,

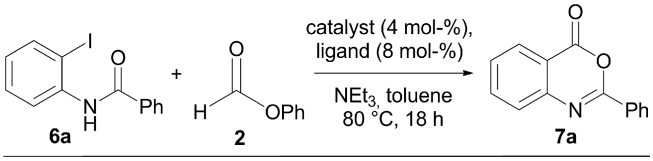
and the corresponding phthalimides **5a** and **5b** were obtained in good yields (Scheme 2).



Scheme 2. Amino acid derived chiral phthalimide synthesis.

Our success with the carbonylative cyclization of *N*-substituted 2-iodobenzamides inspired us to investigate the cyclization of 2-iodoanilides. Initially, the optimized parameters for the phthalimide synthesis were applied to the preparation of a benzoxazinone. However, compound **7a** was formed in poor yield under these conditions (Table 3, Entry 1). We then screened various bidentate nitrogen ligands in toluene as the solvent to increase the yield of **7a**, but the yield of the desired product was still very poor (Table 3, Entries 2–5). Consequently, we changed the ligand and examined various phosphine ligands (Table 3, Entries 6–11). Among them, Xantphos [4,5-bis(diphenylphosphino)-9,9-dimethylxanthene] served as the best ligand and gave compound **7a** in 90% yield (Table 3, Entry 11). Next, the effect of the palladium catalyst was examined (Table 3, Entries 11–13), and we found that $PdCl_2(PhCN)_2$ provided an excellent yield of **7a** (Table 3, Entry 11).

Table 3. Optimization of the reaction conditions for benzoxazinone synthesis.[a]

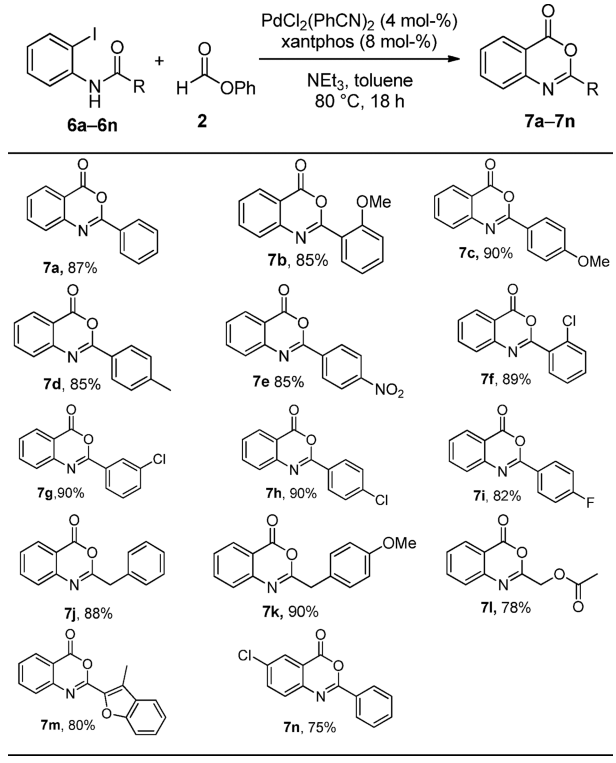


Entry	Catalyst	Ligand	Yield [%][b]
1[c]	$PdCl_2(PhCN)_2$	TMEDA	<10
2	$PdCl_2(PhCN)_2$	TMEDA	<10
3	$PdCl_2(PhCN)_2$	2,2′-bipyridine	<10
4	$PdCl_2(PhCN)_2$	1,10-phenanthroline	<10
5	$PdCl_2(PhCN)_2$	bathophenanthroline	<10
6[d]	$PdCl_2(PhCN)_2$	PPh_3	58
7	$PdCl_2(PhCN)_2$	dppf[e]	65
8	$PdCl_2(PhCN)_2$	dppp[e]	65
9[d]	$PdCl_2(PhCN)_2$	$P(tBu)_3 \cdot HBF_4$	87
10	$PdCl_2(PhCN)_2$	dppb[e]	68
11	$PdCl_2(PhCN)_2$	Xantphos	90
12	$Pd(OAc)_2$	Xantphos	86
13	$Pd(dba)_2$	Xantphos	80

[a] Reagents and conditions: **6a** (0.5 mmol), **2** (1 mmol), catalyst (4 mol-%), ligand (8 mol-%), and NEt_3 (1 mmol) in toluene (1 mL) at 80 °C for 18 h. [b] GC yield. [c] Without solvent in the presence of NEt_3 (2 mmol). [d] Ligand (16 mol-%) was used. [e] dppf = 1,1′-bis(diphenylphosphino)ferrocene, dppp = 1,3-bis(diphenylphosphino)propane, dppb = 1,4-bis(diphenylphosphino)butane.

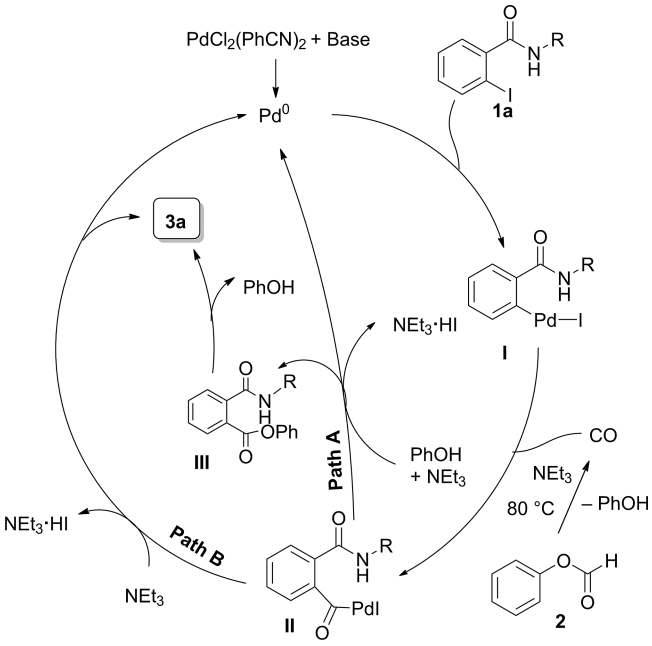
With these optimized reaction parameters, we were pleased to find that various 2-iodoanilides could be converted into the corresponding benzoxazinones in good to excellent yields (Table 4). Various substituted aryl rings such as those with an electron-donating or electron-withdrawing group (**7b**–**7e**), a halo group (**7f**–**7i**), and a benzyl or substituted benzyl group (**7j** and **7k**) as well as a functionalized alkyl group (**7l**) were introduced at the second position of the benzoxazinone. Compound **7m**, which has antifungal and antibacterial activity, was also prepared in high yield under the optimized reaction conditions.[16] When we submitted the 2-iodoanilide with a *m*-chloro substituent to the reaction, the corresponding benzoxazinone **7n** was furnished in 75% yield.

Table 4. Substrate scope for benzoxazinone synthesis.[a]



[a] Reagents and conditions: **6a**–**6n** (0.5 mmol), **2** (1 mmol), catalyst (4 mol-%), ligand (8 mol-%), and NEt_3 (1 mmol) in solvent (1 mL). The reaction mixture was stirred at 80 °C for 18 h.

On the basis of previous reports, we have proposed a plausible reaction mechanism for the phthalimide synthesis (Scheme 3). Initially, the in situ generated Pd^0 species[17] underwent an oxidative addition to 2-iodobenzamide to give arylpalladium intermediate **I**. Next, the arylpalladium species **I** is converted into acylpalladium species **II** in the presence of CO that is generated from the decomposition of phenyl formate.[11] The conversion of acylpalladium species **II** into product **3a** may occur through two pathways. Path A proceeds through a phenoxycarbonylation of acylpalladium species **II**,[11c] which undergoes an intramolecular cyclization to form **3a**, whereas path B proceeds through an intramolecular attack of the nucleophile on acylpalladium species **II** to form **3a**.



Scheme 3. Plausible reaction mechanism for the phthalimide synthesis.

Conclusions

In summary, the present protocol provides the highly efficient $PdCl_2(PhCN)_2$-catalyzed carbonylative cyclization of 2-iodobenzamides and 2-iodoanilides by using phenyl formate as a CO source to furnish the corresponding phthalimides and benzoxazinones, respectively. The protocol is phosphine- and solvent-free for the synthesis of various phthalimide derivatives. Moreover, for the first time, the process was successfully applied to the carbonylative cyclization of amino acid derived *N*-substituted 2-iodobenzamides.

Experimental Section

General Methods: All reactions were performed in oven-dried glassware under nitrogen. The progress of the reactions were monitored by TLC on Merck silica gel 60 F254 plates, and the developed plates were visualized by UV light at 254 nm. The products were purified by column chromatography on silica gel (120–200 mesh). All yields that are reported in Tables 2 and 4 as well as in Scheme 2 refer to isolated yields, and the yields that are reported in Tables 1 and 3 are GC yields. The ^1H and ^{13}C NMR spectroscopic data were recorded with a Bruker-400 MHz spectrometer, and tetramethylsilane was used as the internal standard in $CDCl_3$. Chemical shifts of the ^1H and ^{13}C NMR signals are reported as δ values in parts per million (ppm) relative to TMS and $CDCl_3$, respectively. Proton coupling patterns are described as a singlet (s), doublet (d), triplet (t), quartet (q), or multiplet (m). Optical rotations were measured by using a Rudolph Autopol IV Polarimeter. All gas chromatography was performed on a Perkin–Elmer Clarus 400 GC that was equipped with a flame ionization detector (FID) and a capillary column (30 m × 0.25 mm × 0.25 μm).

General Procedure for the Synthesis Phthalimides from 2-Iodobenzamides and Phenyl Formate: An oven-dried Schlenk tube was evacuated, backfilled with nitrogen, and charged with $PdCl_2(PhCN)_2$ (7.6 mg, 0.02 mmol), TMEDA (4.64 mg, 0.04 mmol), the 2-iodobenzamide (0.5 mmol), phenyl formate (122.12 mg, 1 mmol), and triethylamine (202.38 mg, 2 mmol) under nitrogen. The reaction mixture was stirred at 80 °C for 18 h and then was diluted with EtOAc. The resulting mixture was washed with aqueous $NaHCO_3$ (2× 10 mL). The combined aqueous phases were extracted with ethyl acetate (3× 10 mL), and the combined organic layers were washed with brine and dried with Na_2SO_4. The solvent was removed under reduced pressure to give the crude residue, which was purified by column chromatography on silica gel (ethyl acetate/petroleum ether) to give the corresponding phthalimide.

General Procedure for the Synthesis Benzoxazinones from 2-Iodoanilides and Phenyl Formate: An oven-dried Schlenk tube was evacuated, backfilled with nitrogen, and charged with $PdCl_2(PhCN)_2$ (7.6 mg, 0.02 mmol), Xanthphos (23.14 mg, 0.04 mmol), the 2-iodoanilide (0.5 mmol), phenyl formate (1 mmol), and triethylamine (1 mmol) in toluene (1 mL) under nitrogen. The reaction mixture was stirred at 80 °C for 18 h and then was diluted with EtOAc. The resulting mixture was washed with aqueous $NaHCO_3$ (2× 10 mL). The combined aqueous phases were extracted with ethyl acetate (3× 10 mL), and the combined organic layers were washed with brine and dried with Na_2SO_4. The solvent was removed under reduced pressure to give the crude residue, which was purified by column chromatography on silica gel (ethyl acetate/petroleum ether) to give the corresponding benzoxazinone.

Characterization of Selected Compounds

2-(2-Fluorophenyl)isoindoline-1,3-dione (3b):[5e] White solid (102 mg, 85% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.97 (dd, J = 5.2, 3.2 Hz, 2 H), 7.81 (dd, J = 5.2, 3.2 Hz, 2 H), 7.48–7.43 (m, 1 H), 7.37 (t, J = 6.8 Hz, 1 H), 7.31–7.25 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 159.1, 131.9, 130.8, 130.7, 129.8, 124.6, 124.6, 123.9, 116.6 ppm.

2-(3-Chlorophenyl)isoindoline-1,3-dione (3c):[5e] White solid (115 mg, 90% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (dd, J = 5.2, 3.2 Hz, 2 H), 7.81 (dd, J = 5.2, 3.2 Hz, 2 H), 7.50–7.37 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.8, 134.6, 132.8, 131.5, 130.0, 128.2, 126.6, 124.5, 123.9, 123.7 ppm.

2-[4-(*tert*-Butyl)benzyl]isoindoline-1,3-dione (3i):[5e] White solid (118 mg, 81% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (dd, J = 5.2, 3.2 Hz, 2 H), 7.64 (dd, J = 5.2, 3.2 Hz, 2 H), 7.38 (d, J = 8.4 Hz, 2 H), 7.32 (d, J = 8.4 Hz, 2 H), 4.81 (s, 2 H), 1.27 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.9, 150.6, 134.1, 133.8, 133.4, 128.4, 125.5, 123.2, 41.1, 34.4, 31.2 ppm.

2-Methylisoindoline-1,3-dione (3j):[5e] White solid (70 mg, 87% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, J = 5.2, 3.2 Hz, 2 H), 7.71 (dd, J = 5.2, 3.2 Hz, 2 H), 3.18 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.4, 133.8, 132.2, 123.1, 23.9 ppm.

2-(2-Methoxyethyl)isoindoline-1,3-dione (3l):[5e] White solid (73 mg, 72% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.83 (m, 2 H), 7.73–7.71 (m, 2 H), 3.90 (t, J = 5.6 Hz, 2 H), 3.64 (t, J = 5.6 Hz, 2 H), 3.35 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 133.6, 132.1, 123.5, 69.5, 58.6, 37.3 ppm.

2-Cyclopropylisoindoline-1,3-dione (3m):[5e] White solid (79 mg, 85% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.82 (dd, J = 5.2, 3.2 Hz, 2 H), 7.71 (dd, J = 5.2, 3.2 Hz, 2 H), 2.74–2.68 (m, 1 H), 1.07–0.97 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 133.9, 131.7, 123.4, 20.9, 5.2 ppm.

2-Cyclopentylisoindoline-1,3-dione (3n):[5e] White solid (96 mg, 90% yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, J = 5.2, 3.2 Hz,

2 H), 7.69 (dd, J = 5.2, 3.2 Hz, 2 H), 4.67–4.58 (m, 1 H), 2.13–2.06 (m, 2 H), 2.00–1.88 (m, 4 H), 1.68–1.60 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 133.7, 132.1, 122.9, 50.9, 29.5, 25.0 ppm.

2-(Cyclohexylmethyl)isoindoline-1,3-dione (3o):[5e] White solid (102 mg, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, J = 5.2, 3.2 Hz, 2 H), 7.71 (dd, J = 5.2, 3.2 Hz, 2 H), 3.52 (d, J = 7.2 Hz, 2 H), 1.82–1.67 (m, 6 H), 1.25–1.14 (m, 3 H), 1.05–0.90 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 133.5, 132.0, 123.4, 43.9, 36.8, 30.5, 26.2, 26.1 ppm.

2-(Quinoline-3-yl)isoindoline-1,3-dione (3s):[5d] White solid (109 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.06 (d, J = 2 Hz, 1 H), 8.813 (d, J = 2 Hz, 1 H), 8.17 (d, J = 8.4 Hz, 1 H), 8.02–8.00 (m, 2 H), 7.91–7.77 (m, 4 H), 7.62 (t, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.0, 147.9, 146.9, 134.7, 132.6, 131.6, 130.1, 129.4, 128.0, 127.6, 127.3, 125.6, 124.0 ppm.

(*S*)-2-[1-(Naphthalene-2-yl)ethyl]isoindoline-1,3-dione (3t): White solid (120 mg, 80% yield). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 137.6, 133.9, 133.2, 132.8, 132.0, 128.2, 128.1, 127.5, 126.3, 126.1, 126.0, 125.5, 123.2, 49.7, 17.5 ppm. $[\alpha]_D^{20}$ = 120.0 (c = 0.1, CH_2Cl_2). HRMS (ESI): calcd. for $[(C_{20}H_{15}NO_2)H]^+$ 302.1181; found 302.1178.

(*S*)-2-[1-(*p*-Tolyl)ethyl]isoindoline-1,3-dione (3u): White solid (113 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.76 (m, 2 H), 7.68–7.63 (m, 2 H), 7.39 (d, J = 8 Hz, 2 H), 7.12 (d, J = 8 Hz, 2 H), 5.53 (q, J = 7.2 Hz, 1 H), 2.30 (s, 3 H), 1.90 (d, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 137.4, 137.3, 133.9, 132.0, 129.2, 127.4, 123.2, 49.4, 21.1, 17.6 ppm. $[\alpha]_D^{20}$ = –33.5 (c = 0.1, CH_2Cl_2).

Ethyl (*S*)-2-(1,3-Dioxoisoindolin-2-yl)-3-phenylpropanoate (5a): Light yellow oil (119 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (dd, J = 5.4, 3.1 Hz, 2 H), 7.68 (dd, J = 5.5, 3.0 Hz, 2 H), 7.20–7.11 (m, 5 H), 5.14 (dd, J = 11.2, 5.3 Hz, 1 H), 4.26–4.23 (m, J = 7.1, 2.7 Hz, 2 H), 3.57 (m, 2 H), 1.25 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 167.5, 136.8, 134.0, 131.6, 128.8, 128.5, 126.8, 123.4, 62.0, 53.4, 34.6, 14.1 ppm. $[\alpha]_D^{20}$ = –58.00 (c = 0.1, CH_2Cl_2). HRMS (ESI): calcd. for $[(C_{19}H_{17}NO_4)H]^+$ 324.1236; found 324.1232.

Methyl (*S*)-2-(1,3-Dioxoisoindolin-2-yl)propanoate (5b): Yellow oil (99 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, J = 5.5, 3.0 Hz, 2 H), 7.73 (dd, J = 5.5, 3.1 Hz, 2 H), 4.96 (q, J = 7.3 Hz, 1 H), 3.73 (s, 3 H), 1.68 (d, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 167.4, 134.1, 131.9, 123.5, 52.7, 47.4, 15.2 ppm. $[\alpha]_D^{20}$ = –3.0 (c = 0.1, CH_2Cl_2). HRMS (ESI): calcd. for $[(C_{12}H_{11}NO_4)H]^+$ 234.0766; found 234.0769.

2-Phenyl-4*H*-benzo[*d*][1,3]oxazin-4-one (7a):[6d] White solid (97 mg, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30–8.21 (m, 3 H), 7.83–7.79 (m, 1 H), 7.68 (d, J = 8.0 Hz, 1 H), 7.58–7.48 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.5, 157.0, 146.9, 136.5, 132.6, 130.2, 128.9, 128.7, 128.5, 128.2, 127.2, 117.0 ppm.

2-(2-Methoxyphenyl)-4*H*-benzo[*d*][1,3]oxazin-4-one (7b): White solid (107 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (dd, J = 8.0, 1.6 Hz, 1 H), 7.86–7.78 (m, 2 H), 7.69 (d, J = 8.0 Hz, 1 H), 7.54–7.47 (m, 2 H), 7.07–7.01 (m, 2 H), 3.92 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 158.6, 157.7, 147.0, 136.5, 133.3, 131.4, 128.5, 128.4, 127.3, 120.6, 120.5, 117.0, 112.1, 56.1 ppm.

2-(4-Methoxyphenyl)-4*H*-benzo[*d*][1,3]oxazin-4-one (7c):[6d] White solid (113 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (d, J = 8.4 Hz, 2 H), 8.22 (d, J = 7.9 Hz, 1 H), 7.80 (t, J = 7.7 Hz, 1 H), 7.64 (d, J = 8.0 Hz, 1 H), 7.47 (t, J = 7.6 Hz, 1 H), 7.00 (d, J = 8.5 Hz, 2 H), 3.89 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 159.8, 157.1, 147.3, 136.5, 130.2, 128.5, 127.7, 126.9, 122.5, 116.7, 114.1, 55.5 ppm. HRMS (ESI): calcd. for $[(C_{15}H_{11}NO_3)H]^+$ 254.0817; found 254.0819.

2-(*p*-Tolyl)-4*H*-Benzo[*d*][1,3]oxazin-4-one (7d):[6d] White solid (100 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22–8.17 (m, 3 H), 7.80 (t, J = 8.0 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1 H), 7.49 (t, J = 8.0 Hz, 1 H), 7.29 (d, J = 8.0 Hz, 2 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 157.2, 147.1, 143.3, 136.4, 129.5, 128.5, 128.3, 127.9, 127.4, 127.0, 116.9, 21.6 ppm. HRMS (ESI): calcd. for $[(C_{15}H_{11}NO_2)H]^+$ 238.0868; found 238.0869.

2-(2-Chlorophenyl)-4*H*-benzo[*d*][1,3]oxazin-4-one (7f): White solid (114 mg, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, J = 7.6 Hz, 1 H), 7.92–7.85 (m, 2 H), 7.73 (d, J = 8.0 Hz, 1 H), 7.61–7.55 (m, 2 H), 7.49–7.41 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 156.6, 146.6,136.6, 133.5, 132.3, 131.4, 131.1, 129.7, 128.9, 128.6, 127.4,126.9, 117.0 ppm.

(4-Oxo-4*H*-benzo[*d*][1,3]oxazin-2-yl)methyl Acetate (7l): White solid (85 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, J = 8.0 Hz, 1 H), 7.71–7.58 (m, 1 H), 7.46 (dd, J = 10.8, 5.0 Hz, 2 H), 4.71 (s, 2 H), 2.15 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 166.3, 150.3, 141.0, 135.5, 123.3, 121.6, 120.6, 114.8, 62.9, 20.5 ppm. HRMS (ESI): calcd. for $[(C_{11}H_9NO_4)H]^+$ 220.0610; found 220.0613.

2-(3-Methylbenzofuran-2-yl)-4*H*-benzo[*d*][1,3]oxazin-4-one (7m):[16] White solid (110 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, J = 8.0 Hz, 1 H), 7.85–7.76 (m, 2 H), 7.66–7.60 (m, 2 H), 7.53–7.45 (m, 2 H), 7.33–7.29 (m, 1 H), 2.76 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 154.9, 151.7, 146.9, 140.5, 136.7, 129.6, 128.7, 128.5, 128.0, 127.8, 125.1, 123.3, 120.9, 116.6, 112.1, 9.9 ppm.

6-Chloro-2-phenyl-4*H*-benzo[*d*][1,3]oxazin-4-one (7n):[6d] White solid (96 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31–8.28 (m, 2 H), 8.16 (d, J = 8.0 Hz, 1 H), 7.69 (d, J = 4 Hz, 1 H), 7.62–7.46 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.7, 158.3, 148.0, 142.9, 133.0, 129.9, 129.8, 128.8, 128.7, 128.5, 127.0, 115.8 ppm. HRMS (ESI): calcd. for $[(C_{14}H_8ClNO_2)H]^+$ 258.0322; found 258.0321.

Supporting Information (see footnote on the first page of this article): Decomposition study of phenyl formate and copies of ^{1}H and ^{13}C NMR spectra.

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[1] a) H. Miyachi, A. Azuma, A. Ogasawara, E. Uchimura, N. Watanabe, Y. Kobayashi, F. Kato, M. Kato, Y. Hashimoto, *J. Med. Chem.* **1997**, *40*, 2858–286; b) W. Figg, S. Raje, K. Bauer, A. Tompkins, D. Venzon, R. Bergan, A. Chen, M. Hamilton, J. Pluda, E. Reed, *J. Pharm. Sci.* **1999**, *88*, 121–125; c) J. Balzarini, E. D. Clercq, B. Kaminska, A. Orzeszko, *Antiviral Chem. Chemother.* **2003**, *14*, 139–144; d) A. A. Abdel-Hafez, *Arch. Pharmacal Res.* **2004**, *27*, 495–501; e) M. Gutschow, L. Kuerschner, U. Neumann, M. Pietsch, R. Loser, N. Koglin, K. Eger, *J. Med. Chem.* **1999**, *42*, 5437–5457; f) K. Shreder, Y. Hu, A. Fraser, Y. Kohno, A. Kojima, J. Ishiyama, K. Akihiko, I. Junichi, K. Yasu, Y. Ishiyama, Patent US7879846-B2, **2011**; g)

F. Clemence, O. Le Martret, J. Collard, *J. Heterocycl. Chem.* **1984**, *21*, 1345–1353; h) T. Jian-Bo, L. Yun-Feia, L. Shu-Ling, M. Yuan-Liang, *Chinese J. Struc. Chem.* **2010**, *29*, 1893–1899.

[2] a) J. C. Sheehan, D. W. Chapman, R. W. Roth, *J. Am. Chem. Soc.* **1952**, *74*, 3822–3825; b) M. Sani, G. Fossati, F. Huguenot, M. Zanda, *Angew. Chem. Int. Ed.* **2007**, *46*, 3526–3529; *Angew. Chem.* **2007**, *119*, 3596; c) T. Han, C. F. Chen, *J. Org. Chem.* **2007**, *72*, 7287–7293.

[3] a) J. R. Beck, J. A. Yahner, *J. Org. Chem.* **1973**, *38*, 2450–2452; b) E. P. Papadopoulos, C. D. Torres, *Heterocycles* **1982**, *19*, 1039–1042; c) D. T. Zentmyer, E. C. Wagner, *J. Org. Chem.* **1949**, *14*, 967–981.

[4] a) X.-F. Wu, H. Neumann, M. Beller, *Chem. Rev.* **2013**, *113*, 1–35; b) B. Gabriele, R. Mancuso, G. Salerno, *Eur. J. Org. Chem.* **2012**, 6825–6839; c) K. C. Majumdar, S. Samanta, B. Sinha, *Synthesis* **2012**, *44*, 817–847; d) G. Zeni, R. C. Larock, *Chem. Rev.* **2004**, *104*, 2285–2309; e) B. Gabriele, G. Salerno, M. Costa, *Synlett* **2004**, 2468–2483; f) B. E. Ali, H. Alper, *Synlett* **2000**, 161–171; g) Y. Tamaru, Z. Yoshida, *J. Organomet. Chem.* **1987**, *334*, 213–223; h) J. P. Wolfe, *Eur. J. Org. Chem.* **2007**, 571–582; i) K. Khumtaveeporn, H. Alper, *Acc. Chem. Res.* **1995**, *28*, 414–422; j) M. D. Mihovilovic, P. Stanetty, *Angew. Chem. Int. Ed.* **2007**, *46*, 3612–3615; *Angew. Chem.* **2007**, *119*, 3684; k) T.-S. Mei, L. Kou, S. Ma, K. M. Engle, J.-Q. Yu, *Synthesis* **2012**, *44*, 1778–1791; l) X.-F. Wu, H. Neumann, M. Beller, *Chem. Soc. Rev.* **2011**, *40*, 4986–5009; m) S. T. Gadge, B. M. Bhanage, *RSC Adv.* **2014**, *4*, 10367–10389.

[5] a) R. J. Perry, S. R. Turner, *J. Org. Chem.* **1991**, *56*, 6573–6579; b) S. Inoue, H. Shiota, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2009**, *131*, 6898–6899; c) H. Cao, H. Alper, *Org. Lett.* **2010**, *12*, 4126–4129; d) M. V. Khedkar, S. R. Khan, D. N. Sawant, D. B. Bagal, B. M. Bhanage, *Adv. Synth. Catal.* **2011**, *353*, 3415–3422; e) M. V. Khedkar, A. R. Shinde, T. Sasaki, B. M. Bhanage, *J. Mol. Catal. A* **2014**, *385*, 91–97.

[6] a) S. Cacchi, G. Fabrizi, F. Marinelli, *Synlett* **1996**, 997–338; b) R. Giri, J. K. Lam, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 686–693; c) C. Larksarp, H. Alper, *Org. Lett.* **1999**, *1*, 1619–1622; d) X.-F. Wu, J. Schranck, H. Neumann, M. Beller, *Chem. Eur. J.* **2011**, *17*, 12246–12249; e) X.-F. Wu, H. Neumann, M. Beller, *Chem. Eur. J.* **2012**, *18*, 12599–12602.

[7] a) L. Wu, Q. Liu, I. Fleischer, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2014**, *53*, 6310–6320; b) T. Morimoto, K. Kakiuchi, *Angew. Chem. Int. Ed.* **2004**, *43*, 5580–5588; *Angew. Chem.* **2004**, *116*, 5698.

[8] a) A. Wieckowska, R. Fransson, L. R. Odell, M. Larhed, *J. Org. Chem.* **2011**, *76*, 978–981; b) B. Roberts, D. Liptrot, L. Alcaraz, T. Luker, M. J. Stocks, *Org. Lett.* **2010**, *12*, 4280–4283; c) E. Ren, M. Yamane, *J. Org. Chem.* **2010**, *75*, 3017–3020; d) E. J. Corey, L. S. Hegedus, *J. Am. Chem. Soc.* **1969**, *91*, 1233–1234; e) R. F. Cunico, B. C. Maity, *Org. Lett.* **2003**, *5*, 4947–4949.

[9] a) S. Ko, Y. Na, S. Chang, *J. Am. Chem. Soc.* **2002**, *124*, 750–751; b) G. Jenner, A. Ben Taleb, *J. Organomet. Chem.* **1994**, *470*, 257–261; c) S. Ko, H. Han, S. Chang, *Org. Lett.* **2003**, *5*, 2687–2690; d) K. Hosoi, K. Nozaki, T. Hiyama, *Org. Lett.* **2002**, *4*, 2849–2851; e) V. V. Grushin, H. Alper, *Organometallics* **1993**, *12*, 3846–3850; f) T. Morimoto, K. Fuji, K. Tsutsumi, K. Kakiuchi, *J. Am. Chem. Soc.* **2002**, *124*, 3806–3807; g) T. Ueda, H. Konishi, K. Manabe, *Angew. Chem. Int. Ed.* **2013**, *52*, 8611–8615; *Angew. Chem.* **2013**, *125*, 8773.

[10] C. Brancour, T. Fukuyama, Y. Mukai, T. Skrydstrup, I. Ryu, *Org. Lett.* **2013**, *15*, 2794–2797.

[11] a) T. Ueda, H. Konishi, K. Manabe, *Org. Lett.* **2013**, *15*, 5370–5373; b) T. Ueda, H. Konishi, K. Manabe, *Tetrahedron Lett.* **2012**, *53*, 5171–5175; c) T. Ueda, H. Konishi, K. Manabe, *Org. Lett.* **2012**, *14*, 3100–3103; d) T. Fujihara, T. Hosoki, Y. Katafuchi, T. Iwai, J. Terao, Y. Tsuji, *Chem. Commun.* **2012**, *48*, 8012–8014.

[12] Y. Katafuchi, T. Fujihara, T. Iwai, J. Terao, Y. Tsuji, *Adv. Synth. Catal.* **2011**, *353*, 475–482.

[13] H. Wang, B. Dong, Y. Wang, J. Li, Y. Shi, *Org. Lett.* **2014**, *16*, 186–189.

[14] H. Li, H. Neumann, M. Beller, X.-F. Wu, *Angew. Chem. Int. Ed.* **2014**, *53*, 3183–3186.

[15] a) P. J. Tambade, Y. P. Patil, M. J. Bhanushali, B. M. Bhanage, *Tetrahedron Lett.* **2008**, *49*, 2221–2224; b) D. N. Sawant, Y. S. Wagh, K. D. Bhatte, B. M. Bhanage, *Eur. J. Org. Chem.* **2011**, 6719–6724; c) D. N. Sawant, Y. S. Wagh, K. D. Bhatte, B. M. Bhanage, *J. Org. Chem.* **2011**, *76*, 5489–5494.

[16] H. A. Abdel-Aziz, A. A. I. Mekawey, K. M. Dawood, *Eur. J. Med. Chem.* **2009**, *44*, 3637–3644.

[17] a) J. P. Collman, L. S. Hegedus, J. R. Norton, R. G. Finke, *Principles and Applications of Organotransition Metal Chemistry*, University Science Books, Mill Valley, CA, **1987**, p. 725; b) R. McCrindle, G. Ferguson, G. J. Arsenault, A. J. McAlees, D. K. Stephenson, *J. Chem. Res. Synop.* **1984**, 360–361.

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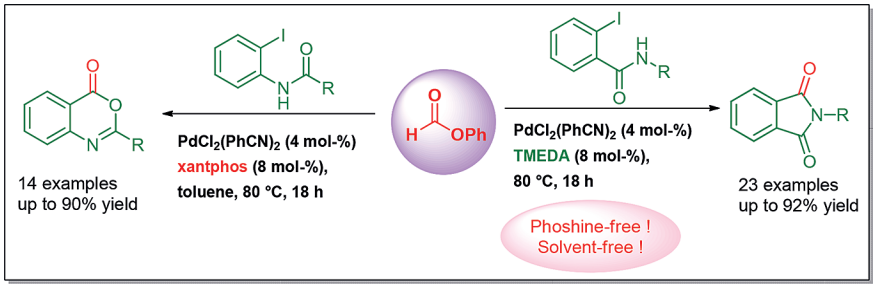

A simple and efficient palladium-catalyzed carbonylative cyclization of *N*-substituted 2-iodobenzamides and 2-iodoanilides was investigated for the synthesis of phthalimides and benzoxazinones, respectively, by using phenyl formate as a CO source.

Keywords: Synthetic methods / Nitrogen heterocycles / Carbonylation / Cyclization / Palladium

