

Depalladation Reactions of Iminoacyl- and 2-Acetylaryl palladium(II) Complexes

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Reaction with Tl(TfO) (TfO = triflate, CF₃SO₃), in some cases in the presence of CO or EtOH, causes the depalladation of complexes *trans*-[Pd{C(=NR)C₆H₄{C(O)Me}-2}Br(CNR)₂] [R = 2,6-dimethylphenyl (Xy) (**1a**), R = ^tBu (**1a'**)], *trans*-[Pd{C(=NXY)C₆H₄(OMe)₃-2,3,4-{C(O)Me}-6}Br(CNXY)₂] (**1b**), *trans*-[Pd{C(=NR)C₆H₄(CH=CH₂)-2}Br(CNR)₂] [R = Xy (**2**), ^tBu (**2'**)], *trans*-[Pd{C(=NXY)C(NHXY)=CC₆H₄{C(O)NXY}-2}Br(CNXY)₂] (**3**), *trans*-[Pd{C₆H₄-{C(O)Me}-2}Br(PPh₃)₂] (**4**), and [Pd{C₆H₄{C(O)Me}-2}Br(bpy)] (bpy = 2,2'-bipyridine) (**5**) to give organic compounds. Complexes **1a**, **1a'**, and **1b** react with Tl(TfO) in Me₂CO or CH₂Cl₂ to give the isoindolinones 2-(2,6-dimethylphenyl)-3-methylene-2,3-dihydroisoindol-1-one (**6a**), 2-*tert*-butyl-3-methylene-2,3-dihydroisoindol-1-one (**6a'**), and 2-(2,6-dimethylphenyl)-5,6,7-trimethoxy-3-methylene-2,3-dihydroisoindol-1-one (**6b**), respectively. When the reaction with **1a'** is carried out in the presence of a small amount of EtOH, in addition to **6a'**, the isoindolinone 2-*tert*-butyl-3-ethoxy-3-methyl-2,3-dihydroisoindol-1-one (**7**) and 2-acetyl-*N*-*tert*-butylbenzamide (**8**) are obtained. Complex **2** reacts with Tl(TfO) in the presence of CO to give *N*-(2,6-dimethylphenyl)-2-vinylbenzamide (**9**); however, the analogous compound **2'** reacts with Tl(TfO) to give a mixture containing *ortho*-cyanostyrene (**10**). Complex **3** reacts with Tl(TfO) to give a separable mixture of *N*-(2,6-dimethylphenyl)-2-(2,6-dimethylphenyl-amino)-2-[2-(2,6-dimethylphenyl)-3-oxo-2,3-dihydroisoindol-1-ylidene]acetamide (**11**) and *N*-(2,6-dimethylphenyl)-2-(2,6-dimethylphenylamino)-2-[2-(2,6-dimethylphenyl)-3-oxo-2,3-dihydroisoindol-1-ylidene]acetamidic acid (**12**). When this reaction is carried out in the presence of a small amount of EtOH, **11**, **12**, and its ethyl ester **13** are obtained. Complex **4** or **5** reacts with CO and Tl(TfO) in Me₂CO to give 3-methylenephthalide (**14**) or a complex mixture, respectively. Complexes **4** and **5** react with Tl(TfO) in CH₂Cl₂ in the presence of a small amount of EtOH, affording 3-ethoxy-3-methyl-3*H*-isobenzofuran-1-one (**15**). The crystal and molecular structures of **6a**, **6b**, **8**·0.11H₂O, **9**, **11**·0.5Et₂O, **13**, and **14** have been determined by X-ray diffraction studies.

Introduction

The insertion of unsaturated molecules into carbon–palladium bonds constitutes a key step in many palladium-mediated organic reactions.^{1,2} However, very few such reactions involving isocyanides have been reported. Thus, some organopalladium complexes react with isocyanides, forming, after depalladation, indazolines,³ indazoles,⁴ ketenimines,^{5–7} or 2-*R*-aminoisoindolinium

(R = Ph, Xy, ^tBu) salts.^{8,9} It has been reported that the reactions of aryliminoacylpalladium complexes with Grignard reagents, followed by hydrolysis, produce aryl ketones.¹⁰ Very recently, palladium-catalyzed syntheses of amidines from aryl halides, isocyanides, and organotin compounds¹¹ as well as mappicines, camptothecins, and homocamptothecins have been described.¹² Finally, the polymerization of isonitriles catalyzed by organopalladium complexes has also been reported.^{13–15}

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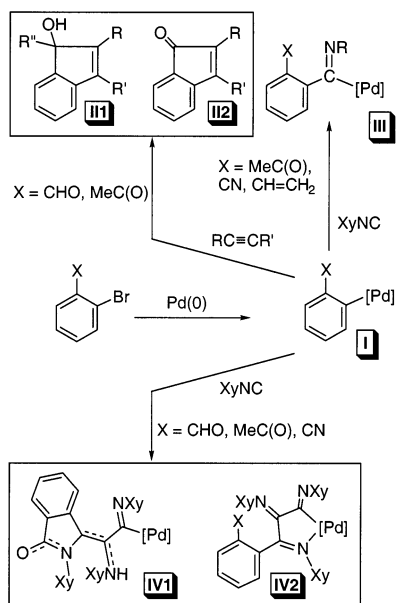
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Scheme 1



We have recently reported the synthesis of ortho-substituted arylpalladium complexes $[\text{Pd}(\text{C}_6\text{H}_4\text{X}-2)\text{BrL}_2]$ (**I**, Scheme 1) [$\text{L}_2 = \text{trans}(\text{PR}_3)_2$, $\text{R} = \text{Ph}$, $\text{X} = \text{CH}=\text{CH}_2$, CHO , $\text{C}(\text{O})\text{Me}$, CN ; $\text{R} = p\text{-To} = 4\text{-tolyl}$, $\text{X} = \text{CH}=\text{CH}_2$; $\text{L}_2 = \text{bpy} = 2,2'\text{-bipyridine}$, $\text{X} = \text{CHO}$, $\text{C}(\text{O})\text{Me}$, CN ; $\text{L}_2 = \text{tmeda} = N,N,N',N'\text{-tetramethylethylenediamine}$, $\text{X} = \text{CHO}$, CN]¹⁶ and studied their reactivity toward alkynes,¹⁷ to give indenols (**II1**) or indenones (**II2**), and toward XyNC , to give aryliminopalladium complexes (**III**) or some products resulting after a tri-insertion process (**IV1** and **IV2**).¹⁸ Some of the above complexes were reacted with $\text{Ti}(\text{TfO})$ to substitute the bromo ligand, whereby we expected either (i) coordination of the ortho groups or the imine-N to give cyclometalated or polynuclear complexes or (ii) decomposition of the resulting cationic or triflate complex to give N-heterocyclic compounds; we have already reported those reactions that lead to new stable complexes.¹⁸ In this paper we describe (i) the synthesis of new complexes of type **III** ($\text{R} = \text{Xy}$, tBu); (ii) the reactivity toward $\text{Ti}(\text{TfO})$, sometimes in the presence of CO or EtOH , of these new complexes, and some of those of types **III** and **IV1** previously reported; and (iii) the reactivity of some ortho-substituted arylpalladium complexes of type **I** toward CO and $\text{Ti}(\text{TfO})$, to force the cleavage of the $\text{Pd}-\text{C}$ bond giving organic compounds. These reactions constitute a stoichiometric synthesis of functionalized arenes from their corresponding bromoarenes and an incentive for future studies on the catalytic synthesis of such functionalized arenes.

Among the organic species we have synthesized, the isoindolinones are especially important. These compounds, particularly those with an alkylidene substituent

in position 3 (see **6**, **11**–**13** in Schemes 2 and 4), have attracted considerable interest because of their reported pharmacological activity.^{19–26} Several natural alkaloids such as neuvamine,^{19,20} lennoxamine,^{19,21} pictonamine,²⁷ or molecules having antitumor activity²⁸ contain an isoindolinone moiety. However, there are few methods reported for the synthesis of this type of compound.^{29–33}

Imidic acids $[\text{RC}(=\text{NR}')\text{OH}]$, usually existing in equilibrium with their tautomers, the amides $[\text{RC}(=\text{O})\text{NHR}']$, are unstable compounds. Both circumstances make imidic acids very difficult to isolate.³⁴ We report here the synthesis of a mixture of an amide and its tautomeric imidic acid form, their separation, and also the synthesis of the ethyl ester of this acid.

Experimental Section

The IR and NMR spectra, elemental analyses, conductivity measurements in Me_2CO , and melting point determinations were performed as described previously.⁸ The long-range $^{13}\text{C}-^1\text{H}$ correlations (HMBC) of **7**, **14**, and **15** were measured in a 200 MHz Bruker Avance spectrometer equipped with a QNP probe. The syntheses of **1a**, **2**, **3**,¹⁸ **4**, and **5**¹⁶ have been reported previously. The compound $[\text{Pd}\{\text{C}_6\text{H}_4(\text{OMe})_3-2,3,4\text{-}\{\text{C}(\text{O})\text{Me}\}-6\}\text{Br}(\text{bpy})]$ was prepared by the reaction of the analogous $[\text{Pd}\{\text{C}_6\text{H}_4(\text{OMe})_3-2,3,4\text{-}\{\text{C}(\text{O})\text{Me}\}-6\}\text{Cl}(\text{bpy})]$ ³⁵ with NaBr . The isonitriles XyNC ($\text{Xy} = 2,6\text{-dimethylphenyl}$) and tBuNC were purchased from Fluka. The preparations of the compounds were carried out at room temperature and without precautions against light, moisture, and O_2 , unless otherwise stated. The preparative thin layer chromatographic separations were performed using silica gel 60 A.C.C. (70–200 μm). For colorless substances fluorescent silica gel (GF₂₅₄) was added (approximately 5%). Elemental analyses and mass fragment data of all compounds and the synthesis and spectroscopic properties of **2'** and **10** have been included in the Supporting Information.

Synthesis of $\text{trans}[\text{Pd}\{\text{C}(=\text{N}^t\text{Bu})\text{C}_6\text{H}_4\{\text{C}(\text{O})\text{Me}\}-2\}\text{Br}(\text{CN}^t\text{Bu})_2]$ (1a'**).** tBuNC (0.196 cm^3 , 1.73 mmol) was added to a solution of $[\text{Pd}\{\text{C}_6\text{H}_4\{\text{C}(\text{O})\text{Me}\}-2\}\text{Br}(\text{bpy})]$ ($\text{bpy} = 2,2'\text{-bipyridine}$) (**5**) (200 mg, 0.43 mmol) in CH_2Cl_2 (15 cm^3). The resulting yellow solution was stirred for 30 min, the solvent

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was evaporated, and addition of Et₂O (20 cm³) produced the precipitation of a yellow solid, which was filtered, washed with Et₂O (2 × 5 cm³), and air-dried, giving yellow **1a'**. Yield: 180 mg, 75%. Mp: 103 °C dec. IR (cm⁻¹): ν(C≡N) 2194, ν(C=O) 1682, 1686, ν(C=N) 1606. ¹H NMR (200 MHz, CDCl₃): δ 8.24 (d, 1H, ³J_{HH} = 8 Hz), 7.42 (t, 1H, ³J_{HH} = 8 Hz), 7.31 (t, 1H, ³J_{HH} = 7 Hz), 7.13 (d, 1H, ³J_{HH} = 7 Hz), 2.44 (s, MeCO, 3H), 1.55 (s, 'Bu, 9H), 1.42 (s, 2×'Bu, 18H). ¹³C{¹H} NMR (50 MHz, CDCl₃): δ 204.5 (C=O), 164.6 (C=N), 141.8 (quaternary C), 140.6 (quaternary C), 133.1 (CH), 128.5 (CH), 127.9 (CH), 125.3 (CH), 58.0 (quaternary C), 57.5 (quaternary C), 32.3 (MeCO), 30.5 (3×Me, 'Bu), 29.7 (6×Me, 2×'Bu).

Synthesis of trans-[Pd{C(=NXy)C₆H(OMe)₃-2,3,4-{C(O)Me}-6}Br(CNXy)₂] (1b). [Pd{C₆H(OMe)₃-2,3,4-{C(O)Me}-6}Br(bpy)] (200 mg, 0.39 mmol) and XyNC (153 mg, 1.17 mmol) were mixed in CH₂Cl₂ (15 cm³) under N₂ to give a yellow solution, which was immediately concentrated in vacuo to dryness. Et₂O (20 cm³) was added and then the solvent partially evaporated, precipitating a solid, which was filtered and air-dried to give yellow **1b**. Yield: 237 mg, 77%. Mp: 118 °C dec. IR (cm⁻¹): ν(C≡N) 2186, 2214, ν(C=O) 1702, ν(C=N) 1618. ¹H NMR (200 MHz, CDCl₃): δ 7.26–7.15 (m, 2H), 7.05–7.01 (m, 4H), 6.90–6.84 (m, 4H), 4.07 (s, 3H, MeO), 3.92 (s, 3H, MeO), 3.64 (b s, 3H, MeO), 2.64 (s, MeCO, 3H), 2.35 (s, 6H, 2×Me), 2.26 (s, 12H, 4×Me).

Synthesis of 2-(2,6-dimethylphenyl)-3-methylene-2,3-dihydroisoindol-1-one (6a). Complex **1a** (300 mg, 0.43 mmol) and Ti(TfO) (152 mg, 0.43 mmol) were mixed in Me₂CO (15 cm³) and stirred for 16 h. The resulting black suspension was filtered over Celite, and the filtrate was concentrated (ca. 3 cm³) and applied to a preparative TLC plate. Eluant: *n*-hexane/Et₂O, 1:1. The colorless band at *R*_f = 0.7 was collected and extracted with Me₂CO (30 cm³). The resulting solution was stirred with anhydrous MgSO₄ for 1 h and filtered. The solution was evaporated to dryness and the residue recrystallized from Et₂O, affording colorless crystals of **6a**. Yield: 70 mg, 65%. Mp: 83 °C. IR (cm⁻¹): ν(C=O) 1794. ¹H NMR (300 MHz, CDCl₃): δ 7.87 (apparent dt, C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.70 (apparent dt, C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.58 (td, C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.49 (td, C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.21–7.09 (m, C₆H₃, 3 H), 5.07 (d, CH₂, 1H, ²J_{HH} = 2 Hz), 4.32 (d, CH₂, 1H, ²J_{HH} = 2 Hz), 2.04 (s, 2×Me, 6 H). ¹³C NMR (75 MHz, CDCl₃): δ 166.2 (C=O), 141.5 (quaternary C), 137.3 (2×CMe), 136.3 (quaternary C), 132.1 (CH), 129.6 (CH), 129.5 (quaternary C), 129.0 (CH), 128.4 (2×CH–CMe), 123.6 (CH), 120.2 (CH), 89.7 (CH₂), 17.7 (2×Me). Single crystals were grown by cooling solutions of **6a** in *n*-pentane.

Synthesis of 2-tert-Butyl-3-methylene-2,3-dihydroisoindol-1-one (6a'). Complex **1a'** (1.100 g, 1.98 mmol) was reacted with Ti(TfO) (701 mg, 1.98 mmol) in Me₂CO for 16 h. The resulting black suspension was filtered over Celite, the filtrate was evaporated to dryness, and the residue was extracted with *n*-pentane (25 cm³). The extract was filtered through a layer of anhydrous MgSO₄, and the filtrate was applied to a preparative TLC plate. Eluant: *n*-hexane/Et₂O, 1:2. The colorless band at *R*_f = 0.7 was collected and extracted with Me₂CO (30 cm³). The extract was treated with anhydrous MgSO₄ for 1 h and filtered. Evaporation to dryness afforded **6a'** as a colorless liquid. This product is unstable and it decomposes completely in 2 days. For this reason it was not possible to obtain correct elemental analyses. Yield: 179 mg, approximately 45%. IR (cm⁻¹): ν(C=O) 1716. ¹H NMR (300 MHz, CDCl₃): δ 7.72 (apparent dt, C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.60 (apparent dt, C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.51 (td, C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.43 (td, C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 5.27 and 5.22 (AB system, CH₂, 2H, ²J_{HH} = 2 Hz), 1.75 (s, 'Bu, 9H). ¹³C NMR (75 MHz, CDCl₃): δ 168.5 (C=O), 142.1 (quaternary C), 137.4 (quaternary C), 131.5 (CH), 129.7 (C=CH₂), 129.0 (CH), 122.6 (CH), 118.8 (CH), 92.5 (CH₂), 57.7 (CMe₃), 29.9 (CMe₃).

Synthesis of 2-(2,6-Dimethylphenyl)-5,6,7-trimethoxy-3-methylene-2,3-dihydroisoindol-1-one (6b). Complex **1b** (300 mg, 0.38 mmol) and Ti(TfO) (134 mg, 0.38 mmol) were mixed in CH₂Cl₂ (15 cm³) and stirred for 16 h. The resulting black suspension was filtered over Celite, and the filtrate was evaporated to dryness. The residue was extracted with Et₂O (25 cm³), and the extract was filtered through a layer of anhydrous MgSO₄. The solution was applied to a preparative TLC plate. Eluant: Et₂O. The colorless band at *R*_f = 0.75 was collected and extracted with Me₂CO (30 cm³). The extract was treated with anhydrous MgSO₄ for 1 h and filtered. Evaporation to dryness afforded a solid, which was recrystallized from Et₂O/*n*-hexane to give white **6b**. Yield: 88 mg, 68%. Mp: 194 °C. IR (cm⁻¹): ν(C=O) 1698, 1694. ¹H NMR (300 MHz, CDCl₃): δ 7.25–7.12 (m, C₆H₃, 3H), 7.01 (s, C₆H, 1H), 5.00 (d, CH₂, 1H, ²J_{HH} = 2 Hz), 4.26 (d, CH₂, 1H, ²J_{HH} = 2 Hz), 4.15 (s, MeO, 3H), 3.97 (s, MeO, 3H), 3.91 (s, MeO, 3H), 2.09 (s, 2×Me, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 164.2 (C=O), 157.7 (quaternary C), 151.4 (quaternary C), 143.3 (quaternary C), 141.3 (quaternary C), 137.4 (2×CMe), 133.6 (quaternary C), 132.4 (quaternary C), 128.7 (CH), 128.3 (2×CH–CMe), 114.1 (quaternary C), 98.6 (CH), 88.1 (CH₂), 59.4 (MeO), 58.3 (MeO), 53.3 (MeO), 14.6 (2×Me). Single crystals were grown by slow evaporation of solutions of **6b** in Et₂O.

Synthesis of 2-tert-Butyl-3-ethoxy-3-methyl-2,3-dihydroisoindol-1-one (7) and 2-Acetyl-N-(tert-butyl)benzamide (8). Ti(TfO) (701 mg, 1.98 mmol) and EtOH (1 drop) were added to a solution of **1a'** in CH₂Cl₂ (15 cm³). The resulting black suspension was stirred for 16 h and filtered over Celite. The filtrate was evaporated to dryness, and the residue was extracted with Et₂O (25 cm³), leaving an oily mixture (327 mg) that could not be resolved. The yellow ethereal solution was concentrated and applied to a preparative TLC plate (eluant: *n*-hexane/Et₂O, 1:2). Three bands were collected and extracted with Me₂CO (30 cm³), the extracts were treated with anhydrous MgSO₄ for 1 h, then filtered, and the filtrates were evaporated to dryness, affording the corresponding compounds: **6a'**, *R*_f = 0.89, yield: 67 mg, 17%. **7**, *R*_f = 0.74, yield: 117 mg, 24%, white oily solid (this fraction must be separated very carefully from the previous one in order to obtain pure **7**; a 1.5% discrepancy in %C of **7** is due to this separation difficulty). **8**, *R*_f = 0.24, yield: 134 mg, 32%, white solid which was washed with *n*-hexane and dried in vacuo.

Compound 7. Mp: 38–42 °C. IR (cm⁻¹): ν(C=O) 1692 (b). ¹H NMR (200 MHz, CDCl₃): δ 7.72 (apparent dt, H₂ C₆H₄ next to C=O, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.53 (apparent dt, H₄ C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.43 (td, H₃ C₆H₄, 1H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 7.36 (td, H₅ C₆H₄ next to the ethoxy group, 2H, ³J_{HH} = 7 Hz, ⁴J_{HH} = 1 Hz), 3.02 (AB system coupled with the Me group, ddq, CH₂, 2H, ²J_{HH} = 9 Hz, ³J_{HH} = 7 Hz), 1.88 (s, Me, 3 H), 1.66 (s, 'Bu, 9 H), 1.11 (t, CH₂Me, 3H, ³J_{HH} = 7 Hz). ¹³C NMR (50 MHz, CDCl₃): δ 168.0 (C=O), 146.4 (C₆ CCOEt), 132.1 (CCO), 131.8 (CH₄), 129.1 (CH₃), 122.8 (CH₂), 120.9 (CH₅), 95.1 (C(OEt)Me), 58.4 (CH₂), 55.9 (CMe₃), 28.7 (CMe₃), 28.1 (Me), 14.9 (CH₂Me).

Compound 8. Mp: 108–110 °C. IR (cm⁻¹): ν(NH) 3306, ν(C=O) 1682. ¹H NMR (200 MHz, CDCl₃): δ 7.57–7.53 (m, 1H), 7.46–7.43 (m, 3H), 5.74 (b s, 1H), 2.56 (s, C(O)Me, 3H), 1.47 (s, 'Bu, 9H). ¹³C NMR (50 MHz, CDCl₃): δ 201.8 (C=O), 168.4 (C(O)NH), 139.2 (quaternary C), 137.1 (quaternary C), 130.8 (CH), 129.7 (CH), 127.8 (CH), 127.4 (CH), 52.0 (CMe₃), 29.4 (C(O)Me), 28.7 (CMe₃). Single crystals of **8**·0.11H₂O were grown by slow evaporation of solutions of **8** in Et₂O.

Synthesis of 2-Vinyl-N-(2,6-dimethylphenyl)benzamide (9). CO was bubbled through a solution of **2** (100 mg, 0.15 mmol) in Me₂CO (10 cm³) for 1 min, and then Ti(TfO) (53 mg, 0.15 mmol) was added. CO was bubbled again for 30 min, the reaction flask was then closed, and the reaction was continued for 16 h. The resulting suspension containing metallic palladium was filtered over Celite, and the red filtrate

was concentrated and applied to a preparative TLC plate (eluant: *n*-hexane/Et₂O, 1:1). A colorless band at $R_f = 0.4$ was extracted with Me₂CO (30 cm³). The extract was stirred with anhydrous MgSO₄ and filtered. Evaporation to dryness of the resulting solution afforded a white solid, which was recrystallized from *n*-hexane to give **9**. Yield: 26 mg, 68%. Mp: 124 °C. IR (cm⁻¹): $\nu(\text{NH})$ 3280, $\nu(\text{C=O})$ 1650. ¹H NMR (300 MHz, CDCl₃): δ 7.64 (d, C₆H₄, 2H, ³ $J_{\text{HH}} = 7$ Hz), 7.47 (t, C₆H₄, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.36 (t, C₆H₄, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.24 (dd, CH=CH₂, 1H, ³ $J_{\text{HH}} = 17$ Hz, ³ $J_{\text{HH}} = 11$ Hz), 7.14–7.12 (m, 3H, C₆H₃), 7.06 (bs, NH, 1H), 5.77 (dd, 1H, CH=CH₂ H *trans* to H, ³ $J_{\text{HH}} = 17$ Hz, ² $J_{\text{HH}} = 1$ Hz), 5.39 (dd, 1H, CH=CH₂ H *cis* to H, ³ $J_{\text{HH}} = 11$ Hz, ² $J_{\text{HH}} = 1$ Hz), 2.33 (s, 2×Me, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 167.6 (C=O), 136.4 (quaternary C), 135.5 (2×CMe), 135.3 (quaternary C), 134.6 (CH), 133.7 (quaternary C), 130.5 (CH), 128.4 (2×CHCMe), 127.8 (CH), 127.6 (CH), 127.4 (CH), 126.5 (CH), 117.1 (CH₂), 18.7 (2×Me). Single crystals were grown by slow evaporation of solutions of **9** in Et₂O.

Synthesis of *N*-(2,6-Dimethylphenyl)-2-(2,6-dimethylphenylamino)-2-[2-(2,6-dimethylphenyl)-3-oxo-2,3-dihydroisindol-1-ylidene]acetamide (11**) and *N*-(2,6-Dimethylphenyl)-2-(2,6-dimethylphenylamino)-2-[2-(2,6-dimethylphenyl)-3-oxo-2,3-dihydroisindol-1-ylidene]acetamidic Acid (**12**).** Tl(TfO) (314 mg, 0.89 mmol) was added to a suspension of **3** (844 mg, 0.89 mmol) in Me₂CO (20 cm³). The resulting red suspension was stirred for 20 h. During this time decomposition to metallic palladium was observed and a dark brownish suspension formed. This was filtered over Celite, and the filtrate was concentrated and applied to a preparative TLC plate (eluant: *n*-hexane/Et₂O, 1:2). A yellow band at $R_f = 0.21$ was collected and extracted with Me₂CO (30 cm³). The resulting solution was dried with anhydrous MgSO₄ for 1 h and filtered, and the filtrate was evaporated to dryness, giving a 2:3 mixture of both tautomers **11** and **12**. Yield: 326 mg, 71%. A sample of this mixture (200 mg) was dissolved in Et₂O (30 cm³), the solution was evaporated to dryness, and the residue was treated with Et₂O (30 cm³), causing the precipitation of a solid, which was filtered and air-dried to give yellow **12** (83 mg, 41%). The same process was repeated with the mother liquor, giving **11** (54 mg, 27%).

Compound 11. Mp: 136–138 °C. IR (cm⁻¹): $\nu(\text{NH})$ 3388, 3366, 3262 b, $\nu(\text{C=O})$ 1698, 1660. ¹H NMR (300 MHz, CDCl₃): δ 7.97 (d, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.73 (d, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.43 (td, 1H, ³ $J_{\text{HH}} = 7$ Hz, ⁴ $J_{\text{HH}} = 1$ Hz), 7.37 (td, 1H, ³ $J_{\text{HH}} = 7$ Hz, ⁴ $J_{\text{HH}} = 1$ Hz), 7.3–7.2 (m, 3H), 7.1–6.95 (m, 6H), 6.86 (s, NH, 1H), 5.07 (s, NH, 1H), 2.36 (s, 2×Me, 6H), 2.20 (s, 2×Me, 6H), 1.66 (s, 2×Me, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 165.8 (C=O), 161.6 (C=O), 137.8 (quaternary C), 137.0 (quaternary C), 135.9 (quaternary C), 135.7 (quaternary C), 135.6 (quaternary C), 134.9 (quaternary C), 132.7 (quaternary C), 132.1 (CH), 129.9 (CH), 129.14 (CH), 129.11 (CH), 128.6 (CH), 127.54 (CH), 127.48 (quaternary C), 127.3 (quaternary C), 127.0 (CH), 126.8 (CH), 124.0 (CH), 122.0 (CH), 112.9 (quaternary C), 18.8 (2×Me), 18.3 (2×Me), 18.1 (2×Me). Single crystals of **11**·0.5Et₂O were grown by slow evaporation of solutions of **11** in *n*-hexane/Et₂O, 1:1.

Compound 12. Mp: 206–208 °C. IR (cm⁻¹): $\nu(\text{OH})$, $\nu(\text{NH})$ 3420, 3232 b, $\nu(\text{C=O})$, $\nu(\text{C=N})$ 1682, 1668. ¹H NMR (300 MHz, CDCl₃): δ 8.15 (d, 1H, ³ $J_{\text{HH}} = 7$ Hz), 8.04 (d, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.63 (td, 1H, ³ $J_{\text{HH}} = 7$ Hz, ⁴ $J_{\text{HH}} = 1$ Hz), 7.56 (b t, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.05–7.02 (m, 4H), 6.95–6.79 (m, 5H), 5.58 (s, NH, 1H), 2.39 (s, 2×Me, 6H), 2.24 (s, 2×Me, 6H), 1.54 (s, OH, 1H), 1.48 (s, 2×Me, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 166.5 (C=O), 160.9 (quaternary C), 138.5 (quaternary C), 137.1 (quaternary C), 136.5 (quaternary C), 135.4 (quaternary C), 135.1 (quaternary C), 133.0 (quaternary C), 132.7 (CH), 130.7 (quaternary C), 130.4 (quaternary C), 130.3 (CH), 129.2 (CH), 128.7 (quaternary C), 128.5 (CH), 128.2 (CH), 128.0 (CH), 126.8 (CH), 124.7 (CH), 124.1 (CH), 123.1 (CH), 122.2 (quaternary C), 18.9 (2×Me), 18.6 (2×Me), 17.7 (2×Me).

Synthesis of the Ethyl Ester of the *N*-(2,6-Dimethylphenyl)-2-(2,6-dimethylphenylamino)-2-[2-(2,6-dimethylphenyl)-3-oxo-2,3-dihydroisindol-1-ylidene]acetamidic Acid (13**).** Tl(TfO) (374 mg, 1.06 mmol) and EtOH (one drop) were added to a solution of **3** (1.000 g, 1.06 mmol) in CH₂Cl₂ (20 cm³). The resulting black suspension was stirred for 20 h and filtered over Celite, and the yellow filtrate was concentrated and applied to a preparative TLC plate (eluant: *n*-hexane/Et₂O, 1:2), where two main yellow bands separated. From the band at $R_f = 0.26$ a 2:1 mixture of **11** and **12** was obtained. Yield: 317 mg, 51%. The band at $R_f = 0.61$ was collected and extracted with Me₂CO (30 cm³). The extract was treated with anhydrous MgSO₄ for 1 h, filtered, and evaporated to dryness, affording the yellow ester **13**. Yield: 98 mg, 18%. Mp: 206–208 °C. IR (cm⁻¹): $\nu(\text{NH})$ 3384, $\nu(\text{C=O})$, $\nu(\text{C=N})$ 1698, 1694, 1660. ¹H NMR (300 MHz, CDCl₃): δ 7.99 (d, 1H, ³ $J_{\text{HH}} = 8$ Hz), 7.59–7.58 (m, 2H), 7.43 (q, 1H, ³ $J_{\text{HH}} = 4$ Hz), 7.10–7.05 (m, 3H), 6.80–6.69 (m, 6H), 4.79 (s, NH, 1H), 4.39 (q, CH₂, 2H, ² $J_{\text{HH}} = 7$ Hz), 2.22 (s, 2×Me, 6H), 1.48 (bs, 4×Me, 12H), 1.39 (t, CH₂Me, 3H, ² $J_{\text{HH}} = 7$ Hz). ¹H NMR (300 MHz, CDCl₃, –60 °C): δ 8.04 (d, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.66 (t, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.55–7.45 (m, 2H), 7.14–7.10 (m, 3H), 6.87–6.81 (m, 4H), 6.72–6.64 (m, 2H), 4.81 (s, NH, 1H), 4.40 (m, CH₂), 2.35 (s, Me, 3H), 2.30 (s, Me, 3H), 2.16 (s, Me, 3H), 2.01 (s, Me, 3H), 1.43 (t, CH₂Me, 3H, ² $J_{\text{HH}} = 7$ Hz), 0.89 (s, Me, 3H), 0.63 (s, Me, 3H). Single crystals were grown by slow evaporation of solutions of **13** in Et₂O.

Synthesis of 3-Methylenephthalide (14**).** CO was bubbled for 1 min through a solution of **4** (850 mg, 1.02 mmol) in Me₂CO (20 cm³). Tl(TfO) (360 mg, 1.02 mmol) was added and CO bubbled again for 30 min. The flask was closed, and the mixture was stirred for 16 h. The resulting dark red suspension was filtered over Celite, the filtrate was evaporated to dryness, and the residue was extracted with Et₂O (20 cm³). The extract was concentrated and applied to a preparative TLC plate (eluant: *n*-hexane/Et₂O, 1:1). A colorless band ($R_f = 0.62$) was collected and extracted with Me₂CO (30 cm³), and the extract was treated with anhydrous MgSO₄ for 1 h. The suspension was filtered and the filtrate was evaporated to dryness, affording **14** as a white oil. Yield: 48 mg, 32%. ¹H NMR (200 MHz, CDCl₃): δ 7.91 (dt, H₂ C₆H₄ next to C=O, 1H, ³ $J_{\text{HH}} = 8$ Hz, ⁴ $J_{\text{HH}} = 1$ Hz), 7.74–7.71 (m, H₄ and H₅ C₆H₄ next to C=CH₂, 2H), 7.64–7.54 (m, H₃ C₆H₄, 1H), 5.23 (AB system, CH₂, 2H, ² $J_{\text{HH}} = 3$ Hz). ¹³C NMR (75 MHz, CDCl₃): δ 166.8 (C=O), 151.9 (C=CH₂), 139.0 (C₆ CC=CH₂), 134.4 (CH₄), 130.4 (CH₃), 125.3 (CH₂), 125.2 (C₁ CCO), 120.6 (CH₅), 91.2 (CH₂). These data are coincident with those described previously.³⁷ Single crystals were grown by slow evaporation of solutions of **14** in CDCl₃/Et₂O.

Synthesis of 3-Ethoxy-3-methyl-3H-isobenzofuran-1-one (15**).** This was prepared from **4** or **5** (1.2 g, 2.60 mmol), Tl(TfO) (919 mg, 2.60 mmol), and CO following the procedure used to prepare **14** but adding a drop of EtOH to the solvent (CH₂Cl₂, 20 cm³) ($R_f = 0.59$ in the preparative TLC). Yield (preparation from **5**): 370 mg, 74% (yellowish liquid). IR (cm⁻¹): $\nu(\text{C=O})$ 1672. ¹H NMR (200 MHz, CDCl₃): δ 7.88 (d, H₂ C₆H₄ next to C=O, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.75 (t, H₄ C₆H₄, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.60 (t, H₃ C₆H₄, 1H, ³ $J_{\text{HH}} = 7$ Hz), 7.53 (d, H₅ C₆H₄ next to the ethoxy group, 1H, ³ $J_{\text{HH}} = 7$ Hz), 3.18 (ddq, AB part of an ABM₃ system, CH₂, 2H, ² $J_{\text{HH}} = 9$ Hz, ³ $J_{\text{HH}} = 7$ Hz), 1.85 (s, Me, 3H), 1.15 (t, CH₂Me, 3H, ³ $J_{\text{HH}} = 7$ Hz). ¹³C NMR (50 MHz, CDCl₃): δ 168.0 (C=O), 147.9 (C₆ CCOEt), 134.4 (CH₄), 130.3 (CH₃), 127.1 (C₁ CCO), 125.3 (CH₂), 122.0 (CH₅), 108.5 (COEt), 59.4 (CH₂), 25.5 (Me), 14.9 (CH₂Me).

X-ray Structure Determinations. Data were registered using Mo K α radiation on a Siemens P4 (**6a**,**9**) or Bruker

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Table 1. Summary of X-ray Data for Compound 6a, 6b, 8·0.11H₂O, and 9

	6a	6b	8·0.11H₂O	9
formula	C ₁₇ H ₁₅ NO	C ₂₀ H ₂₁ NO ₄	C ₁₃ H _{17.22} NO _{2.11}	C ₁₇ H ₁₇ NO
<i>M_r</i>	249.30	339.38	221.26	251.32
cryst syst	monoclinic	orthorhombic	tetragonal	monoclinic
space group	<i>P</i> 2 ₁ / <i>c</i>	<i>Pbcn</i>	<i>I</i> 4 ₁ / <i>a</i>	<i>P</i> 2 ₁ / <i>c</i>
<i>a</i> (Å)	8.5260(8)	11.9844(11)	17.8744(14)	12.2829(12)
<i>b</i> (Å)	10.4956(10)	14.5392(14)	17.8744(14)	11.5491(12)
<i>c</i> (Å)	15.3645(16)	19.9966(18)	15.6983(18)	10.1581(11)
α (deg)	90	90	90	90
β (deg)	94.882(9)	90	90	110.02(2)
γ (deg)	90	90	90	90
<i>V</i> (Å ³)	1369.9(2)	3484.3(6)	5015.5(8)	1353.9(2)
<i>Z</i>	4	8	16	4
<i>T</i> (K)	173(2)	133(2)	133(2)	173(2)
<i>D_{calc}</i> (Mg m ^{−3})	1.209	1.294	1.172	1.233
<i>F</i> (000)	528	1440	1906	536
μ (mm ^{−1})	0.075	0.090	0.079	0.076
no. of indep reflns	2400	4219	2571	2377
no. of data/restraints/params	2400/0/174	4219/0/231	2571/0/156	2377/0/178
<i>S</i> (<i>F</i> ²)	0.944	1.025	1.007	0.938
wR2 [all reflns]	0.0925	0.0917	0.0982	0.0867
R1 [<i>I</i> > 2σ(<i>I</i>)]	0.0352	0.0359	0.0369	0.0352
max. Δρ (e Å ^{−3})	−0.183	−0.209	−0.182	−0.192

Table 2. Summary of X-ray Data for Compounds 11·0.5Et₂O, 13, and 14

	11	13	14
formula	C ₃₆ H ₃₈ N ₃ O _{2.5}	C ₃₆ H ₃₇ N ₃ O ₂	C ₉ H ₆ O ₂
<i>M_r</i>	552.69	543.69	146.14
cryst syst	monoclinic	monoclinic	monoclinic
space group	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 2 ₁ / <i>n</i>	<i>Cc</i>
<i>a</i> (Å)	10.9302(11)	12.1747(14)	7.7327(8)
<i>b</i> (Å)	25.491(2)	15.6855(18)	13.3949(14)
<i>c</i> (Å)	21.9214(18)	15.9240(18)	13.5108(14)
α (deg)	90	90	90
β (deg)	94.002(3)	90.116(3)	96.419(3)
γ (deg)	90	90	90
<i>V</i> (Å ³)	6092.8(10)	3040.9(6)	1390.7(3)
<i>Z</i>	8	4	8
<i>T</i> (K)	133(2)	133(2)	133(2)
<i>D_{calc}</i> (Mg m ^{−3})	1.205	1.188	1.396
<i>F</i> (000)	2360	1160	608
μ (mm ^{−1})	0.076	0.074	0.099
no. of indep reflns	11 357	6206	2029
no. of data/ restraints/ params	11357/996/797	6206/110/381	2029/2/199
<i>S</i> (<i>F</i> ²)	0.979	1.003	1.077
wR2 [all reflns]	0.1367	0.1260	0.0818
R1 [<i>I</i> > 2σ(<i>I</i>)]	0.0517	0.0486	0.0310
max. Δρ (e Å ^{−3})	−0.328	−0.371	−0.179

SMART 1000 CCD diffractometer. Structures were solved by direct methods and refined anisotropically on *F*² (program SHELXL-97, G. M. Sheldrick, University of Göttingen, Germany). Treatment of hydrogen atoms: NH freely refined, methyls as rigid groups, other H riding. Crystal data are presented in Tables 1 and 2. *Special features of refinement*: For compound **8**, a significant difference peak was refined as a partially occupied water site, for which the H atoms were not located. Compound **11** crystallizes with two independent molecules and an ether molecule in the asymmetric unit; the latter is disordered over two sites with occupation 0.683, 0.317(6). A small difference peak (0.6 e/Å³) in **13** lies near C9 and may be an alternative position for C10. For compounds **11** and **13**, which diffracted weakly, systems of restraints (to dimensions of the two independent molecules for **11**, to displacement parameters for both structures) were employed to improve refinement stability. Compound **14** crystallizes with two independent molecules; Friedel opposite reflections were merged because the anomalous dispersion was not significant. Tables 1 and 2 give details of data collection and refinement.

Results

The aim of this work was to study the conditions required to demetalate some of the previously reported aryl and iminoacyl complexes of types **I**, **III**, and **IV1** (Scheme 1)¹⁸ to give organic compounds. Previous attempts starting from complexes of the types **I** and **IV2** were unsuccessful.¹⁸ To extend this study, we have prepared some new complexes of type **III** (see below).

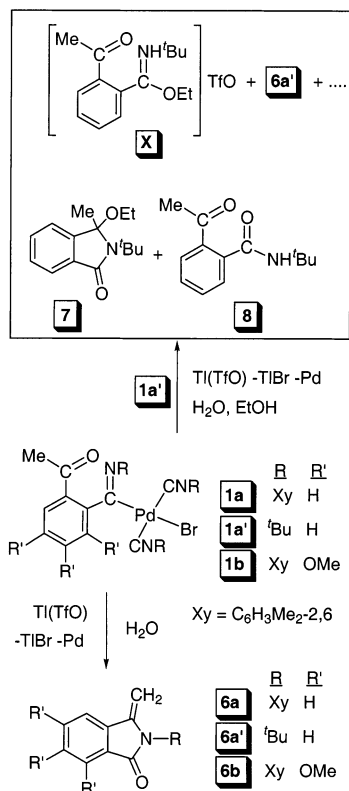
We have attempted to force the cleavage of the Pd–C bond by replacing the bromo ligand for TfO. We have also carried out these reactions in the presence of CO. Only those leading to positive results are reported here. No precautions were taken against light, moisture, and oxygen in these depalladation reactions. The influence of the presence of EtOH in some reactions was also studied.

Synthesis of New Iminoacyl Palladium Complexes. We have prepared the new compounds *trans*-[Pd{C(=N^tBu)C₆H₄[C(O)Me]-2}Br(CN^tBu)₂] (**1a'**), *trans*-[Pd{C(=N^tBu)C₆H₄[C(O)Me]-2,3,4-[C(O)Me]-6}Br(CN^tBu)₂] (**1b**), and *trans*-[Pd{C(=N^tBu)C₆H₄(CH=CH₂)-2}Br(CN^tBu)₂] (**2**) in order to expand the reactivity studies on the analogous **1a** and **2**. They were synthesized following the same procedures used for **1a** and **2**,¹⁸ viz., reactions of the corresponding isocyanide with [Pd(R)-BrL₂] [L₂ = bpy, R = C₆H₄[C(O)Me]-2 (for **1a'**), C₆H₄(OMe)₃-2,3,4-[C(O)Me]-6 (for **1b**); L = PPh₃, R = C₆H₄(CH=CH₂)-2 (for **2**)] (Scheme 2). However, while **1a'** was easily isolated and characterized, the reaction to give **1b** had to be carried out under N₂ and rapidly, as otherwise the Pd(I) dimer [Pd₂Br₂(CN^tBu)₄] is obtained.^{8,18,38,39} We had previously observed this reduction in the reaction of [Pd(R)(μ-Br)]₂ or [Pd(R)Br(L)] with R'NC (Pd:R'NC = 1:3 or 1:2, respectively; R = C, *N*-C₆H₄CH₂NH₂-2-X-5, X = H, MeO, NO₂, F; L = R'NC, R' = Xy, ^tBu)⁸ or that between [Pd(dba)₂], 2-BrC₆H₄-CHO, and an excess of XyNC.¹⁸ It is curious that the synthesis of **1a** did not cause this problem.¹⁸ This difference may be regarded as a consequence of the

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Scheme 2

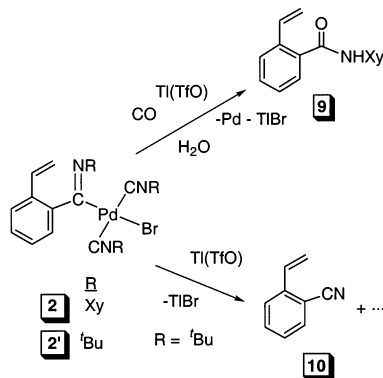


additional reactivity introduced by the three MeO groups. The preparation of **2'** must also be carried out under N_2 and rapidly (as with **2**).¹⁸ However, we have not been able to isolate it as a pure substance, as it forms as the major product together with tenacious minor impurities, of similar solubility in Et_2O and hexane, which significantly affect the carbon analysis (see Supporting Information).

Reactions with $\text{Ti}(\text{TfO})$. The reaction of **1a**, **1a'**, or **1b** with $\text{Ti}(\text{TfO})$ in CH_2Cl_2 or Me_2CO results, after 16 h stirring at room temperature, in the precipitation of TiBr plus metallic palladium and the formation of the isoidolinone **6a**, **6a'** or **6b**, which can be isolated from the resulting solutions in 65, 45 or 68% yield, respectively (Scheme 2). **6a** and **6b** are stable white solids which have been fully characterized, including X-ray diffraction studies. In contrast, **6a'** is a liquid that decomposes completely within 2 days, although it could be characterized by NMR and mass spectroscopy. Our attempts to prepare **6a** using **1a** or $[\text{Pd}(\text{dba})_2]$ as catalyst failed (10% of **1a**, Ti_2CO_3 , Me_2CO at room temperature or DMF at 90 °C; 10% of $[\text{Pd}(\text{dba})_2]$, $\text{Ti}(\text{TfO})$, DMF, 90 °C).

When $\text{Ti}(\text{TfO})$ and a drop of EtOH were added to a solution of **1a'** in CH_2Cl_2 , a mixture of products was obtained, after 16 h stirring at room temperature. The fraction insoluble in Et_2O , an oily mixture, could not be separated, but its spectroscopic data (IR, NMR, and EI-MS) suggested it to be a mixture of two compounds, one of them being probably the triflate salt of the ethyl ester of the 2-acetyl-*N*-*tert*-butyl benzimidic acid (**X** in Scheme 2). The fraction soluble in Et_2O contained a mixture of products that could be separated by preparative TLC. They were identified as 2-*tert*-butyl-3-ethoxy-3-methyl-2,3-dihydroisoidol-1-one (**7**) and 2-acetyl-*N*-

Scheme 3

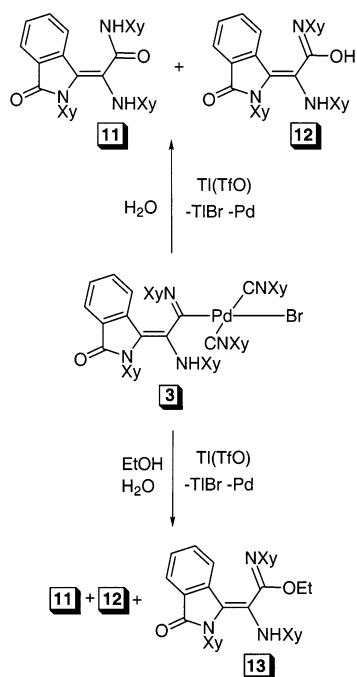


(*tert*-butyl)benzamide (**8**), as well as **6a'**. Indeed, when the reaction of **1a'** with $\text{Ti}(\text{TfO})$ was carried out in 1:15 $\text{EtOH}/\text{CH}_2\text{Cl}_2$ or in EtOH as solvent, more complex mixtures formed; the only component we could identify was compound **8**. Interestingly, the reactivity of **1a** and **1b** with TiOTf in CH_2Cl_2 was not affected in this way by the presence of EtOH . As mentioned in the Introduction, isoidolinones, particularly those with an alkylidene substituent in position 3, have attracted considerable interest because of their reported pharmacological activity.^{19–28} However, there are few methods for the synthesis of 3-alkylidene-isoidolin-1-ones and isonitriles are not employed in any of them.^{29–33}

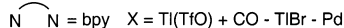
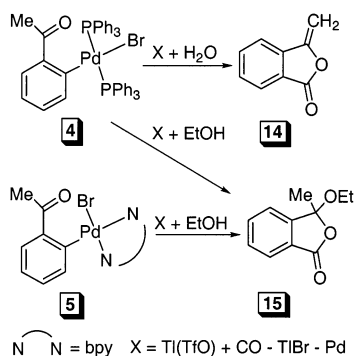
The reactions of **2** or **2'** with $\text{Ti}(\text{TfO})$ in Me_2CO afforded complicated mixtures of compounds. However, when the reaction with **2** was carried out in the presence of CO (see below), a depalladation to 2-vinyl-*N*-(2,6-dimethylphenyl)benzamide (**9**) (Scheme 3) took place. This difference in reactivity due to the presence of CO was not observed with **2'**, which, with or without CO, afforded a complex mixture from which only *ortho*-cyanostyrene (**10**) (39%) could be isolated and characterized. The spectroscopic data of this unexpected product are coincident with those previously described in the literature (see Supporting Information).³⁶ The major product in this reaction was a solid which could not be identified (see Supporting Information). This different and unexpected behavior of **2'** with respect to **2** could be due to the above-mentioned impurities present in **2'**.

Complex **3** reacts with $\text{Ti}(\text{TfO})$ in Me_2CO to give, after 20 h at room temperature, a precipitate of TiBr plus metallic palladium and a solution from which the highly functionalized 3-alkylidene-2,3-dihydroisoidolines **11** and **12** could be isolated (71% total yield, Scheme 4). These tautomers could not be separated by chromatography, but they displayed an exploitable difference in solubility. Thus, when a solution of both products in Et_2O was evaporated to dryness and Et_2O added again, the major tautomer did not redissolve and could be isolated by filtration, while the other could be similarly separated from the mother liquors. In the solid state, **11** and **12** are stable and they do not interconvert. However, if **12** is dissolved in CH_2Cl_2 and refluxed for 16 h, it transforms completely into **11**. The latter is stable at room temperature in CDCl_3 for several days, while under the same conditions **12** transforms partially into **11**. The addition of an acid does not accelerate the interconversion of these products. Several reviews dealing with imido compounds have discussed the question

Scheme 4



Scheme 5



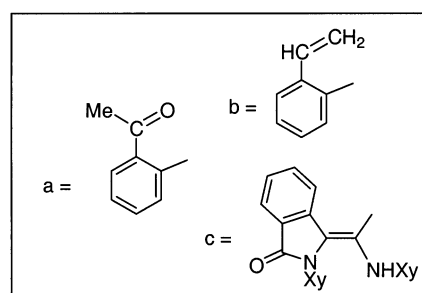
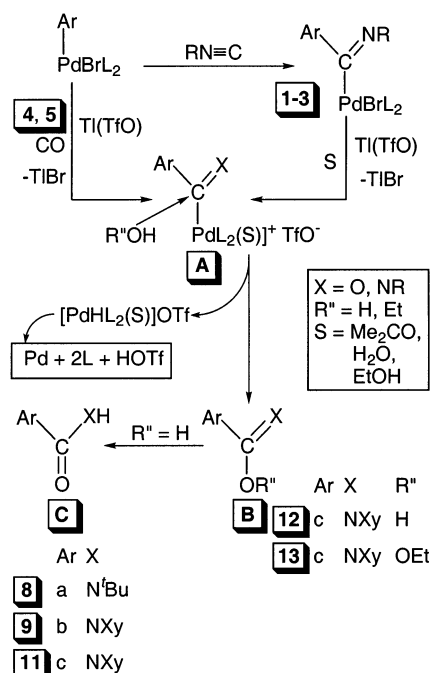
of whether imidic acids can exist in general.³⁴ They are unstable compounds that may be in equilibrium with the stable amide molecule. This is confirmed by theoretical investigations, which demonstrate that the amide form is about 11 kcal/mol more stable than the tautomeric imidic acid.⁴⁰

When the reaction of **3** with $\text{Ti}(\text{TfO})_4$ was carried out in CH_2Cl_2 plus a drop of EtOH , **13**, the ethyl ester of **12**, was obtained in addition to **11** and **12**. The yield of **13** varies from 15 to 40%, depending on the added amount of EtOH .

Reactions with CO and $\text{Ti}(\text{TfO})_4$. The reactions of complexes of types **I** and **III** (Scheme 1) with CO did not lead to complexes resulting from the insertion of CO into the C–Pd bond. Usually, the starting material was recovered or, if TiOTf was added, intractable mixtures formed. The only exceptions were the results described in this section.

By bubbling CO through a solution of **2** in Me_2CO for 1 min, then adding $\text{Ti}(\text{TfO})_4$, bubbling CO again for 30 min, and stirring the reaction mixture for 16 h at room temperature, 2-vinyl-*N*-(2,6-dimethylphenyl)benzamide (**9**) was obtained in 68% yield (Scheme 3). **9** was not

Scheme 6



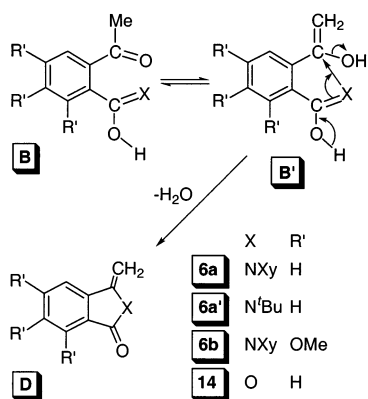
formed without CO, nor if, instead of bubbling CO, N_2 or H_2 was bubbled or a few drops of distilled water were added. As mentioned above, the reactivity of complex **2'** with TiOTf was not similarly affected by the presence of CO. The reaction of **1a**, **1a'**, or **1b** with $\text{Ti}(\text{TfO})_4$ is not affected by the presence of CO either, forming again the isobenzofuranones **6a**, **6a'**, or **6b**, respectively.

By bubbling CO through a suspension of complex **4** and $\text{Ti}(\text{TfO})_4$ in Me_2CO or CH_2Cl_2 , 3-methylenephthalide **14** (32% yield) was obtained (Scheme 5). The same reaction with complex **5** afforded an intractable mixture. Both **4** and **5** reacted with $\text{Ti}(\text{TfO})_4$ and CO in CH_2Cl_2 with a drop of EtOH , giving 3-ethoxy-3-methyl-3H-isobenzofuran-1-one (**15**) (74%).

Discussion

The starting materials for the synthesis of complexes under study were 2-X-bromoarenes, X being $\text{CH}=\text{CH}_2$, CHO , or $\text{C}(\text{O})\text{Me}$. The oxidative addition reactions of these arenes with $[\text{Pd}(\text{dba})_2]$ ($=[\text{Pd}_2(\text{dba})_3]\cdot\text{dba}$; dba = dibenzylideneacetone)¹⁶ and the insertion reactions of isocyanides¹⁸ afforded new organic groups attached to palladium resulting after formation of one or three new C–C bonds (Scheme 1). In addition, in the case of compounds of type **IV1**, the X group ($\text{X} = \text{CHO}$) participated in a C–H bond cleavage and a C–N bond formation. Although we did not isolate products of insertion of CO into the C–Pd bond, the results of

Scheme 7

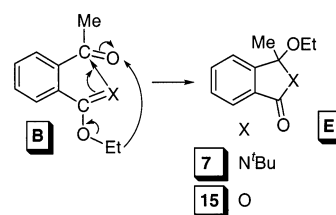


reactions leading to **14** and **15** from **4** and **5**, respectively, show that such an insertion took place. Therefore, the depalladation of these inserted complexes represents a stoichiometric synthesis of functionalized arenes, N- or O-heterocyclic compounds from bromoarenes. As mentioned above, we fruitlessly attempted the synthesis of some of these organic compounds under catalytic conditions. However, catalytic applications of these stoichiometric reactions could still be an objective for future studies.

We believe that all depalladation reactions reported here share three common steps: (i) The substitution of the bromo ligand in the iminoacyl complexes $[\text{Pd}\{\text{C}(\text{=NR})\text{Ar}\}\text{BrL}_2]$ (**1**–**3**) by TfO to give the intermediates **A** (Scheme 6), which are formulated as cationic, assuming that the very labile TfO is substituted by Me_2CO , H_2O , or EtOH ; when starting from the aryl complexes $[\text{Pd}(\text{Ar})\text{BrL}_2]$ (**4**, **5**) the corresponding acyl complexes $[\text{Pd}\{\text{C}(\text{=O})\text{Ar}\}\text{BrL}_2]$, resulting after insertion of CO, were not isolated but the nature of compounds resulting after the reaction with $\text{Ti}(\text{TfO})$, **14** and **15** (Schemes 5 and 7), demonstrate that such insertion took place. The formation of **9** in the reaction of **2** with $\text{Ti}(\text{TfO})$ requires the presence of CO, although it is not incorporated into the molecule. In this case, it is possible that the intermediate **A** was a cationic carbonyl complex ($\text{S} = \text{CO}$, Scheme 6). (ii) The nucleophilic attack on the iminoacyl ($\text{X} = \text{NXy}$, N'Bu) or acyl ($\text{X} = \text{O}$) carbon in **A** by EtOH or H_2O ($\text{R}''\text{OH}$, Scheme 6), the latter coming from atmospheric or solvent moisture. (iii) The decomposition of the resulting adduct to give (probably through an intermediate hydrido palladium complex, Scheme 6) metallic palladium, the neutral ligand L, HOTf, and $\text{ArC}(\text{=X})\text{OR}''$, **B**, an imidic acid ($\text{X} = \text{NXy}$, $\text{R}'' = \text{H}$, **12**), or an imidic acid ester (NXy , $\text{R}'' = \text{OEt}$, **13**). When $\text{R}'' = \text{H}$, **B** may cyclize to give **14** (when $\text{X} = \text{O}$ and $\text{Ar} = \text{C}_6\text{H}_4\text{C}(\text{OMe})$; see below and Scheme 7) or may transform into its tautomeric form, the amide **C**, $\text{ArC}(\text{=O})\text{XH}$ [$\text{X} = \text{N'Bu}$, $\text{Ar} = \text{a}$ (**8**, Scheme 6); $\text{X} = \text{NXy}$, $\text{Ar} = \text{b}$ (**9**), c (**11**)]. As mentioned above, amides **C** are more stable than their imidic acid tautomers, **B**. However, when $\text{X} = \text{NXy}$, we have been able to isolate both tautomers **11** and **12** (Scheme 4).

The stability of the bromo precursors toward nucleophiles can be explained as a consequence of the low electrophilic character of the iminoacyl carbon in the neutral bromo complexes, and the instability of **A** should be due to the enhancement of the electrophilic character of such carbon due to its cationic nature. It is very likely

Scheme 8



that reactions of this type constitute an important step in palladium-catalyzed carbonylations,^{1,2,41} as well as in the termination step of the palladium-catalyzed copolymerization of CO and olefins.^{42–44}

When the Ar group was *ortho*-acetylaryl, the intermediate **B** evolved to give an X-heterocycle **D** or **E** depending on the nucleophile (Scheme 7 or 8). When this was H_2O ($\text{R}'' = \text{H}$, Scheme 7), we propose a nucleophilic attack of X on the C–OH carbon of the enol tautomer **B'** to form an X–C bond. The position of the three methoxy groups in **6b** is in agreement with this proposal. An alternative route assuming that the nucleophile was the O atom would require a rearrangement from the O-heterocycle to the N-heterocycle to explain the formation of isindolinones **6**, and this would require very severe conditions.⁴⁵ Similarly, when $\text{R}''\text{OH}$ was EtOH , the nucleophilic attack of X at the carbonyl carbon of the intermediate **B** and migration of the Et group to the oxygen atom of the acetyl group would give **7** ($\text{X} = \text{N'Bu}$, Scheme 8) or **15** ($\text{X} = \text{O}$). However, formation of **7** (from **1a'**, Schemes 2 and 8) was accompanied with that of the corresponding intermediate **C** (compound **8**, Schemes 2 and 6), **D** (compound **6a'**, Schemes 2 and 7), and probably $\text{X} = [\text{HB}]\text{TfO}$ ($\text{R}'' = \text{Et}$, $\text{X} = \text{NH'Bu}$, Schemes 2 and 6). This complicated behavior of **1a'** in the presence of EtOH contrasts with that of its homologues **1a** and **1b** (Scheme 2), whose reactivity with TiOTf is not affected by the presence or absence of added nucleophiles ($\text{EtOH} + \text{H}_2\text{O}$; Scheme 2). This difference could be explained by the different nature of the isocyanide (XyNC in **1a** and **1b** and tBuNC in **1a'**): the more basic character of the N'Bu group, with respect to the NXy group, could favor in **B** the formation of **C** to give **8** or of $[\text{HB}]\text{TfO} = \text{X}$ (Schemes 2 and 6). Such processes would thus compete with the cyclization reactions $\text{B} \rightarrow \text{B}' \rightarrow \text{D}$ (**6a'**; Scheme 7) or $\text{B} \rightarrow \text{E}$ (**7**; Scheme 8), which for **1a** and **1b** would be the main reaction pathways. Additionally, as noted above, **6a** and **6b** are stable, while **6a'** decomposes within 2 days. This difference in stability could be due to the additional conjugation effect of the xylyl group in the isindolinones **6a** and **6b**, which is not present in **6a'** containing the tBu group. The instability of **6a'** could also explain the formation of other products in the reaction of **1a'** with $\text{Ti}(\text{OTf})$ in the presence of EtOH .

Although the very simple reaction pathways proposed in Schemes 6–8 allow a systematization of the formation of such different products as **6**–**15**, some questions remain unanswered because too many factors can

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Table 3. Hydrogen Bonds for Compounds 6a, 6b, 8·0.11H₂O, 9, 11·0.5Et₂O, 13, and 14

	D—H···A	d(D—H) (Å)	d(H···A) (Å)	d(D···A) (Å)	∠(DHA) (deg)	symmetry transformations used to generate equivalent atoms
6a	C(6)—H(6)···O(1)#1	0.95	2.64	3.4839(18)	148.6	#1 -1+x,y,z
6b	C(2)—H(2B)···O(1)#1	0.95	2.44	3.3600(16)	161.7	#1 -x+1/2,y-1/2,z
	C(7)—H(7)···O(1)#1	0.95	2.47	3.3865(16)	162.8	
	C(15)—H(15)···O(2)#2	0.95	2.58	3.4515(15)	152.5	#2 -x+1/2,-y+3/2,z+1/2
	C(18)—H(18B)···O(3)#3	0.98	2.51	3.2568(16)	133.2	#3 -x,y,-z+1/2
	C(9)—H(9B)···O(4)#4	0.98	2.57	3.5438(16)	174.9	#4 -x,-y+1,-z
8	N—H(0)···O(1)#1	0.887(15)	1.999(16)	2.8839(16)	175.9(13)	#1 -y+1/4,x-1/4,z-1/4
9	N—H(0)···O#1	0.871(15)	2.087(16)	2.9528(15)	172.3(13)	#1 x,-y+1/2,z+1/2
11	N(3')—H(03')···O(1)	0.875(15)	2.094(16)	2.969(2)	178.0(19)	
	N(3)—H(03)···O(99)#1	0.867(16)	2.078(18)	2.904(3)	159(2)	#1 x,-y+3/2,z+1/2
	N(3)—H(03)···O(99')#1	0.867(16)	2.197(18)	3.051(8)	168(2)	
	C(27)—H(27A)···O(1')#2	0.98	2.47	3.393(3)	157.6	#2 x,1.5-y,-0.5+z
	C(27')—H(27F)···O(1)	0.98	2.46	3.414(3)	163.3	
13	C(33)—H(33)···O(1)#1	0.95	2.42	3.345(2)	163.9	#1 x+1,y,z
14	C(8)—H(8B)···O(1)#1	0.95	2.41	3.356(2)	176.2	#1 x,-y+1,z+1/2
	C(8')—H(8'2)···O(1')#2	0.95	2.46	3.360(2)	157.8	#2 x+1/2,y-1/2,z

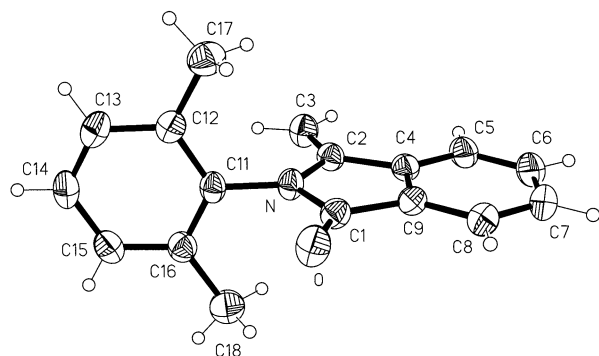


Figure 1. Ellipsoid representation of **6a** with 50% probability ellipsoids and the labeling scheme. Selected bond lengths (Å) and angles (deg): O—C(1) = 1.2152(16), C(1)—N = 1.3853(17), C(1)—C(9) = 1.4862(18), C(2)—C(3) = 1.3260(19), C(2)—N = 1.4173(16), C(2)—C(4) = 1.4698(19), N—C(11) = 1.4355(16); O—C(1)—N = 125.25(12), O—C(1)—C(9) = 129.50(13), N—C(1)—C(9) = 105.25(11), C(3)—C(2)—N = 125.06(12), C(3)—C(2)—C(4) = 129.61(13), N—C(2)—C(4) = 105.33(11), C(1)—N—C(2) = 112.35(11), C(1)—N—C(11) = 124.89(11), C(2)—N—C(11) = 122.62(10).

influence the results. Thus, the reaction of **5** with CO and Tl(TfO) in the absence of EtOH gave an intractable mixture of products instead of the phthalide **14** obtained in the reaction starting from **4**. Although this is most likely due to the different nature of the neutral ligands (PPh₃ in **4** and bpy in **5**) and/or the geometry of complexes, it is unclear how these factors influence so markedly the course of such reactions. Finally, we do not attempt to explain the formation of *ortho*-cyanostyrene in the reaction of **2'** with Tl(TfO), as we cannot account for the influence of the impurities present in the starting material. In any case, *ortho*-cyanostyrene was not among the impurities of **2'**.

X-ray Diffraction Studies of 6a, 6b, 8·0.11H₂O, 9, 11·0.5Et₂O, 13, and 14. The structures of **6a** (Figure 1) and **6b** (Figure 2) consist of an almost planar arrangement of the atoms in the indoline rings, the O, and the methylene C atoms. This plane and that of the carbon atoms of the xyllyl ring (both with mean deviation 0.01 Å) subtend an angle of 88°. The distances and bond angles are similar to those of other 3-alkylideneisoindolin-1-ones.^{32,46,47} In **6a**, there is only one contact that

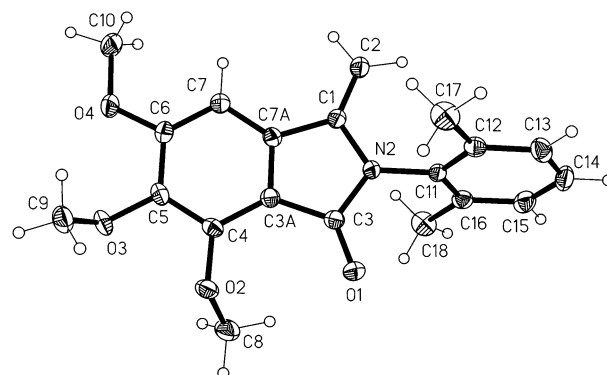


Figure 2. Ellipsoid representation of **6b** with 50% probability ellipsoids and the labeling scheme. Selected bond lengths (Å) and angles (deg): O(1)—C(3) = 1.2214(14), C(1)—C(2) = 1.3283(17), C(1)—N(2) = 1.4171(15), C(1)—C(7A) = 1.4713(17), N(2)—C(3) = 1.3853(15), N(2)—C(11) = 1.4352(15), C(3)—C(3A) = 1.4760(16); C(2)—C(1)—N(2) = 125.51(11), C(2)—C(1)—C(7A) = 129.36(11), N(2)—C(1)—C(7A) = 105.13(10), C(3)—N(2)—C(1) = 112.26(10), C(3)—N(2)—C(11) = 123.35(10), C(1)—N(2)—C(11) = 124.18(9), O(1)—C(3)—N(2) = 124.34(11), O(1)—C(3)—C(3A) = 130.20(11), N(2)—C(3)—C(3A) = 105.46(10).

could be a C—H···O hydrogen bond, namely, H(6)···O (Table 3 summarizes hydrogen bonds for all structures presented here), which links the molecules by translation parallel to the *x* axis. In **6b**, there are five intermolecular C—H···O hydrogen bonds with H···O < 2.67 Å; the three shortest, including a bifurcated system at O(1), combine to form layers parallel to *xy* at *z* = 0.25 and 0.75 (Figure 3).

The amide **8** (Figure 4) shows typical structural values,⁴⁸ confirming the presence of an amidic carbon—oxygen double bond. The structure of **9** (Figure 5) is very similar to that of **8**. In both cases, the molecules are connected by intermolecular hydrogen bonds N—H···O forming chains parallel to the *z* axis (Figures 6 and 7). In **8**, the role of the partially occupied water site may also be to form hydrogen bonds (O_{water}···O(2) 2.65 Å), and the chains are reinforced by a weak C—H···O(2) interaction.

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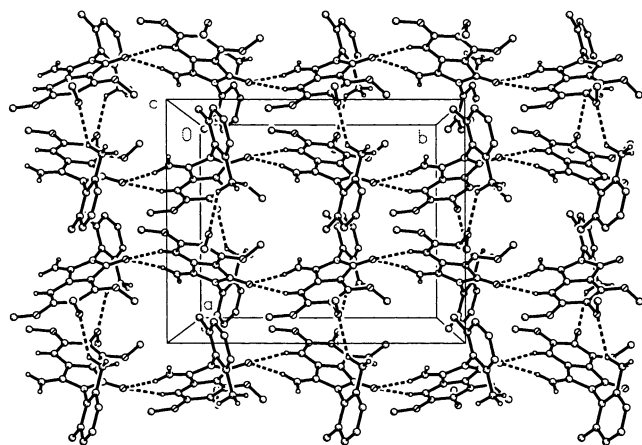


Figure 3. Packing diagram of **6b**, showing hydrogen bonds (dashed lines). Only H atoms involved in H bonds, together with their geminal neighbors, are included. View direction parallel to the *z* axis.

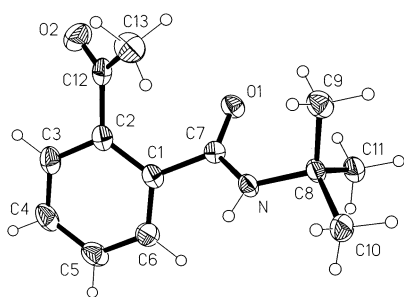


Figure 4. Ellipsoid representation of **8** with 50% probability ellipsoids and the labeling scheme. Selected bond lengths (Å) and angles (deg): C(1)–C(7) = 1.5033(19), C(2)–C(12) = 1.501(2), C(7)–O(1) = 1.2400(16), C(7)–N = 1.3354(17), C(8)–N = 1.4804(17), C(12)–O(2) = 1.2178(18); C(6)–C(1)–C(2) = 119.29(13), C(6)–C(1)–C(7) = 119.82(13), C(2)–C(1)–C(7) = 120.58(13), C(3)–C(2)–C(1) = 118.94(14), C(3)–C(2)–C(12) = 117.37(13), C(1)–C(2)–C(12) = 123.69(13), O(1)–C(7)–N = 124.33(13), O(1)–C(7)–C(1) = 120.11(12), N–C(7)–C(1) = 115.54(12), O(2)–C(12)–C(2) = 119.03(14), O(2)–C(12)–C(13) = 120.47(15), C(2)–C(12)–C(13) = 120.35(13), C(7)–N–C(8) = 124.97(12).

The structure of **11**·0.5Et₂O (Figure 8) shows two independent molecules of **11** with slight differences in the bonding distances and angles. The alkylideneisoindolinone fragment is similar to that found in compounds **6**. The alkylidene C=C bond [C(8)–C(20) 1.357(3) Å] is somewhat longer than the C=CH₂ bond in **6a** [C(2)–C(3), 1.3260(19) Å] or **6b** [1.3283(17) Å]; this may be due to the conjugation with the alkylidene substituents. The C(20)–N(2) [1.372(3) Å] and C(30)–N(3) [1.358(3) Å] bond lengths are typical of sp² carbon atoms bonded through a single bond to planar NHR groups.⁴⁸ The carbonyl C(1)–O(1) and C(30)–O(2) bond lengths [1.234(2) and 1.244(2) Å, respectively] are characteristic of C_{sp}²=O in amides.⁴⁸ The delocalization of electron density over the groups of atoms N(3), C(30), O(2) and N(2), C(20), C(8) is shown by the coplanarity of the groups of atoms C(31), N(3), H(3), C(30), O(2), C(20) and C(21), N(2), H(02), C(20), C(30), C(8), with mean deviations of 0.01 and 0.03 Å, respectively (0.04 and 0.10 Å in the second molecule). The angle between both planes is 80° and 83° in molecules 1 and 2, respectively. The molecules of **11** are connected through N–H···O hydrogen bonds from N(3)–H(03) to both oxygen positions of

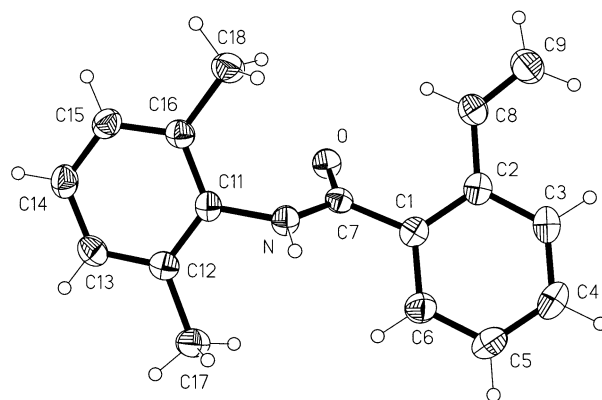


Figure 5. Ellipsoid representation of **9** with 50% probability ellipsoids and the labeling scheme. Selected bond lengths (Å) and angles (deg): C(1)–C(7) = 1.4989(18), C(7)–O = 1.2348(15), C(7)–N = 1.3472(17), C(8)–C(9) = 1.319(2), C(11)–N = 1.4381(17); C(6)–C(1)–C(2) = 120.06(13), C(6)–C(1)–C(7) = 117.92(12), C(2)–C(1)–C(7) = 121.84(12), O–C(7)–N = 122.63(12), O–C(7)–C(1) = 121.73(12), N–C(7)–C(1) = 115.56(11), C(9)–C(8)–C(2) = 126.23(14), C(16)–C(11)–C(12) = 122.20(12), C(16)–C(11)–N = 119.81(12), C(12)–C(11)–N = 117.96(12), C(7)–N–C(11) = 122.68(11).

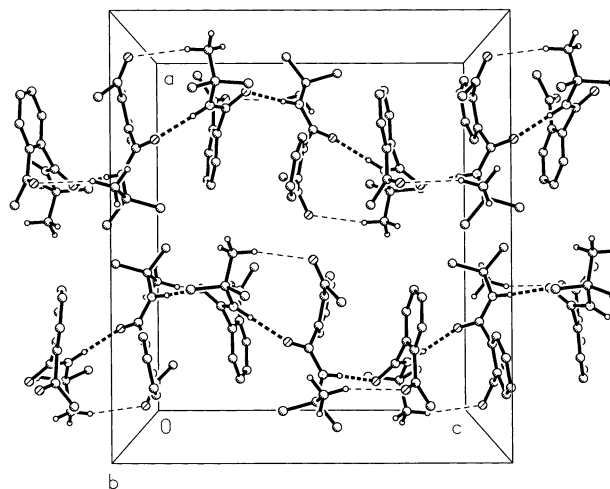


Figure 6. Packing diagram of **8**, showing helical chains of molecules (related by the *a*₁ operator) connected by hydrogen bonds (dashed lines). Only H atoms involved in H bonds, together with their geminal neighbors, are included. The partially occupied water site (see text) is omitted. View direction parallel to the *z* axis.

the disordered ether molecule, and from N(3')–H(03') to O(1). The hydrogens at N(2) and N(2') do not form hydrogen bonds but lie close to the ring at C(11)/C(11'), with H(02)···C(11) 2.30 Å and H(02')···C(11') 2.29 Å. Finally there are two short C–H···O interactions from methyl hydrogens. The net effect is to connect the molecules in helical chains parallel to the *y* axis, but the packing diagram is too congested to be easily assimilated. The compound **13** (Figure 9) has a very similar structure to **11**, but, in agreement with its proposed structure (Scheme 4), the C(30)–N(3) distance [1.265(2) Å] corresponds to a C=N bond, while the C(30)–O(2) distance [1.352(2) Å] is close to the value expected for a single bond. Again, there are no hydrogen bonds involving N(2)–H(02) (cf. H(02)···C(11) 2.25 Å), but one short C–H···O contact that connects the molecules by translation parallel to the *x* axis.

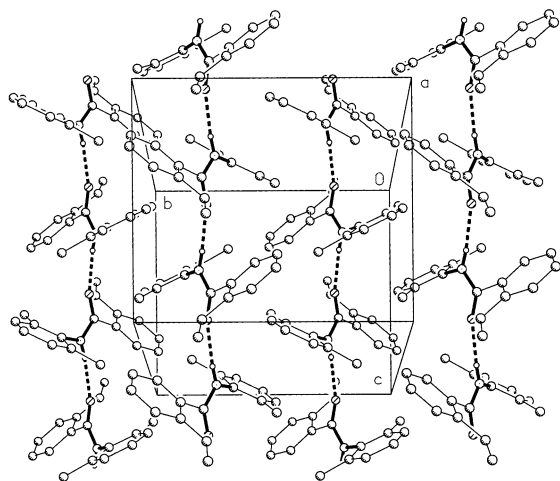


Figure 7. Packing diagram of **9**, showing chains of molecules connected by hydrogen bonds (dashed lines). Only H atoms involved in H bonds, together with their geminal neighbors, are included. View direction perpendicular to the *xy* plane.

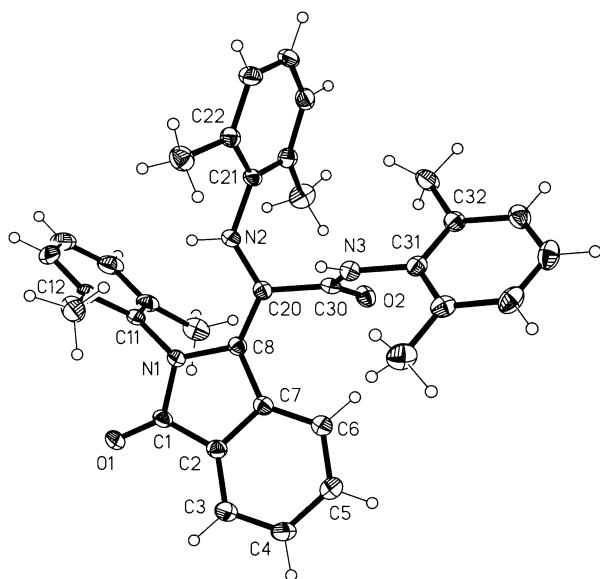


Figure 8. Ellipsoid representation of **11** with 30% probability ellipsoids and the labeling scheme, excluding the disordered ether molecule. Selected bond lengths (Å) and angles (deg) for one of two independent molecules in the crystal: C(1)–O(1) = 1.234(2), C(1)–N(1) = 1.379(3), C(1)–C(2) = 1.458(3), C(7)–C(8) = 1.465(3), C(8)–C(20) = 1.357(3), C(8)–N(1) = 1.438(2), C(11)–N(1) = 1.442(3), C(20)–N(2) = 1.372(3), C(20)–C(30) = 1.519(3), C(21)–N(2) = 1.432(3), C(30)–O(2) = 1.224(2), C(30)–N(3) = 1.358(3), C(31)–N(3) = 1.445(3); O(1)–C(1)–N(1) = 124.1(2), O(1)–C(1)–C(2) = 129.88(19), N(1)–C(1)–C(2) = 106.00(17), C(3)–C(2)–C(7) = 121.9(2), C(3)–C(2)–C(1) = 128.7(2), C(7)–C(2)–C(1) = 109.34(18), C(6)–C(7)–C(2) = 118.83(19), C(6)–C(7)–C(8) = 133.56(19), C(2)–C(7)–C(8) = 107.60(18), C(20)–C(8)–N(1) = 125.57(19), C(20)–C(8)–C(7) = 129.02(19), N(1)–C(8)–C(7) = 105.17(17), C(8)–C(20)–N(2) = 123.67(19), C(8)–C(20)–C(30) = 118.38(18), N(2)–C(20)–C(30) = 117.83(18), O(2)–C(30)–N(3) = 123.43(19), O(2)–C(30)–C(20) = 119.80(18), N(3)–C(30)–C(20) = 116.73(18), C(1)–N(1)–C(8) = 111.79(17), C(1)–N(1)–C(11) = 120.86(17), C(8)–N(1)–C(11) = 126.79(16), C(20)–N(2)–C(21) = 128.62(19), C(30)–N(3)–C(31) = 123.47(18).

The compound **14** (Figure 10) has been previously described,³⁷ but its X-ray structure had not been deter-

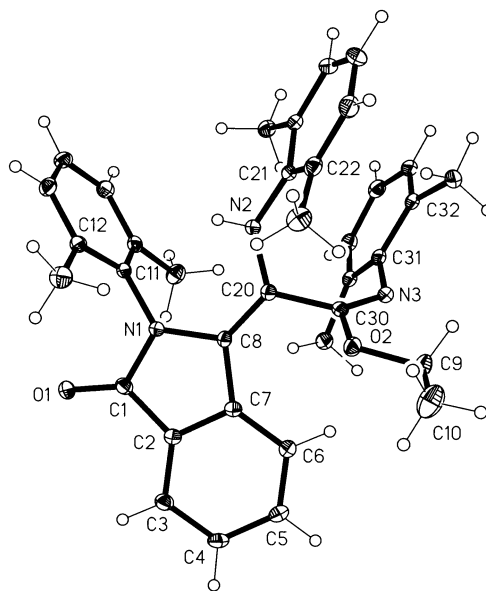


Figure 9. Ellipsoid representation of **13** with 50% probability ellipsoids and the labeling scheme. Selected bond lengths (Å) and angles (deg): C(1)–O(1) = 1.222(2), C(1)–N(1) = 1.390(2), C(1)–C(2) = 1.467(2), C(2)–C(3) = 1.394(2), C(7)–C(8) = 1.476(2), C(8)–C(20) = 1.358(2), C(8)–N(1) = 1.440(2), C(9)–O(2) = 1.452(2), C(11)–N(1) = 1.442(2), C(20)–N(2) = 1.386(2), C(20)–C(30) = 1.514(2), C(21)–N(2) = 1.424(2), C(30)–N(3) = 1.265(2), C(30)–O(2) = 1.352(2), C(31)–N(3) = 1.423(2); O(1)–C(1)–N(1) = 124.27(16), O(1)–C(1)–C(2) = 129.81(16), N(1)–C(1)–C(2) = 105.89(14), C(20)–C(8)–N(1) = 125.42(15), C(20)–C(8)–C(7) = 130.04(15), N(1)–C(8)–C(7) = 104.53(13), O(2)–C(9)–C(10) = 107.77(16), C(8)–C(20)–N(2) = 123.05(15), C(8)–C(20)–C(30) = 120.19(15), N(2)–C(20)–C(30) = 116.63(14), N(3)–C(30)–O(2) = 120.28(15), N(3)–C(30)–C(20) = 129.03(16), O(2)–C(30)–C(20) = 110.68(14), C(1)–N(1)–C(8) = 111.84(13), C(1)–N(1)–C(11) = 119.33(14), C(8)–N(1)–C(11) = 128.07(13), C(20)–N(2)–C(21) = 129.05(15), C(30)–N(3)–C(31) = 125.65(15), C(30)–O(2)–C(9) = 116.18(13).

mined. It shows the presence of two independent molecules with slight differences in the bonding distances and angles, but all of them within the expected ranges.⁴⁸ The two molecules also pack independently of each other, forming short hydrogen bonds C(8)–H(8B)···O(1) and C(8')–H(8'2)···O(1'); these connect the molecules to chains parallel to the *z* axis or the diagonals [–110] and [110], respectively.

Other Structural Studies. The spectroscopic data of **7** and **15** are in accordance with their proposed structures (Schemes 2 and 5). Thus, the very strong IR band at 1692 and 1672 cm^{–1}, respectively, and a peak at 168 ppm in their ¹³C NMR spectra indicate the presence of the carbonyl group. In the ¹H NMR spectrum, the diastereotopic methylene protons of the Et group appear as characteristic doublets of doublets of quartets, as expected for the AB part of an ABM₃ system. ¹³C–¹H long-range correlations (HMBC) have allowed the assignment of all the aromatic carbons in these two compounds. The quaternary aromatic carbons close to the CMeOEt groups appear at considerably higher frequencies (146.4 ppm in **7** and 147.9 ppm in **15**) than the ones close to the carbonyl groups (132.1 ppm in **7** and 127.1 ppm in **15**). The isoindolinones **6a**, **6a'**, and **6b** show the ¹³C carbonyl resonance at 166.2, 168.5, and 164.8 ppm, respectively. In their ¹H NMR

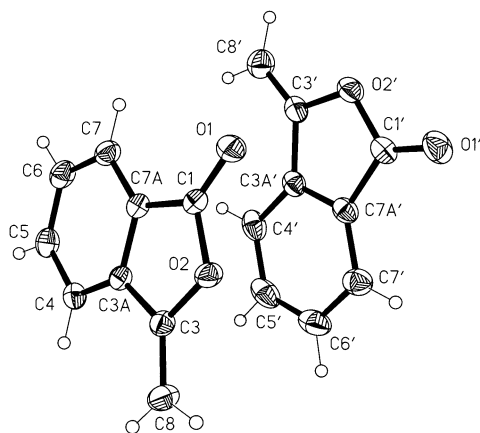


Figure 10. Ellipsoid representation of **14** with 50% probability ellipsoids and the labeling scheme. Selected bond lengths (Å) and angles (deg) for one of the two independent molecules (unprimed atom names): C(1)–O(1) = 1.202(2), C(1)–O(2) = 1.3804(19), C(1)–C(7A) = 1.472(2), O(2)–C(3) = 1.4027(19), C(3)–C(8) = 1.323(2), C(3)–C(3A) = 1.463(2); O(1)–C(1)–O(2) = 121.18(14), O(1)–C(1)–C(7A) = 131.40(15), O(2)–C(1)–C(7A) = 107.41(13), C(1)–O(2)–C(3) = 109.98(12), C(8)–C(3)–O(2) = 121.57(14), C(8)–C(3)–C(3A) = 131.00(15), O(2)–C(3)–C(3A) = 107.43(13), C(4)–C(3A)–C(7A) = 121.26(14), C(4)–C(3A)–C(3) = 131.34(15), C(7A)–C(3A)–C(3) = 107.39(13), C(3A)–C(7A)–C(7) = 121.81(14), C(3A)–C(7A)–C(1) = 107.72(13), C(7)–C(7A)–C(1) = 130.45(15).

spectra, the two inequivalent protons of the methyldene group appear as characteristic doublets, with $^2J_{\text{HH}} = 2$ Hz. The difference in chemical shift between these two protons is much higher in **6a** and **6b** (0.75 and 0.74 ppm,

respectively) than in **6a'** (0.05 ppm), where they clearly show second-order character. This difference might be due to the anisotropic effect of the xyllyl group, which strongly differentiates the two methyldene protons in **6a** and **6b**. In the 3-methylenephthalide **14**, the second-order character of the methyldene protons is much stronger, and they appear as an AB system. The carbonylic carbon resonance is at 166.8 ppm. The aromatic carbons in **14** have also been assigned through a ^{13}C – ^1H long-range correlation (HMBC). Again, the quaternary aromatic carbon close to the carbonyl group has a lower chemical shift (127.1 ppm) than the other one, close to the vinylidene group (139.0 ppm), although the difference here is lower than in **7** and **15**. Finally, the FAB mass spectra show signals corresponding to the molecular ion and its protonated species, respectively. In the case of **15** the fragment resulting from the loss of CO_2 was also observed.

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Supporting Information Available: Listing of all refined and calculated atomic coordinates, anisotropic thermal parameters, and bond lengths and angles for **6a**, **6b**, **8**·0.11 H_2O , **9**, **11**·0.5 Et_2O , **13**, and **14**; synthesis and spectroscopic properties of **2'** and **10**; elemental analyses, mass fragment data; packing of the two independent molecules in **14**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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