Palladium-Catalyzed Cyclocarbonylation of *o*-Iodoanilines with Heterocumulenes: Regioselective Preparation of 4(3*H*)-Quinazolinone Derivatives

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A catalyst system comprising palladium acetate−bidentate phosphine is effective for the cyclocarbonylation of *o*-iodoanilines with heterocumulenes at 70−100 °C for 12−24 h to give the corresponding 4(3*H*)-quinazolinone derivatives in good yields. Utilizing *o*-iodoaniline with isocyanates, carbodiimides, and ketenimines for the reaction, 2,4-(1*H*,3*H*)-quinazolinediones, 2-amino-4(3*H*)-quinazolinones and 2-alkyl-4(3*H*)-quinazolinones were obtained, respectively. The nature of the substrates including the electrophilicity of the carbon center of the carbodiimide, and the stability of the ketenimine, influence the product yields of this reaction. Urea-type intermediates are believed to be generated first in situ from the reaction of *o*-iodoanilines with heterocumulenes, followed by palladium-catalyzed carbonylation and cyclization to yield the products.

Introduction

4(3*H*)-Quinazolinone derivatives are of considerable interest because of their pharmacological properties;[1] e.g., protein tyrosine kinase inhibitor,[2] cholecystokinin inhibitor,[3] antimicrobial,[4] anticonvulsant,[5] sedative and hypotensive,[6] antidepressant and antiinflammatory,[7] as well as antiallergy.[8] In addition, more than 40 alkaloids comprised of a 4(3*H*)-quinazolinone moiety were isolated from natural sources.[9] Some of these have interesting biological properties such as antimalarial activity and biofungicide[10] and diuretic properties. There are a number of methods described for the preparation of the compounds. The main synthetic routes to such compounds utilize 2-aminobenzoic acid or its derivatives,[11] 2-aminobenzonitrile,[12] isatoic anhydride,[13] 2-carbomethoxyphenyl isocyanate,[14] *N*-arylnitrilium salts,[15] and 4*H*-3,1-benzoxazinones.[16] Recently, the solid-phase synthesis of 2,4-(1*H*, 3*H*)-quinazolinediones have been reported.[17] The direct ortho substitution of *N*-(*tert*-butoxycarbonyl)aniline by a lithium reagent was also described.[18] Transition metals were utilized in the preparation of these compounds; e.g., Akazome et al.[19] described the use of ruthenium and platinum complexes for the catalytic reduction N-heterocyclization of *N*-(2-nitrobenzoyl)amides under carbon monoxide pressure. A 2,4-(1*H*,3*H*)-quinazolinedione was synthesized by the reaction of azobenzene with a stoichiometric amount of dicobalt octacarbonyl under CO pressure at 230 °C.[20] The reaction of aromatic 2-carbamoylaniline with carbon monoxide

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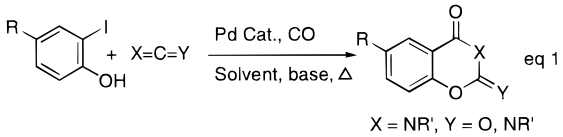
and a stoichiometric or excess amount of selenium in the presence of *N*-methylpyrrolidine afforded 2,4-(1*H*,3*H*)-quinazolinediones in fine yields.[21] A combination of $PdCl_2$-$(PPh_3)_2$ and $SnCl_2$ was reported for the intermolecular reductive N-heterocyclization of 2-nitrobenzamide to give the corresponding quinazolines.[22]

Palladium-catalyzed carbonylation reactions can serve as effective tools for the synthesis of heterocyclic-containing carbonyl moieties. The palladium-catalyzed carbonylation of aniline derivatives afforded 4*H*-3,1-benzoxazinones.[23] We recently examined the utility of palladium catalysts for the preparation of benzo[*e*]-1,3-oxazin-4-one derivatives from *o*-iodophenols with heterocumulenes and carbon monoxide (eq 1).[24]

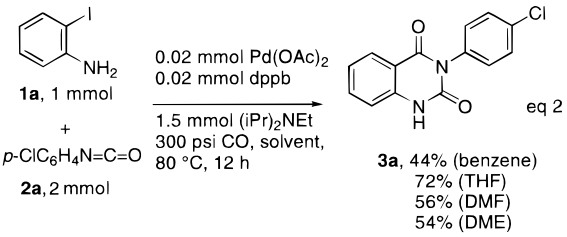


Palladium-catalyzed carbonylation of a mixture of *o*-iodoanilines and lactams resulted in 3−52% yields.[25] Encouraged by the usefulness of 4(3*H*)-quinazolinone derivatives, we decided to explore the preparation of the title compounds by palladium catalyzed cyclocarbonylation reactions of *o*-iodoanilines with heterocumulenes.

We now wish to report a convenient method for the synthesis of 4(3*H*)-quinazolinone derivatives by treatment of *o*-iodoanilines with heterocumulenes such as isocyanates, carbodiimides, and ketenimines in the presence of a palladium catalyst under carbon monoxide pressure.

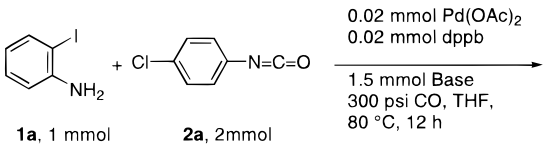
Results and Discussion

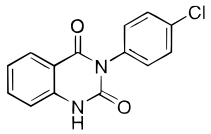
Treatment of *o*-iodoaniline, **1a** (1 mmol), and *p*-chlorophenylisocyanate, **2a** (2 mmol),[26] with 300 psi CO in benzene, in the presence of 0.02 mmol of $Pd(OAc)_2$, 0.02 mmol of 1,4-bis(diphenylphosphino)butane (dppb), and $(i\text{-}Pr)_2NEt$ for 12 h at 80 °C afforded 3-(*p*-chlorophenyl)-2,4-(1*H*,3*H*)-quinazolinedione (**3a**) in 44% isolated yield (eq 2). Performing the same reaction but using THF instead of benzene resulted in the isolation of **3a** in 72% yield. Lower product yields were obtained when using DMF (56%) or DME (54%) as the solvent.



Using the $Pd_2(dba)_3$·$CHCl_3$-dppb catalytic system under the same reaction conditions in THF furnished **3a** in 72% isolated yield. The effect of base used in the reaction was investigated in the reaction of **1a** (1 mmol) and **2a** (2 mmol) in the presence of 0.02 mmol each of $Pd(OAc)_2$ and dppb under 300 psi CO in THF, and the results are summarized in Table 1. Potassium carbonate (entry 2) gave results similar to those obtained by using diisopropylethylamine (entries 1 and 3), while slightly lower yields of **3a** resulted from the reaction using triethylamine and sodium carbonate as the base (entries 2 and 4).

Table 1. Determination of the Effect of Base on the Palladium-Catalyzed Cyclocarbonylation Reaction of 1a with 2a[a]





3a

entry	base (1.5 mmol)	isolated yield[b] (%)
1	$(^iPr)_2NEt$	72
2	Et_3N	63
3	K_2CO_3	75
4	Na_2CO_3	60

[a] Reaction conditions: **1a** (1 mmol), **2a** (2 mmol), base (1.5 mmol), $Pd(OAc)_2$ (0.02 mmol), dppb (0.02 mmol), THF (5 mL), 300 psi CO, 80 °C, 12 h. [b] Isolated yield by silica gel column chromatography.

Similar yields of **3a** were observed in the reaction of **1a** with **2a** and K_2CO_3 under 300 psi CO, in the presence of 2 mol % $Pd(OAc)_2$ in THF, using PCy_3 (71%) compared to the same reaction employing dppb as the added ligand. Higher yields of **3a** were obtained from the reaction employing PPh_3 (85%) or 1,1′-bis(diphenylphosphino) ferrocene (dppf) (88%) as the ligand. It is worth noting that the use of dppb and dppf in some cases gave the same isolated product yield. Therefore, dppb and dppf were chosen to use as added ligands in this study.

A variety of 3-substituted 2,4-(1*H*,3*H*)-quinazolinediones (**3**) can be prepared in moderate to good yields by the reaction of *o*-iodoanilines (**1**) with isocyanates (**2**) under carbon monoxide pressure in the presence of 2 mol % $Pd(OAc)_2$-bidentate phosphine (dppb or dppf) catalyst and 1.5 mol % K_2CO_3 in THF at 70−80 °C for 12 h (see Table 2 for results). Two equivalents of isocyanates to *o*-iodoaniline was used since lower product yields may be obtained if 1 equiv is used.[26] Isocyanates containing either electron-withdrawing or electron-donating groups on the aromatic ring react with *o*-iodoaniline to form 3-substituted 2,4-(1*H*,3*H*)-quinazolinediones (**3**) in good yields. *o*-Iodoaniline (**1a**), *p*-chloro-*o*-iodoaniline (**1b**), and *p*-methyl-*o*-iodoaniline (**1c**) were converted to **3** in this reaction. However, none of the desired product was isolated, using *o*-iodoaniline with a hydroxyl group

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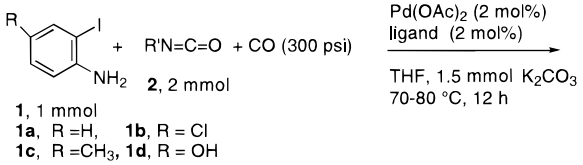
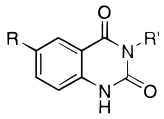
(26) As reported in ref 24, using 2 mol equiv of isocyanate in the reaction with 1 mol of *o*-iodophenol gave better product yields than performing the reaction using a 1:1 ratio, possibly because dimerization or trimerization of the isocyanate may occur in the presence of base. See: (a) Hofmann, A. W. *Ber* **1860**, *3*, 761. Snape, H. L. *J. Chem. Soc.* **1886**, *49*, 254. (b) Hofmann, A. W. *Ber* **1885**, *18*, 764.

Table 2. Cyclocarbonylation Reactions of *o*-Iodoaniline (1) with Isocyanates (2) Catalyzed by $Pd(OAc)_2$−Bidentate Phosphine Complexes[a]



1, 1 mmol
1a, R =H, **1b**, R = Cl
1c, R =CH_3, **1d**, R = OH



3

entry	**1**	R′N=C=O, **2**, R′ =	product	isolated yield[b] (%)
1	**1a**	*p*-ClC_6H4, **2a**	**3a**	88[d]
2	**1b**	**2a**	**3b**	68[d]
3	**1c**	**2a**	**3c**	72[c]
4	**1a**	*p*-BrC_6H_4, **2b**	**3d**	68[d]
5	**1a**	*p*-CH_3OC_6H4, **2c**	**3e**	80[d]
6	**1c**	**2c**	**3f**	90[c]
7	**1d**	**2c**	**3g**	0[d]
8	**1a**	C_6H_5, **2d**	**3h**	87[d]
9	**1c**	**2d**	**3i**	89[d]
10	**1a**	*p*-$CH_3C_6H_4$, **2e**	**3j**	83[c]
11	**1c**	**2e**	**3k**	77[c]

[a] Reaction conditions: **1**/**2**/K_2CO_3/$Pd(OAc)_2$/bidentate phosphine ligand, 1:2:1.5:0.02:0.02 mmol in 5 mL of THF, 70−80 °C, 300 psi CO, 12 h. [b] Isolated yield by silica gel column chromatography. [c] dppb was used in this reaction. [d] dppf was used in this reaction.

substituted at the C-4 of the phenyl ring (**1d**) in reaction with *p*-methoxyphenylisocyanate (**2c**) (entry 7). The latter may be due to competitive reactions of the hydroxyl and amine groups with the isocyanate, or to differences in the electrophilicity of the central carbon in isocyanates vs carbodiimides.

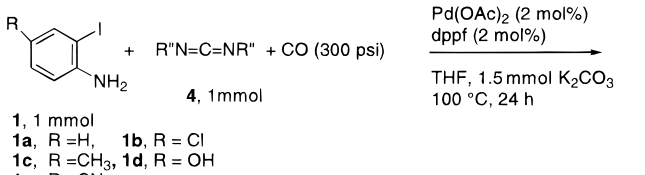
2-Amino-4(3*H*)-quinazolinones (**5**) can be prepared in moderate to good yields by utilizing the developed method with *o*-iodoaniline (**1,** 1 mmol), carbodiimide (**4,** 1 mmol), and 300 psi carbon monoxide, catalyzed by 2 mol % $Pd(OAc)_2$ and dppf in the presence of 1.5 mmol K_2CO_3 in THF at 100 °C for 24 h (Table 3).

Using *o*-iodoanilines with electron-withdrawing or electron-donating groups substituted on the phenyl ring does not have any effect on the selectivity of the reaction. The reaction tolerates nitrile as well as hydroxyl functional groups of *o*-iodoanilines (entries 4, 7, and 8). In contrast, using carbodiimides containing an electron-donating substituent on nitrogen, such as **4d**−**f**, gave recovered starting material (entries 10−12).

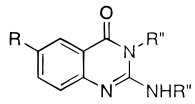
A possible mechanism for the palladium-catalyzed cyclocarbonylation reaction of *o*-iodoanilines (**1**) with isocyanates (**2**) or carbodiimides (**4**) is outlined in Scheme 1. Initial reaction of *o*-iodoaniline with an isocyanate or carbodiimide can give a urea (**6a**) or a guanidine (**6b**). Oxidative addition of the palladium catalyst to the C−I bond of **6a** or **6b** would afford **7**. Carbonyl insertion into the latter and possible coordination of the NHR″ moiety to the metal would afford the aroylpalladium intermediate **8**. Reductive elimination would result in the formation of 3-substituted-4(3*H*)-quinazolinone derivatives.

When carbodiimides are used as reactants, 4(3*H*)-quinazolinone-2-imine intermediates **9** may be generated that, on rearrangement, would afford the more stable 2-amino-4(3*H*)-quinazolinones **5** (eq 3). Evidence for this process came from the reaction of *N*-methyl-*o*-iodoaniline

Table 3. 2-Amino-(3*H*)-quinazolin-4-ones (5) from the Palladium-Catalyzed Reaction of *o*-Iodoanilines (1) with Carbodiimides (4) and Carbon Monoxide[a]



1, 1 mmol
1a, R =H, **1b**, R = Cl
1c, R =CH_3, **1d**, R = OH
1e, R =CN

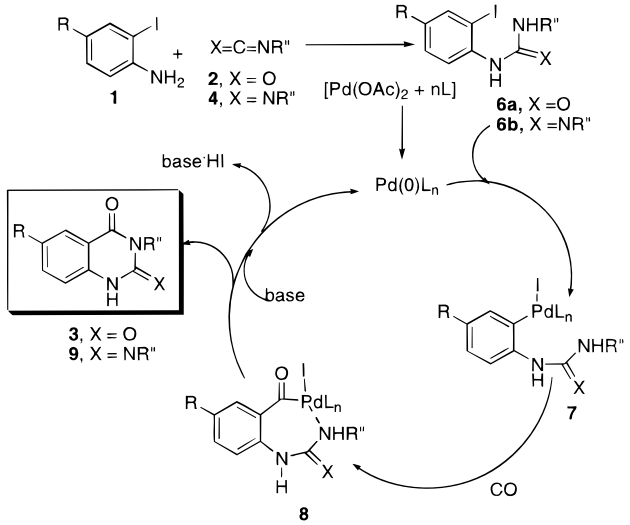


5

entry	**1**	R″N=C=NR″, **4**, R″ =	product	isolated yield[b] (%)
1	**1**	*p*-ClC_6H4, **4a**	**5a**	75
2	**1b**	**4a**	**5b**	67
3	**1c**	**4a**	**5c**	55
4	**1d**	**4a**	**5d**	90
5	**1a**	C_6H_5, **4b**	**5e**	64
6	**1b**	**4b**	**5f**	64
7	**1d**	**4b**	**5g**	78
8	**1e**	**4b**	**5h**	74
9	**1a**	*p*-BrC_6H_4, **4c**	**5i**	73 (61)[c]
10	**1a**	*p*-$CH_3C_6H_4$, **4d**		0
11	**1a**	C_6H_{11}, **4e**		0
12	**1b**	*i*C_3H_7, **4f**		0

[a] Reaction conditions: refer to the Experimental Section for the general procedure for the cyclocarbonylation of *o*-iodoanilines (**1**) with carbodiimides (**4**). [b] The products (**5**) were purified by silica gel column chromatography. [c] The yield in parentheses was obtained from the reaction using dppb as the ligand.

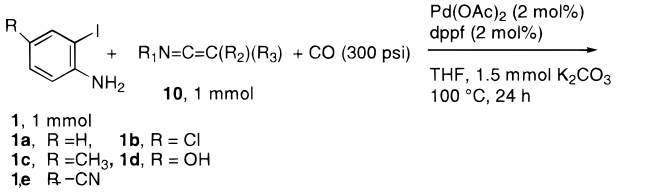
Scheme 1

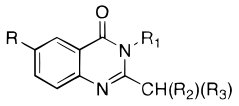


(**1f**) with bis(*p*-chlorophenyl)carbodiimide (**4a**), which under the same reaction conditions afforded 1-methyl-3-(*p*-chlorophenyl)-*N*-(*p*-chlorophenyl)-4(3*H*)-quinazolinone-2-imine (**9j**) in 61% isolated yield (eq 4). Rearrangement did not occur here, since such a process would require a methyl rather than a hydrogen transfer.

2-Alkyl-4(3*H*)-quinazolinone derivatives can be synthesized by using ketenimines rather than carbodiimides in the reaction with *o*-iodoanilines and CO. Treatment of *o*-iodoaniline (**1**) with an equimolar amount of a ketenimine (**10**) at 300 psi CO, in the presence of 2 mol % each of $Pd(OAc)_2$ and dppf, gave 2-alkyl-4(3*H*)-quinazolinones (**11**) in good to excellent isolated yields (see Table 4 for results). Ketenimines **10a**−**c** are quite

Table 4. Palladium-Catalyzed Cyclocarbonylation Reactions of *o*-Iodoanilines (1) with Ketenimines (10)[a]

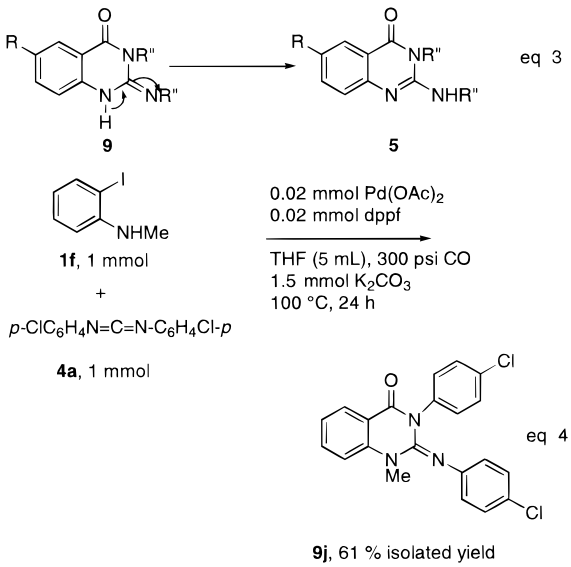




11

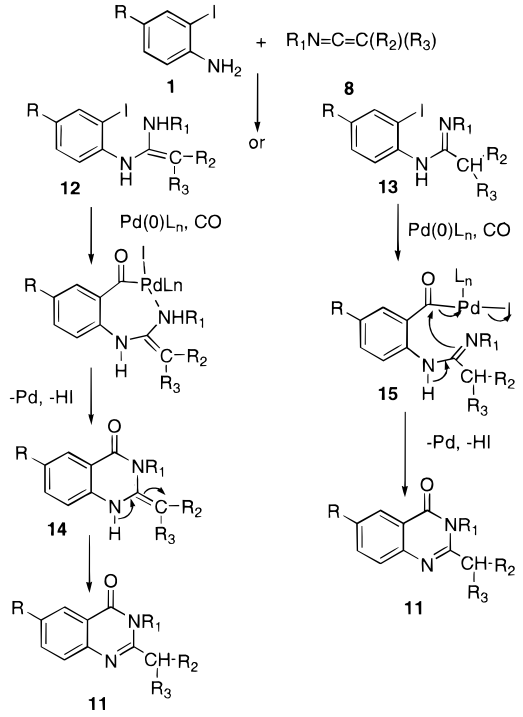
entry	1	10	product	Isolated yield[b] (%)
1	**1a**	PhN=C=C(CH$_3$)(COOEt) **10a**	**11a**	98
2	**1b**	**10a**	**11b**	87
3	**1c**	**10a**	**11c**	99
4	**1d**	**10a**	**11d**	45
5	**1e**	**10a**	**11e**	47
6	**1a**	^{n}BuN=C=C(CH$_3$)(COOEt) **10b**	**11f**	72
7	**1c**	**10b**	**11g**	74
8	**1a**	PhN=C=C(CH$_3$)(COPh) **10c**	**11h**	95
9	**1c**	**10c**	**11i**	95
10	**1a**	PhN=C=C(COOEt)$_2$	**11j**	71
11	**1b**	**10d**	**11k**	94
12	**1b**	PhN=C=C(Ph)$_2$ **10e**		0
13	**1b**	*p*-tolylN=C=C(Ph)$_2$ **10f**		0

[a] Reaction conditions: refer to the Experimental Section for the general procedure for the cyclocarbonylation of *o*-iodoanilines (**1**) with ketenimines (**10**). [b] The products (**11**) were purified by silica gel column chromatography.



stable and can be used in the reaction to obtain high product yields. However, ketenimine **10d** is not stable in air and should be kept under nitrogen at low temperature at all times. Therefore, freshly prepared **10d** gave better product yields than a sample that was kept for more than 1 month. For example, **11k** was obtained in 94% isolated yield (entry 11) when freshly prepared **10d** was used and in 60% yield using **10d** prepared 1 month earlier. Note that ketenimines, which are fully substituted with aromatic groups, do not react with *o*-iodoanilines (entries 12 and 13).

Scheme 2



The palladium-catalyzed cyclocarbonylation reaction of ketenimines with *o*-iodoanilines may proceed in a pathway similar to that of isocyanates and carbodiimides. There are two conceivable amidine intermediates that can be formed in situ from the reaction of an *o*-iodoaniline with a ketenimine, namely **12** and **13**. If **12** is formed, oxidative addition and carbonyl insertion followed by coordination of the amine unit to palladium, and subsequent reductive elimination would afford **14**. Rearrangement of **14** would form the more stable 2-alkyl-4(3*H*)-quinazolinone (**11**). An alternate pathway to **11** may involve oxidative addition and carbonyl insertion of **13** to give **15** Base-catalyzed intramolecular cyclization of **15** would form **11**.

In summary, the research reported herein constitutes simple methods for the synthesis of 2,4(1*H*,3*H*)-quinazolinediones, 2-amino-4(3*H*)-quinazolinones, and 2-alkyl-4(*3H*)-quinazolinone derivative by palladium-catalyzed cyclocarbonylation reaction of *o*-iodoanilines with isocyanates, carbodiimides, and ketenimines, respectively.

Experimental Section

General Methods. Pd(OAc)$_2$, phosphine ligands, *o*-iodoaniline (**1a**), dicyclohexylcarbodiimide (**4e**), diisopropylcarbodiimide (**4f**), and isocyanates (**2**) were purchased from commercial sources and were used as received. Carbodiimides (**4a**−**d**),[27] *p*-chloro-*o*-iodoaniline (**1b**),[28] *p*-methyl-*o*-iodoaniline (**1c**),[28] *p*-hydroxy-*o*-iodoaniline (**1d**),[29] *p*-cyano-*o*-iodoaniline (**1e**),[30] *N*-methyl-*o*-iodoaniline (**1f**),[31] ketenimines (**10a**−**c**,[32]

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10d,[33] **10e**−**f** [34]) and $Pd_2(dba)_3$·$CHCl_3$[35] were prepared according to literature procedures. Organic solvents were dried and distilled prior to use.

General Procedure for the Palladium-Catalyzed Cyclocarbonylation of *o*-Iodoanilines (1) with Isocyanates (2a−e). An autoclave, its glass liner, and a magnetic stirring bar were dried in an oven and then cooled in a desiccator before use. The liner was charged with the palladium catalyst (2 mol %), 1 equiv of bidentate phosphine ligand, and 3 mL of dried solvent. After the mixture was stirred under nitrogen for 15 min, *o*-iodoaniline (**1**, 1 mmol), isocyanate (**2**, 2 mmol), 1.5 mmol of base, and another 2 mL of solvent were added to the mixture. The autoclave was then attached to a gauge block assembly and was flushed three times with CO and pressurized to 300 psi. After 12 h in an oil bath at 70−80 °C, the autoclave was removed and allowed to cool to room temperature. The excess gas was discharged and the system disassembled. The reaction mixture was then filtered, and the filtrate was concentrated and purified by column chromatography on silica gel using 1:1 mixture of ethyl acetate/pentane as the eluant. Melting points, IR, NMR, MS, and analytical data of selected 2,4-(1*H*,3*H*)-quinazolinediones **3** are as follows (see the Supporting Information for all other examples of **3**).

3-(*p*-Chlorophenyl)-2,4-(1*H*,3*H*)-quinazolinedione (3a)[11j] (R = H, R″ = *p*-ClC_6H_4): mp 296−297 °C (lit.[11j] mp 295−296 °C); IR 1725, 1649 cm^{-1}; ^1H ($CDCl_3$ + DMSO-d_6, 200 MHz) δ 6.59−7.10 (m, 7H), 7.45 (d, 1H, J = 7.94 Hz), 10.99 (s, 1H, NH); ^{13}C ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 113.1, 114.5, 118.7, 121.6, 126.7, 127.4, 128.0, 129.2, 132.8, 134.0, 138.6, 149.3, 161.3; MS (*m*/*e*) 272 $[M]^+$.

3-(*p*-Methoxyphenyl)-2,4-(1*H*,3*H*)-quinazolinedione (3e) (R = H, R″ = *p*-$CH_3OC_6H_4$): mp 293−295 °C (lit.[11j] mp 297−299 °C); IR 1735, 1649 cm^{-1}; ^1H ($CDCl_3$ + DMSO-d_6, 200 MHz) δ 3.20 (s, 3H), 6.29 (m, 2H), 6.57−6.75 (m, 2H), 7.03−7.12 (m, 3H), 9.30 (s (br), 1H, NH); ^{13}C ($CDCl_3$ + DMSO-d_6, 75 MHz) δ 54.1, 112.6, 120.5, 123.4, 127.1, 129.8, 135.3, 148.8, 149.8, 154.3, 158.3; MS (*m*/*e*) 268 $[M]^+$. Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.02; H, 4.45; N, 10.45.

General Procedure for the Palladium-Catalyzed Cyclocarbonylation of *o*-Iodoanilines (1) with Carbodiimides (4a−f) or with Ketenimines (10a−f). The cyclocarbonylation reactions of *o*-iodoanilines with carbodiimides or ketenimines were performed in the same manner as that for isocyanates except for the use of 1 equiv of a carbodiimide or ketenimine in THF. Two mol % of the $Pd(OAc)_2$−ddpf catalyst system and K_2CO_3 were used for all reactions. The reaction mixture was stirred in an oil bath at 100 °C for 24 h, cooled, and filtered. The filtrate was concentrated and then purified by silica gel column chromatography using a 1:1 mixture of ethyl acetate/pentane as the eluant. Melting points, IR, NMR, MS, and analytical data of selected examples of of **5** and **11** are as follows. (See the Supporting Information for all other examples of **5** and **11**.)

2-(*p*-Chlorophenylamino)-3-(*p*-Chlorophenyl)-4(3*H*)-quinazolinone (5a) (R = H, R″ = *p*-ClC_6H_4): mp 175−177 °C; IR 1684, 1607 cm^{-1}; ^1H ($CDCl_3$ 200 MHz) δ 5.89 (s (br), 1H, NH), 7.22−7.66 (m, 11H), 8.15 (dd, 1H, J = 7.90, and 1.50 Hz); ^{13}C ($CDCl_3$ 75 MHz) δ 118.2, 122.2, 124.0, 125.6, 127.2, 128.9, 129.2, 130.5, 131.1, 132.7, 135.0, 136.2, 136.6, 145.7, 148.1, 162.2; MS (*m*/*e*) 380 $[M - 2]^+$, 382 $[M]^+$. Anal. Calcd for $C_{20}H_{13}Cl_2N_3O$: C, 62.84; H, 3.43; N, 10.99. Found: C, 63.00; H, 3.45; N, 10.98.

6-Methyl-2-(phenylamino)-3-phenyl-4(3*H*)-quinazolinone (5f) (R = CH_3, R″ = C_6H_5): mp 184−185 °C; IR 1686, 1606 cm^{-1}; ^1H ($CDCl_3$ 200 MHz) δ 5.98 (s (br), 1H, NH), 7.08−7.67 (m, 12H), 8.10 (d, 1H, J = 2.38 Hz); ^{13}C ($CDCl_3$ 75 MHz) δ 110.1, 121.0, 124.3, 126.4, 127.2, 128.9, 130.4, 130.9, 134.2, 135.0, 137.5, 146.5, 147.0, 161.4; MS (*m*/*e*) 346 $[M - 1]^+$, 347 $[M]^+$. Anal. Calcd for $C_{20}H_{14}ClN_3O$; C, 69.07; H, 4.06; N, 12.08. Found: C, 68.75; H, 4.11; N, 12.02.

2-(1-Ethoxycarbonylethyl)-3-phenyl-4(3*H*)-quinazolinone (11a) (R = H, R_1= C_6H_5, R_2 = CH_3, R_3 = COOEt): mp 75−76 °C; IR 1735, 1686 cm^{-1}; ^1H ($CDCl_3$ 200 MHz) δ 1.15 (m, 3H), 1.50 (m, 3H), 3.58 (m, 1H), 4.08 (m, 2H), 7.20−7.80 (m, 8H), 8.24 (m, 1H); ^{13}C ($CDCl_3$ 75 MHz) δ 13.9, 15.7, 61.3, 120.9, 126.9, 126.9, 127.5, 128.2, 129.0, 129.4, 129.9, 134.4, 136.8, 147.3, 154.6, 162.3, 171.0; MS (*m*/*e*) 322 $[M]^+$. Anal. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.58; H, 5.68; N, 8.65.

2-(1-Ethoxycarbonylethyl)-3-*n*-butyl-4(3*H*)-quinazolinone (11g) (R = H, R_1 = C_4H_9, R_2 = CH_3, R_3 = COOEt): mp 54−55 °C; IR 1744, 1681 cm^{-1}; ^1H ($CDCl_3$ 200 MHz) δ 0.95 (t, 3H), 1.17 (t, 3H), 1.43 (m, 2H), 1.63 (m, 5H), 2.42 (s, 3H), 3.92−4.21 (m, 5H), 7.50 (m, 2H), 8.00 (s, 1H); ^{13}C ($CDCl_3$ 75 MHz) δ 13.6, 14.0, 16.0, 20.1, 21.2, 31.1, 43.6, 44.1, 61.5, 120.3, 125.9, 127.1, 135.4, 136.7, 145.0, 153.8, 162.1, 170.9; MS (*m*/*e*) 316 $[M]^+$. Anal. Calcd for $C_{18}H_{24}N_2O_3$: C, 68.33; H, 7.65; N, 8.85. Found: C, 68.47; H, 7.66; N, 8.97.

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Supporting Information Available: Spectral data of compounds **3a**−**f**,**h**−**k**, **5a**−**i**, and **11a**−**k**; ^1H and ^{13}C NMR spectra of compounds **3b**,**d**, **5g**,**i**, and **11f**. This material is available free of charge via the Internet at http:/pubs.acs.org.

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