# Regioselective Palladium(II)-Catalyzed Synthesis of Five- or Seven-Membered Ring Lactones and Five-, Six- or Seven-Membered Ring Lactams by Cyclocarbonylation Methodology

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**Abstract:** 2-Allylphenols react with carbon monoxide and hydrogen in the presence of catalytic quantities of a cationic palladium(II) complex $[(PCy_3)_2Pd(H)(H_2O)]^+BF_4^-$ or palladium acetate and 1,4-bis(diphenylphosphino)butane, affording five- or seven-membered ring lactones (bicyclic, tricyclic, and pentacyclic) as the principal products, often in excellent yields. Use of 2-aminostyrenes as reactants and catalytic quantities of palladium acetate and tricyclohexylphosphine, affords five-membered ring lactams in high yield and selectivity. Bicyclic and tricyclic heterocycles containing six-membered ring lactams can be synthesized from the reaction of 2-allylanilines with $CO/H_2$ using the catalytic system $Pd(OAc)_2/PPh_3$, while use of 1,4-bis(diphenylphosphino)butane instead of $PPh_3$ in the latter process results in the formation of the seven-membered lactams benzazepinones in good yield. The regiochemical control depends on the nature of the palladium catalyst, the relative pressures of the gases, and the solvent.

Transition-metal-catalyzed carbonylation reactions are of broad applicability, in terms of both basic research and commercial applications. A specific class of carbonylation reactions concerns the intramolecular cyclization of unsaturated alcohols and amines, leading to the formation of lactones and lactams.[1−4] An attractive strategy is the use of cyclocarbonylation reactions since they can provide access to cyclic compounds which are often difficult to synthesize by other methods. Most of the lactone syntheses by this methodology are concerned with monocyclic five-membered ring lactones by the carbonylation of allylic and homoallylic alcohols.[5−8] There are no examples of the selective conversion of 2-allylphenols to lactones. We reasoned that the cyclocarbonylation of 2-allylphenols could result in the efficient syntheses of bicyclic and polycyclic lactones of different ring size.

The selective synthesis of lactams, fused to an aromatic ring, is of considerable interest due to their presence in biologically and pharmacologically active compounds.[9−12] Examples of the synthesis of 5−7-membered ring bicyclic lactams include the preparation of 2-oxindoles via radical cyclization of *o*-bromo-*N*-acryloylanilines in the presence of tri-*n*-butylstannane,[13] the photocyclization of enamides affording six-membered ring lactams in modest yields (∼40%),[14] and the photorearrangement of spirooxaziridines to form benzazepinones in 30−40% yield.[15] There are no reports, to our knowledge, on the intramolecular cyclocarbonylation of 2-aminostyrenes to form five- or six-membered ring lactams or of 2-allylanilines to give five-, six-, or seven-membered ring lactams. We anticipated that this approach would have considerable potential for the construction of the noted heterocycles.

This paper describes the synthesis of five- or seven-membered ring lactones and of five-, six-, or seven-membered ring lactams, usually in high regioselectivity, by the use of appropriate palladium catalysts, and added phosphine ligands for the reaction of allylphenols, allylanilines, or aminostyrenes with carbon monoxide and hydrogen. Noteworthy characteristics of these reactions include the dependence of regiochemical control on the nature of the palladium catalyst and phosphine ligand, the relative pressures of the gases, and the solvent.

## Results and Discussion

**Cyclocarbonylation of 2-Allylphenols.** The first reaction examined was the carbonylation of 2-allylphenol, **1a**, $R^1 = R^2 = R^3 = H$ (eq 1). Treatment of **1a** in dichloromethane with a 1/1 mixture of carbon monoxide and hydrogen, a catalytic amount of the cationic hydridoaquopalladium(II) complex[16] $Pd(PCy_3)_2(H)(H_2O)^+BF_4^-$ (**A**), and 1,4-bis(diphenylphosphino)butane (dppb; 100/1/4 ratio of **1a**/**A**/dppb), at 120 °C and 600 psi for 16 h (Table 1, entry 1) resulted in the formation of

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(1) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991; see also references cited therein.
(2) Barrett, A. G. M.; Sturgess, M. A. *Tetrahedron* **1988**, *44*, 5615.
(3) Kondo, T.; Kodoi, K.; Mitsudo, T. A.; Watanabe, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 755.
(4) Zhou, J. Q.; Alper, H. *J. Org. Chem.* **1992**, *57*, 3328. El Ali, B.; Alper, H. *J. Org. Chem.* **1991**, *56*, 5357.
(5) Chiusoli, G. P. *Transition Met. Chem.* **1991**, *16*, 553.
(6) Hosokawa, T.; Murahashi, S. I. *Heterocycles* **1992**, *33*, 1079.
(7) Tamaru, Y.; Hojo, M.; Yoshida, Z. I. *J. Org. Chem.* **1991**, *56*, 1099; Copéret, C.; Sugihara, T.; Wu, G.; Shimayama, I.; Negishi, E. I. *J. Am. Chem. Soc.* **1995**, *117*, 3422.
(8) Matsushita, K.; Komori, T.; Oi, S.; Inoue, Y. *Tetrahedron Lett.* **1994**, *35*, 5889. Alper, H.; Leonard, D. *J. Chem. Soc., Chem. Commun.* **1985**, 511. Alper, H.; Hamel, N. *J. Chem. Soc., Chem. Commun.* **1990**, 112.
(9) Raphael, R. A.; Ravenscroft, P. *J. Chem. Soc., Perkin Trans. 1* **1988**, *7*, 1823.
(10) Dueholm, K. L.; Pederson, L. B. *Synthesis* **1992**, 1.
(11) Robertson, D. W.; Krushinski, J. H.; Utterback, B. G.; Kauffman, R. F. *J. Med. Chem.* **1989**, *32*, 1476.
(12) Bjeldanes, L. F. *J. Org. Chem.* **1977**, *42*, 2333. Weidner-Wells, M. A.; Decamp, A.; Mazzocchi, P. H. *J. Org. Chem.* **1989**, *54*, 5746.
(13) Jones, K.; Thompson, M.; Wright, C. *J. Chem. Soc., Chem. Commun.* **1986**, 115.
(14) Ninomiya, I.; Hashimoto, C.; Kiguchi, T.; Naito, T. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2967.
(15) Johnson, C. P.; Marples, B. A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3399.
(16) (a) Huh, K. T.; Orita, A.; Alper, H. *J. Org. Chem.* **1993**, *58*, 6956. Piotti, M. E.; Alper, H. *J. Org. Chem.* **1994**, *59*, 1956. (b) Leoni, P.; Sommovigo, M.; Pasquali, M.; Midollini, S.; Braga, D.; Sabatino, P. *Organometallics* **1991**, *10*, 1038.

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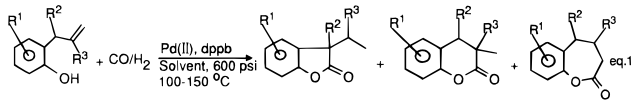
**Table 1.** Cyclocarbonylation of 2-Allylphenols by Pd(II)/dppb/CO/$H_2$[a]

| | | | | | | | | | product distribution,[c] % | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| entry | substrate | solvent | *T*, °C | time, h | $P_{CO}$, psi | $P_{H_2}$, psi | catalyst | yield,[b] % | **2** | **3** | **4** |
| 1 | **1a** | $CH_2Cl_2$ | 120 | 16 | 300 | 300 | **A** | 97 | 27 | 21 | 52 |
| 2 | **1a** | THF | 120 | 46 | 300 | 300 | **A** | 98 | 13 | 28 | 59 |
| 3 | **1a** | toluene | 120 | 16 | 300 | 300 | **A** | 93 | 1 | 7 | 92 |
| 4 | **1a** | $CH_2Cl_2$ | 120 | 16 | 100 | 500 | **A** | 98 | 76 | 18 | 6 |
| 5 | **1a** | $CH_2Cl_2$ | 120 | 16 | 500 | 100 | **A** | 48 | 14 | 70 | 16 |
| 6 | **1a** | toluene | 100 | 24 | 300 | 300 | **B** | 96 | 2 | 3 | 95 |
| 7 | **1b** | $CH_2Cl_2$ | 120 | 16 | 300 | 300 | **A** | 100 | 54 | 39 | 8 |
| 8 | **1b** | $CH_2Cl_2$ | 120 | 16 | 100 | 500 | **A** | 87 | 77 | 19 | 4 |
| 9 | **1b** | toluene | 100 | 16 | 300 | 300 | **A** | 94 | 0 | 7 | 93 |
| 10 | **1c** | $CH_2Cl_2$ | 120 | 16 | 100 | 500 | **A** | 89 | 66 | 17 | 17 |
| 11 | **1c** | toluene | 120 | 16 | 300 | 300 | **A** | 76 | 4 | 9 | 87 |
| 12 | **1d** | $CH_2Cl_2$ | 120 | 24 | 100 | 500 | **A**, **B** | traces | | | |
| 13 | **1d** | toluene | 120 | 24 | 300 | 300 | **A** | 75 | 11 | 0 | 89 |
| 14 | **1e** | $CH_2Cl_2$ | 120 | 24 | 100 | 500 | **A**, **B** | traces | | | |
| 15 | **1e** | toluene | 120 | 24 | 300 | 300 | **A** | 80 | 0 | 3 | 97 |
| 16 | **1f** | $CH_2Cl_2$ | 120 | 24 | 100 | 500 | **A**, **B** | traces | | | |
| 17 | **1f** | toluene | 120 | 24 | 300 | 300 | **B** | 85 | 1 | 1 | 98 |
| 18 | **1g** | toluene | 120 | 16 | 300 | 300 | **A** | 77 | 2 | 7 | 91 |
| 19 | **1g** | toluene | 120 | 16 | 300 | 300 | **B** | 84 | 0 | 12 | 88 |
| 20 | **1h** | toluene | 120 | 16 | 300 | 300 | **A** | 70 | 0 | 9 | 91 |
| 21 | **1i** | toluene | 120 | 24 | 300 | 300 | **A** | 95 | 0 | 0 | 100 |

[a] Reaction conditions: catalyst (0.01 mmol); **A** = $Pd(PCy_3)_2(H)(H_2O)^+BF_4^-$; **B** = $Pd(OAc)_2$; dppb (0.04 mmol); substrate (1.0 mmol); solvent (5 mL). See the general procedure. [b] Isolated yield. [c] The ratio of **2**/**3**/**4** was determined by GC and $^1$H NMR spectroscopy.




1 2 3 4

1a, $R^1$=$R^2$=$R^3$=H

1b, $R^1$=6-$CH_3$; $R^2$=$R^3$=H

1c, $R^1$=4-Cl; $R^2$=$R^3$=H

1d, $R^2$=$CH_3$; $R^1$=$R^3$=H

1e, $R^1$=4-$(CH_3)_3C$; $R^2$=$CH_3$; $R^3$=H

1f, $R^3$=$CH_3$; $R^1$=$R^2$=H

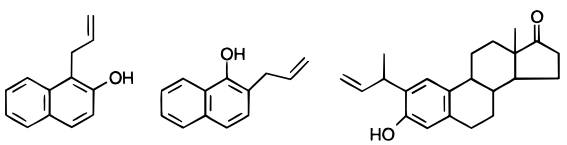
lactones in excellent yield (97%), and with moderate selectivity for the seven-membered ring heterocycle (27/21/52 ratio of **2a**/**3a**/**4a**). A quite similar product distribution resulted using tetrahydrofuran (THF) in place of $CH_2Cl_2$ (entry 2). The seven-membered ring lactone **4a** could be formed in high regioselectivity using *toluene* as the solvent (entry 3). Neutral palladium acetate (**B**) was as equally effective as the cationic complex under these conditions.

When the reaction of **1a** was conducted using a *1/5* mixture of CO/$H_2$ and catalyzed by the cationic palladium catalyst **A** and dppb in $CH_2Cl_2$ (entry 4), the five-membered ring lactone **2a** was formed in good regioselectivity (76%). It is conceivable that the use of excess $H_2$ in the mixture generates a high concentration of a palladium hydride species, [Pd−H], which can catalyze efficient double bond isomerization,[17] followed by CO insertion, giving the five-membered ring lactone as the principal product of the reaction. In contrast, the use of a 5/1 mixture of CO/$H_2$ (entry 5) afforded the six-membered ring lactone **3a** as the major product (70% of the product distribution) using **A**/dppb as the catalytic system, although in a lower total yield of lactones (48%). It is noteworthy that the reaction of **1a**, in either $CH_2Cl_2$ or toluene, *in the absence of* $H_2$, and catalyzed by **A** or **B** and dppb, gave only traces of lactones and nearly all the starting material was recovered. Other bidentate phosphine ligands such as 1,2-bis(diphenylphosphino)ethane and 1,3-bis(diphenylphosphino)propane, or a monodentate phosphine ligand such as triphenylphosphine, afforded lactones in low yields (<10%) and poor regioselectivity.

(17) Cruikshank, R.; Davies, N. R. *Aust. J. Chem.* **1966**, *19*, 815.

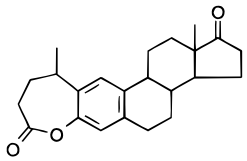
The cyclocarbonylation reaction of 2-allylphenols is relatively insensitive to electronic effects [e.g., compare **1a**−**1c** under identical conditions (Table 1, entries 4, 8, and 10 or 3, 6, and 9)]. The five-membered ring was obtained as the major product (66−79%) using $CH_2Cl_2$ as the solvent (entries 8 and 10) with a 1/5 mixture of CO/$H_2$, and the seven-membered ring lactone was formed (87−93%) (entries 9 and 11) using a 1/1 ratio of CO/$H_2$, toluene as the solvent, and **A** plus dppb as the catalytic system. Attempts to form six-membered ring lactones from **1b** and **1c** using a 5/1 mixture of CO/$H_2$ and **A**/dppb/$CH_2Cl_2$ as the catalytic system for 48 h resulted in low yields of lactones (10−20%). 2-Allylphenols **1d**, **1e**, and **1f** containing a methyl group as a substituent on the allyl chain were converted to seven-membered ring lactones in 89−95% selectivity (entries 13, 15, and 17), and in fine yields, using either palladium complex **A** or **B** as the catalyst and dppb in toluene. The selectivity for formation of the seven-membered ring products **4** is insensitive to the substitution on the allyl group. However, using $CH_2Cl_2$ as the solvent, under a variety of conditions, gave the isomerized vinylphenol (entries 12, 14, and 16). The latter compounds, in which the double bond is trisubstituted, are quite unreactive in the cyclocarbonylation reaction.

The effectiveness of this new approach for the synthesis of five- and seven-membered lactones was further demonstrated with the isomeric allylnaphthols **1g** and **1h**, and with the 2-(1-methyl-2-propenyl) derivative of the steroid estrone (**1i**). Seven-




1g 1h 1i

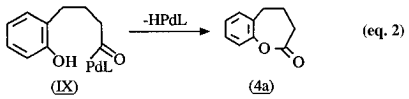
membered ring lactones were obtained in 88−91% selectivity in toluene using *either* **A** or **B**, dppb, and 1/1 CO/$H_2$ (Table 1, entries 18−20). Finally, pentacyclic **4i**, containing a seven-membered ring lactone, was isolated in 95% yield as the only product from the reaction of **1i** with CO/$H_2$, **A**, and dppb in toluene (no reaction in $CH_2Cl_2$) (Table 1, entry 21).



4i

A possible mechanism for the formation of the seven-membered ring lactone is outlined in Scheme 1 (illustrated for 2-allylphenol (**1a**)). Oxidative addition of palladium(0) (generated from **A** or **B** on exposure to CO and hydrogen) to the OH bond of **1a**, and coordination of the olefinic unit to Pd, would give **I** in which dppb is coordinated to the metal in a monodentate fashion. Intramolecular hydropalladation and coordination of carbon monoxide would form **II**. Carbonyl insertion (via ligand migration), with dppb becoming a bidentate ligand in coordinating to Pd, would afford **III**, and the lactone **4a** would arise by subsequent reductive elimination.

Competitive with the oxidative addition of Pd(O) into the OH bond of an allylphenol is the reaction with hydrogen to form a palladium hydride (**IV**; Scheme 2). Isomerization to **VI** may occur via an addition−elimination pathway (**V**)[17] which on decomplexation would generate **VII**. The five- and six-membered ring lactones can be obtained by oxidative addition of Pd(0) to **VII** to form **VIII**, with the subsequent steps being analogous to those in Scheme 1. Note that it is conceivable that, instead of oxidative addition into the OH bond of the allylphenol, the OH unit does not participate in the reaction until the final cyclization step (e.g., **IX** → **4a**, eq 2).

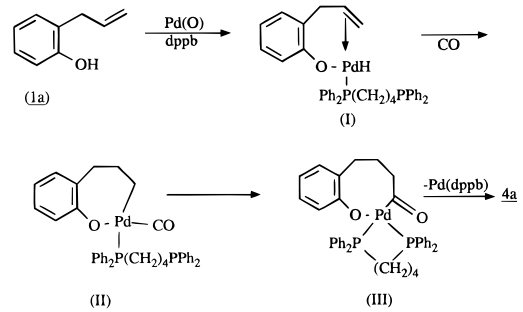


(eq. 2)

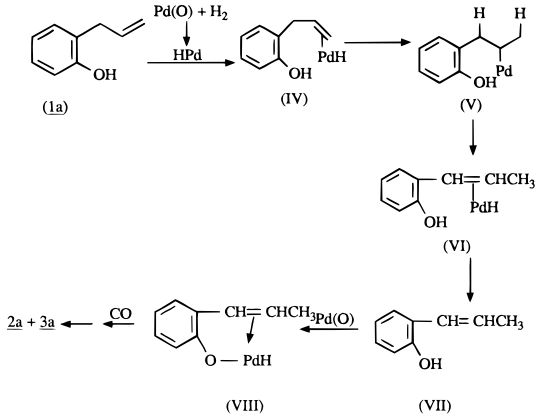
Consistent with these pathways are the following observations: (a) Use of a lower temperature for the reaction in $CH_2Cl_2$ gives the seven- rather than the five-membered ring bicyclic lactone as the major product. Specifically, when allylphenol was reacted in $CH_2Cl_2$, as described in entry 4 of Table 1, except at 70 °C for 48 h instead of 120 °C for 16 h, the combined product yield was 40% with the distribution of **2**/**3**/**4** being 2/12/86. Similarly, use of **1b** as the reactant in $CH_2Cl_2$ at 70 °C for 24 h gave **3** and **4** in a 8/92 ratio, the combined yield being 12% (compared with a 77/19/4 ratio of **2**/**3**/**4** and a total yield of 87%, using the conditions in entry 8, Table 1). The product distribution is a reflection of the extent of isomerization of the allylphenol to **VII**. At 120 °C in $CH_2Cl_2$, the isomerization is quite facile, and that is why the five-membered ring product is favored, while at 70 °C the rate of isomerization is reduced and the seven-membered ring lactone is the major product, albeit in lower combined yield. (b) When allylphenols **1d**−**1f** were reacted at 120 °C in $CH_2Cl_2$, only traces of lactones were formed. However, the isomerized *o*-vinylphenol was obtained in high yield (e.g., 81% from **1f**) in which the double bond is trisubstituted in all cases. (c) When toluene was used as the solvent, whether at 120 or 160 °C, the seven-membered ring product was the dominant one (repetition of the experiment in entry 3, Table 1, at 160 °C gave **2**/**3**/**4** in a ratio of 0/8/92, and in 87% total yield). Clearly isomerization of allylphenols is not favored in toluene, in contrast to $CH_2Cl_2$. This difference in behavior may be a consequence of the sensitivity of the isomerization reaction to solvent polarity.

**Cyclocarbonylation of 2-Aminostyrenes.** The carbonylation of a variety of 2-aminostyrenes **5a**−**j** was effected in dry dichloromethane with carbon monoxide (500 psi) and hydrogen

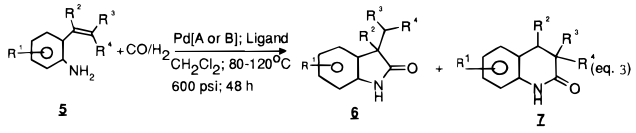
**Scheme 1**



**Scheme 2**



(100 psi) in the presence of a catalytic quantity of either neutral palladium acetate (**B**) and a monodentate (tricyclohexylphosphine or triphenylphosphine) or a bidentate [1,4-bis(diphenylphosphino)butane (dppb)] phosphine ligand, or the cationic hydridoaquopalladium complex $Pd(PCy_3)_2(H)(H_2O)^+BF_4^-$ (**A**) (eq 3). These reactions were run at 80−120 °C using a 100/1 ratio of substrate to palladium catalyst, and the results are presented in Table 2.



(eq. 3)

a) $R^1=R^2=R^3=R^4=H$
b) $R^1=R^3=R^4=H$; $R^2=CH_3$
c) $R^1=R^2=R^4=H$; $R^3=CH_3$
d) $R^1$=3-$OCH_3$; $R^2=R^4=H$; $R^3=CH_3$
e) $R^1$=4,5-O-$CH_2$-O; $R^3=CH_3$; $R^2=R^4=H$
f) $R^1=R^2=R^4=H$; $R^3$=Ph
g) $R^1=R^2=R^4=H$; $R^3$=2-Furyl
h) $R^1=R^2=R^3=H$; $R^4$=2-Furyl
i) $R^1=R^2=R^4=H$; $R^3$=2-Thienyl
j) $R^1=R^2=R^3=H$; $R^4$=2-Thienyl

The catalytic system consisting of $Pd(OAc)_2$ and tricyclohexylphosphine is an excellent one for the synthesis of five-membered ring lactams **6**. The process is completely selective for 2-aminostyrenes **5a**−**e**, affording oxindoles **6** in 86−98% yield of pure products. The reaction was less selective for 2-aminostilbene (**5f**), although the combined yield of **6** and **7** was 84%. The isomeric aminostyrenes **5g** and **5h** afforded **6** in 92−93% selectivity and reasonable yield, while lactams **6** and **7** were obtained in low combined yield in the case of the isomeric 2-thienyl systems **5i** and **5j**.

These reactions can be effected using CO alone or $CO/H_2$ (e.g., Table 2, compare entries 7, 8, 15, and 16). In comparison with $PCy_3$, the use of a less basic and less bulky phosphine, $PPh_3$, with $Pd(OAc)_2$ gave lower combined yields and reduced selectivity for **6** (e.g., **5b** afforded **6b** and **7b** in a ratio of 84/

**Table 2.** Cyclocarbonylation of 2-Aminostyrenes by Pd(II)/Ligand/CO/$H_2$[a]

| | | | | | | | | product distribution,[c] % | |
|---|---|---|---|---|---|---|---|---|---|
| entry | substrate **5** | Pd catalyst | ligand | $P_{CO}$, psi | $P_{H_2}$, psi | $T$, °C | yield,[b] % | **6** | **7** |
| 1 | **a** | **A** | dppb | 500 | 100 | 100 | 90 | 55 | 45 |
| 2 | **a** | **B** | dppb | 600 | 0 | 80 | 62 | 25 | 75 |
| 3 | **a** | **B** | $PCy_3$ | 500 | 100 | 100 | 95 | 100 | 0 |
| 4 | **b** | **A** | dppb | 500 | 100 | 100 | 75 | 0 | 100 |
| 5 | **b** | **B** | dppb | 500 | 100 | 100 | 90 | 0 | 100 |
| 6 | **b** | **B** | dppb | 600 | 0 | 100 | NR | 0 | 0 |
| 7 | **b** | **B** | $PCy_3$ | 500 | 100 | 100 | 98 | 100 | 0 |
| 8 | **b** | **B** | $PCy_3$ | 600 | 0 | 100 | 89 | 100 | 0 |
| 9 | **c** | **B** | dppb | 500 | 100 | 100 | 98 | 41 | 59 |
| 10 | **c** | **B** | dppb | 600 | 0 | 100 | NR | 0 | 0 |
| 11 | **c** | **B** | $PCy_3$ | 500 | 100 | 100 | 98 | 100 | 0 |
| 12 | **c** | **A** | $PCy_3$ | 500 | 100 | 100 | 90 | 100 | 0 |
| 13 | **d** | **B** | dppb | 500 | 100 | 100 | 30 | 61 | 39 |
| 14 | **d** | **B** | dppb | 500 | 100 | 120 | 87 | 66 | 34 |
| 15 | **d** | **B** | $PCy_3$ | 500 | 100 | 100 | 92 | 100 | 0 |
| 16 | **d** | **B** | $PCy_3$ | 600 | 0 | 100 | 88 | 100 | 0 |
| 17 | **e** | **B** | dppb | 500 | 100 | 120 | 83 | 63 | 37 |
| 18 | **e** | **B** | $PCy_3$ | 500 | 100 | 120 | 86 | 100 | 0 |
| 19 | **f** | **B** | dppb | 500 | 100 | 120 | 85 | 74 | 26 |
| 20 | **f** | **B** | $PCy_3$ | 500 | 100 | 120 | 84 | 77 | 23 |
| 21 | **f** | **B** | dppb | 600 | 0 | 120 | 64 | 69 | 31 |
| 22 | **g** | **B** | $PCy_3$ | 500 | 100 | 140 | 52 | 92 | 8 |
| 23 | **h** | **B** | $PCy_3$ | 500 | 100 | 140 | 47 | 93 | 7 |
| 24 | **i** | **B** | $PCy_3$ | 500 | 100 | 140 | 34 | 63 | 37 |
| 25 | **j** | **B** | $PCy_3$ | 500 | 100 | 140 | 24 | 63 | 37 |

[a] Reaction conditions: **B** = $Pd(OAc)_2$; **A** = $Pd(PCy_3)_2(H)(H_2O)^+BF_4^-$; 0.01 mmol of catalyst; 0.04 mmol of dppb or 0.08 mmol of $PCy_3$; 1.0 mmol of substrate; 5 mL of $CH_2Cl_2$; 48 h. See the general procedure. [b] Isolated yield. [c] The product ratio was determined by GC and $^1H$ NMR spectroscopy.

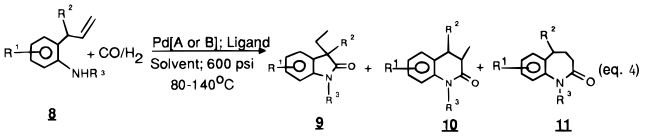
**Table 3.** Cyclocarbonylation of 2-Allylanilines by Pd(II)/Ligand/CO/$H_2$[a]

| | | | | | | | product distribution,[c] % | | |
|---|---|---|---|---|---|---|---|---|---|
| entry | substrate **8** | Pd catalyst | ligand | solvent | $T$, °C | yield,[b] % | **9** | **10** | **11** |
| 1 | **a** | **B** | $PCy_3$ | $CH_2Cl_2$ | 80 | 97 | 34 | 50 | 16 |
| 2 | **a** | **B** | $PPh_3$ | $CH_2Cl_2$ | 80 | 85 | 0 | 94 | 6 |
| 3[d] | **a** | **A** | dppb | toluene | 100 | 90 | 57 | 20 | 23 |
| 4[d] | **a** | **A** | dppb | $CH_2Cl_2$ | 100 | 85 | 32 | 38 | 30 |
| 5 | **a** | **B** | dppb | $CH_2Cl_2$ | 100 | 90 | 1 | 24 | 75 |
| 6 | **a** | **A** | $PPh_3$ | $CH_2Cl_2$ | 80 | 94 | 27 | 50 | 23 |
| 7[d] | **b** | **A** | dppb | toluene | 120 | 90 | 40 | 24 | 36 |
| 8 | **b** | **B** | dppb | $CH_2Cl_2$ | 100 | 95 | 1 | 21 | 78 |
| 9 | **b** | **B** | $PPh_3$ | $CH_2Cl_2$ | 100 | 95 | 5 | 92 | 3 |
| 10 | **c** | **B** | $PCy_3$ | $CH_2Cl_2$ | 100 | 93 | 27 | 56 | 17 |
| 11 | **c** | **B** | $PPh_3$ | $CH_2Cl_2$ | 100 | 90 | 6 | 91 | 3 |
| 12 | **c** | **B** | dppb | $CH_2Cl_2$ | 100 | 97 | 4 | 20 | 76 |
| 13[d] | **c** | **A** | dppb | toluene | 120 | 85 | 50 | 20 | 30 |
| 14 | **d** | **B** | $PCy_3$ | $CH_2Cl_2$ | 100 | 91 | 34 | 57 | 7 |
| 15 | **d** | **B** | $PPh_3$ | $CH_2Cl_2$ | 100 | 77 | 25 | 72 | 3 |
| 16 | **d** | **B** | dppb | $CH_2Cl_2$ | 120 | 96 | 10 | 38 | 52 |
| 17 | **d** | **A** | dppb | toluene | 150 | 89 | 4 | 34 | 62 |
| 18 | **e** | **B** | dppb | $CH_2Cl_2$ | 120 | 60 | 7 | 52 | 41 |
| 19 | **e** | **B** | dppb | $CH_2Cl_2$ | 140 | 84 | 20 | 64 | 24 |
| 20 | **e** | **B** | $PPh_3$ | $CH_2Cl_2$ | 140 | 86 | 13 | 71 | 18 |
| 21[d] | **e** | **A** | dppb | toluene | 140 | 70 | 11 | 70 | 18 |
| 22[d] | **f** | **A** | dppb | toluene | 140 | 96 | 51 | 24 | 25 |
| 23 | **f** | **B** | dppb | $CH_2Cl_2$ | 100 | 89 | 3 | 33 | 64 |
| 24 | **f** | **B** | $PPh_3$ | $CH_2Cl_2$ | 120 | 88 | 17 | 58 | 25 |
| 25 | **g** | **A** | dppb | toluene | 120 | 90 | 2 | 6 | 92 |
| 26 | **g** | **B** | dppb | $CH_2Cl_2$ | 120 | 84 | 4 | 12 | 84 |
| 27 | **g** | **B** | $PPh_3$ | $CH_2Cl_2$ | 100 | 79 | 23 | 30 | 47 |

[a–c] See footnotes *a*–*c* of Table 2 (same conditions except 5 mL of toluene or $CH_2Cl_2$, 0.08 mmol of $PCy_3$ or $PPh_3$, $CO/H_2$ = 5/1, 600 psi of CO + $H_2$). [d] $CO/H_2$ = 1/1.

16, with the total yield being 72%). Variable results were obtained using dppb as the ligand and either $Pd(OAc)_2$ or $Pd(PCy_3)_2(H)(H_2O)^+BF_4^-$ as the catalytic system (e.g., see Table 2, entries 1, 4, 5, and 9), with hydrogen necessary in some cases (compare entries 5 and 6, or 9 and 10) and not in others (Table 2, entries 19 and 21).

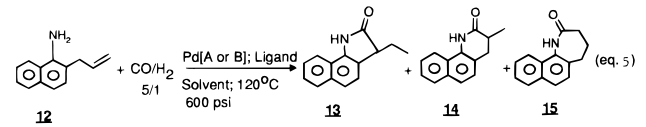
**Cyclocarbonylation of 2-Allylanilines.** Application of the $Pd(OAc)_2/PCy_3$ catalytic system to the reaction of 2-allylaniline (**8a**) with CO and $H_2$ resulted in the formation, in 97% combined yield, of a mixture of five-, six-, and seven-membered ring lactams in low selectivity (ratio of **9a**/**10a**/**11a** = 34/50/16) (Table 3, entry 1). Similar results were obtained with substrates **8c** and **8d** (Table 3, entries 10 and 14). However, the replacement of $PCy_3$ by $PPh_3$ resulted in the synthesis of six-membered ring lactams, **10** in high selectivity and good total yield of the three heterocyclic products **9**−**11** (eq 4). For




8 9 10 11

a) $R^1=R^2=R^3=H$
b) $R^1$=4-$CH_3$; $R^2=R^3=H$
c) $R^1$=4-$OCH_3$; $R^2=R^3=H$
d) $R^1$=6-$OCH_3$; $R^2=R^3=H$
e) $R^1$=4-$CO_2C_2H_5$; $R^2=R^3=H$
f) $R^1=R^2=H$; $R^3=CH_3$
g) $R^1=R^3=H$; $R^2=CH_3$

example, 2-allylaniline (**8a**) gave **10a** and **11a** in a ratio of 94/6 and in 85% total yield (entry 2). Similarly $Pd(OAc)_2/PPh_3$-catalyzed reaction of 2-allylanilines **8b**−**e** afforded the 3,4-dihydrobenzoquinolones **10b**−**e** in excellent selectivity (71−92%) and yield (entries 9, 11, 15, and 20). Although the selectivity for **10f** from **8f** is less impressive (entry 24), the results are still of synthetic merit. The process is not useful for the transformation of **8g** into **10g**. Finally, 2-allyl-1-aminonaphthalene (**12**) afforded the tricyclic compound **14**, containing a six-membered ring, in excellent yield (90%) and selectivity (88%) (eq 5).




12 13 14 15

| d cat./L | Solvent | Yield % | Product distribution, % | | |
|---|---|---|---|---|---|
| B/$PPh_3$ | $CH_2Cl_2$ | 90 | 7 | 88 | 5 |
| B/dppb | $CH_2Cl_2$ | 78 | 0 | 20 | 80 |
| A/dppb | $PhCH_3$ | 88 | 0 | 27 | 73 |

The intramolecular cyclocarbonylation reaction is remarkably sensitive to the nature of the phosphine. Substitution of monodentate $PPh_3$ by bidentate dppb in the $Pd(OAc)_2$-catalyzed reaction affords the seven-membered ring benzazepinones, in good to excellent (52−92%) selectivity and yield [see Table 3, entries 5, 8, 12, 17, 23, and 26, and the results for **12** (eq 4)]. It is noteworthy that the cationic palladium complex **A** can, with dppb in toluene, catalyze the conversion of **8g** to **11g** (entry 25) and of **12** to **15** in comparable yield and selectivity to that of $Pd(OAc)_2$/dppb. However, the process involving the cationic palladium complex is not a general one, as **8a**−**c** and **8f** gave the five-membered ring lactams **9a**−**c** (Table 3, entries 3, 7, and 13) and **9f** (Table 3, entry 22), respectively, in modest selectivity, while **8e** afforded mainly **10e** (Table 3, entry 21), and **11d** and **11g** were obtained in high yield and good selectivity from **8d** and **8g** (Table 3, entries 17 and 25), respectively.

In conclusion, this research has resulted in the first regioselective cyclocarbonylation of 2-allylphenols into lactones catalyzed by the novel cationic palladium complex $Pd(PCy_3)_2(H)(H_2O)^+BF_4^-$ or $Pd(OAc)_2$ and dppb under hydroformylation conditions. This methodology is particularly impressive for the synthesis of bicyclic, tricyclic, and pentacyclic compounds containing a seven-membered ring lactone unit. One can also achieve the synthesis of five-, six-, and seven-membered ring lactams, fused to an aromatic ring, usually in excellent selectivity and yield, from 2-aminostyrenes or 2-allylanilines. The optimum conditions for the preparation of bicyclic (or tricyclic) lactams are five-membered rings from 2-aminostyrenes with $Pd(OAc)_2$ and $PCy_3$; six-membered rings from 2-allylanilines with $Pd(OAc)_2$ and $PPh_3$, and seven-membered rings from 2-allylanilines with $Pd(OAc)_2$ and dppb. While the mechanisms for these reactions remain to be elucidated, the processes are of genuine value in organic synthesis, especially for the preparation of five- and seven-membered ring lactones and five-, six-, and seven-membered ring lactams.

## Experimental Section

**General Experimental Procedures.** All $^1H$ NMR and $^{13}C$ NMR spectra were recorded at room temperature on a Gemini 200 spectrometer or on a VXR-500 spectrometer as indicated. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane as the internal standard and referenced to the proton signal of the residual solvent ($CDCl_3$, 7.24 ppm for proton and 77.0 ppm for carbon). Mass spectra were obtained on a VG 7070 E mass spectrometer. Preparative high-performance liquid chromatography was carried out using a JAI LC-908 instrument containing a JAIGEL 2H column. Elemental analyses were performed by MHW Laboratories (Phoenix, AZ) or by the Elemental Analysis Service of the Department of Chemistry at the University of Ottawa, Canada.

**Materials.** Toluene was dried and distilled from Na/benzophenone ketyl under nitrogen prior to use. Dichloromethane was freshly distilled under nitrogen from $P_2O_5$. All chemicals were used as purchased from commercial sources. The palladium(II) complex $(PCy_3)_2Pd(H)(H_2O)^+BF_4^-$ was prepared as described in the literature.[16b] 2-Allylphenol (**1a**), 6-methyl-2-allylphenol (**1b**), and 4-chloro-2-allylphenol (**1c**) are commercially available. The following 2-allylphenols, 2-aminostyrenes, and 2-allylanilines are known compounds prepared according to literature procedures and have spectral properties in accord with literature data: **1d**,[18] **1e**,[19] **1f**,[20] **1g**,[21] **1h**,[22] **1i**,[23] **5a**,[24] **5c**,[25] **5e**,[26] **5f**,[27] **5g**−**j**,[28] **8a**,[29] **8b**,[30] **8c**,[31,32] **8e**,[30,33] **8f**,[34] **8g**,[35] and **8h**.[36]

**General Procedure for the Carbonylation of 2-Allylphenols 1.** A mixture of 1.0 mmol of **1**, 0.010 mmol of palladium(II) catalyst, and 0.04 mmol of dppb was dissolved in 5 mL of dry solvent and placed in a 45 mL autoclave. The autoclave was purged, pressurized, and then heated (see Table 1 for the time, temperature, and pressure in each case). The reaction was then cooled to room temperature, filtered through Celite or silica gel, and concentrated by rotary evaporation. The separation and the purification of lactones were achieved by silica gel chromatography and by HPLC. The products were identified by comparison of spectral data with those for authentic materials, where known, and by elemental analysis as well as by spectral data [IR, NMR ($^1H$, $^{13}C$), MS].

(18) Habich, A.; Barner, R.; Roberts, R. M.; Schmid, H. *Helv. Chim. Acta* **1962**, *45*, 1943.
(19) Sen, A. B.; Rastogi, R. P. J. *Indian Chem. Soc.* **1953**, *30*, 355.
(20) Shulgin, A. T.; Baker, A. W. *J. Org. Chem.* **1963**, *28*, 2468.
(21) Barton, D. H. R.; Fekih, A.; Lusinchi, X. *Bull. Soc. Chim. Fr.* **1988**, 681.
(22) Boddy, I. K.; Cambie, R. C.; Dixon, G.; Rutledge, P. S.; Woodgate, P. D. *Aust. J. Chem.* **1983**, *36*, 803.
(23) Patton, T. L. *J. Org. Chem.* **1962**, *27*, 910.
(24) Subramanian, C.; Noguchi, M.; Weinreb, S. M. *J. Org. Chem.* **1989**, *54*, 5580.
(25) Wehrli, R.; Heimgartner, H.; Schmid, H.; Hansen, H. J. *Helv. Chim. Acta* **1977**, *60*, 2034.
(26) Uchida, S.; Fujihara, M.; Sugasawa, S. *Yakugaku Zasshi* **1965**, *85*, 31; *Chem. Abstr.* **1965**, *63*, 577c.
(27) Ziegler, C. B. Jr.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2941.
(28) Molina, P.; Alajarin, M.; Vidal, A.; Sanchez-Andrala, P. *J. Org. Chem.* **1992**, *57*, 929.
(29) Smith, P. A. S.; Chou, S.-S. P. *J. Org. Chem.* **1981**, *46*, 3970.
(30) Hegedus, L. S.; Allen, G. F.; Bozell, J. J.; Waterman, E. L. *J. Am. Chem. Soc.* **1978**, *100*, 5800.
(31) Hino, K.; Nogai, Y.; Uno, H. *Chem. Pharm. Bull.* **1987**, *35*, 2819.
(32) Jones, K.; Thompson, M.; Wright, C. *J. Chem. Soc., Chem. Commun.* **1986**, 115.
(33) Kozugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301.
(34) Scholl, B.; Hansen, H.-J. *Helv. Chim. Acta* **1980**, *63*, 1823.
(35) Jolidan, S.; Hansen, H.-J. *Helv. Chim. Acta* **1979**, *62*, 2581.
(36) Schmid, M.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 105.

**Lactones.** The following lactones are known compounds and have spectral data in accord with the literature data: **2a**, **2b**, **3b**, **2c**, **3c**, **2d**, **3e**, **2f**, **3f**, **2g**, **3g**, and **2h**,[37] **3a**,[38] and **4a**.[39]

**Characterization Data for New Lactones. 9-Methyl-4,5-dihydro-1-benzoxepin-2(3*H*)-one (4b):** $^1$H NMR ($CDCl_3$) $\delta$ 2.04−2.22 (m, 2H), 2.25 (s, 3H), 2.44 (t, 2H, $J$ = 7.41 Hz), 2.76 (t, 2H, $J$ = 7.30 Hz), 7.00−7.08 (m, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 16.20, 26.45, 28.30, 31.05, 125.40, 127.04, 128.30, 128.60, 128.81, 15.50, 171.74; MS *m*/*e* 176 [$M^+$]. Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.53; H, 7.08.

**7-Chloro-4,5-dihydro-1-benzoxepin-2(3*H*)-one (4c):** $^1$H NMR ($CDCl_3$) $\delta$ 2.11−2.22 (m, 2H), 2.45 (t, 2H, $J$ = 7.34 Hz), 2.75 (t, 2H, $J$ = 7.33 Hz), 7.00−7.22 (m, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 26.10, 28.08, 30.90, 120.60, 128.08, 129.40, 130.70, 131.80, 150.21, 170.81; MS *m*/*e* 196 [$M^+$]. Anal. Calcd for $C_{10}H_9ClO_2$: C, 61.80; H, 4.61. Found: C, 61.75; H, 4.64.

**5-Methyl-4-hydro-1-benzoxepin-2(3*H*)-one (4d):** $^1$H NMR ($CDCl_3$) $\delta$ 1.34 (d, 3H, $J$ = 6.82 Hz), 1.52−1.56 (m, 1H), 2.20−2.40 (m, 3H), 3.20−3.35 (m, 1H), 7.10−7.40 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.00, 31.84, 31.90, 35.50, 119.80, 126.30, 126.60, 128.50, 129.0, 152.10, 172.40; MS *m*/*e* 176 [$M^+$]. Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 75.09; H, 6.88.

**5-Methyl-7-*tert*-butyl-4-hydro-1-benzoxepin-2(3*H*)-one (4e):** $^1$H NMR ($CDCl_3$) $\delta$ 1.22 (s, 9H), 1.28 (d, 3H, $J$ = 7.10 Hz), 1.44−1.64 (m, 1H), 2.34−2.38 (m, 3H), 3.00−3.18 (m, 1H), 6.56−7.40 (m, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 17.18, 30.96, 31.20, 31.30, 34.40, 34.70, 118.30, 122.20, 124.30, 132.60, 148.60, 148.90, 171.90; MS *m*/*e* 232 [$M^+$]. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.65; H, 8.58.

**4-Methyl-4,5-dihydro-1-benzoxepin-2(3*H*)-one (4f):** $^1$H NMR ($CDCl_3$) $\delta$ 0.93 (d, 3H, $J$ = 6.60 Hz), 2.04−2.10 (m, 1H), 2.43 (q, 1H, $J$ = 6.40 Hz), 2.49−2.56 (m, 3H), 2.93 (qd, 1H, $J$ = 7.44 Hz, 6.40 Hz), 7.04−7.26 (m, 4H); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.30, 33.63, 36.08, 38.48, 119.16, 125.54, 128.28, 128.94, 130.20, 151.72, 170.54; MS *m*/*e* 176 [$M^+$]. Anal. Calcd: C, 74.98; H, 6.90. Found: C, 74.60; H, 6.93.

**4,5-Dihydro-1-benzo[*g*]benzoxepin-2-(3*H*)-one (4g):** $^1$H NMR ($CDCl_3$) $\delta$ 2.20−2.40 (m, 2H), 2.50 (t, 2H, $J$ = 6.60 Hz), 3.25 (t, 2H, $J$ = 6.96 Hz), 7.26 (d, 1H, $J$ = 8.08 Hz), 7.43−7.60 (m, 2H), 7.74−7.90 (m, 2H), 7.99−8.04 (d, 1H, $J$ = 8.40 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.50, 26.60, 31.50, 119.00, 122.90, 124.30, 125.40, 127.00, 128.50, 128.80, 131.60, 131.90, 149.30, 171.10; MS *m*/*e* 212 [$M^+$]. Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.50; H, 5.70. Found: C, 79.17; H, 5.54.

**4,5-Dihydro-1-benzo[*i*]benzoxepin-2(3*H*)-one (4h):** $^1$H NMR ($CDCl_3$) $\delta$ 2.16−2.28 (m, 2H), 2.40 (t, 2H, $J$ = 7.50 Hz), 2.88 (t, 2H, $J$ = 7.20 Hz), 7.20 (d, 1H, $J$ = 8.20 Hz), 7.38−7.45 (m, 2H), 7.58 (d, 1H, $J$ = 8.24 Hz), 7.72−8.08 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 27.50, 28.44, 31.41, 121.41, 125.42, 125.50, 126.30, 126.65, 127.10, 127.60, 133.10, 133.70, 146.60, 171.84; MS *m*/*e* 212 [$M^+$]. Anal. Calcd: C, 79.50; H, 5.70. Found: C, 79.52; H, 5.58.

**Pentacyclic Lactone 4i:** $^1$H NMR ($CDCl_3$) $\delta$ 0.91 (d, 3H, $J$ = 7.20 Hz), 1.32 (d, 3H, $J$ = 6.81 Hz), 1.40−1.64 (m, 7H), 1.94−2.16 (m, 4H), 2.24−2.52 (m, 6H), 2.85−2.88 (m, 2H), 3.09−3.15 (m, 1H), 6.80 (s, 1H), 7.12 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.82, 17.50, 21.55, 25.81, 26.33, 28.97, 31.28, 31.31, 31.54, 35.02, 35.80, 38.10, 44.30, 47.90, 50.37, 119.20, 122.60, 130.70, 136.30, 137.20, 149.40, 172.20, 220.70; MS *m*/*e* 352 [$M^+$]. Anal. Calcd: C, 78.40; H, 7.95. Found: C, 78.06; H, 7.85.

**Synthesis of 2-(1-Propenyl)-6-methoxyaniline (5d). 5d** was prepared using ethyltriphenylphosphonium bromide and 3-methoxy-2-nitrobenzaldehyde:[28] yield 70%; oil [eluant *n*-hexane/ether (9/1); *Z*/*E* = 70/30; $^1$H NMR ($CDCl_3$) $\delta$ 1.72−1.77 (dd, 3H, $J$ = 1.75, 6.88 Hz) (*Z*), 1.87−1.91 (dd, 3H, $J$ = 1.69, 6.90 Hz) (*E*), 3.83−3.86 (m, 5H) (*Z* + *E*), 5.82−6.15 (m, 1H) (*Z* + *E*), 6.28−6.40 (m, 1H), 6.67−6.71 (m, 3H) (*Z* + *E*); $^{13}$C NMR ($CDCl_3$) (*Z* + *E*) $\delta$ 14.55, 18.82, 55.43, 55.52, 108.44, 115.85, 117.64, 122.09, 124.06, 134.37, 135.71, 147.23; MS *m*/*e* 163 [$M^+$]. Anal. Calcd for $C_{10}H_{13}NO$ (*Z* + *E*): C, 73.60; H, 8.03; N, 8.60. Found: C, 73.33; H, 8.18; N, 8.66.

**Synthesis of 2-Allyl-6-methoxyaniline (8d). 8d** was prepared by the Claisen rearrangement of 2-methoxy-*N*-allylaniline which can be prepared according to a literature method:[29,40] yield 40%; oil [eluant *n*-hexane/ether (9/1)]; $^1$H NMR ($CDCl_3$) $\delta$ 3.28−3.32 (m, 2H), 3.79−3.82 (m, 5H), 5.04−5.08 (m, 1H), 5.12 (d, 1H, $J$ = 0.73 Hz), 5.86−6.00 (m, 1H), 6.70 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 36.19, 55.54, 108.44, 135.71, 115.85, 117.64, 122.09, 124.06, 134.37, 147.23; MS *m*/*e* 163 [$M^+$]. Anal. Calcd for $C_{10}H_{13}NO$: C, 73.60; H, 8.03; N, 8.60. Found: C, 73.32; H, 8.00; N, 8.73.

**General Procedure for the Carbonylation of 2-Aminostyrenes 5 and 2-Allylanilines 8.** A mixture of 1.0 mmol of **5** or **8**, 0.010 mmol of palladium(II) catalyst, and 0.04 mmol of dppb or 0.08 mmol of $PPh_3$ or $PCy_3$ (see Tables 1 and 2 for the reaction conditions) was dissolved in 5 mL of dry solvent and placed in a 45 mL autoclave. The autoclave was purged, pressurized, and then heated (see Tables 1 and 2 for the time, temperature, and pressure in each case). The reaction was then cooled to room temperature, filtered through Celite or silica gel, and concentrated by rotary evaporation. The separation and the purification of lactams were achieved by silica gel chromatography and by HPLC. The products were identified by comparison of spectral data with those for authentic materials, where known, and by elemental analysis as well as by spectral data [IR, NMR ($^1$H, $^{13}$C), MS].

**Lactams.** The following lactams are known compounds and have spectral data in accord with the literature data: **6a**,[41] **7a**,[41] **6b**,[42] **7b**,[32] **6c**,[43] **7c**,[44] **7e**,[45] **6f**,[41,43] **7f**,[31] **9a or 6c**,[43] **10a or 7c**,[44] **11a**,[46] **11c**,[47] **10f**,[48] **11f**,[48] **9g**,[49] **10g**,[50] **11g**,[51] and **14**.[52]

**Characterization Data for New Lactams. 3-Ethyl-7-methoxyoxindole 6d or 9d:** $^1$H NMR ($CDCl_3$) $\delta$ 0.91 (t, 3H, $J$ = 7.33 Hz), 2.03 (qd, 2H, $J$ = 7.33 Hz, 5.48 Hz), 3.47 (t, 1H, $J$ = 5.30 Hz), 3.87 (s, 3H), 6.79−6.87 (m, 2H), 6.95−7.03 (m, 1H), 8.77 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 10.64, 24.18, 48.39, 56.28, 110.84, 117.05, 123.24, 130.99, 131.30, 144.42, 180.51; MS *m*/*e* 191 [$M^+$]. Anal. Calcd for $C_{11}H_{13}NO_3$: C, 69.08; H, 6.87; N, 7.32. Found: C, 69.16; H, 6.89; N, 7.15.

**3,4-Dihydro-8-methoxy-3-methyl-2(1*H*)-quinolinone 7d or 10d:** $^1$H NMR ($CDCl_3$) $\delta$ 1.29 (d, 3H, $J$ = 6.5 Hz), 2.64−2.75 (m, 2H), 2.94−3.02 (m, 1H), 3.86 (s, 3H), 6.75−6.79 (m, 2H), 6.90−6.98 (m, 1H), 7.75 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.25, 33.30, 34.74, 55.62, 108.83, 119.92, 112.54, 123.82, 130.23, 145.54, 173.10; MS *m*/*e* 191 [$M^+$]. Anal. Calcd for $C_{11}H_{13}NO_3$: C, 69.08; H, 6.87; N, 7.32. Found: C, 69.16; H, 6.89; N, 7.15.

**5,6-Dioxolo-3-ethyloxindole (6e):** $^1$H NMR ($CDCl_3$) $\delta$ 0.90 (t, 3H, $J$ = 7.47 Hz), 1.97 (td, 2H, $J$ = 7.47 Hz, 5.67 Hz), 3.39 (t, 1H, $J$ = 5.67 Hz), 5.93 (s, 2H), 6.51 (s, 1H), 6.75 (s, 1H), 8.60 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 9.77, 23.26, 47.37, 93.35, 100.96, 105.52, 121.11, 135.59, 143.07, 146.94, 180.84; MS *m*/*e* 208 [$M^+$]. Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.37; H, 5.41; N, 6.82. Found: C, 64.41; H, 5.36; N, 7.11.

**3-(Furylmethyl)oxindole (6g):** $^1$H NMR ($CDCl_3$) $\delta$ 2.98 (dd, 1H, $J$ = 9.50 Hz, 15.0 Hz), 3.48 (dd, 1H, $J$ = 4.65 Hz, 15.0 Hz), 3.82 (dd,

(37) Dubois, R. A. U.S. Patent 4,567,281, 1986; *Chem. Abstr.* **1986**, *105*, P42649k.

(38) Patra, A.; Misra, S. K. *Magn. Reson. Chem.* **1991**, *29*, 749. Abe, S.; Nonaka, T.; Fuchigami, T. *J. Am. Chem. Soc.* **1983**, *103*, 3630.

(39) Nicolle, J. P.; Hamon, J. F.; Wakselman, M. *Bull. Soc. Chim. Fr.* **1977**, 83.

(40) Cadogan, J. I. G.; Hickson, C. L.; McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1985**, *9*, 1885.

(41) Canoira, L.; Rodriguez, J. G. *J. Heterocycl. Chem.* **1985**, *22*, 1511.

(42) Storey, J. M. D.; McCarthy, C.; Jones, J. *J. Chem. Soc., Chem. Commun.* **1991**, 892.

(43) Beccalli, E. M.; Marchesini, A. *Synthesis* **1992**, 265.

(44) Chibani, A.; Hazard, R.; Jubault, M.; Tallec, A. *Bull. Soc. Chim. Fr.* **1987**, *5*, 795.

(45) Mali, R. S.; Yadav, V. J. *Synthesis* **1984**, *10*, 862.

(46) Weidner-Wells, M. A.; Decamp, A.; Mazzocchi, P. M. *J. Org. Chem.* **1989**, *54*, 5746.

(47) Masatsugu, T.; Shinsaku, M.; Shojiro, U. *J. Chem. Soc. C* **1969**, *2*, 183.

(48) Patapov, V. M.; Dem'yanovich, V. M.; Vendrova, O. E.; Solov'eva, L. D. *Khim. Geterotsikl. Soedin.* **1984**, *1*, 97; *Chem. Abstr.* **1984**, *100*, 174172f.

(49) Browman, W. R.; Heaney, H.; Jordan, B. M. *Tetrahedron Lett.* **1988**, *29*, 6657.

(50) Naito, T.; Toda, Y.; Ninomiya, I. *Heterocycles* **1984**, *22*, 237.

(51) Johnson, G. P.; Marples, B. A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3399.

(52) Ninomiya, I.; Hashimoto, C.; Kiguchi, T.; Naito, T. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2967.

1H, $J$ = 4.65 Hz, 9.50 Hz), 6.03 (d, 1H, $J$ = 3.07 Hz), 6.29 (dd, 1H, $J$ = 1.87 Hz, 3.07 Hz), 6.77−6.98 (m, 3H), 7.19−7.34 (m, 2H), 8.79 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 29.03, 45.17, 107.29, 109.79, 110.34, 122.22, 124.63, 128.07, 128.74, 141.42, 141.53, 151.89, 179.55; MS *m*/*e* 213 [$M^+$]. Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.21; H, 5.21; N, 6.57. Found: C, 73.17; H, 5.06; N, 6.86.

**3,4-Dihydro-3-(2-Furyl)-2-(1*H*)-quinolinone (7g):** $^1$H NMR ($CDCl_3$) $\delta$ 3.27−3.32 (m, 2H), 4.00 (t, 1H, $J$ = 7.40 Hz), 6.15 (m, 1H), 6.30 (dd, 1H, $J$ = 1.84 Hz, 2.97 Hz), 6.77−7.38 (m, 5H), 8.43 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 30.64, 40.70, 107.25, 110.32, 115.50, 122.60, 123.30, 127.71, 128.02, 136.63, 142.16, 150.83, 169.98; MS *m*/*e* 213 [$M^+$]. Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.21; H, 5.21; N, 6.57. Found: C, 72.96; H, 5.18; N, 6.64.

**3-Ethyl-5-methyloxindole (9b):** $^1$H NMR ($CDCl_3$) $\delta$ 0.92 (t, 3H, $J$ = 7.36 Hz), 1.97−2.10 (m, 2H), 2.33 (s, 3H), 3.43 (t, 1H, $J$ = 5.58 Hz), 6.73−6.84 (m, 1H), 6.95−7.26 (m, 2H), 9.45 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 9.97, 21.10, 23.52, 47.29, 109.55, 124.72, 128.00, 129.60, 131.49, 139.64, 181.30; MS *m*/*e* 175 [$M^+$]. Anal. Calcd for $C_{11}H_{13}NO$: C, 75.38; H, 7.49; N, 7.99. Found: C, 75.53; H, 7.49; N, 7.91.

**3,4-Dihydro-3,6-dimethyl-2(1*H*)-quinolinone (10b):** $^1$H NMR ($CDCl_3$) $\delta$ 1.28 (d, 3H, $J$ = 6.59 Hz), 2.29 (s, 3H), 2.63−2.76 (m, 2H), 2.92−2.98 (m, 1H), 6.74 (d, 1H, $J$ = 8.50 Hz), 6.95−6.99 (m, 2H), 9.08 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.37, 20.73, 33.35, 34.93, 115.06, 123.29, 127.78, 128.62, 132.29, 134.71, 155.04, 174.78; MS *m*/*e* 175 [$M^+$]. Anal. Calcd for $C_{11}H_{13}NO$: C, 75.38; H, 7.49; N, 7.99. Found: C, 75.57; H, 7.49; N, 8.37.

**7-Methyl-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (11b):** $^1$H NMR ($CDCl_3$) $\delta$ 2.17−2.29 (m, 4H), 2.32 (s, 3H), 2.76 (t, 2H, $J$ = 6.63 Hz), 6.88−6.92 (m, 1H), 7.02−7.27 (m, 2H), 8.41 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.94, 28.47, 30.21, 32.70, 121.71, 127.87, 130.36, 134.05, 135.25, 175.55; MS *m*/*e* 175 [$M^+$]. Anal. Calcd for $C_{11}H_{13}NO$: C, 75.38; H, 7.49; N, 7.77. Found: C, 75.32; H, 7.77; N, 8.23.

**3-Ethyl-5-methoxyoxindole (9c):** $^1$H NMR ($CDCl_3$) $\delta$ 0.92 (t, 3H, $J$ = 7.35 Hz), 1.96−2.10 (m, 2H), 3.45 (t, 1H, $J$ = 7.20 Hz), 3.79 (s, 3H), 6.70−6.86 (m, 3H), 9.23 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 9.75, 23.39, 47.58, 55.58, 109.99, 111.20, 111.93, 130.84, 135.53, 155.43, 181.00; MS *m*/*e* 191 [$M^+$]. Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.08; H, 6.87; N, 7.32. Found: C, 69.29; H, 6.88; N, 7.21.

**3,4-Dihydro-6-methoxy-3-methyl-2(1*H*)-quinolinone (10c):** $^1$H NMR ($CDCl_3$) $\delta$ 1.28 (t, 3H, $J$ = 6.55 Hz), 2.63−2.78 (m, 2H), 2.94−3.00 (m, 1H), 3.78 (s, 3H), 6.72 (s, 3H), 8.50 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 15.32, 33.69, 34.78, 55.52, 113.88, 115.96, 122.27, 124.82, 130.73, 155.40, 174.42; MS *m*/*e* 191 [$M^+$]. Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.08; H, 6.87; N, 7.32. Found: C, 68.99; H, 6.83; N, 7.71.

**1,3,4,5-Tetrahydro-9-methoxy-2*H*-1-benzazepin-2-one (11d):** $^1$H NMR ($CDCl_3$) $\delta$ 2.21−2.42 (m, 4H), 2.79 (t, 2H, $J$ = 7.33 Hz), 3.84 (s, 3H), 6.78−6.84 (m, 2H), 7.08 (t, 1H, $J$ = 7.91 Hz), 7.28 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 28.46, 30.30, 33.21, 55.54, 108.98, 121.56, 125.41, 134.77, 135.04, 150.04, 174.23; MS *m*/*e* 191 [$M^+$]. Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.08; H, 6.87; N, 7.32. Found: C, 68.91; H, 6.84; N, 7.61.

**5-Carboethoxy-3-ethyloxindole (9e):** $^1$H NMR ($CDCl_3$) $\delta$ 0.92 (t, 3H, $J$ = 7.34 Hz), 1.40 (t, 3H, $J$ = 7.14 Hz), 2.02−2.12 (m, 2H), 3.53 (t, 1H, $J$ = 7.30 Hz), 4.37 (q, 2H, $J$ = 7.14 Hz), 6.98 (d, 1H, $J$ = 8.06 Hz), 7.91−8.01 (m, 2H), 9.66 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 9.82, 14.32, 23.35, 46.92, 60.83, 109.30, 123.06, 124.50, 125.28, 130.46, 146.19, 166.49, 181.18; MS *m*/*e* 233 [$M^+$]. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.49; N, 6.01. Found: C, 67.07; H, 6.28; N, 5.85.

**6-Carboethoxy-3,4-dihydro-3-methyl-2(1*H*)-quinolinone (10e):** $^1$H NMR ($CDCl_3$) $\delta$ 1.30 (d, 3H, $J$ = 6 Hz), 1.40 (t, 3H, $J$ = 7.1 Hz), 2.72−2.85 (m, 2H), 3.03−3.10 (m, 1H), 4.37 (q, 2H, $J$ = 7.14 Hz), 6.89 (d, 1H, $J$ = 8.79 Hz), 7.87−7.92 (m, 2H), 9.24 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.35, 15.31, 33.03, 34.76, 60.86, 114.88, 123.11, 124.96, 129.42, 129.56, 141.14, 166.18, 174.67; MS *m*/*e* 233 [$M^+$]. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.49; N, 6.01. Found: C, 66.78; H, 6.25; N, 5.90.

**7-Carboethoxy-1,3,4,5-tetrahydro-2*H*-1-benzazepin-2-one (11e):** $^1$H NMR ($CDCl_3$) $\delta$ 1.41 (t, 3H, $J$ = 7.12 Hz), 2.24−2.45 (m, 4H), 2.69−2.90 (m, 2H), 4.37 (q, 2H, $J$ = 7.12 Hz), 7.06 (d, 1H, $J$ = 8.75 Hz), 7.87−7.96 (m, 2H), 8.69 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.33, 28.29, 30.40, 33.06, 61.01, 121.42, 127.34, 129.03, 131.32, 133.82, 142.19, 166.06, 175.63; MS *m*/*e* 233 [$M^+$]. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.49; N, 6.01. Found: C, 66.50; H, 6.44; N, 5.92.

**1,3,4,5-Tetrahydro-2*H*-1-benzo[*i*]benzazepin-2-one (15):** $^1$H NMR ($CDCl_3$) $\delta$ 2.22−2.31 (m, 4H), 2.87 (t, 2H, $J$ = 7.12), 7.24−7.90 (m, 6H), 8.25 (br s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 29.65, 30.70, 32.76, 121.13, 125.80, 126.12, 126.76, 127.32, 127.72, 128.28, 131.71, 132.46, 133.05, 175.88; MS *m*/*e* 211 [$M^+$]. Anal. Calcd for $C_{14}H_{13}NO$: C, 79.60; H, 6.20; N, 6.63. Found: C, 79.84; H, 6.10; N, 6.47.

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