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Selective hetero- and carbo-cycle syntheses via masked cyclopalladated secondary amine and ketone functions

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Abstract

The iodo-bridged or cationic cyclopalladated complexes **1b** and **1c** derived from *N*-phenyl-2-pyridylamine and **4b** derived from phenyl-2-pyridylketone reacted with internal alkynes to yield five-membered heterocyclic **3** and carbocyclic products **6** with high chemoselectivity. The indoles **3b–3f**, formed from **1b** or **1c** and disymmetric alkynes, were obtained regioselectively, suggesting that this reaction might be under both electronic and steric control. Analysis of the regiochemistry of this reaction has led us to propose a pathway involving a nucleophilic addition of the secondary amine function to an alkyne activated by η^2-coordination to palladium. The indenol derivatives **6**, obtained as stable bis(*O*,*N*)-palladated chelates, result from the insertion of the alkyne into the Pd–C bond of **4b** followed by attack of the palladated vinyl carbon atom on the electrophilic carbonyl function. In so far as their reactivities towards alkynes are concerned, **1b** and **1c** behave as masked cyclopalladated secondary amine functions and **4b** as masked cyclopalladated ketone functions.

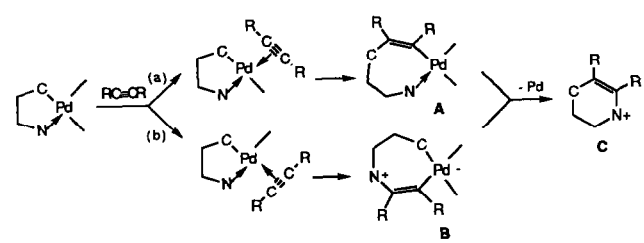
Key words: Palladium; Amine; Indole; Indenol; Alkyne; Heteroannulation

1. Introduction

For several years we have aimed at studying the use of cyclopalladated compounds in organic synthesis. It has long been established that these compounds, in which a Pd–C bond is stabilized by the intramolecular coordination of a heteroatom, can react with various reagents often with a high selectivity [1]. Our attention has mainly focused on the reactivity of N-containing metallated ligands towards disubstituted alkynes. Consequently we and others have shown that such reactions can afford heterocyclic compounds through the selective formation of both a C–C and a C–N bond [2]. The pathway by which these two new bonds are made is of fundamental importance since, if better understood, it might allow one to increase the synthetic scope of such a reaction. Scheme 1 summarizes the two reaction sequences proposed for the reaction of cyclopalladated tertiary amines with alkynes [3].

In pathway (a) the acetylene inserts into the carbon–palladium bond following *trans* coordination to nitrogen. The resulting nitrogen-stabilized chelate in **A** can then transform after palladium extrusion into the heterocyclic product **C**. In pathway (b), formation of a bond between the palladium-bound nitrogen and the *cis* acetylene occurs initially. The resulting zwitterionic complex **B** may then undergo a reductive elimination to form a C–C bond, yielding **C**.

We have so far advocated pathway (a) for two main reasons. First, a large number of inserted complexes of type **A** have been isolated and characterized and it has



Scheme 1.

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often been shown that these complexes can yield related heterocyclic products **C** after depalladation. However, the last process involves the formation of a C–N bond through a formal reductive elimination that would appear to have little precedent [3]. Second, although pathway (b) involves a more common reductive elimination process (C–C bond formation from **B** to **C**) [4], the addition of a tertiary amine function to an alkyne is a difficult process [5].

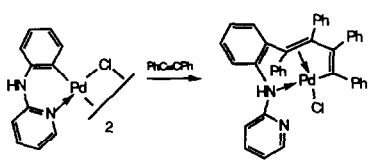
Here, we describe the reactivity of the easily accessible six-membered cyclopalladated complex **1**, derived from *N*-phenyl-2-pyridylamine, with disubstituted alkynes. Cyclometallation of the pyridylamine is possible by virtue of the directing and tertiary nature of the pyridine. However, we envisaged that the pyridine function might serve as a "spectator group", enabling the reactivity to be centred on the nucleophilic secondary amine function. As a comparison we also decided to study the reactivity of compound **4** in which a potentially electrophilic ketone group is incorporated into the metallocyclic ring.

2. Results and discussion

2.1. Reactivity of the cyclopalladated N-phenyl-2-pyridylamine derivatives

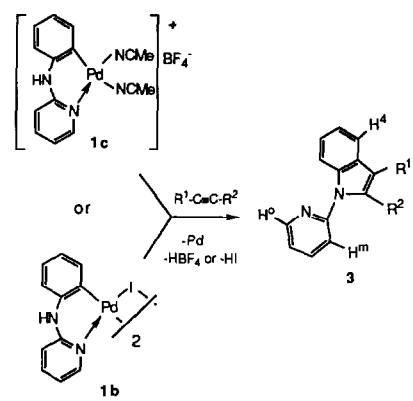
The chloro-dimer **1a**, initially synthesized by Nonoyama [6], was prepared with a better yield (85%) via an indirect C–H activation route [7], by reaction of equimolar quantities of *N*-phenyl-2-pyridylamine and $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)(\mu\text{-}Cl)\}_2]$ [8] in a CH_3CO_2H–CH_2Cl_2 solution ($CH_3CO_2H:CH_2Cl_2 = 1:1$) for 48 h at room temperature. This air-stable yellow solid was converted into its iodo and cationic derivatives **1b** and **1c** by standard procedures [9].

1a reacted with alkynes in a complex manner. However, with diphenylacetylene (DPA) in refluxing chlorobenzene an orange solid could be obtained which was shown by combustion analysis and mass spectroscopy to contain the initial *N*-phenyl-2-pyridylamine-palladium moeity and two DPA molecules. This complex was assigned the structure **2** in which the aniline nitrogen is bound to palladium. It has already been shown that eight-membered ring is favoured over ten-membered ring formation in a similar bis-inserted complex [10].



1a 2

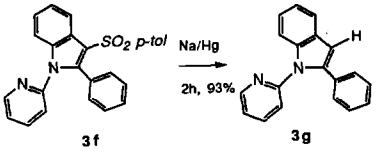
It is remarkable that **1c** reacted with DPA under very similar conditions to give metallic palladium and a product that after work-up was shown by mass spectroscopy to be a palladium-free compound corresponding to a 1:1 *N*-phenyl-2-pyridylamine–alkyne adduct. Such a dramatic difference between the behaviour of chloro-bridged compound and those of the corresponding iodo or cationic cyclopalladated compounds towards alkynes has already been observed and is attributed to the enhanced electrophilicity and facility of the latter two types of complex to undergo reductive elimination [9a,9c]. **1c** also reacted with ethyl-3-phenylproynoate (EPP) to give a palladium-free compound similar to that obtained with DPA, although with other acetylenes **1c** gave uncharacterized mixtures. **1b** proved to be a better starting material and reacted with a range of acetylenes, also giving 1:1 *N*-phenyl-2-pyridylamine/alkyne adducts after depalladation. The IR spectra of these products showed no ν(NH) and, on the basis of mass spectroscopy and ^1H and ^{13}C nuclear magnetic resonance (NMR) spectroscopy, they were formulated as the 2,3-disubstituted indoles **3**.



From Table 1 it is clear that this reaction is operative for alkynes bearing both electron-donating and electron-withdrawing groups. (Note, however, that dimethylacetylene dicarboxylate (DMAD) and 1-phenylpropyne gave uncharacterised mixtures.) The reaction involving asymmetric acetylenes displays a high degree of regioselectivity. For example, the ^1H NMR spectrum of crude **3e** showed that only one regio-isomer was present, even before purification. The regiochemistry of **3d** was established by NOE difference spectroscopy in $CDCl_3$; irradiation of the ^{t}Bu group caused enhancement of both the *ortho* (2.3%) and *meta* (3.6%) pyridine protons, whereas Me irradiation caused a 10.7% enhancement of the indole H^4 proton resonance. For **3f** in CD_2Cl_2, the H^4 proton resonance at 8.4 ppm was assigned by ^1H COSY NMR spectroscopy. A NOESY experiment showed this proton to be interacting with the AB system of the *p*-tolyl group, and therefore that the phenyl group was in the 2-indole

position. The low field shift of this proton is likely to be due to the deshielding effect of the sulphone group. A similar deshielding of the H^4 proton was observed for the oxygen-containing compounds **3b**, **3c** and **3e**, and hence these compounds were assigned the regioselectivity with the oxygen-bearing substituents in the 3-indole position.

3f can be readily desulphonylated, enabling the starting acetylenic sulphone to be employed as a phenylacetylene equivalent [11a].



Although a preliminary attempt with the sodium dithionite protocol of Julia and coworkers [11b] seemed unsuccessful, the sodium amalgam method of Trost *et al.* [11c] gave a virtually quantitative conversion of **3f** to **3g**. This was rather encouraging since it is well established that terminal and trimethylsilyl-substituted acetylenes are not compatible with our cyclopalladated compounds.

We have thus shown that, upon reaction with disubstituted alkynes, cyclopalladated *N*-phenyl-2-pyridylamine behaves more like a metallated secondary amine than a cyclopalladated pyridine. Two observations support this.

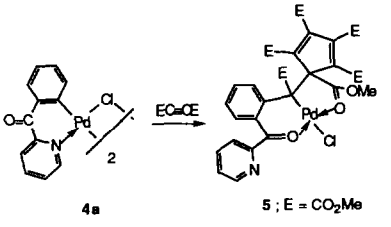
(i) A cyclopalladated 2-benzylpyridine complex (like **1b** but with a CH_2 group instead of an NH unit) was shown to react with DPA to furnish a seven-membered heterocyclic derivative [9b].

(ii) It was recently shown that the reaction between various *N*-substituted 2-iodoanilines and a series of alkynes in the presence of catalytic amounts of palladium affords indoles with regioselectivities that match those observed here (see Table 1, entry 5) [12].

Analysis of the regioisomers obtained in this study suggests that this reaction may well indeed be under electronic control. The fact that the electron-withdrawing substituents in **3b**, **3c**, **3d** and **3f** end up in the 3-indole position strongly points to a 1,4-Michael addition of the secondary amine to the activated alkyne, as in Scheme 1, pathway (b). Steric effects could also explain the regiochemistry observed for **3d** as it is usually accepted that the insertion of asymmetric alkynes into a Pd–X bond (X = Cl, aryl,...) is under steric control such that in the resultant vinyl–Pd species the bulkiest group is further from the "bulky" palladium [13]. In our case, the addition of the NH group to the *cis*-coordinated alkyne could occur so that the "small" methyl group is adjacent to the palladium.

2.2. Reactivity of the cyclopalladated phenyl-2-pyridylketone derivatives

The chloro-bridged dimer **4a** [14] was found to be quite unreactive towards alkynes, although with excess DMAD the triply inserted cyclopentadiene complex **5** was obtained.



Similar triply inserted complexes have already been reported and characterized, including one with a benzylpyridine complex [1]. The iodo-bridged homologue **4b** was found to react with DMAD, DPA and EPP in PhCl within 0.25 h to afford the rather interesting palladium-containing indenols **6a–6c** which were characterized by ^1H NMR spectroscopy and elemental analysis.

TABLE 1

Entry	Precursor	Product	R^2	R^1	Yield [a] (%)	Reflux time (h)	Solvent
1	**1c**	**3a**	Ph	Ph	57	0.25	$C_2H_4Cl_2$
2	**1b**	**3b**	Ph	CO_2Et	57	0.25	$C_2H_4Cl_2$
3	**1c**	**3b**	Ph	CO_2Et	46	0.25	PhCl, 85°C
4	**1b**	**3c**	Me	CO_2Et	59	0.25	$C_2H_4Cl_2$
5	**1b**	**3d** [b]	^{t}Bu	Me	95	0.3	$C_2H_4Cl_2$
6	**1b**	**3e**	Ph	CHO	63	0.75	$C_2H_4Cl_2$
7	**1b**	**3f** [c]	Ph	SO_2p-tol	60	0.5	$C_2H_4Cl_2$

[a] After work-up, compound gave satisfactory IR, NMR, mass spectral or analytical data. [b] Regiochemistry obtained by NOE difference spectroscopy. [c] Regiochemistry obtained by COSY and NOESY spectroscopy.

Reactions with other acetylenes gave uncharacterised mixtures. The IR spectrum of **6b** shows no ν(C=O). The ^{1}H NMR spectra of **6a** and **6b** are rather simple, suggesting that only one geometrical isomer has been formed [15] and, given the chirality of the newly formed *spiro* junction, **6a** and **6b** would also appear to be formed as single diastereoisomers. Unfortunately we were not able to grow suitable crystals of **6a** for X-ray analysis nor of **6c** which was obtained as a mixture of isomers that could be separated by fractional crystallization. These two isomers are likely to be regioisomers resulting from the non-regioselective insertion of the alkyne into the Pd–C bond of **4b**.

The mechanism by which **6a–6c** are formed may be assimilated to pathway (a) in Scheme 1. Following alkyne insertion into the Pd–C bond of **4b**, nucleophilic addition of the palladated vinyl group to the ketone function leads to the five-membered carbocyclic unit. The homoleptic bis-chelate **6** is likely to be the result of ligand rearrangements, and the driving force for the reaction could be related to the high stability constants that are well known for similar [Pd(chelate–$N,O)_2$] complexes [15].

Preliminary attempts to displace the palladium from **6** to liberate the carbocyclic product were unfortunately unsuccessful. Alternative routes to metal-free indenols, involving the reaction of cyclometallated compounds of palladium or manganese with alkynes, have already been documented [16].

3. Conclusion

We have shown that the cyclopalladated complexes derived from *N*-phenyl-2-pyridylamine and phenyl-2-pyridylketone behave as masked cyclopalladated secondary amine and ketone entities in their reactions with internal alkynes. They lead to heterocyclic or carbocyclic products resulting from the reaction of both the N and the C atoms of these masked functions. In the first case, indoles are obtained in both a regioselective and chemoselective manner via a process assumed to involve initial addition of the secondary amine function onto an activated alkyne function. This mechanism is in sharp contrast with the mechanism that we have already established for the reaction of the corresponding cyclopalladated complexes derived from tertiary amines towards alkynes. Compounds **6a–6c** are likely to result from an initial insertion of the alkyne into the Pd–C bond of **4b** followed by nucleophilic addition of the resulting palladated vinyl unit onto the ketone function.

4. Experimental section

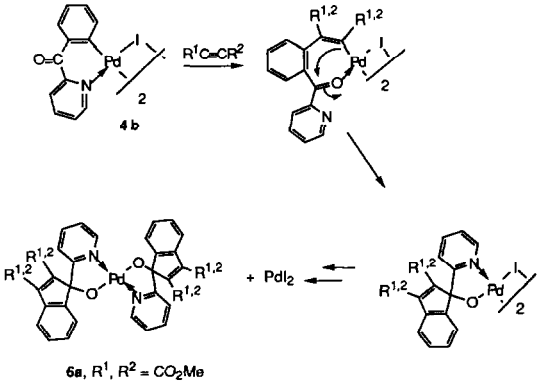
4.1. Reagents and general techniques

All reactions were run in air and starting products were used as obtained from commercial sources. 1-Phenyl-1-paratolylsulphonylethyne [17] and complex **4** [14] were synthesized according to methods given in the literature. "Flash" chromatographic separation of the products was carried out on silica or aluminum oxide (activity II–III) [Merck 70 – 230 mesh] (typical size of the column, 10 cm × 2 cm). IR spectra were recorded as KBr discs. Mass spectra of compounds were carried out on a Thompson THW 208 (70 eV) spectrometer by the Laboratoire de Spectroscopie de Masse (Strasbourg). Analyses were performed by the Service de Micronalyses du CNRS in Strasbourg. ^{1}H and ^{13}C–{^{1}H} spectra were recorded (at 200.1 MHz and 50.3 MHz respectively) on a Bruker SY200 spectrometer in $CDCl_3$ (unless stated otherwise) using tetramethylsilane as internal standard. The NOE experiment for **3d** was run in a sealed tube in $CDCl_3$, after usual freeze–pump–thaw degassing.

4.2. [{Pd{2-C_6H_4NH(2-C_5H_4N)}(μ-X)}$_2$] (X = Cl (1a), I (1b))

[{Pd(2-$C_6H_4CH_2NMe_2$)(μ-Cl)}$_2$] (1 g, 3.6 mmol) and *N*-phenyl-2-pyridylamine (0.65 g, 3.8 mmol) were stirred for 48 h in a mixture of CH_2Cl_2 (70 ml) and acetic acid (70 ml). After 48 h the yellow precipitate was collected by filtration, washed thoroughly with hexane and dried (yield, 0.95 g (85%)). Anal. Found: C, 42.51; H, 3.19; N, 8.56. $C_{22}H_{18}Cl_2N_4Pd_2$ calc.: C, 42.47; H, 2.92; N, 9.01%.

1b was obtained according to a well-known general procedure by treating **1a** with a large excess of NaI in acetone [9].



4.3. [Pd{2-$C_6H_4NH(2-C_5H_4N)$}$(MeCN)_2$]BF_4 (1c)

The yellow solid (yield, 84%) was prepared *in situ* from $AgBF_4$ and **1a** in CH_2Cl_2–MeCN (CH_2Cl_2 : MeCN = 10 : 1) according to the general procedure [9]. NMR ^1H ($CDCl_3$, CD_3CN): 1.97 and 1.99 (s, 3H, MeCN); 6.58–8.35 (m, 8H, Ar); 8.20 (s, 1H, NH) ppm. IR: 1084 cm^{-1}.

4.4. [Pd{CPh=CPhCPh=CPh(2-C_6H_4)NH(2-C_5H_4N)}-Cl] (2)

Complex **1a** (200 mg, 0.16 mmol) and DPA (350 mg, 1.97 mmol) were heated under reflux in PhCl (25 ml) for 0.25 h. After cooling and filtration through Celite, the resulting orange filtrate was evaporated to dryness. After dissolution of the latter in CH_2Cl_2 (5 ml), the addition of hexane (30 ml) afforded an orange solid which was collected by filtration. A further amount of **2** could be obtained by concentration of the filtrate and addition of hexane. The orange solids were combined and dried *in vacuo* (yield, 260 mg (61%)). Anal. Found: C, 69.83; H, 4.21; N, 4.16. $C_{39}H_{29}ClN_2Pd$ calc.: C, 70.16; H, 4.39; N, 4.20%. ^1H NMR: 7.0–7.8 (m, Ar) ppm. *m/z*. Found: 668 (M^+ + H). Calc.: 667.

4.5. 2,3-diphenyl-1-(2-pyridyl)indole (3a)

1c (250 mg, 0.56 mmol) and DPA (200 mg, 1.1 mmol) were heated for 0.25 h in refluxing 1,2-dichloroethane (20 ml). After removal of metallic palladium over Celite, the red filtrate was evaporated and washed with hexane (50 ml). Silica gel chromatography enabled the separation of the excess acetylene (hexane eluent, 50 ml) and the heterocycle (orange band) was eluted with CH_2Cl_2 and then acetone. Evaporation of the combined fractions left a brown solid (yield, 110 mg (57%)). ^1H NMR: 6.90–7.97 (m, 17H, Ar); 8.60 (dd, 1H, ^3J(HH) = 4.9 Hz, ^4J(HH) = 1.3 Hz, H^0) ppm. ^{13}C NMR: 111.57; 119.70; 121.52; 122.27; 123.41; 125.88; 126.20; 127.46; 127.75; 127.90; 128.08; 128.3 (m); 129.56; 129.94; 130.34; 130.98; 131.80; 137.57; 149.12 ppm. IR: 3000, 2900, 1585, 1438, 1360, 743, 698 cm^{-1}. *m/z*. Found: 346 (M^+, 100%). $C_{25}H_{18}N_2$ calc.: 346.

4.6. 3-ethoxycarbonyl-2-phenyl-1-(2-pyridyl)indole (3b)

1b (210 mg, 0.5 mmol) and EPP (160 mg, 0.95 mmol) were heated in refluxing 1,2-dichloroethane (20 ml) for 0.25 h. After cooling and filtration over Celite, the dark-red filtrate was evaporated to dryness. The excess of alkyne was removed on a short silica column (6 cm; CH_2Cl_2 eluant, 100 ml) and the crude product eluted with acetone (red band). This was concentrated to dryness, extracted with alkaline ethanol (50 ml + KOH) and evaporated. **3b** was then extracted from the resulting residue with CH_2Cl_2. Evaporation and drying left a red oil (yield, 95 mg (57%)). ^1H NMR: 1.26 (t, 3H, CH_3, ^3J(HH) = 7.2 Hz); 4.28 (q, 2H, CH_2, ^3J(HH) = 7.2 Hz); 6.83 (d, 1H, ^3J(HH) = 8 Hz, Ar); 7.20–7.58 (m, 10H, Ar); 8.31 (dd, ^3J(HH) = 7.0 Hz, ^4J(HH) = 1.6 Hz, H^4); 8.59 (dd, 1H, ^3J(HH) = 4.9 Hz, ^4J(HH) = 1.1 Hz, H^0) ppm. ^{13}C NMR: 14.20 (CH_3); 59.69 (CH_2); 107.47; 111.47; 122.02; 122.63; 122.84; 123.75; 126.93; 127.54; 128.21; 128.51; 128.71; 131.05; 131.32; 137.07; 137.9; 145.26; 149.30; 150.72; 165.04 (C=O) ppm. IR: 1685, 1590, 1468, 1454, 1399, 1190, 749, 702 cm^{-1}. *m/z*. Found: 342 (M^+, 100%). $C_{22}H_{18}N_2O_2$ calc.: 342.

4.7. 3-ethoxycarbonyl-2-methyl-1-(2-pyridyl)indole (3c)

A yield of 59% was obtained using a procedure identical to that for **3b**. ^1H NMR: 1.47 (t, 3H, ^3J(HH) = 7.1 Hz, CH_3); 2.71 (s, 3H, CH_3); 4.43 (q, 2H, ^3J(HH) = 7.1 Hz, CH_2); 7.16–7.5 (m, 5H, Ar); 7.96 (dt, 1H, ^3J(HH) = 5.7 Hz, ^3J(HH) = 2.0 Hz, Ar); 8.17 (dd, 1H, ^3J(HH) = 6.3 Hz, ^4J(HH) = 1.3 Hz, H^4); 8.73 (dd, 1H, H^0) ppm. ^{13}C NMR: 13.14; 14.58 (2 Me); 59.61 (CH_2); 106.1; 110.29; 121.47; 122.12; 122.31; 122.70; 123.30; 126.73; 128.7; 136.59; 138.55; 145.02; 150.02; 166.00 (CO) ppm. IR: ν(CO) 1697, 1470, 1193 cm^{-1}. *m/z*. Found: 280 (M^+, 100%); 251 (M^+ – Et, 45%). $C_{17}H_{16}O_2N_2$ calc.: 280.

4.8. 2-tert-butyl-3-methyl-1-(2-pyridyl)indole (3d)

1b (150 mg, 0.37 mmol) and 4,4-dimethyl-2-pentyne (60 mg, 0.63 mmol) were heated in refluxing 1,2-dichloroethane (20 ml) for 0.3 h. After filtration over Celite, the red filtrate was evaporated to dryness. The excess alkyne was removed on a short silica column (8 cm; hexane eluant) and the crude product eluted with acetone. Concentration of the solution left a red solid which was dissolved in a minimum of CH_2Cl_2 (4 ml). Addition of hexane (20 ml) precipitated an organometallic residue, leaving an orange filtrate. The latter gave, after concentration, a yellow–orange oil (yield, 100 mg (95%)). ^1H NMR: 1.31 (s, 9H, ^{t}Bu); 2.51 (s, 3H, Me); 6.74–7.90 (m, 7H, Ar); 8.62 (d, 1H, ^3J(HH) = 4.6 Hz, H^0) ppm. ^{13}C NMR: 11.83 (Me); 31.75 (^{t}Bu); 34.84 (quart. C); 109.95; 117.83; 120.00; 121.87; 123.05; 124.07; 125.00; 130.50 (m); 138.06; 149.58; 155.00 ppm. IR: 2952, 1599, 1585, 1506, 1465, 1355, 740, 668 cm^{-1}. *m/z*. Found: 264 (M^+, 64%), 249 (M^+ – Me, 100%), 234 (M^+ – 2Me, 32%). $C_{18}H_{20}N_2$ calc.: 264.

4.9. 3-formyl-2-phenyl-1-(2-pyridyl)-indole (3e)

1b (150 mg, 0.37 mmol) and phenylpropargyl aldehyde (65 mg, 0.48 mmol) were heated under reflux for 0.75 h in 1,2-dichloroethane (20 ml). After addition of K_2CO_3 and filtration of the Pd black over Celite, the dark-red filtrate was evaporated to dryness. Addition of acetone (5 ml) and hexane (20 ml) gave a brown solid that was filtered off, and an orange filtrate. The latter was evaporated to dryness and washed with

hexane, giving a brown solid (yield, 70 mg (63%)). Anal. Found: C, 80.56; H, 4.38; N, 9.15. $C_{20}H_{14}N_2O$ calc.: C, 80.52; H, 4.73; N, 9.39%. ^{1}H NMR: 6.91–7.86 (m, 11H, Ar); 8.50 (dd, ^3J(HH) = 4.8 Hz, ^4J(HH) = 1.4 Hz, H^4); 8.64 (dd, ^3J(HH) = 4.0 Hz, ^4J(HH) = 1.1 Hz, H^0); 9.97 (s, 1H, C*H*O) ppm. ^{13}C NMR: 111.46; 116.93; 122.21; 122.33; 123.04; 123.88; 124.79; 125.47; 128.41; 128.88; 129.43; 131.08; 137.47; 138.18; 149.58; 149.83; 150.31; 187.44 (CHO) ppm. IR: 1654, 1467, 1456, 1385, 1227, 1084, 758 cm^{-1}. *m/z*. Found: 298 (M^+, 100%); 269 ($M^+ - CH_2O$, 74%). Calc.: 298.

4.10. *3-paratolylsulphonyl-2-phenyl-1-(2-pyridyl)indole (3f)*

The method was the same as for **3e**; **3f**, however, was obtained pure by short-column alumina chromatography (ether and then acetone as eluents), giving an orange solid (yield, 60%). Anal. Found: C, 71.02; H, 4.52; N, 5.46. $C_{26}H_{20}N_2SO_2 \cdot 0.25\ CH_2Cl_2$ calc.: C, 70.73; H, 4.63; N, 6.28%. ^{1}H NMR: 2.29 (s, 3H, Me); 6.81 (d, 1H, ^3J(HH) = 7.2 Hz, Ar); 7.03–7.58 (m, 14H, Ar); 8.40 (dd, 1H, ^3J(HH) = 5.7 Hz; ^4J(HH) = 1.3 Hz, H^4); 8.54 (dd, 1H, ^3J(HH) = 4.8 Hz; ^4J(HH) = 1.2 Hz, H^0) ppm. ^{13}C NMR: 21.45 (Me); 111.79; 121.09; 122.60; 123.13; 123.43; 124.52; 126.72; 127.64; 128.91; 129.2 (m); 131.74; 136.56; 138.21; 141.00; 143.10; 149.45 ppm. IR: 1590, 1463, 1373, 1333, 1153 ($\nu(SO_2)$), 757, 743, 661, 589, 540 cm^{-1}. *m/z*. Found: 424. $C_{26}H_{20}N_2SO_2$ calc.: 424.

4.11. *3-phenyl-1-(2-pyridyl)indole (3g)*

3f (85 mg, 0.2 mmol), Na_2HPO_4 (540 mg, 3.8 mmol) and sodium amalgam (6 mol.% Na) were stirred at room temperature in MeOH under N_2. After 2 h the mixture was poured into water, extracted with Et_2O and washed with saturated ammonium chloride solution, followed by $MgSO_4$ drying. After filtration of the $MgSO_4$, the pale-yellow filtrate was evaporated to dryness and ^{1}H NMR analysis showed no *p*-tolyl methyl signal. A white paste (50 mg, 93%) was obtained after filtration (Et_2O) over a short silica column. ^{1}H NMR: 6.83 (1H, s, Ar); 6.90–7.73 (13H, m, Ar); 8.64 (1H, m, H^0) ppm. IR: 2922, 2851, 1465, 1457, 1378, 745, 697 cm^{-1}. *m/z*. Found: 270 (M^+, 100%). $C_{19}H_{14}N_2$ calc.: 270.

4.12. *Synthesis of compound 5*

DMAD (0.264 g, 1.86 mmol) was added to a suspension of **4a** (0.20 g, 0.16 mmol) in PhCl (40 ml). After heating for 0.25 h at 100°C, filtration through a short silica column (acetone eluent, 50 ml), the orange residue was evaporated to dryness. After pentane washing, yellow crystals could be obtained from CH_2Cl_2–pentane (yield, 0.25 g (54%)). Anal. Found: C, 45.71; H, 3.55; N, 1.66. $C_{30.5}H_{27}Cl_2NO_{13}$ (**5** + 0.5 CH_2Cl_2) calc.: C, 46.18; H, 3.41; N, 1.76%. ^{1}H NMR: 3.70, 3.73, 3.92, 3.96, 4.09 (5s, 18H, CO_2CH_3); 7.42 (dd, 1H, ^3J(HH) = 7.1 Hz, ^4J(HH) = 1.3 Hz, Ar); 7.7d, 1H, ^3J(HH) = 7.7 Hz, ^4J(HH) = 1.4 Hz, Ar); 8.75 (dd, 1H, ^3J(HH) = 5.2 Hz, H^0) ppm. IR: ν(CO) 1750–1630 cm^{-1}.

4.13. *Synthesis of compound 6a*

A mixture of **4b** (0.19 g, 0.23 mmol) and DMAD (0.195 g, 0.68 mmol of dimer) in PhCl (40 ml) was heated just below reflux temperature for 0.1 h. The metallic palladium formed was removed by filtration through a silica column and the crude product was eluted with acetone (40 ml), affording a red–brown solution. This was concentrated to 3 ml and hexane addition gave a brown precipitate and yellow filtrate, the latter being evaporated to dryness giving a yellow solid. CH_2Cl_2–pentane recrystallization yielded 120 mg (66%) (yield based on phenyl-2-pyridylketone) of **6a**. Anal. Found: C, 56.74; H, 3.87; N, 3.61. $C_{36}H_{28}N_2O_{10}Pd$ calc.: C, 57.26; H, 3.74; N, 3.74%. ^{1}H NMR: 3.83, 3.86, 3.91, 3.92 (4s, 12H, CO_2Me); 6.62 (d, 1H, ^3J(HH) = 6.8 Hz, Ar); 7.06–7.81 (m, 6H, Ar); 8.29 (dd, 1H, ^3J(HH) = 5.5 Hz, H^0) ppm. IR: ν(CO) 1710 cm^{-1}.

4.14. *Synthesis of 6b*

The method was as for **6a**. However, the reaction time required to yield **6b** was 0.15 h (PhCl reflux) and then 1 h at room temperature (yield, 61% (based on phenyl-2-pyridylketone ligand). Anal. Found: C, 75.64; H, 4.50; N, 3.39. $C_{52}H_{36}N_2O_2Pd$ calc.: C, 75.49; H, 4.40; N, 3.39%. ^{1}H NMR: 6.79 (d, 1H, ^3J(HH) = 7.8 Hz, Ar); 7.02 (t, 1H, ^3J(HH) = 6.3 Hz, Ar); 7.11–7.5 (m, 14H, Ar); 7.83 (m, 1H, Hm); 8.34 (d, 1H, ^3J(HH) = 4.8 Hz, H^0) ppm.

4.15. *Synthesis of 6c*

The method was as for **6a**. However, the reaction time required to yield **6c** (mixture of two regioisomers) was 0.25 h (PhCl reflux) (yield, 52%). Anal. Found: C, 66.57; H, 4.51; N, 3.30. $C_{46}H_{36}N_2O_6Pd$ calc.: C, 67.43; H, 4.44; N, 3.45%. First isomer, ^{1}H NMR: 1.05 (t, 3H, ^3J(HH) = 7.1 Hz, CH_2); 4.14 (q, 2H, ^3J(HH) = 7.1 Hz, CH_3); 6.65 (d, 1H, ^3J(HH) = 7.8 Hz, Ar); 7.00–7.72 (m, 12H, Ar); 8.19 (dd, 1H, ^3J(HH) = 5.3 Hz, H^0) ppm. IR: 1700 cm^{-1}. Second isomer, ^{1}H NMR: 1.04 (t, 3H, ^3J(HH) = 7.1, CH_2); 4.14 (q, 2H, ^3J(HH) = 7.1 Hz, MHz, CH_3); 6.64 (d, 1H, ^3J(HH) = 7.8 Hz, Ar); 7.00–7.72 (m, 12H, Ar); 8.18 (dd, 1H, ^3J(HH) = 5.3 Hz, H^0) ppm. IR: 1700 cm^{-1}.

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