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Reactivity of Ortho-Palladated Benzamides toward CO, Isocyanides, and Alkynes. Synthesis of Functionalized Isoindolin-1-ones and 4,5-Disubstituted Benzo[*c*]azepine-1,3-diones

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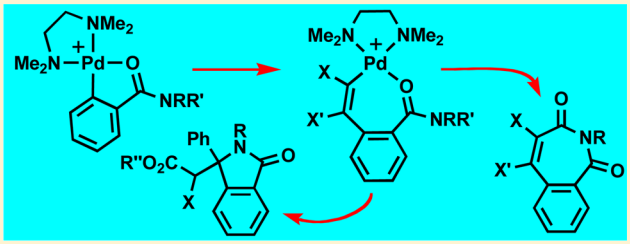
Supporting Information

ABSTRACT: Aryl palladium complexes [Pd{$C_6H_4C(O)NRR'$-2}I(tmeda)] [NRR′ = NH_2 (**1a**), NHMe (**1b**), NMe_2 (**1c**); tmeda = *N,N,N′,N′*-tetramethylethylenediamine] are prepared by oxidative addition of the corresponding 2-iodophenylbenzamides to "$Pd(dba)_2$" ($[Pd_2(dba)_3]$·dba; dba = dibenzylideneacetone) in the presence of tmeda. Cationic cyclometalated derivatives [Pd{κ^2C,O-$C_6H_4C(O)NRR'$-2}(tmeda)]TfO (**2a–c**) are obtained by iodide abstraction from the appropriate complex **1** with AgTfO, while the deprotonation of the amide function of **1a** or **1b** with KO^{t}Bu gives the neutral amidate complexes [Pd{κ^2C,N-$C_6H_4C(O)NR$-2}(tmeda)] [R = H (**3a**), Me (**3b**)]. Complexes **2a,b** and **3a,b** react with CO under mild conditions to yield phthalimide (**4a**) or *N*-methylphthalimide (**4b**), whereas the reactions of derivatives **1c** and **2c** with CO are very slow and give N^1,N^1,N^2,N^2-tetramethylphthalamide and phthalic anhydride. The reaction of **1b** with 1 equiv of XyNC (Xy = 2,6-dimethylphenyl) or ^{t}BuNC affords Pd(0), (tmedaH)I, and 3-(2,6-dimethylphenylimino)-2-methylisoindolin-1-one (**5b**) or 3-(*tert*-butylimino)-2-methylisoindolin-1-one (**5b′**), respectively, while complex **1c** reacts with 3 equiv of XyNC to give *trans*-[Pd{$C(=NXy)C_6H_4C(O)NMe_2$-2}I$(CNXy)_2$] (**6**). The seven-membered palladacycles [Pd{κ^2C,O-C(X)=C(X′)$C_6H_4C(O)NRR'$-2}(tmeda)]TfO [NRR′ = NH_2 and X = Ph, X′ = Me (**7a**); NRR′ = NHMe and X = Ph, X′ = Me (**7b**), X = X′ = Ph (**8b**), Et (**9b**), CO_2Me (**10b**), X = CO_2Me, X′ = Ph (**11b**), X = CO_2Et, X′ = Ph (**12b**); NRR′ = NMe_2 and X = X′ = Ph (**8c**), Et (**9c**)] are obtained from the reactions of **2a–c** with alkynes. Treatment of complexes **7a**, **7b**, **8b**, and **9b** with CO at room temperature gives the corresponding 2*H*-benzo[*c*]azepine-1,3-diones (**14**), resulting from the insertion of a molecule of CO into the Pd–C bond followed by a C–N reductive coupling. In contrast, the reactions of **11b** or **12b** with CO in the presence of residual water or 2 equiv of ROH (R = Me, Et) lead to 2-methyl-3-phenylisoindolin-1-one derivatives (**15**), resulting from a CO insertion followed by an intramolecular aza-Michael addition of the NHMe moiety to the activated vinyl group and subsequent hydrolysis or alcoholysis of the acyl–Pd bond. The neutral complex [Pd(κ^2C,O-$C_{14}H_{13}O_5$)(tmeda)] (**18**) was synthesized by reacting the cationic derivative **10b** with NaOMe in MeOH. Depalladation of **18** gives (*E*)-4-[methoxy(methoxycarbonyl)methylene]-2-methylisoquinoline-1,3(2*H*,4*H*)-dione (**19**).



INTRODUCTION

Ortho-palladated benzamides are involved as intermediates in certain palladium-catalyzed C–C and C–heteroatom cross-coupling processes, including methodologies for the arylation,[1] trifluoromethylation,[2] and alkenylation[3] of benzamides and the preparation of diverse heterocyclic systems.[4−7] Most often, they are produced by oxidative addition of 2-halobenzamides to Pd(0) or amide-directed C–H activations by Pd(II). Despite their important role, only a few of these complexes have been isolated and structurally characterized, and studies of their reactivity are very limited. Examples of isolated ortho-palladated benzamides include acyclic complexes of the type **I**[5,8] (Chart 1) and five-membered *C,O*-palladacycles (**II**).[6,8] Deprotonation of the amide function can lead to *C,N*-palladacyclic amidates (**III**).[2,7] To the best of our knowledge, there are no examples of *C,N*-cyclopalladated arylamides; the coordination of an amide through the nitrogen is highly unfavorable because the nitrogen lone pair is conjugated with the carbonyl group, and therefore amides usually coordinate through the oxygen atom. Several pincer-type complexes containing the type **III** structure are also known.[9] Our research group has recently reported the synthesis

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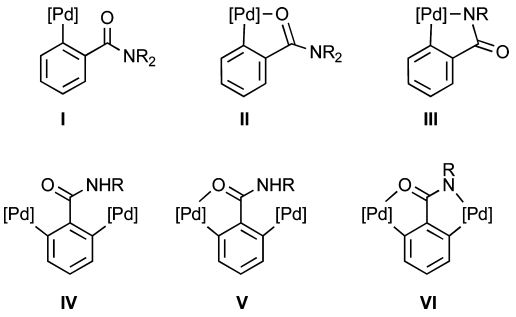
Chart 1



of ortho-dipalladated benzamides, as well as *C,O*-cyclopalladated and *C,O*/*C,N*-dicyclopalladated ("akimbo") derivatives (**IV**–**VI**).[10]

As part of our ongoing research on the reactivity of ortho-functionalized arylpalladium complexes, we have recently shown that ortho-palladated phenylacetamides[11] and 3-phenylpropanamides[12] undergo C–N reductive coupling after the insertion of CO or isocyanides into the Pd–C bond, leading to six- or seven-membered heterocycles under mild conditions. Eight- and nine-membered heterocycles were also obtained via sequential insertion of alkynes and CO into the Pd–C bond followed by reductive C–N coupling.[12,13] In this paper, we report the synthesis of a family of ortho-palladated benzamides and their *C,O*- and *C,N*-palladacyclic derivatives and the study of their reactivity toward CO, isocyanides, and alkynes, with the main objective of exploring the feasibility of heterocycle formation from these systems. A series of new functionalized isoindoline-1-ones and 4,5-disubstituted benzazepine-1,3-diones have been obtained. Both of these heterocyclic frameworks are of great importance because they are found in a variety of bioactive compounds displaying a wide range of therapeutic activities.[14] Benzazepine-1,3-diones are particularly scarce,[15] and, to the best of our knowledge, there are no precedents for 4,5-disubstituted derivatives.

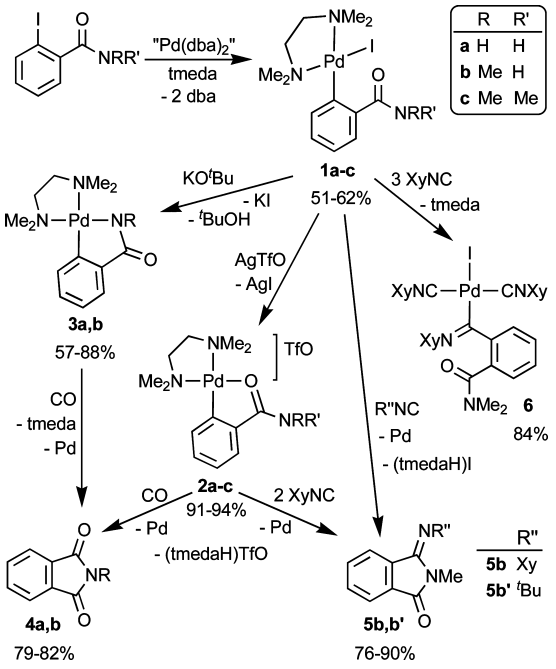
RESULTS AND DISCUSSION

Synthesis of Ortho-Palladated Benzamides and Cyclometalated Derivatives. Reactions with CO and Isocyanides. The aryl palladium complexes [Pd{$C_6H_4C(O)NRR'$-2}I(tmeda)] [NRR′ = NH_2 (**1a**), NHMe (**1b**), NMe_2 (**1c**); tmeda = *N,N,N′,N′*-tetramethylethylenediamine; Scheme 1] were obtained in moderate yields by oxidative addition of the corresponding 2-iodobenzamides to "$Pd(dba)_2$" ($[Pd_2(dba)_3]$·dba; dba = dibenzylideneacetone) in the presence of tmeda in CH_2Cl_2 at room temperature.

The cationic derivatives [Pd{κ^2*C,O*-$C_6H_4C(O)NRR'$-2}(tmeda)]TfO (**2a**–**c**) were obtained in high yields from **1a**–**c** via iodide abstraction with AgTfO. In these complexes, the amide function is coordinated through the oxygen atom, as usually observed for amide complexes,[8,10−13,16] thus forming five-membered palladacycles.

Treatment of complex **1a** or **1b** with KO^{t}Bu in MeOH led to the deprotonation of the amide function and the formation of the neutral palladacyclic derivatives [Pd{κ^2*C,N*-$C_6H_4C(O)NR$-2}(tmeda)] [R = H (**3a**), Me (**3b**)]. These complexes result from the displacement of the iodo ligand by the nitrogen of the amidate group and can be isolated in moderate to good yields. Attempts to deprotonate the methyl group in the NMe_2 derivative **1c** with KO^{t}Bu were unsuccessful.

Scheme 1



Complexes **2a,b** and **3a,b** were treated with CO (1.4 bar) in order to verify the possible CO insertion/C–N reductive coupling process. The reactions were complete in about 3 h at room temperature in acetone-D_6 (**2a,b**) or $CDCl_3$ (**3a,b**), quantitatively giving colloidal Pd, (tmedaH)TfO or free tmeda, and phthalimide (**4a**, from **2a** or **3a**) or *N*-methylphthalimide (**4b**, from **2b** or **3b**). On a preparative scale, these organic compounds were isolated in ca. 80% yield from **2a** or **2b**, respectively.

The reactions of the NMe_2 derivative **1c** or **2c** with CO were also carried out to check the possible activation of the methyl groups, which has been shown to be catalyzed by Pd(0) for a series of 2-bromo-*N*-alkyl-*N*-methylbenzamides.[5] However, complete decomposition of these complexes to Pd(0) required 3 days under CO (1.4 bar) at 68 °C in $CHCl_3$ and resulted in the formation of a mixture of (tmedaH)X (X = I^- or TfO^-), phthalic anhydride,[17] and N^1,N^1,N^2,N^2-tetramethylphthalamide,[18] which were identified by their NMR data. In addition to these products, the ESI(+) mass spectrum of the crude reaction mixture showed a small amount of *N,N*-dimethylphthalamic acid. It is reasonable to assume that this compound arises from the hydrolysis of an acyl complex by residual water, after which it undergoes internal *O*-cyclization to give phthalic anhydride and dimethylamine (Scheme 2).[19] Further molecules of the acyl complex can then undergo aminolysis by dimethylamine to give N^1,N^1,N^2,N^2-tetramethylphthalamide.

The reaction of **1b** with 1 equiv of XyNC (Xy = 2,6-dimethylphenyl) or ^{t}BuNC at room temperature gave colloidal Pd, (tmedaH)I, and 3-(2,6-dimethylphenyimino)-2-methylisoindolin-1-one (**5b**) or 3-(*tert*-butylimino)-2-methylisoindolin-1-one (**5b′**), respectively (Scheme 1), which resulted from the insertion of a molecule of isocyanide into the Pd–C bond and a subsequent intramolecular C–N coupling. The intermediate iminoacyl complex could not be isolated because it rapidly decomposed to give the organic product. Compound **5b** was also obtained from **2b** and XyNC, but in this case 2 equiv of the isocyanide was required. In contrast, the reaction of the NH_2 derivative **1a** or **2a** with 1 or 2 equiv, respectively,

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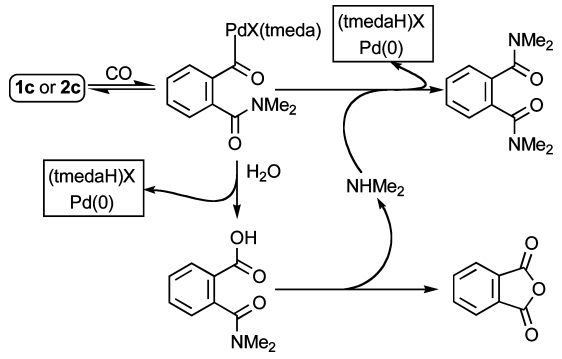
Scheme 2



of XyNC gave mixtures of two products that could not be separated, while the NMe_2 derivative **1c** reacted with 3 equiv of XyNC to give *trans*-[Pd{C(=NXy)C_6H_4C(O)NMe_2-2}I-$(CNXy)_2$] (**6**), resulting from the displacement of the tmeda ligand by two of the isocyanide molecules and the insertion of a third isocyanide into the Pd–C bond. Complex **6** was also obtained when only 1 equiv of isocyanide was employed, leaving part of the starting complex unreacted.

Insertion of Alkynes. The reactions of palladacycles **2a–c** with a series of internal alkynes XC≡CX′ at room temperature afforded good yields of the seven-membered palladacycles [Pd{κ^2C,O-C(X)=C(X′)C_6H_4C(O)NRR′-2}(tmeda)]TfO [NRR′ = NH_2, X = Ph, X′ = Me (**7a**); NRR′ = NHMe, X = Ph, X′ = Me (**7b**), X = X′ = Ph (**8b**), Et (**9b**), CO_2Me (**10b**), X = CO_2Me, X′ = Ph (**11b**), X = CO_2Et, X′ = Ph (**12b**); NRR′ = NMe_2, X = X′ = Ph (**8c**), Et (**9c**)], resulting from the insertion of one molecule of the alkyne into the Pd–C bond (Scheme 3). These reactions required an excess of the alkyne and reaction times in the range of 1–5 days to complete and were thus considerably slower than those of the six- and seven-membered palladacycles [Pd{κ^2C,O-$C_6H_4(CH_2)_n$C(O)NRR′-2}(tmeda)]-TfO (n = 1,[13] 2[12]). The insertion of alkynes into the Pd–C bond of aryl complexes requires the coordination of the alkyne and the migration of the aryl group to the coordinated alkyne. This process has been shown to be faster as the nucleophilicity of the metalated arylic carbon increases and when alkynes bearing smaller substituents or of a higher electron-withdrawing character are employed.[20] The slower alkyne-monoinsertion reactions of **2a–c** can be ascribed to the higher stability of the five-membered palladacycle, which makes the alkyne coordination step more difficult, and the lower nucleophilicity of the metalated arylic carbon caused by the electron-withdrawing amide function directly bonded to the aryl ring. The required reaction conditions for each case (Table 1) clearly reflect the effects of the NRR′ group and the alkyne. For example, the NMe_2 derivative **2c** required a lower excess of the alkyne (5-fold) and a shorter reaction time (1 day) than did the NHMe derivative **2b** for the insertion of diphenylacetylene (10-fold excess, 5 days), while in the case of the NH_2 derivative **2a** no reaction was observed with a 10-fold excess of this alkyne at room temperature. The attempts to obtain the monoinsertion products by reacting **2a** or **2b** with diphenylacetylene at higher temperatures led to partial decomposition to metallic Pd and complex mixtures. The increasing reactivity toward the insertion of alkynes in the order **2a** < **2b** < **2c** can thus be associated with an increasing nucleophilicity of the metalated arylic carbon as the number of methyl substituents of the amide function increases. The effect of the alkyne is also in line with previously observed trends,[20] as the reactions of more electrophilic or less sterically demanding alkynes with **2a** or **2b** were faster. Thus, the insertion of 1-phenylpropyne into the Pd–C bond of **2a** was feasible at room temperature, and the reaction times required in the case of **2b** decreased in the sequence diphenylacetylene > methyl phenylpropiolate ~ ethyl phenylpropiolate > 1-phenylpropyne ~ 3-hexyne ~ dimethylacetylenedicarboxylate. Compound **2a** also reacted with 3-

Scheme 3

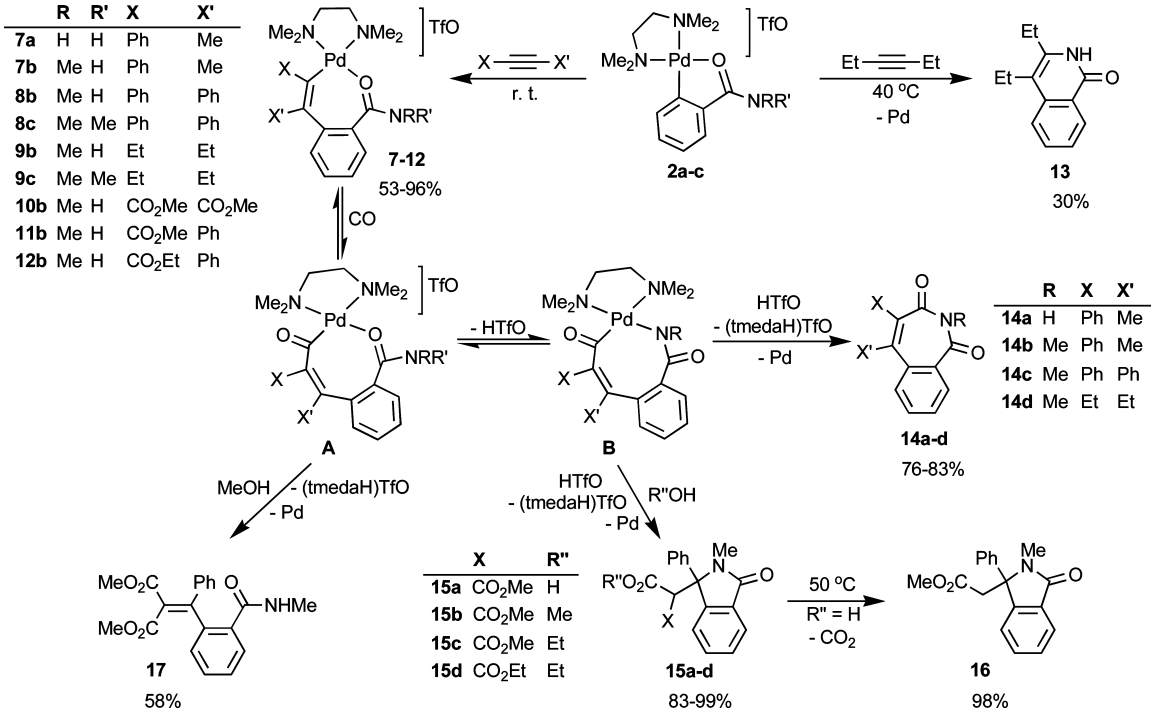


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Table 1. Molar Ratios, Reaction Times, and Yields of the Alkyne-Monoinsertion Reactions

starting complex	alkyne	molar ratio	reaction time (h)	product	yield (%)
2a	1-phenylpropyne	1:10	64	**7a**	65
2b	1-phenylpropyne	1:10	24	**7b**	76
	diphenylacetylene	1:10	120	**8b**	74
	3-hexyne	1:10	24	**9b**	53
	dimethylacetylenedicarboxylate	1:10	24	**10b**	96
	methyl phenylpropiolate	1:10	48	**11b**	71
	ethyl phenylpropiolate	1:10	48	**12b**	67
2c	diphenylacetylene	1:5	24	**8c**	88
	3-hexyne	1:5	24	**9c**	87

hexyne at room temperature, although the resulting monoinsertion product is unstable and could not be obtained in pure form; when the reaction mixture was heated at 40 °C for 24 h, a partial decomposition to colloidal Pd, (tmedaH)TfO, and 3,4-diethylisoquinolin-1(2*H*)-one[21] (**13**) was observed.

Di- or triinsertion products were not observed in any of the cases, which is striking considering the presence of an excess of alkyne and the larger size of palladacycles **7**−**12**, which should facilitate the ring-opening and the coordination of additional alkyne molecules. This is possibly associated with the relatively low nucleophilicity of the vinylic carbon bonded to Pd, because of the electron-withdrawing effect of the amide carbonyl group.

The regiochemistry of the insertions of the unsymmetrical alkynes 1-phenylpropyne, methyl phenylpropiolate, and ethyl phenylpropiolate was established by means of $^{1}H/^{13}C$ heteronuclear multiple-bond correlation (HMBC) experiments and confirmed by the crystal structures of **7a** and **11b** (see below). We have reviewed the regiochemistry of the insertion of alkynes into the Pd−C bond of aryl palladium complexes.[22] The insertion of 1-phenylpropyne led to only the regioisomer with the most sterically demanding substituent in the α-position with respect to the metal (**7a**,**b**), which is the usual pattern observed for the insertion of unsymmetrical alkynes.[23,24] However, methyl and ethyl phenylpropiolate led to an approximately 1:0.2 mixture of regioisomers, the major one with the ester group in the α-position, and only this regioisomer was isolated after workup (**11b**, **12b**). The insertion of phenylpropiolate derivatives into the Pd−C bond of five-membered palladacycles has previously been shown to give preferentially the regioisomer with the ester group in the β-position.[25] We have recently shown this also to be the case for six-membered palladacycles.[24] Nevertheless, this pattern can be reversed for palladacycles with weakly chelating aryl ligands,[22,26,27] such as **2a**−**c**, or a highly electron-deficient character.[27,28]

Reactions of Alkyne-Monoinsertion Products with CO. Palladacycles **7a**, **7b**, **8b**, and **9b** reacted with CO (1.4 bar) at room temperature in $CHCl_3$ to give colloidal Pd, (tmedaH)TfO, and the corresponding 4,5-disubstituted benzo[*c*]azepine-1,3-diones **14** (Scheme 3), resulting from a CO insertion/C−N reductive coupling sequence. The formation of these derivatives probably involves an eight-membered cyclic acyl intermediate **A**, in equilibrium with the amidate **B**, resulting from the deprotonation of the amide function. The latter would ultimately undergo the C−N reductive coupling. In line with our previous observations,[11−13] the NHMe derivatives **7**−**9b** required a longer reaction time (24 h) than did the NH_2 derivative **7a** (3 h), because the steric repulsion of the methyl substituent makes the C−N coupling slower. The reactions of the NMe_2 derivatives **8c** and **9c** with CO in $CHCl_3$ at 50 °C gave mixtures of decomposition products. The complex with inserted DMAD, **10b**, also reacted with CO in $CHCl_3$ at room temperature, but gave a mixture of at least three compounds that could not be properly identified.

The palladacycles containing inserted phenylpropiolate derivatives showed a different behavior. Thus, the room-temperature reaction of **11b** with CO (1.4 bar) in CH_2Cl_2 gave colloidal Pd, (tmedaH)TfO, and 3-[carboxy(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**15a**). The NMR data of this compound showed two sets of signals in approximately 1:1 ratio corresponding to the two possible diastereomeric pairs of enantiomers (see the Supporting Information). The cyclization to give the isoindolinone ring is formally the result of an aza-Michael addition of the NHMe moiety to the vinyl group originating from the alkyne. This process probably takes place from the amidate intermediate **B** (Scheme 3) and is certainly favored because the vinyl group is highly activated toward conjugated additions. Similar intramolecular aza-Michael additions of an amine or amide function to an α,β-unsaturated ester, ketone, or aldehyde moiety are a key step in several methodologies employed for the synthesis of isoindolines or isoindolinones.[29] Finally, the depalladation step takes place through the hydrolysis of the acyl−Pd bond by residual water. Our attempts to isolate compound **15a** from the reaction mixture were unsuccessful because decarboxylation easily occurred to give 3-(methoxycarbonylmethyl)-2-methyl-3-phenylisoindolin-1-one (**16**); indeed, the latter compound was obtained in pure form after refluxing the reaction mixture in CH_2Cl_2 for 24 h. The facile decarboxylation of phenylmalonic diacids and hemiesters is well known.[30]

When the reaction of **11b** with CO was carried out in the presence of 2 equiv of MeOH or EtOH, the same process took place, but in these cases the depalladation step is an alcoholysis leading to the diester 3-[di(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**15b**) or 3-[ethoxycarbonyl(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**15c**), respectively. Analogously, the reactions of **12b** with CO in the presence of 2 equiv of MeOH or EtOH gave **15c** or 3-[di(ethoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (**15d**), respectively.

The use of MeOH as solvent for the reaction of **11b** and CO led to the formation of dimethyl 2-((2-(methylcarbamoyl)phenyl)(phenyl)methylene)malonate (**17**), resulting from the methanolysis of the intermediate acyl complex **A**, and only trace quantities of the heterocyclic compound **15b** were detected in the reaction mixture. Logically, in the presence of a large excess of MeOH, the methanolysis of **A** is much faster than the cyclization. The attempt to cyclize **17** by heating a $CDCl_3$ solution at 70 °C for 24 h in the presence of an excess of tmeda

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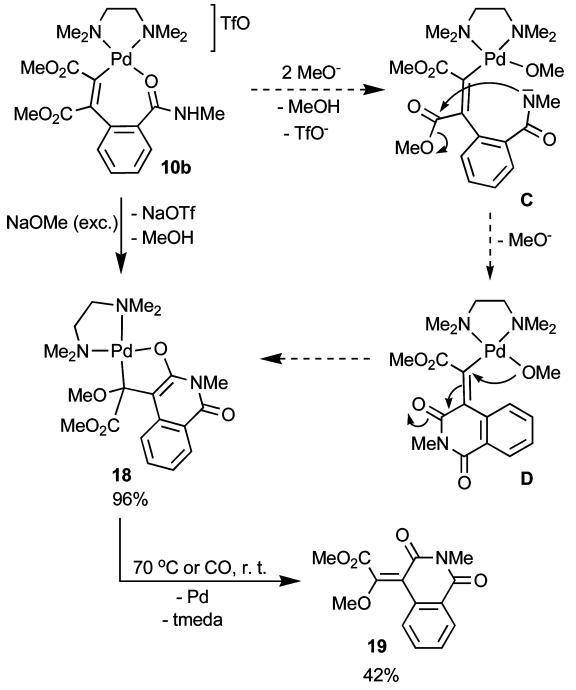
was unsuccessful, suggesting that the aza-Michael addition leading to **15a–d** is assisted by the Pd(II) center, which is consistent with the participation of an amidate intermediate.

Formation and Depalladation of a Neutral Alkyl-Alcoholate Complex. The deprotonation of the amide function in complex **10b** with NaOMe was attempted in order to obtain a seven-membered cyclic amidate and use it as a precursor for the preparation of an additional benzo[*c*]azepine-1,3-dione derivative. However, the reaction of this complex with excess NaOMe in MeOH led to the formation of the unexpected neutral complex [Pd(κ^2*C*,*O*-$C_{14}H_{13}O_5$)(tmeda)] (**18**), which contains a chelating alkyl-alcoholate ligand based on the isoquinoline-1,3-dione scaffold (Scheme 4). The formation of this ligand must involve the nucleophilic attack of an amidate group (intermediate **C**) to the ester group in β with respect to the metal to generate a six-membered cyclic imide (**D**). Subsequently a methoxide anion would attack the metalated carbon atom.

Scheme 4



The depalladation of complex **18** was achieved by refluxing it in $CHCl_3$ for 2 d and led to the organic compound (*E*)-4-[methoxy(methoxycarbonyl)methylene]-2-methylisoquinoline-1,3(2*H*,4*H*)-dione (**19**). The same product was observed by ^{1}H NMR after reacting complex **18** with CO (1.4 bar) in $CDCl_3$ for 6 h at room temperature (93%). In this case the insertion of CO into the Pd–C bond did not take place, but probably the excess CO assisted the reduction process.

Crystal Structures. The structure of **2a** is shown in Figure 1. The amide group is coordinated to the Pd atom through the oxygen, forming a practically planar five-membered *C*,*O*-palladacycle [mean deviation from plane Pd–C1–C2–C7–O1: 0.03 Å]. The square-planar coordination environment around the Pd center is slightly distorted, because of the small bite of both the chelating benzamide unit [angle C(1)–Pd–O(1): 82.38(6)°] and the tmeda ligand [angle N(2)–Pd–N(3): 85.43(7)°]. The Pd–O(1) bond distance of 2.0220(12) Å is similar to that found for the ortho-palladated benzamide derivative [Pd{κ^2*C*,*O*-C_6H_4{C(O)NH^{t}Bu}-6-$(OMe)_3$-2,3,4}-(bpy)]TfO [2.009(2) Å].[8] The two H atoms of the NH_2 group are involved in hydrogen bonds with two oxygen atoms of different triflate anions, forming infinite chains parallel to [110].

The amidate group of **3a** is coordinated to the Pd atom through the nitrogen atom, forming an almost planar (mean deviation: 0.05 Å) five-membered ring (Figure 2). The Pd–N(1) bond distance of 1.9943(16) Å is similar to or slightly shorter than that found for previously reported five-,[10,31] six-,[11,32] or seven-membered[12] cyclic palladium amidate complexes. The O(1)–C(7) bond distance of 1.252(2) Å is longer than the average C–O distance found in amides (1.234 Å),[33] as expected because of the delocalization of the negative charge over the N–C═O group. The molecules are connected

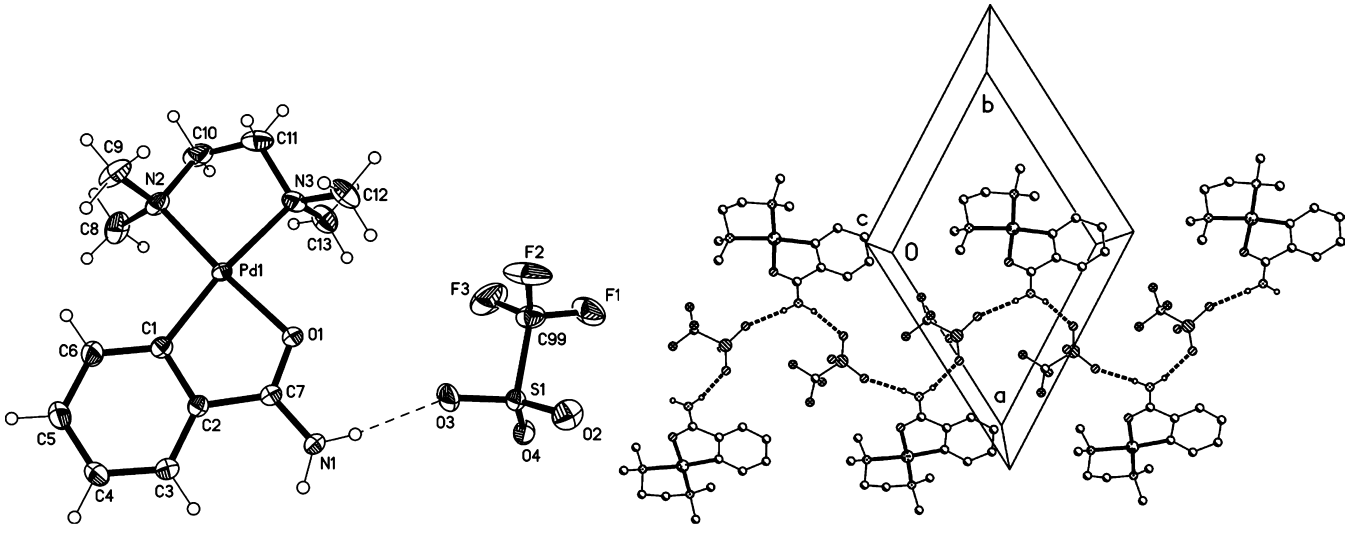


Figure 1. Left: Thermal ellipsoid plot (50% probability) of complex **2a**. Selected bond distances (Å) and angles (deg): Pd–C(1) 2.0025(18), Pd–O(1) 2.0220(12), Pd–N(2) 2.0728(15), Pd–N(3) 2.1494(16), O(1)–C(7) 1.272(2), N(1)–C(7) 1.318(2); C(1)–Pd–O(1) 82.38(6), N(2)–Pd–N(3) 85.43(7), C(7)–O(1)–Pd 114.03(11), O(1)–C(7)–C(2) 118.02(15), N(1)–C(7)–C(2) 123.10(16). Right: Chain of residues connected by hydrogen bonds (dashed bonds).

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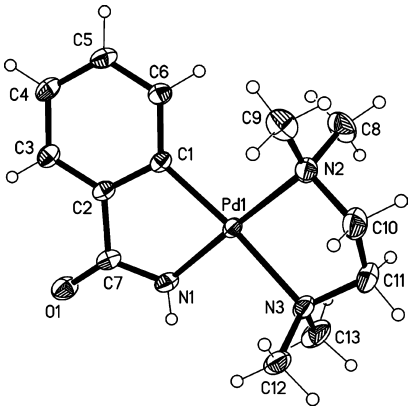

Figure 2. Thermal ellipsoid plot (50% probability) of complex **3a**. Selected bond distances (Å) and angles (deg): Pd–N(1) 1.9943(16), Pd–C(1) 2.0058(15), Pd–N(2) 2.1228(16), Pd–N(3) 2.1575(14), O(1)–C(7) 1.252(2), N(1)–C(7) 1.328(2); N(1)–Pd–C(1) 80.56(6), N(2)–Pd–N(3) 84.15(6), C(7)–N(1)–Pd(1) 119.03(12), O(1)–C(7)–C(2) 122.59(15), N(1)–C(7)–C(2) 110.83(15).

to form inversion-symmetric dimers by a hydrogen bond N1–H01···O1.

The crystal structures of complexes **7a** (Figure 3) and **11b** (Figure 4) show that the 1-phenylpropyne or methyl phenylpropiolate molecule, respectively, has inserted in a syn fashion and the amide function remains coordinated to the metal through the oxygen. The resulting ring shows a folded conformation dictated by the constraints of the planar vinyl, benzene, and amide groups; the atoms C1, C2, C9, and O1 are essentially coplanar, with the atoms Pd, C3, and C4 lying ca. 1.2, 0.9, and 0.9 Å to the same side of the plane. The Pd atom is in a square planar environment, slightly distorted by the small bite of the tmeda ligand and the strain of the seven-membered ring. The latter leads to a C(1)–Pd–O(1) angle of 86.17(7)° (**7a**) or 85.50(6)° (**11b**), which is appreciably narrower than the corresponding angle in the larger palladacycles [Pd{κ^2*C*,*O*-C(Ph)=C(Ph)$C_6H_4(CH_2)_n$C(O)NH_2-2}(tmeda)]TfO (n = 1, 94.00°;[13] n = 2, 90.47°[12]). In **7a**, the H atoms of the NH_2 group are involved in hydrogen bonds with one oxygen atom of a triflate anion and another oxygen atom of an adjacent molecule, forming inversion-symmetric dimers. In **11b**, the NHMe group is connected to the triflate anion through a hydrogen bond.

The crystal structure of compound **14b** is shown in Figure 5. The seven-membered ring shows a twisted conformation (N2, C3, C4 lie 0.7, 1.4, 0.65 Å to the same side of the plane C1–C9A–C5A–C5) involving a nonplanar imide group (angle of 48° between the C(9A)–C(1)–O(1)–N(2) and C(4)–C(3)–O(2)–N(2) mean planes). Only a few structures of cyclic imides of this size have been reported to date, and these display a similar conformation.[34]

Compound **15b** crystallized with two independent molecules in the asymmetric unit (Figure 6), for which a least-squares fit gave an rms deviation of 0.28 Å. The bond distances and angles within the isoindoline fragment are comparable to those found in analogous compounds.[35]

The structure of complex **18** (Figure 7) proved to be a CH_2Cl_2 monosolvate. It shows the isoquinoline-1,3-dione-based ligand coordinated through one of the oxygen atoms and the deprotonated methoxy(methoxycarbonyl)methyl group, forming a nearly planar five-membered palladacycle (mean deviation 0.04 Å). The Pd–O(1) distance of 2.0267(11) Å is comparable to that found in some Pd(II) phenolato complexes.[36]

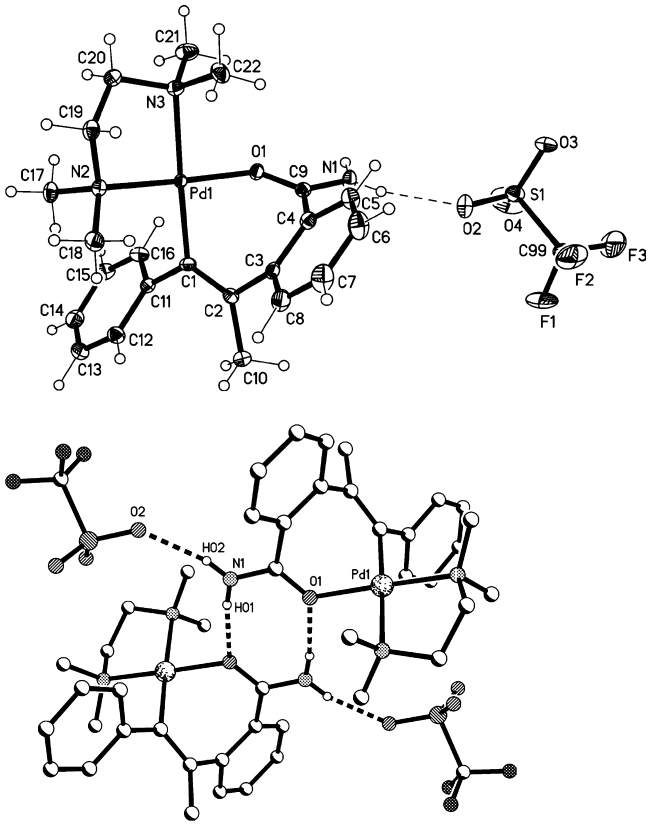

Figure 3. Above: Thermal ellipsoid plot (50% probability) of complex **7a**. Selected bond distances (Å) and angles (deg): Pd–C(1) 1.9936(19), Pd–O(1) 2.0525(13), Pd–N(2) 2.0672(16), Pd–N(3) 2.1715(17), O(1)–C(9) 1.266(2), N(1)–C(9) 1.317(3), C(1)–C(2) 1.344(3); C(1)–Pd–O(1) 86.17(7), N(2)–Pd–N(3) 85.37(6), C(9)–O(1)–Pd 120.42(13), C(2)–C(1)–Pd 118.94(15), C(1)–C(2)–C(3) 120.85(18), O(1)–C(9)–C(4) 122.54(17), N(1)–C(9)–C(4) 118.43(18). Below: Inversion-symmetric dimer of **7a** connected by hydrogen bonds (dashed lines).

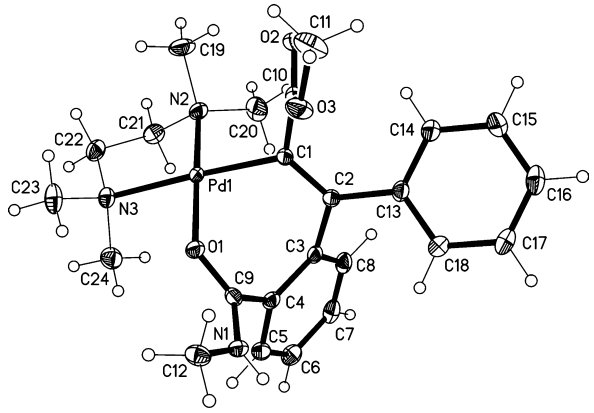

Figure 4. Thermal ellipsoid plot (50% probability) the cation of complex **11b**. Selected bond distances (Å) and angles (deg): Pd–C(1) 1.9962(18), Pd–O(1) 2.0580(12), Pd–N(2) 2.0628(15), Pd–N(3) 2.1474(15), C(1)–C(2) 1.345(3), C(9)–O(1) 1.265(2); C(1)–Pd–O(1) 85.50(6), N(2)–Pd–N(3) 85.14(6), C(2)–C(1)–C(10) 124.58(17), C(2)–C(1)–Pd 119.59(14), C(9)–O(1)–Pd 117.92(12), C(1)–C(2)–C(3) 119.39(17), O(1)–C(9)–N(1) 120.28(17), O(1)–C(9)–C(4) 123.27(16).

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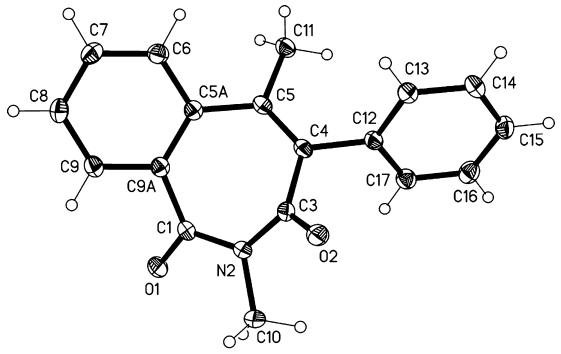

Figure 5. Thermal ellipsoid plot (50% probability) of compound **14b**. Selected bond distances (Å) and angles (deg): C(1)−O(1) 1.2194(12), C(1)−N(2) 1.3901(13), C(1)−C(9A) 1.4982(14), N(2)−C(3) 1.4036(13), C(3)−O(2) 1.2164(12), C(3)−C(4) 1.4941(13), C(4)−C(5) 1.3458(14); O(1)−C(1)−N(2) 119.25(9), O(1)−C(1)−C(9A) 120.27(9), N(2)−C(1)−C(9A) 120.06(8), C(1)−N(2)−C(3) 126.46(8), O(2)−C(3)−N(2) 119.37(9), O(2)−C(3)−C(4) 120.86(9), N(2)−C(3)−C(4) 118.85(8), C(5)−C(4)−C(3) 125.71(9), C(4)−C(5)−C(5A) 123.11(9).

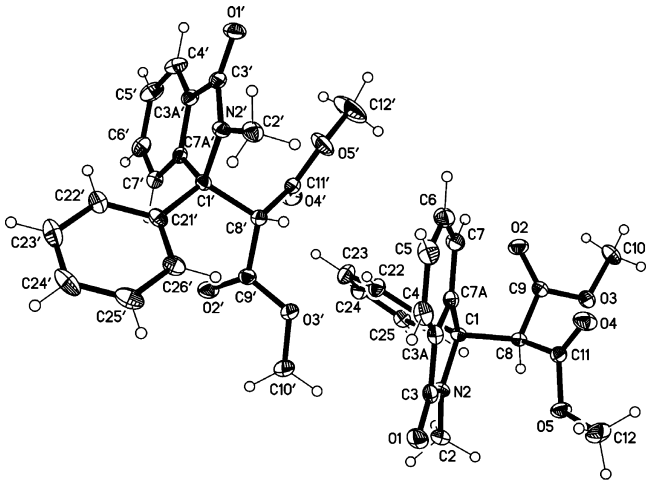

Figure 6. Thermal ellipsoid plot (50% probability) of compound **15b**. Selected bond distances (Å) and angles (deg): O(1)−C(3) 1.2290(15), C(1)−N(2) 1.4877(15), C(1)−C(7A) 1.5303(17), N(2)−C(3) 1.3591(16), C(3)−C(3A) 1.4763(18), C(3A)−C(7A) 1.3883(17); N(2)−C(1)−C(7A) 100.41(9), N(2)−C(1)−C(21) 109.52(9), C(7A)−C(1)−C(21) 113.89(10), N(2)−C(1)−C(8) 107.48(9), C(7A)−C(1)−C(8) 112.89(10), C(21)−C(1)−C(8) 111.81(10), C(3)−N(2)−C(2) 121.38(10), C(3)−N(2)−C(1) 113.92(10), C(2)−N(2)−C(1) 124.33(10), O(1)−C(3)−N(2) 125.31(12), O(1)−C(3)−C(3A) 128.18(12), N(2)−C(3)−C(3A) 106.50(10).

The crystal structure of compound **19** (Figure 8) reveals that the C4−C9 double bond has an *E* configuration, which must be the most sterically favored.

CONCLUSIONS

Ortho-palladated benzamides can be obtained by oxidative addition of 2-iodobenzamide or its *N*-methyl- or *N,N*-dimethyl-substituted derivatives to $Pd(dba)_2$ in the presence of tmeda. Five-membered cationic *C,O*- or neutral *C,N*-palladacyclic derivatives are easily accessible via iodide abstraction or deprotonation of the NH_2 or NHMe group, respectively. The insertion of CO or isocyanides into the Pd−C bond of some of these complexes triggers C−N reductive coupling under mild

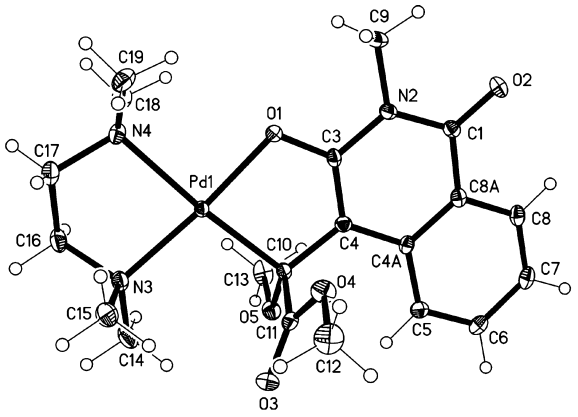

Figure 7. Thermal ellipsoid plot (50% probability) of complex **18**. Selected bond distances (Å) and angles (deg): Pd−O(1) 2.0267(11), Pd−C(10) 2.0635(14), Pd−N(3) 2.1058(12), Pd−N(4) 2.1783(12), C(1)−O(2) 1.2422(19), C(1)−N(2) 1.388(2), N(2)−C(3) 1.3967(19), C(3)−O(1) 1.3075(18), C(3)−C(4) 1.368(2), C(4)−C(10) 1.507(2); O(1)−Pd−C(10) 84.38(5), N(3)−Pd−N(4) 83.42(5), C(4)−C(10)−Pd(1) 105.48(9), C(3)−O(1)−Pd 110.72(10), C(1)−N(2)−C(3) 122.90(13), O(1)−C(3)−C(4) 122.66(15), O(1)−C(3)−N(2) 116.22(14), C(4)−C(3)−N(2) 121.10(15), C(3)−C(4)−C(10) 115.87(14), C(3)−C(4)−C(4A) 119.76(15).

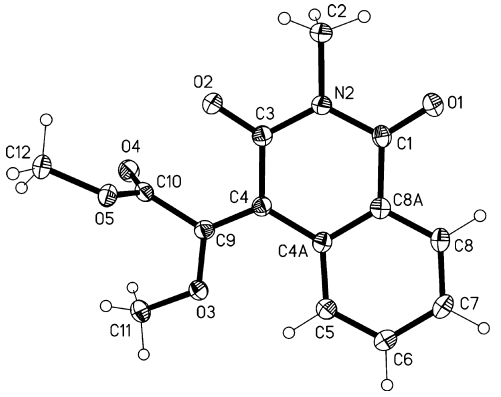

Figure 8. Thermal ellipsoid plot (50% probability) of compound **19**. Selected bond distances (Å) and angles (deg): O(1)−C(1) 1.2194(14), O(2)−C(3) 1.2285(14), C(1)−N(2) 1.3917(14), C(1)−C(8A) 1.4820(15), N(2)−C(3) 1.3823(14), C(3)−C(4) 1.4838(15), C(4)−C(9) 1.3573(16), C(4)−C(4A) 1.4707(15); O(1)−C(1)−N(2) 120.45(10), O(1)−C(1)−C(8A) 122.68(10), N(2)−C(1)−C(8A) 116.86(9), C(3)−N(2)−C(1) 125.01(9), C(3)−N(2)−C(2) 116.94(9), C(1)−N(2)−C(2) 118.03(9), O(2)−C(3)−N(2) 119.41(10), O(2)−C(3)−C(4) 122.24(10), N(2)−C(3)−C(4) 118.34(10), C(9)−C(4)−C(4A) 126.22(10), C(9)−C(4)−C(3) 114.69(10), C(4A)−C(4)−C(3) 119.08(10).

conditions, leading to the formation of isoindoline-1,3-diones (phthalimides) or 3-iminoisoindolin-1-ones.

Cationic *C,O*-cyclopalladated benzamides react with internal alkynes to give seven-membered palladacycles resulting from the insertion of the alkyne into the Pd−C bond. These insertions are, in general, much slower than those from analogous cyclopalladated phenylacetamides and 3-phenylpropanamides previously reported by us, presumably because of the higher stability of the five-membered palladacyclic precursors and the lower nucleophilicity of the metalated carbon of the benzamide. In addition, the substitution degree of the amidic nitrogen clearly affects the rate of the insertion

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reaction, which increases significantly with the number of methyl substituents. Two different types of heterocyclic compounds can be obtained from the reactions of the enlarged palladacycles with CO, depending on the nature of the inserted alkyne. Thus, the complexes containing inserted 1-phenylpropyne, diphenylacetylene, or 3-hexyne (NH_2 or NHMe derivatives) lead to 4,5-disubstituted benzo[*c*]azepine-1,3-diones, resulting from a CO insertion into the Pd−C bond followed by a C−N reductive coupling. For the complexes with inserted methyl or ethyl phenylpropiolate (NHMe derivatives), an aza-Michael addition of the NHMe moiety to the vinyl group takes place after the insertion of CO, finally leading to the formation of isoindolin-1-one derivatives.

EXPERIMENTAL SECTION

General Considerations, Materials, and Instrumentation. Unless otherwise noted, all preparations were carried out at room temperature under atmospheric conditions. Synthesis grade solvents were obtained from commercial sources. CH_2Cl_2 was degassed and dried using a Pure Solv MD-5 solvent purification system from Innovative Technology, Inc. The compound $[Pd_2(dba)_3]$·dba was prepared according to the published procedure.[37] The preparations of 2-iodo-*N*-methylbenzamide and 2-iodo-*N*,*N*-dimethylbenzamide are given in the Supporting Information. All other reagents were obtained from commercial sources and used without further purification. NMR spectra were recorded on Bruker Avance 200, 300, or 400 spectrometers at 298 K. Chemical shifts are referred to internal TMS. The assignments of the ^1H and $^{13}C\{^1H\}$ NMR spectra were made with the help of HMBC and HMQC experiments. Inserted and coordinated XyNC are denoted by $XyNC^i$ and $XyNC^c$, respectively, and the 1,2-C_6H_4 arylene group is denoted by Ar. Melting points were determined on a Reichert apparatus and are uncorrected. Elemental analyses were carried out with Carlo Erba 1106 and LECO CHNS-932 microanalyzers. Infrared spectra were recorded in the range 4000−200 cm^{-1} on a Perkin-Elmer Spectrum 100 spectrophotometer using Nujol mulls between polyethylene sheets or CH_2Cl_2 solutions. High-resolution ESI mass spectra were recorded on an Agilent 6220 Accurate-Mass TOF LC/MS.

X-ray Structure Determinations. Crystals suitable for X-ray diffraction studies were obtained by liquid−liquid diffusion from acetone/Et_2O (**2a**), CH_2Cl_2/Et_2O (**3a**), CH_2Cl_2/Et_2O (**7a**), $CDCl_3$/Et_2O (**11b**), $CDCl_3$/*n*-hexane (**15b**), or CH_2Cl_2/*n*-hexane (**18**·CH_2Cl_2) or by sublimation at low pressure (**14b** and **19**). Numerical details are given in the Supporting Information (Tables S1 and S2). The data for **3a**, **7a**, **11b**, **15b**, and **18**·CH_2Cl_2 were collected on an Oxford Diffraction Xcalibur E diffractometer using monochromated Mo Kα radiation in ω-scan mode. The data for **2a**, **14b**, and **19** were collected on an Oxford Diffraction Nova A diffractometer using mirror-focused Cu Kα radiation in ω-scan mode. Absorption corrections were based on multiscans. The structures were solved by direct methods and refined anisotropically on F^2 using the program SHELXL-97 (G. M. Sheldrick, University of Göttingen).[38] Treatment of hydrogen atoms was as follows: NH (where present) freely refined, methyls as idealized rigid groups allowed to rotate but not tip, other H using a riding model starting from calculated positions.

Exceptions and Special Features. The Flack parameter refined to −0.019(4) for **2a** and −0.025(12) for **18**. For **15b**, no absorption correction was applied. For **3a**, a significant isolated difference peak near the 2-fold axis was tentatively refined as a water oxygen, but no water hydrogens were located.

Synthesis of [Pd{C_6H_4C(O)NRR′-2}I(tmeda)] [NRR′ = NH_2 (1a), NHMe (1b), NMe_2 (1c)]. To a suspension of $Pd(dba)_2$ (1234 mg, 2.15 mmol) in CH_2Cl_2 (20 mL) were added tmeda (0.4 mL, 2.66 mmol) and 2-iodobenzamide, 2-iodo-*N*-methylbenzamide, or 2-iodo-*N*,*N*-dimethylbenzamide (2.15 mmol), and the mixture was stirred for 90 min under an N_2 atmosphere. The resulting black suspension was filtered through anhydrous $MgSO_4$, and the clear orange filtrate was concentrated (1 mL). The addition of Et_2O (20 mL) led to the formation of a precipitate, which was filtered off, washed with a 1:2 MeOH/Et_2O mixture (3 × 5 mL) (**1a**) or Et_2O (3 × 5 mL) (**1b**,**c**), and vacuum-dried to give the corresponding complex **1**.

1a. Yellow solid. Yield: 53%. Anal. Calcd for $C_{13}H_{22}IN_3OPd$: C, 33.25; H, 4.72; N, 8.95. Found: C, 33.34; H, 4.80; N, 8.60. Mp: 130−132 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3307; ν(CO), 1647. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.26 (br s, 1 H, NH), 7.63 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.55 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.03 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.93 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.02 (br s, 1 H, NH), 2.73 (br s, 6 H, Me), 2.82−2.59 (m, 4 H, CH_2), 2.27 (br s, 6 H, Me). $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$): δ 172.7 (CO), 144.0, 140.1 (C, Ar), 137.6, 129.3, 128.7, 123.4 (CH, Ar), 62.2, 58.5 (CH_2), 50.0 (br, Me).

1b. Yellow solid. Yield: 62%. Anal. Calcd for $C_{14}H_{24}IN_3OPd$: C, 34.76; H, 5.00; N, 8.69. Found: C, 34.77; H, 4.68; N, 8.66. Mp: 158−161 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3321; ν(CO), 1650. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.22 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.56 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.50 (dd, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.99 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 6.91 (td, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 3.08 (d, $^3J_{HH}$ = 4.8 Hz 1 H, NH*Me*), 2.72 (br s, 6 H, Me, tmeda), 2.72−2.58 (m, 4 H, CH_2, tmeda), 2.22 (br s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 171.0 (CO), 142.6, 140.9 (C, Ar), 137.4, 128.9, 128.2, 123.3 (CH, Ar), 62.2, 58.4 (CH_2), 50.1 (br, Me, tmeda), 26.3 (NHMe).

1c. Pale orange solid. Yield: 51%. Anal. Calcd for $C_{15}H_{26}IN_3OPd$: C, 36.20; H, 5.27; N, 8.44. Found: C, 36.25; H, 5.18; N, 8.40. Mp: 165−168 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1612. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.27 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 6.96 (m, 1 H, Ar), 6.86 (m, 1 H, Ar), 6.80 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 3.27−3.20 (m, 1 H, CH_2), 3.08 (s, 3 H, Me, benzamide), 2.93 (s, 3 H, Me, benzamide), 2.77 (m, 1 H, CH_2), 2.71 (s, 3 H, Me, tmeda), 2.68 (s, 3 H, Me, tmeda), 2.61 (s, 3 H, Me, tmeda), 2.37−2.30 (m, 2 H, CH_2), 2.19 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 175.0 (CO), 144.3, 143.1 (C, Ar), 135.4, 127.0, 125.0, 121.8 (CH, Ar), 61.5, 58.4 (CH_2), 51.4, 51.2, 48.3, 47.7 (Me, tmeda), 40.4, 35.4 (Me, benzamide).

Synthesis of [Pd{κ^2*C*,*O*-C_6H_4C(O)NRR′-2}(tmeda)]TfO [NRR′ = NH_2 (2a), NHMe (2b), NMe_2 (2c)]. To a suspension of the appropriate complex **1** (1.02 mmol) in acetone (15 mL) was added AgTfO (1.02 mmol). The mixture was stirred for 30 min and filtered through Celite. Partial evaporation of the filtrate (2 mL) and addition of Et_2O (20 mL) led to the precipitation of a colorless solid, which was collected by filtration, washed with Et_2O (5 × 3 mL), and vacuum-dried to give **2**.

2a. Yield: 94%. Anal. Calcd for $C_{14}H_{22}F_3N_3O_4PdS$: C, 34.19; H, 4.51; N, 8.54; S, 6.52. Found: C, 34.10; H, 4.77; N, 8.42; S, 6.08. Mp: 179−181 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3334, 3215, 3180; ν(CO), 1663. ^1H NMR (400.9 MHz, $(CD_3)_2CO$): δ 8.76 (br, 1 H, NH), 8.34 (br, 1 H, NH), 7.66 (m, 1 H, Ar), 7.40−7.35 (m, 2 H, Ar), 7.22−7.18 (m, 1 H, Ar), 3.13−3.10 (m, 2 H, CH_2), 3.06 (s, 6 H, Me), 2.92−2.89 (m, 2 H, CH_2), 2.75 (s, 6 H, Me). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $(CD_3)_2CO$): δ 183.8 (CO), 153.8, 142.0 (C, Ar), 133.2, 133.0, 127.8, 125.9 (CH, Ar), 65.9, 58.2 (CH_2), 52.1, 47.8 (Me).

2b. Yield: 91%. Anal. Calcd for $C_{15}H_{24}F_3N_3O_4PdS$: C, 35.62; H, 4.78; N, 8.31; S, 6.34. Found: C, 35.65; H, 4.87; N, 8.31; S, 6.12. Mp: 209−210 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3283; ν(CO), 1615. ^1H NMR (400.9 MHz, $(CD_3)_2CO$): δ 9.04 (br, 1 H, NH), 7.57 (m, 1 H, Ar), 7.36−7.31 (m, 2 H, Ar), 7.21−7.14 (m, 1 H, Ar), 3.14−3.11 (m, 2 H, CH_2), 3.07 (s, 6 H, Me, tmeda), 3.06 (d, $^3J_{HH}$ = 4.4 Hz, 3 H, NH*Me*), 2.94−2.91 (m, 2 H, CH_2), 2.82 (s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $(CD_3)_2CO$): δ 180.7 (CO), 152.6, 142.3 (C, Ar), 132.9, 132.7, 126.5, 125.9 (CH, Ar), 66.0, 58.1 (CH_2), 52.1, 48.0 (Me, tmeda), 27.1 (NHMe).

2c. Yield: 91%. Anal. Calcd for $C_{16}H_{26}F_3N_3O_4PdS$: C, 36.97; H, 5.04; N, 8.08; S, 6.17. Found: C, 36.90; H, 4.75; N, 8.09; S, 6.54. Mp: 132−133 °C. IR (Nujol, cm^{-1}): ν(CO), 1586. ^1H NMR (400.9 MHz, $(CD_3)_2CO$): δ 7.64 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.39 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.33 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.19 (ddd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$

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= 7.6 Hz, 1 H, Ar), 3.63 (s, 3 H, Me, benzamide), 3.30 (s, 3 H, Me, benzamide), 3.14−3.11 (m, 2 H, CH_2), 3.05 (s, 6 H, Me, tmeda), 2.91−2.88 (m, 2 H, CH_2), 2.79 (s, 6 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $(CD_3)_2CO$): δ 180.6 (CO), 153.7, 141.9 (C, Ar), 133.1, 132.0, 130.1, 125.4 (CH, Ar), 66.0, 58.0 (CH_2), 52.0, 48.1 (Me, tmeda), 41.9, 39.1 (Me, benzamide).

Synthesis of [Pd{κ^2*C*,*N*-$C_6H_4C(O)NR$-2}(tmeda)] [R = H (3a), Me (3b)]. To a solution of the appropriate complex **1** (0.40 mmol) in MeOH (20 mL) was added KO^{t}Bu (0.45 mmol), and the mixture was stirred for 1 h. The solvent was removed under reduced pressure, and the residue was extracted with CH_2Cl_2 (6 × 5 mL); the combined extracts were filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (2 mL) and slow addition of *n*-pentane (20 mL) led to the formation of a pale yellow precipitate, which was filtered off, washed with *n*-pentane (3 × 3 mL), and vacuum-dried to give the corresponding complex **3**.

3a. Yield: 88%. Anal. Calcd for $C_{13}H_{21}N_3OPd$: C, 45.69; H, 6.19; N, 12.30. Found: C, 45.55; H, 6.25; N, 12.17. Mp: 183−184 °C. IR (Nujol, cm^{-1}): ν(NH), 3252; ν(CO), 1608. ^1H NMR (300.1 MHz, $CDCl_3$): δ 7.48−7.42 (m, 1 H, Ar), 7.18−7.12 (m, 1 H, Ar), 7.10−7.04 (m, 2 H, Ar), 4.36 (br, 1 H, NH), 2.95 (s, 6 H, Me), 2.77−2.74 (m, 2 H, CH_2), 2.63 (s, 6 H, Me), 2.63−2.61 (m, 2 H, CH_2). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 181.8 (CO), 146.4, 144.4 (C, Ar), 129.7, 128.7, 127.4, 124.3 (CH, Ar), 63.5, 58.5 (CH_2), 51.0, 48.8 (Me).

3b*·*H*$_2$*O. Yield: 57%. Anal. Calcd for $C_{14}H_{25}N_3O_2Pd$: C, 44.99; H, 6.74; N, 11.24. Found: C, 45.02; H, 6.60; N, 11.25. Mp: 92−93 °C (dec). IR (Nujol, cm^{-1}): ν(OH), 3399; ν(CO), 1589. ^1H NMR (300.1 MHz, $CDCl_3$): δ 7.48 (dd, $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 6.9 Hz, 1 H, Ar), 7.12 (m, 1 H, Ar), 7.07−6.96 (m, 2 H, Ar), 3.02 (s, 3 H, Me, benzamide), 2.92 (s, 6 H, Me, tmeda), 2.72 (m, 8 H, CH_2 + Me, tmeda), 2.61 (br, 2 H, CH_2, tmeda), 2.15 (s, 2 H, H_2O). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 180.2 (CO), 146.0, 145.1 (C, Ar), 129.0, 127.6, 127.0, 124.4 (CH, Ar), 63.7, 60.3 (CH_2), 51.1, 48.8 (Me, tmeda), 34.8 (Me, benzamide).

Synthesis of Isoindoline-1,3-dione (Phthalimide) (4a). A solution of **2a** (130 mg, 0.26 mmol) in acetone (15 mL) was stirred under a CO atmosphere (1.4 bar) for 3 h. A black precipitate of Pd gradually formed. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel, using a 2:1 EtOAc/Et_2O mixture as the eluent. Compound **4a** was obtained as a colorless solid after evaporation of the solvents. Yield: 32 mg, 82%. Mp: 235 °C (lit. 237−238 °C[39]). The ^1H NMR data are in agreement with those reported in the literature.[40]

Synthesis of 2-Methylisoindoline-1,3-dione (*N*-Methylphthalimide) (4b). A solution of **2b** (139 mg, 0.27 mmol) in acetone (15 mL) was stirred under a CO atmosphere (1.4 bar) for 3 h. A black precipitate of Pd gradually formed. The solvent was evaporated under reduced pressure, and the residue was extracted with Et_2O (6 × 5 mL). The combined extracts were filtered through anhydrous $MgSO_4$, and the filtrate was evaporated to dryness to give **4b** as a colorless solid. Yield: 35 mg, 79%. Mp: 134 °C (lit. 134 °C[41]). The ^1H NMR data are in agreement with those reported in the literature.[41,42]

Synthesis of 3-(2,6-Dimethylphenylimino)-2-methylisoindolin-1-one (5b). Method A: To a solution of **1b** (100 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) was added XyNC (27.1 mg, 0.21 mmol), and the mixture was stirred for 6 h. A black suspension was obtained. The solvent was removed under vacuum, the residue was extracted with *n*-hexane (8 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. Compound **5b** was obtained as a yellow solid after evaporation of the solvent. Yield: 46 mg, 84%. Method B: To a solution of **2b** (127 mg, 0.25 mmol) in acetone (15 mL) was added XyNC (66 mg, 0.50 mmol). The mixture was stirred for 6 h, and the solvent was removed under vacuum. Compound **5b** was isolated as described for method A. Yield: 60 mg, 90%. Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 76.92; H, 5.92; N, 10.51. Mp: 92−94 °C. IR (Nujol, cm^{-1}): ν(CO), 1743; ν(C═N), 1669. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{17}H_{17}N_2O$ $[M + H]^+$ requires 265.1335, found 265.1344, error = 3.08 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.84 (m, 1 H, H7), 7.52 (td, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.31 (td, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, H5), 7.11 (br d, $^3J_{HH}$ = 7.6 Hz, 2 H, *m*-H, Xy), 7.03−6.98 (m, 1 H, *p*-H, Xy), 6.50 (d, $^3J_{HH}$ = 7.6 Hz, 1 H, H4), 3.43 (s, 3 H, NMe), 2.04 (s, 6 H, Me, Xy). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 167.8 (CO), 151.3 (C═N), 146.0 (*i*-C, Xy), 133.2 (C5), 132.2 (C7a), 132.0 (C7), 130.1 (C3a), 128.3 (*m*-C, Xy), 126.7 (*o*-C, Xy), 123.8 (C4), 123.7 (*p*-C, Xy), 123.1 (C7), 25.2 (NMe), 18.1 (Me, Xy).

Synthesis of 3-(*tert*-Butylimino)-2-methylisoindolin-1-one (5b′). This compound was obtained as a colorless solid using the procedure described for **5b** (method A), from **1b** (148 mg, 0.31 mmol) and ^{t}BuNC (35 μL, 0.31 mmol). Yield: 50 mg, 76%. Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.11; H, 7.29; N, 12.92. Mp: 133−135 °C. IR (Nujol, cm^{-1}): ν(CO), 1728; ν(C═N), 1650. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{13}H_{17}N_2O$ $[M + H]^+$ requires 217.1335, found 217.1335, error = 0.03 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.99 (br d, $^3J_{HH}$ = 7.6 Hz, 1 H, H7), 7.89 (m, 1 H, H4), 7.62 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.58 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H5), 3.18 (s, 3 H, NMe), 1.55 (s, 9 H, ^{t}Bu). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 167.5 (CO), 147.3 (C═N), 134.4 (C3a), 131.8 (C6), 130.9 (C5), 129.0 (C7a), 127.0 (C7), 123.1 (C4), 53.6 (CMe_3), 30.8 (CMe_3), 25.2 (NMe).

Synthesis of *trans*-[Pd{C(═NXy)$C_6H_4C(O)NMe_2$-2}I$(CNXy)_2$] (6). To a solution of **1c** (132 mg, 0.27 mmol) in CH_2Cl_2 (10 mL) was added XyNC (105 mg, 0.80 mmol), and the mixture was stirred for 30 min. Partial evaporation of the solvent (3 mL) and addition of *n*-pentane (15 mL) led to the precipitation of a yellow solid, which was filtered off, washed with *n*-pentane (5 × 3 mL), and vacuum-dried to give **6**. Yield: 173 mg, 84%. Anal. Calcd for $C_{36}H_{37}IN_4OPd$: C, 55.79; H, 4.81; N, 7.23. Found: C, 55.89; H, 4.70; N, 7.21. Mp: 154−155 °C (dec). IR (Nujol, cm^{-1}): ν(C≡N), 2184; ν(CO), 1623; ν(C═N), 1584. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.07 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.45 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.37 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.26 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.20 (t, $^3J_{HH}$ = 7.6 Hz, 2 H, *p*-H, XyNC[c]), 7.04 (m, 4 H, *m*-H, XyNC[c]), 6.85 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, *p*-H, XyNC[i]), 6.90−6.60 (br, 2 H, *m*-H, XyNC[i]), 3.08 (s, 3 H, Me, benzamide), 3.075 (s, 3 H, Me, benzamide), 2.24 (s, 12 H, Me, XyNC[c]), 2.40−2.00 (br, 6 H, Me, XyNC[i]). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 175.8 (C═N), 171.2 (CO), 150.2 (*i*-C, XyNC[i]), 143.9 (C, Ar), 136.0 (C, Ar + *o*-C, XyNC[c]), 129.85 (CH, XyNC[c]), 129.76, 128.4, 128.3 (CH, Ar), 128.2 (CH, XyNC[i]), 127.9 (CH, XyNC[c]), 127.1 (*o*-C, XyNC[i]), 126.1 (CH, Ar), 123.3 (CH, XyNC[i]), 39.7, 34.6 (NMe), 18.8 (Me, XyNC); C≡N and *i*-C of XyNC[c] not observed.

Synthesis of [Pd{κ^2*C*,*O*-C(X)═C(X′)$C_6H_4C(O)NRR'$-2}(tmeda)]-TfO [NRR′ = NH_2 and X = Ph, X′ = Me (7a); NRR′ = NHMe and X = Ph, X′ = Me (7b), X = X′ = Ph (8b), Et (9b), CO_2Me (10b), X = CO_2Me, X′ = Ph (11b), X = CO_2Et, X′ = Ph (12b); NRR′ = NMe_2 and X = X′ = Ph (8c), Et (9c)]. A solution of the appropriate complex **2** (0.47 mmol) and the alkyne (4.70 mmol for NH_2 and NHMe derivatives; 2.35 mmol for NMe_2 derivatives) in a 1:2 acetone/CH_2Cl_2 mixture (15 mL) (**7a**) or CH_2Cl_2 (10 mL) (other complexes) was stirred for 64 h (**7a**), 24 h (**7b**, **9b**, **10b**, **8c**, **9c**), 48 h (**11b**, **12b**), or 5 d (**8b**). The mixture was filtered through anhydrous $MgSO_4$, and the filtrate was concentrated to ca. 4 mL (**11b**, **12b**) or 1 mL (other complexes). The addition of Et_2O (20 mL) led to the precipitation of a yellow solid, which was filtered off, washed with Et_2O (3 × 3 mL), recrystallized from CH_2Cl_2/Et_2O, and vacuum-dried to give the corresponding complex **7**−**12**.

7a. Yield: 65%. Anal. Calcd for $C_{23}H_{30}F_3N_3O_4PdS$: C, 45.44; H, 4.97; N, 6.91; S, 5.27. Found: C, 45.37; H, 4.89; N, 6,79; S, 5.27. Mp: 146−147 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3330, 3197; ν(CO), 1662. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.89 (br s, 1 H, NH), 7.66 (m, 1 H, Ar), 7.58 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.51−7.47 (m, 3 H, Ar + Ph), 7.39−7.33 (m, 3 H, Ar + Ph), 7.26−7.23 (m, 2 H, NH + Ph), 2.65−2.50 (m, 5 H, CH_2 + NMe), 2.34 (s, 3 H, NMe), 2.27−2.18 (m, 2 H, CH_2), 2.10 (s, 3 H, NMe), 2.08 (s, 3 H, CMe), 1.83 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 178.8 (CO), 144.8 (PdC), 143.4 (C, Ar), 142.5 (C, Ph), 133.3 (C,

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Ar), 131.7, 129.2 (CH, Ar), 128.5 (*C*Me), 128.4, 128.3 (CH, Ph), 127.2, 126.4 (CH, Ar), 125.9 (CH, Ph), 63.7, 57.1 (CH_2), 52.8, 48.9, 48.8, 45.9 (NMe), 20.7 (*C*Me).

7b. Yield: 76%. Anal. Calcd for $C_{24}H_{32}F_3N_3O_4PdS$: C, 46.34; H, 5.19; N, 6.76; S, 5.16. Found: C, 46.10; H, 5.27; N, 6.71; S, 5.10. Mp: 80−82 °C. IR (Nujol, cm^{-1}): ν(NH), 3280; ν(CO), 1600. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.50 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.60 (dd, $^4J_{HH}$ = 0.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.53 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.48−7.44 (m, 3 H, Ar + Ph), 7.36−7.31 (m, 3 H, Ar + Ph), 7.27−7.23 (m, 1 H, Ph), 3.00 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.62−2.51 (m, 5 H, CH_2 + Me, tmeda), 2.34 (s, 3 H, Me, tmeda), 2.29−2.21 (m, 2 H, CH_2), 2.07 (s, 3 H, Me, tmeda), 2.06 (s, 3 H, CMe), 1.84 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.4 (CO), 144.5 (PdC), 143.3 (C, Ar), 142.7 (C, Ph), 134.1 (C, Ar), 131.2, 128.8 (CH, Ar), 128.7 (CMe), 128.3, 128.2 (CH, Ph), 127.5, 126.4 (CH, Ar), 125.8 (CH, Ph), 63.6, 57.1 (CH_2), 52.7, 48.9, 48.8, 46.0 (Me, tmeda), 28.1 (Me, benzamide), 20.6 (*C*Me).

8b·H_2O. Yield: 74%. Anal. Calcd for $C_{29}H_{36}F_3N_3O_5PdS$: C, 49.61; H, 5.17; N, 5.98; S, 4.57. Found: C, 49.21; H, 5.13; N, 6.14; S, 4.73. Mp: 178−180 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3273; ν(CO), 1600. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.51 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.64 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.53 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.48 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.35−7.30 (m, 3 H, Ar + Ph), 7.18−7.07 (m, 5 H, Ph), 7.04−6.98 (m, 3 H, Ph), 3.07 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.64−2.53 (m, 2 H, CH_2), 2.53 (s, 3 H, Me, tmeda), 2.50 (s, 3 H, Me, tmeda), 2.34−2.21 (m, 2 H, CH_2), 2.07 (s, 3 H, Me, tmeda), 2.00 (s, 3 H, Me, tmeda), 1.68 (s, 2 H, H_2O). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 176.6 (CO), 151.6 (PdC), 142.6 (C, Ph), 141.6 (C, Ar), 140.5 (C, Ph), 135.4 (PdC=*C*), 135.3 (C, Ar), 131.2, 130.0 (CH, Ar), 129.4, 128.1, 128.0, 127.9 (CH, Ph), 127.3, 126.7 (CH, Ar), 126.2, 125.8 (CH, Ph), 63.7, 57.2 (CH_2), 53.0, 49.01, 48.95, 46.2 (Me, tmeda), 28.2 (Me, benzamide).

8c. Yield: 88%. Anal. Calcd for $C_{30}H_{36}F_3N_3O_4PdS$: C, 51.61; H, 5.20; N, 6.02; S, 4.59. Found: C, 51.52; H, 5.19; N, 5.93; S, 5.06. Mp: 210−212 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1587. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.73 (m, 1 H, Ar), 7.61 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.49−7.41 (m, 2 H, Ar), 7.34−7.32 (m, 2 H, Ph), 7.18−7.05 (m, 6 H, Ph), 7.00−6.98 (m, 2 H, Ph), 3.29 (s, 3 H, Me, benzamide), 2.93 (s, 3 H, Me, benzamide), 2.76−2.62 (m, 2 H, CH_2), 2.59 (s, 3 H, Me, tmeda), 2.48 (s, 3 H, Me, tmeda), 2.42−2.32 (m, 2 H, CH_2), 2.14 (s, 3 H, Me, tmeda), 1.95 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.6 (CO), 152.9 (PdC), 142.5 (C, Ph), 142.3 (C, Ar), 140.3 (C, Ph), 135.2 (C, Ar), 135.1 (PdC=*C*), 130.8, 129.7 (CH, Ar), 128.8, 128.2, 128.1, 128.0 (CH, Ph), 126.6 (CH, Ar), 126.3, 125.9 (CH, Ph), 125.7 (CH, Ar), 64.0, 57.4 (CH_2), 53.1, 49.1, 49.0, 46.2 (Me, tmeda), 41.5, 36.6 (Me, benzamide).

9b. Yield: 53%. Anal. Calcd for $C_{21}H_{34}F_3N_3O_4PdS$: C, 42.90; H, 5.83; N, 7.15; S, 5.45. Found: C, 42.57; H, 5.81; N, 7.04; S, 5.39. Mp: 127−129 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3237; ν(CO), 1608. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.34 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.50 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.47 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.34 (m, 1 H, Ar), 7.28 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 2.93 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, NH*Me*), 2.62 (s, 3 H, Me, tmeda), 2.50 (s, 3 H, Me, tmeda), 2.64−2.45 (m, 4 H, CH_2, tmeda), 2.34 (s, 3 H, Me, tmeda), 2.30−2.17 (m, 2 H, CH_2CH_3), 2.13−2.04 (m, 1 H, CH_2CH_3), 2.04 (s, 3 H, Me, tmeda), 2.02−1.88 (m, 1 H, CH_2CH_3), 1.29 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3), 0.70 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.7 (CO), 150.2 (PdC), 141.9, 136.7 (C, Ar), 133.5 (PdC=*C*), 130.8, 128.3, 126.6, 126.0 (CH, Ar), 63.4, 56.8 (CH_2), 52.2, 51.2, 47.5, 47.0 (Me, tmeda), 27.9 (NHMe), 26.5, 26.3 (CH_2CH_3), 15.5, 14.4 (CH_2CH_3).

9c. Yield: 87%. Anal. Calcd for $C_{22}H_{36}F_3N_3O_4PdS$: C, 43.89; H, 6.03; N, 6.98; S, 5.33. Found: C, 43.83; H, 6.06; N, 6.99; S, 5.34. Mp: 137−138 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1587. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 7.53 (m, 1 H, Ar), 7.42 (m, 1 H, Ar), 7.36 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.31 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 3.13 (s, 3 H, Me, benzamide), 3.00 (s, 3 H, Me, benzamide), 2.73−2.64 (m, 1 H, CH_2CH_3), 2.63−2.61 (m, 1 H, CH_2, tmeda), 2.61 (s, 3 H, Me, tmeda), 2.51 (s, 3 H, Me, tmeda), 2.58−2.48 (m, 2 H, CH_2, tmeda), 2.31 (s, 3 H, Me, tmeda), 2.34−2.21 (m, 2 H, CH_2, tmeda, + CH_2CH_3), 2.14−2.04 (m, 1 H, CH_2CH_3), 2.04 (s, 3 H, Me, tmeda), 1.96−1.87 (m, 1 H, CH_2CH_3), 1.25 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3), 0.73 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.4 (CO), 152.0 (PdC), 142.7, 135.8 (C, Ar), 133.4 (PdC=*C*), 130.5, 128.6, 125.9, 125.5 (CH, Ar), 63.6, 56.9 (CH_2, tmeda), 52.2, 51.2, 47.5, 47.1 (Me, tmeda), 41.3, 36.3 (Me, benzamide), 26.4, 25.7 (CH_2CH_3), 15.6, 14.7 (CH_2CH_3).

10b. Yield: 96%. Anal. Calcd for $C_{21}H_{30}F_3N_3O_8PdS$: C, 38.93; H, 4.67; N, 6.48; S, 4.95. Found: C, 39.09; H, 4.94; N, 6.34; S, 4.54. Mp: 149−151 °C. IR (Nujol, cm^{-1}): ν(NH), 3333; ν(COO), 1695; ν(CO), 1618. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 8.65 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.70 (m, 1 H, Ar), 7.59 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.50−7.45 (m, 2 H, Ar), 3.87 (s, 3 H, CO_2Me), 3.65 (s, 3 H, CO_2Me), 2.99 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.75 (s, 3 H, Me, tmeda), 2.81−2.73 (m, 2 H, CH_2, tmeda), 2.553 (s, 3 H, Me, tmeda), 2.549 (s, 3 H, Me, tmeda), 2.37−2.30 (m, 2 H, CH_2), 2.13 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 175.7 (CONHMe), 171.4 (CO_2Me), 164.0 (PdC), 161.5 (CO_2Me), 136.1, 134.4 (C, Ar), 131.3, 131.1 (CH, Ar), 129.3 (PdC=*C*), 127.94, 127.91 (CH, Ar), 64.6, 58.1 (CH_2), 54.4 (Me, tmeda), 52.2, 52.0 (CO_2Me), 49.7, 48.2, 46.4 (Me, tmeda), 28.3 (NHMe).

11b. Yield: 71%. Anal. Calcd for $C_{25}H_{32}F_3N_3O_6PdS$: C, 45.08; H, 4.84; N, 6.31; S, 4.81. Found: C, 44.67; H, 4.66; N, 6.22; S, 4.51. Mp: 175−177 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3233; ν(COO), 1693; ν(CO), 1600. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 9.04 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.72 (m, 1 H, Ar), 7.48−7.40 (m, 2 H, Ar), 7.25−7.14 (m, 4 H, Ar + Ph), 7.03−7.00 (m, 2 H, Ph), 3.49 (CO_2Me), 3.03 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.88 (s, 3 H, Me, tmeda), 2.81−2.79 (m, 2 H, CH_2), 2.70 (s, 3 H, Me, tmeda), 2.58 (s, 3 H, Me, tmeda), 2.35−2.29 (m, 2 H, CH_2), 2.16 (s, 3 H, Me, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 176.3 (CONHMe), 171.5 (CO_2Me), 141.6 (C, Ar), 140.6 (C, Ph), 140.4 (PdC=*C*), 138.2 (PdC), 134.6 (C, Ar), 131.4, 130.9 (CH, Ar), 128.5, 128.1 (CH, Ph), 127.7, 127.6 (CH, Ar), 127.3 (CH, Ph), 64.5, 57.9 (CH_2), 54.4 (Me, tmeda), 51.8 (CO_2Me), 49.9, 48.2, 46.6, 28.4 (NHMe).

12b. Yield: 67%. Anal. Calcd for $C_{26}H_{34}F_3N_3O_6PdS$: C, 45.92; H, 5.04; N, 6.18; S, 4.72. Found: C, 45.93; H, 5.15; N, 6.18; S, 4.63. Mp: 199−200 °C (dec). IR (Nujol, cm^{-1}): ν(NH), 3240; ν(COO), 1690; ν(CO), 1604. ^{1}H NMR (400.9 MHz, $CDCl_3$): δ 9.01 (br q, $^3J_{HH}$ = 4.8 Hz, 1 H, NH), 7.63 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.44 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.38 (dd, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, Ar), 7.22−7.14 (m, 4 H, Ar + Ph), 7.02−6.99 (m, 2 H, Ph), 4.06, 3.89 (AB part of ABX_3 system, $^2J_{HH}$ = 10.8 Hz, $^3J_{HH}$ = 6.8 Hz, 2 H, CH_2CH_3), 3.00 (d, $^3J_{HH}$ = 4.8 Hz, 3 H, Me, benzamide), 2.88 (s, 3 H, Me, tmeda), 2.81−2.78 (m, 2 H, CH_2, tmeda), 2.68 (s, 3 H, Me, tmeda), 2.56 (s, 3 H, Me, tmeda), 2.38−2.30 (m, 2 H, CH_2, tmeda), 2.13 (s, 3 H, Me, tmeda), 0.89 (t, $^3J_{HH}$ = 6.8 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 176.4 (CONHMe), 171.0 (CO_2Et), 141.6 (C, Ar), 140.5 (PdC=*C* + C, Ph), 138.9 (PdC), 134.5 (C, Ar), 131.3, 130.9 (CH, Ar), 128.7, 127.9 (CH, Ph), 127.6, 127.5 (CH, Ar), 127.2 (CH, Ph), 64.5 (CH_2, tmeda), 60.4 (CH_2CH_3), 57.9 (CH_2, tmeda), 54.4, 49.8, 48.2, 46.5 (Me, tmeda), 28.3 (NHMe), 13.7 (CH_2CH_3).

Synthesis of 3,4-Diethylisoquinolin-1(2*H*)-one (13). A mixture of **2a** (122 mg, 0.25 mmol) and 3-hexyne (285 μL, 2.50 mmol) in acetone (20 mL) was stirred at 40 °C for 24 h. The solvent was evaporated under vacuum, the residue was extracted with Et_2O (6 × 5 mL), and the combined extracts were filtered through anhydrous $MgSO_4$. The pale yellow filtrate was evaporated to dryness, and the residue was stirred in *n*-pentane (10 mL) for 16 h, whereupon a colorless precipitate formed, which was filtered off and vacuum-dried to give **13**. Yield: 15 mg, 30%. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{13}H_{16}NO$ $[M + H]^+$ requires 202.1226, found 202.1233, error = 3.41 ppm. Mp: 180 °C (lit. 173−175 °C[21]). The ^{1}H NMR data are in agreement with those reported in the literature.[21]

Synthesis of (*Z*)-5-Methyl-4-phenyl-2*H*-benzo[*c*]azepine-1,3-dione (14a), (*Z*)-2,5-Dimethyl-4-phenyl-2*H*-benzo[*c*]azepine-

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1,3-dione (14b), (*Z*)-2-Methyl-4,5-diphenyl-2*H*-benzo[*c*]-azepine-1,3-dione (14c), and (*Z*)-4,5-Diethyl-2-methyl-2*H*-benzo[*c*]azepine-1,3-dione (14d). A solution of complex **7a**, **7b**, **8b**, or **9b** (0.45 mmol) in $CHCl_3$ (15 mL) was stirred under a CO atmosphere (1.4 bar) for 3 h (**7a**) or 24 h (**7**−**9b**), whereupon a black precipitate of Pd gradually formed. The suspension was filtered through anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel, using as the eluent Et_2O [R_f = 0.8−0.9 (**14a**), 0.9 (**14d**)], a 1:1 EtOAc/*n*-hexane mixture [R_f = 0.8−0.9 (**14b**)], or a 2:1 Et_2O/*n*-hexane mixture [R_f = 0.7−0.8 (**14c**)]. The compounds were isolated as colorless solids (**14a**−**c**) or as a yellow oil (**14d**) after evaporation of the solvents.

14a. Yield: 81%. Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.64; H, 4.90; N, 5.34. Mp: 200−202 °C. IR (Nujol, cm^{-1}): ν(CO), 1688, 1655. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{17}H_{14}NO_2$ $[M + H]^+$ requires 264.1019, found 264.1025, error = 2.29 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.64 (br, 1 H, H2), 8.20 (m, 1 H, H9), 7.72 (m, 1 H, H6), 7.67 (m, 1 H, H7), 7.55 (m, 1 H, H8), 7.46−7.41 (m, 2 H, Ph), 7.39−7.35 (m, 1 H, Ph), 7.25−7.22 (m, 2 H, Ph), 2.18 (s, 3 H, Me). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 166.7 (C1), 166.5 (C3), 142.4 (C5), 139.1 (C, Ph), 136.7 (C5a), 136.6 (C4), 132.8 (C7), 131.7 (C9), 131.3 (C9a), 129.4 (C8), 129.0 (CH, Ph), 128.7 (C6), 128.6, 127.9 (CH, Ph), 23.7 (Me).

14b. Yield: 83%. Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.03; H, 5.57; N, 4.98. Mp: 98−99 °C. IR (Nujol, cm^{-1}): ν(CO), 1687, 1649. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{18}H_{16}NO_2$ $[M + H]^+$ requires 278.1176, found 278.1184, error = 2.89 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.91 (m, 1 H, H9), 7.59 (m, 2 H, H7 + H6), 7.50−7.46 (m, 1 H, H8), 7.44−7.34 (m, 3 H, Ph), 7.28−7.26 (m, 2 H, Ph), 3.44 (s, 3 H, NMe), 2.10 (s, 3 H, CMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 170.9 (C1), 170.7 (C3), 139.2 (C4), 138.0 (C5), 137.4 (C, Ph), 136.0 (C5a), 134.1 (C9a), 131.6 (C7), 131.0 (C9), 129.1 (CH, Ph), 128.9 (C8), 128.5, 127.8 (CH, Ph), 127.1 (C6), 33.6 (NMe), 21.2 (*C*Me).

14c. Yield: 76%. Anal. Calcd for $C_{23}H_{17}NO_2$: C, 81.40; H, 5.05; N, 4.13. Found: C, 81.25; H, 4.81; N, 4.19. Mp: 151−153 °C. IR (Nujol, cm^{-1}): ν(CO), 1689, 1645. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{23}H_{18}NO_2$ $[M + H]^+$ requires 340.1332, found 340.1338, error = 1.74 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.96 (m, 1 H, H9), 7.45 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, H8), 7.37 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, H7), 7.29−7.27 (m, 2 H, Ph), 7.15−7.11 (m, 6 H, Ph), 6.97−6.94 (m, 3 H, Ph + H6), 3.44 (s, 3 H, Me). $^{13}C\{^1H\}$ NMR (100.8 MHz, $CDCl_3$): δ 170.86, 170.84 (CO), 142.5 (C5), 139.6, 137.2 (C, Ph), 136.3 (C4), 135.7 (C5a), 134.7 (C9a), 131.1 (C7), 130.8 (C9), 130.6 (CH, Ph + C6), 129.2 (C8), 127.9, 127.50, 127.45, 127.3 (CH, Ph), 33.9 (Me).

14d*·0.25*H*$_2$*O. Yield: 79%. Anal. Calcd for $C_{15}H_{17.5}NO_{2.25}$: C, 72.70; H, 7.12; N, 5.65. Found: C, 72.84; H, 6.92; N, 5.49. IR (Nujol, cm^{-1}): ν(CO), 1700, 1662. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{15}H_{18}NO_2$ $[M + H]^+$ requires 244.1332, found 244.1341, error = 3.71 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.81−7.79 (m, 1 H, H9), 7.53−7.50 (m, 2 H, H6, H7), 7.43−7.37 (m, 1 H, H8), 3.41 (NMe), 2.70 (q, $^3J_{HH}$ = 7.6 Hz, 2 H, CH_2), 2.63 (q, $^3J_{HH}$ = 7.6 Hz, 2 H, CH_2), 1.62 (br, 0.5 H, H_2O), 1.12 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3), 1.05 (t, $^3J_{HH}$ = 7.6 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 173.0 (C3), 171.1 (C1), 140.3 (C5), 137.9 (C4), 135.5 (C5a), 134.9 (C9a), 131.3 (C7), 130.7 (C9), 128.1 (C8), 126.4 (C6), 33.0 (NMe), 26.5, 25.6 (CH_2CH_3), 14.0, 13.9 (CH_2CH_3).

Synthesis of 3-[Di(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (15b). To a solution of **11b** (137 mg, 0.21 mmol) in $CHCl_3$ (15 mL) was added MeOH (17 μL, 0.42 mmol), and the mixture was stirred under a CO atmosphere (1.4 bar) for 6 h, whereupon a black precipitate of Pd gradually formed. The suspension was filtered through anhydrous $MgSO_4$, the filtrate was evaporated to dryness, and the residue was purified by column chromatography on silica gel, using Et_2O as the eluent (R_f = 0.50). Compound **15b** was isolated as a colorless solid after evaporation of the solvent. Yield: 60 mg, 83%. Mp: 120−121 °C. Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.87; H, 5.34; N, 4.23. IR (Nujol, cm^{-1}): ν(CO), 1759, 1739, 1687. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{20}H_{20}NO_5$ $[M + H]^+$ requires 354.1336, found 354.1343, error = 2.07 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.85 (m, 1 H, H7), 7.79 (m, 1 H, H4), 7.55 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, H5), 7.49 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.33−7.29 (m, 3 H, Ph), 7.06−7.03 (m, 2 H, Ph), 4.86 (s, 1 H, $CHCO_2Me$), 3.64 (s, 3 H, CO_2Me), 3.48 (s, 3 H, CO_2Me), 2.97 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 168.0 (C1), 166.6, 166.3 (CO_2Me), 146.6 (C3a), 138.0 (C, Ph), 131.9 (C5), 131.8 (C7a), 128.92 (C6), 128.87 (CH, Ph), 128.4, 125.9 (CH, Ph), 125.0 (C4), 123.1 (C7), 70.4 (C3), 55.6 ($CHCO_2Me$), 52.79, 52.77 (CO_2Me), 25.6 (NMe).

Synthesis of 3-[Ethoxycarbonyl(methoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (15c). This compound was obtained as a colorless oil using the method described for **15b**, either from **11b** (160 mg, 0.24 mmol) and EtOH (29 μL, 0.50 mmol) or from **12b** (161 mg, 0.24 mmol) and MeOH (20 μL, 0.49 mmol), and purified by column chromatography using Et_2O as the eluent (R_f = 0.60−0.70). An approximately 1:1 mixture of the two diastereomeric pairs of enantiomers was obtained. Yield: 97%. Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.43; H, 5.76; N, 3.74. IR (CH_2Cl_2, cm^{-1}): ν(CO), 1760, 1736, 1696. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{21}H_{22}NO_5$ $[M + H]^+$ requires 368.1492, found 368.1506, error = 3.74 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.86−7.83 (m, 3 H, H4, H7), 7.74 (m, 1 H, H4), 7.55−7.47 (m, 4 H, H5, H6), 7.32−7.28 (m, 6 H, Ph), 7.08−7.02 (m, 4 H, Ph), 4.85 (s, 1 H, CHCOO), 4.84 (s, 1 H, CHCOO), 4.08−4.05 (m, 2 H, CH_2CH_3), 3.95−3.89 (m, 2 H, CH_2CH_3), 3.65 (s, 3 H, CO_2Me), 3.50 (s, 3 H, CO_2Me), 3.02 (s, 3 H, NMe), 2.95 (s, 3 H, NMe), 1.08 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH_2CH_3), 0.98 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 168.2, 167.9 (C1), 166.8, 166.5 (CO_2Me), 166.1, 165.8 (CO_2Et), 147.0, 146.5 (C3a), 138.2, 138.0 (C, Ph), 132.1 (C7a), 131.9 (C5), 131.6 (C7a), 128.93 (C6), 128.90 (CH, Ph), 128.81 (C6), 128.80, 128.4, 128.3, 126.0, 125.7 (CH, Ph), 125.3, 124.6 (C4), 123.2, 123.1 (C7), 70.5, 70.4 (C3), 62.0, 61.9 (CH_2CH_3), 56.2, 55.6 (CHCOO), 52.72, 52.71 (CO_2Me), 26.0, 25.4 (NMe), 13.7, 13.6 (CH_2CH_3).

Synthesis of 3-[Di(ethoxycarbonyl)methyl]-2-methyl-3-phenylisoindolin-1-one (15d). This compound was obtained as a colorless oil using the method described for **15b**, from **12b** (192 mg, 0.28 mmol) and EtOH (33 μL, 0.56 mmol), and purified by column chromatography using Et_2O as the eluent (R_f = 0.70). Yield: 107 mg, 99%. Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.28; H, 6.08; N, 3.67. Found: C, 69.13; H, 5.94; N, 3.78. IR (CH_2Cl_2, cm^{-1}): ν(CO), 1757, 1733, 1696. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{22}H_{24}NO_5$ $[M + H]^+$ requires 382.1649, found 382.1661, error = 3.2 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.85 (m, 1 H, H7), 7.82 (m, 1 H, H4), 7.54 (td, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H5), 7.48 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.33−7.28 (m, 3 H, Ph), 7.07−7.04 (m, 2 H, Ph), 4.83 (s, 1 H, CHCOO), 4.09 (m, 2 H, CH_2CH_3), 3.94 (m, 2 H, CH_2CH_3), 3.00 (s, 3 H, NMe), 1.11 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH_2CH_3), 1.00 (t, $^3J_{HH}$ = 7.2 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 168.0 (C1), 166.2, 165.9 (CO_2Et), 146.8 (C3a), 138.3 (C, Ph), 131.92 (C7a), 131.86 (C5), 128.8 (C6 + CH, Ph), 128.3, 125.9 (CH, Ph), 125.0 (C4), 123.1 (C7), 70.4 (C3), 61.85, 61.77 (CH_2CH_3), 56.1 ($CHCO_2Et$), 25.7 (NMe), 13.8, 13.6 (CH_2CH_3).

Synthesis of 3-(Methoxycarbonylmethyl)-2-methyl-3-phenylisoindolin-1-one (16). A solution of **11b** (118 mg, 0.18 mmol) in $CHCl_3$ (15 mL) was stirred under a CO atmosphere (1.4 bar) at room temperature for 6 h and then at 50 °C for 24 h. The resulting black suspension was filtered through anhydrous $MgSO_4$, and the filtrate was concentrated to dryness. The residue was chromatographed on silica gel, using Et_2O as the eluent [R_f = 0.4−0.5]. Compound **16** was isolated as a colorless solid after evaporation of the solvent. Yield: 51 mg, 98%. Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.22; H, 5.93; N, 4.67. Mp: 98−100 °C. IR (Nujol, cm^{-1}): ν(CO), 1732, 1686. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{18}H_{18}NO_3$ $[M + H]^+$ requires 296.1281, found 296.1288, error = 2.35 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.87 (m, 1 H, H7), 7.48 (td, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, H5), 7.44 (td, $^4J_{HH}$ =

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1.2 Hz, $^3J_{HH}$ = 7.2 Hz, 1 H, H6), 7.37−7.28 (m, 3 H, Ph), 7.24 (m, 1 H, H4), 7.15−7.12 (m, 2 H, Ph), 3.57, 3.37 (AB system, $^2J_{HH}$ = 14.0 Hz, 2 H, CH_2), 3.39 (s, 3 H, CO_2Me), 2.91 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 168.9 (CO_2Me), 168.5 (C1), 148.7 (C3a), 138.9 (C, Ph), 131.8 (C5), 131.1 (C7a), 129.1 (CH, Ph), 128.5 (C6), 128.3, 125.8 (CH, Ph), 123.4 (C7), 122.3 (C4), 68.2 (C3), 51.9 (CO_2*Me*), 39.1 (CH_2), 25.0 (NMe).

Synthesis of Dimethyl 2-((2-(Methylcarbamoyl)phenyl)-(phenyl)methylene)malonate (17). A solution of **11b** (154 mg, 0.23 mmol) in MeOH (15 mL) was stirred under a CO atmosphere (1.4 bar) for 3 h, whereupon a black precipitate of Pd gradually formed. The suspension was filtered through Celite, and the filtrate was concentrated to dryness. The residue was chromatographed on silica gel, using Et_2O as the eluent [R_f = 0.35]. Compound **17** was isolated as a colorless solid after evaporation of the solvent. Yield: 47 mg, 58%. Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.65; H, 5.57; N, 4.04. Mp: 152−154 °C. IR (Nujol, cm^{-1}): ν(NH), 3250; ν(CO), 1729, 1632. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{20}H_{20}NO_5$ [M + H]$^+$ requires 354.1336, found 354.1340, error = 1.05 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 7.64−7.61 (m, 1 H, Ar), 7.48−7.43 (m, 2 H, Ar), 7.35−7.25 (m, 4 H, Ar + Ph), 7.03−7.00 (m, 2 H, Ph), 6.81 (br q, $^3J_{HH}$ = 5.2 Hz, 1 H, NH), 3.67 (s, 3 H, CO_2Me), 3.65 (s, 3 H, CO_2Me), 2.80 (d, $^3J_{HH}$ = 5.2 Hz, 1 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 168.8 (CONH), 167.0, 166.1 (CO_2Me), 157.6 (C═CCO_2Me), 137.9 (C, Ar), 137.8 (C, Ph), 136.1 (C, Ar), 130.2 (CH, Ph), 130.1, 129.5, 129.0 (CH, Ar), 128.6 (CH, Ph), 128.33 (CH, Ar), 128.29 (CH, Ph), 125.5 (C═CCO_2Me), 52.8, 52.5 (CO_2*Me*), 26.7 (NHMe).

Synthesis of [Pd(κ^2*C*,*O*-$C_{14}H_{13}O_5$)(tmeda)] (18). To a solution of **10b** (110 mg, 0.17 mmol) in MeOH (15 mL) was added NaOMe (92 mg, 1.70 mmol), and the mixture was stirred for 15 h. The solvent was removed under reduced pressure, and the remaining residue was extracted with CH_2Cl_2 (6 × 5 mL). The combined extracts were filtered through anhydrous $MgSO_4$. Partial evaporation of the filtrate (4 mL) and slow addition of *n*-hexane (30 mL) led to the formation of an orange precipitate, which was filtered off, washed with *n*-hexane (3 × 3 mL), and vacuum-dried to give **18**·CH_2Cl_2. Yield: 95 mg, 96%. Anal. Calcd for $C_{21}H_{31}Cl_2N_3O_5Pd$: C, 43.28; H, 5.36; N, 7.21. Found: C, 42.88; H, 4.96; N, 7.10. Mp: 167−168 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1688, 1632. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.19 (m, 1 H, H8), 7.33 (m, 1 H, H6), 7.25 (m, 1 H, H5), 6.98 (m, 1 H, H7), 5.30 (s, 2 H, CH_2Cl_2), 3.61 (s, 3 H, CO_2Me), 3.51 (s, 3 H, COMe), 3.49 (s, 3 H, NMe), 3.05−2.98 (m, 1 H, CH_2, tmeda), 2.80−2.74 (m, 1 H, CH_2, tmeda), 2.74 (s, 3 H, Me, tmeda), 2.72 (s, 3 H, Me, tmeda), 2.69 (s, 3 H, Me, tmeda), 2.66 (s, 3 H, Me, tmeda), 2.49−2.40 (m, 2 H, CH_2, tmeda). $^{13}C\{^1H\}$ APT NMR (75.5 MHz, $CDCl_3$): δ 177.1 (CO_2Me), 164.2 (CONMe), 137.5 (C4a), 131.7 (C6), 128.2 (C8), 119.71, 119.70 (C7, C5), 117.9 (C8a), 93.9 (C4), 79.4 (PdC), 64.5, 57.1 (CH_2, tmeda), 54.1 (OMe), 51.8 (CO_2*Me*), 50.7, 49.7, 48.1, 46.1 (Me, tmeda), 26.7 (NMe) (C3 not observed).

Synthesis of (*E*)-4-[Methoxy(methoxycarbonyl)methylene]-2-methylisoquinoline-1,3(2*H*,4*H*)-dione (19). A solution of **18**·CH_2Cl_2 (127 mg, 0.22 mmol) in $CHCl_3$ (15 mL) was stirred at 70 °C for 2 d, whereupon a black precipitate of Pd gradually formed. The solvent was evaporated to dryness, and the residue was extracted with Et_2O (8 × 5 mL). The combined extracts were filtered through anhydrous $MgSO_4$, and the resulting pale orange filtrate was evaporated to dryness. The residue was purified by column chromatography on silica gel, using Et_2O as the eluent [R_f = 0.8]. Compound **19** was isolated as a colorless solid after evaporation of the solvent. Yield: 25 mg, 42%. Anal. Calcd for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 61.01; H, 4.42; N, 5.19. Mp: 116−119 °C (dec). IR (Nujol, cm^{-1}): ν(CO), 1734, 1696, 1657. HRMS (ESI+, *m*/*z*): exact mass calcd for $C_{14}H_{14}NO_5$ [M + H]$^+$ requires 276.0866, found 276.0874, error = 2.90 ppm. ^1H NMR (400.9 MHz, $CDCl_3$): δ 8.36 (m, 1 H, H5), 8.31 (dd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H8), 7.62 (ddd, $^4J_{HH}$ = 1.6 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 7.6 Hz, 1 H, H6), 7.43 (m, 1 H, H7), 4.09 (s, 3 H, COMe), 4.03 (s, 3 H, CO_2Me), 3.39 (s, 3 H, NMe). $^{13}C\{^1H\}$ APT NMR (100.8 MHz, $CDCl_3$): δ 165.4 (C3), 164.1 (C1), 163.1 (CO_2Me), 161.7 (MeO*C*═C), 133.4 (C6), 131.3 (C4a), 129.1 (C8), 127.6 (C7), 126.6 (C5), 123.8 (C8a), 104.7 (C4), 58.4 (COMe), 53.0 (CO_2*Me*), 27.0 (NMe).

■ ASSOCIATED CONTENT

Supporting Information

Syntheses of 2-iodo-*N*-methylbenzamide and 2-iodo-*N*,*N*-dimethylbenzamide. ^1H NMR data of the mixture of **15a** and (tmedaH)TfO. Crystallographic data in CIF format for **2a**, **3a**, **7a**, **11b**, **14b**, **15b**, **18**·CH_2Cl_2, and **19**. Tables of crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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