Cyclometallation of indole derivatives: cyclopalladation of gramine and 1-methyl gramine and CO insertion

Stefano Tollari [a,*], Francesco Demartin [b], Sergio Cenini [a], Giovanni Palmisano [c], Paolo Raimondi [a]

[a] *Dipartimento di Chimica Inorganica, Metallorganica ed Analitica and CNR Center, Via Venezian 21, 20133 Milan, Italy*
[b] *Dipartimento di Chimica Strutturale e Stereochimica Inorganica, Via Venezian 21, 20133 Milan, Italy*
[c] *Dipartimento di Scienza e Tecnologia del Farmaco, Via Giuria 9, 10100 Turin, Italy*

Abstract

Li_2PdCl_4, in methanol, with gramine 1 and 1-methyl gramine 2 gave the dimeric complexes 1a and 2a with chlorine bridges and having the indole nucleus metallated at position 2. The corresponding bromo derivatives 1b and 2b were isolated from the reactions of $Pd(OAc)_2$ with 1 and 2, followed by treatment with LiBr. Complexes 1a,b and 2a,b gave the monomeric, cyclometallated derivatives 3a–d by reaction with PPh_3 in methylene chloride. When the cyclopalladation of 1-methyl gramine 1 was attempted by reacting $PdCl_2$, PPh_3 and 2 in methanol in the presence of AcONa, an unexpected compound 4 was obtained. A structural determination of 4 showed it consisted of the known $[Pd(PPh_3)Cl_3]^-$ anion packed with the dimethyl-bis(3-methylene-1-methyl indole) ammonium cation.

When compounds 1a and 2a were reacted with carbon monoxide at atmospheric pressure in methanol or ethanol and in the presence of NEt_3, the corresponding 2-carboalkoxy indole derivatives 5 and 6 were isolated in high yields.

Keywords: Gramine; Cyclopalladation; CD insertion; 1-methyl gramine

1. Introduction

The cyclometallation reaction represents one of the most useful methods for the activation and ortho-functionalisation of $C(sp^2)$–H bonds in aromatic compounds [1]. The metallation at one definitive position of the organic molecule is crucial for its selective functionalisation [2]. The presence of a tethered donor group allows the initial coordination of the ligand to the metal and favourable intramolecular cyclisation. Whereas heteroatom-directed cyclometallation of benzenoid and heteroaromatic systems has been exhaustively investigated [1–3], the chemistry of the analogous indole derivatives has remained virtually unexplored.

In the last 10 years this gap has been partially filled, and within this context we have reported on the *peri*-palladation of hydrazones of 1H-indole-3-carboxaldehyde [4] and on the *ortho*-platination of indoles such as gramine, tryptamine and (S)-tryptophan methyl ester [5].

We report in this paper the synthesis and reactivity towards carbon monoxide of hitherto unknown five-membered indole-fused *ortho*-palladacycles which incorporate gramine [N,N-dimethyl-1H-indole-3-methanamine] 1 and its 1-Me derivative 2 as C,N-bidendate ligands.

2. Results and discussion

Our initial investigations focused on the efficacy of various Pd(II) metallating agents in promoting the desired cyclometallation. The palladation was achieved in good yields by reacting compounds 1 and 2 with $Li_2[PdCl_4]$ in the

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* Corresponding author.

presence of NaOAc as a proton scavenger. The orange, probably dimeric, cyclopalladated complexes **1a** and **2a** precipitated from the solution (Eq. (1)) (Table 1):

(1)

1 R = H
2 R = Me

1a R = H
2a R = Me
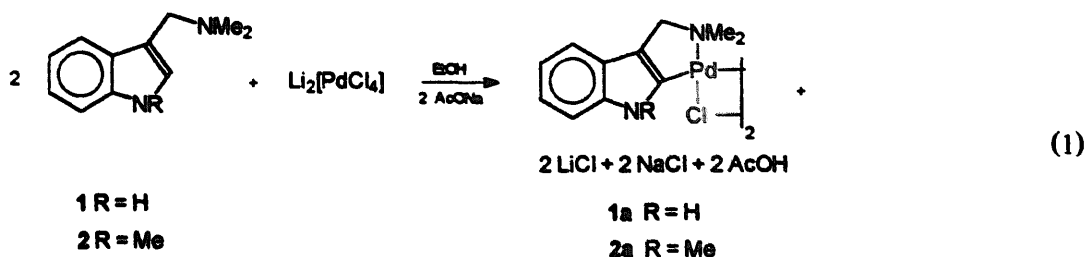
Both these compounds have poor solubility in common organic solvents, and hence unambiguous structure identification by using NMR spectroscopy was precluded. Nevertheless, their structures have been indirectly confirmed by the spectroscopic properties of the corresponding monomeric derivatives, obtained by cleavage of the chlorine bridges by reaction with PPh_3 (vide infra).

The substitution of chlorine for bromine in **1a** and **2a** was not a trivial task, and metathetical reactions with LiBr in acetone were unsuccessful. The corresponding bromo derivatives **1b** and **2b** were satisfactorily obtained by reaction of $Pd(OAc)_2$ with **1** and **2** respectively in CH_2Cl_2, followed, after evaporation of the solvent, by treatment of the residue with an excess of LiBr in ethanol in situ without isolating the intermediate dimeric acetate derivatives (Eq. (2)) (Table 1):

1 R = H
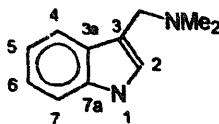**2 R = Me**

(2)

1b R = H
2b R = Me
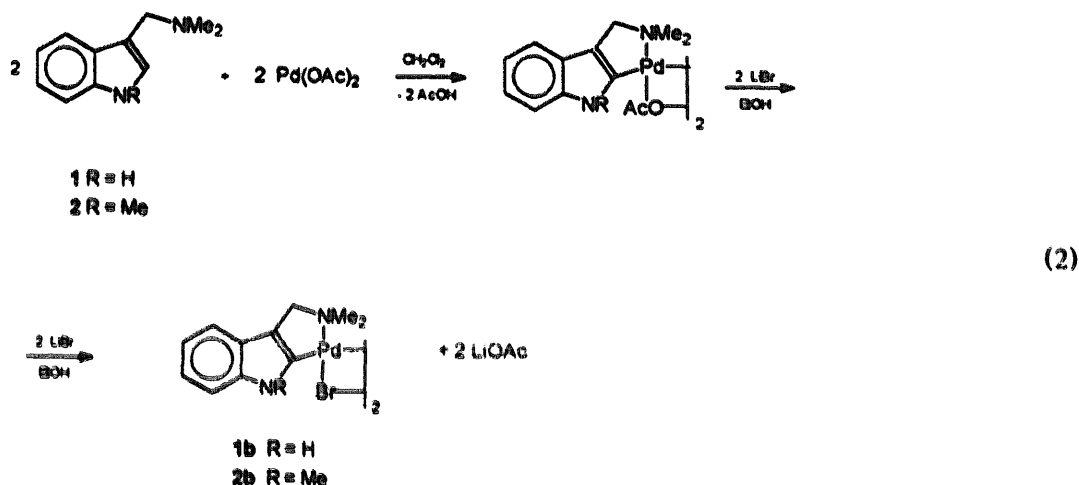
This methodology has already been applied [6].

Like **1a** and **2a**, the deep orange products **1b** and **2b** are insoluble in the common organic solvents. In order to obtain derivatives suitable for a spectroscopic characterisation, compounds **1a,b** and **2a,b** were treated with PPh_3 in dichloromethane.

Table 1
Analytical and infrared data

Compound	Colour	Yield (%)	Analytical data calc. (found)(%)			IR data ν(Pd–Cl) (cm^{-1})
			C	H	N	
1a	Orange	93	41.93 (42.09)	4.16 (4.11)	8.89 (8.81)	306, 250
2a	Orange	86	43.79 (43.68)	4.59 (4.5)	8.51 (8.45)	288, 248
1b	Orange	92	36.75 (36.8)	3.64 (3.55)	7.79 (7.72)	
2b	Orange	86	38.58 (38.62)	4.05 (3.92)	7.5 (7.41)	
3a	Yellow	83	60.33 (60.28)	4.89 (4.8)	4.85 (4.79)	273
3b	Yellow	78	60.93 (60.81)	5.11 (5.01)	4.74 (4.66)	278
3c	Yellow	87	56.01 (55.97)	4.54 (4.46)	4.5 (4.56)	
3d	Yellow	77	56.67 (56.81)	4.76 (4.69)	4.41 (4.37)	

Table 2
^{1}H ^{a} and ^{31}P ^{b} NMR data

Compound	δ(H(1))	δ(H(2))	δ(H(4))	δ(H(5))	δ(H(6))	δ(H(7))	δ(CH₂N)	δ(NMe₂)	δ(PPh₃)	δ³¹P
1	8.5	7.1	7.43 dd J_{H-H} 8.6; 3.2	7.23 m	7.21 m	7.7 dd J_{H-H} 8.5; 3.3	3.58	2.35		
2	3.78	7.08	7.22 dd J_{H-H} 8.6; 3.1	7.25 m	7.23 m	7.77 dd J_{H-H} 8.7; 3.1	3.56	2.38		
3a	9.22		7.22 dd J_{H-H} 8.6; 3.1	6.78 m	6.78 m	7.22 dd J_{H-H} 8.7; 3.2	4.12	3.01	7.6–7.22 brm	34.93
3b	3.8		7.31 dd J_{H-H} 8.8; 3.1	6.83 m	6.73 m	7.32 dd J_{H-H} 8.7; 3.1	4.1	2.85	7.5–7.1 brm	33.82
3c	9.31		7.42 dd J_{H-H} 8.6; 3.3	6.88 m	6.71 m	7.48 dd J_{H-H} 8.5; 3.1	3.67	2.86	7.8–7.2 brm	33.38
3d	3.7		7.38 dd J_{H-H} 8.7; 3.2	6.85 m	6.73 m	7.25 dd J_{H-H} 8.6; 3.2	3.71	2.96	7.7–7.3 brm	33.88

^{a} Spectra measured at 200 MHz, $CDCl_3$; chemical shifts δ(ppm) with Me_4Si as internal standard; coupling constants J (Hz).
^{b} Spectra measured at 32.4 MHz, $CDCl_3$; chemical shifts δ(ppm) with 85% H_3PO_4 as internal standard; coupling constants J (Hz).

From these reactions, the yellow, monomeric cyclopalladated complexes 3a–d were isolated (Eq. (3)) (Tables 1–3):
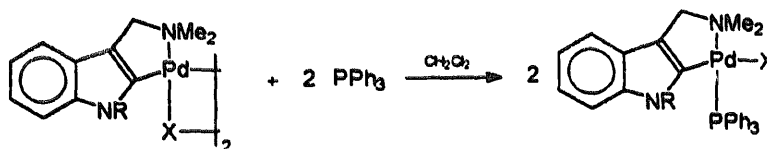
1a R = H, X = Cl	3a R = H, X = Cl
1b R = H, X = Br	3c R = H, X = Br
2a R = Me, X = Cl	3b R = Me, X = Cl
2b R = Me, X = Br	3d R = Me, X = Br

$$(3)$$

The ^{1}H, ^{13}C and ^{31}P NMR spectra indicated the presence of a single isomer for compounds 3a–d. Comparison of the ^{1}H NMR (Table 2) with those of compounds 1 and 2 [7] showed that cyclometallation has occurred on the 2-position in all cases.

The ^{1}H NMR signals were assigned on the basis of the chemical shifts and spin–spin coupling and were confirmed by selective decoupling experiments (for ^{1}H and ^{13}C NMR special assignments of cyclopalladated compounds, see Ref. [8]). The aromatic protons and the NH proton are shifted upfield by cyclometallation; this effect must be attributed to the anisotropy of the phenyl rings of the phosphine ligands and/or to a decrease in the ring current of the heteroaromatic system [9]. Furthermore, the relatively large diamagnetic shift of H-6, a position unaffected by steric interaction, clearly indicates the presence of some metal-to-ligand back-bonding [10].

The loss of a broad singlet at 7.12 ppm (H-2) and the presence of a quaternary carbon (at 140–142 ppm) are consistent with ortho-metallation (C(2) as σ donor) rather than peri-metallation (C(4) as σ donor). The signal of C(2) in the cyclometallated complexes 3a–d exhibits low intensity due to the nuclear Overhauser effect and underwent a paramagnetic shift (ca. 18 ppm). The C(3) resonance was shifted towards higher frequency and there was no noticeable quadrupole broadening due to coupling with the ^{105}Pd nucleus (22.5% natural abundance, $I = 5/2$).

Table 3
^{13}C NMR data ^{a}

Compound	C(2)	C(3)	C(3a)	C(4)	C(5)	C(6)	C(7)	C(7a)	C(CH₂N)	C(NMe₂)	C(N–Me)
3a	140.7	118.7	124.9	114.9	116.8	119.7	110.3	135.3	68.2	53.3	
3b	140.1	119.1	124.5	115.3	116.3	119.8	110.6	135.2	68.5	53.6	31.5
3c	141.8	118.9	125.4	115.6	116.9	121.1	111.3	136.9	67.9	54.1	
3d	142.1	119.6	125.1	115.4	117.5	120.9	111.1	137.1	67.5	54.5	32.1

^{a} Spectra measured at 50.3 MHz, $CDCl_3$; chemical shifts δ(ppm) with Me_4Si as internal standard.

On N-coordination with the palladium centre in 3a–d, a puckered five-membered ring is formed.

The ^{1}H NMR signals of NMe_2 and CH_2N undergo a paramagnetic shift owing to the anisotropy of the metal [11] and resonate as singlets: this could reasonably be due to a rapid on–off movement of these groups, or to a fast inversion on the NMR time scale. We attempted to obtain spectroscopic evidence for a fluxional behaviour. On taking the ^{1}H NMR spectra (CDCl$_3$) of 3a–d at 200 K (the temperature was lowered in steps of 10 K) no appreciable change in the spectra were evident. Solubility problems precluded measurements below this temperature.

Detection of a band in the range 273–278 cm^{-1} in the far-infrared spectrum of 3a,b due to $\nu_{(Pd-Cl)}$ (Table 1) was consistent with a halogen trans to the ligand (carbon σ donor) of strong trans influence [12]. Additionally, the phosphorus resonance in the ^{31}P-{^{1}H} NMR spectrum of 3a–b is in the range 33.8–34.9 ppm, suggesting that the phosphine is trans to the N donor. A C–Pd–PPh$_3$ trans arrangement would shift the ^{31}P resonance to lower frequency [13].

As with the platination [4] of gramine 1, the CH_2NMe_2 moiety present in this compound is capable of directing cyclometallation to the 2-position with the (SP-4-4) [12] stereoisomer being formed as the sole organometallic product.

The outcome of the cyclometallation of 1 depends on the Pd(II) metallating agent and the solvent in which it is carried out. Thus, attempts to achieve a tandem cyclometallation-halide bridge splitting by reaction of 1(L) with PdCl$_2$ and PPh$_3$ in a 1:2 molar ratio in MeOH at room temperature were unsuccessful. Surprisingly, under these conditions, and in the presence of AcONa, 1-methyl gramine 2 gave the ionic complex 4, albeit in low yield (Eq. (4)):

$$\text{(4)}$$

4
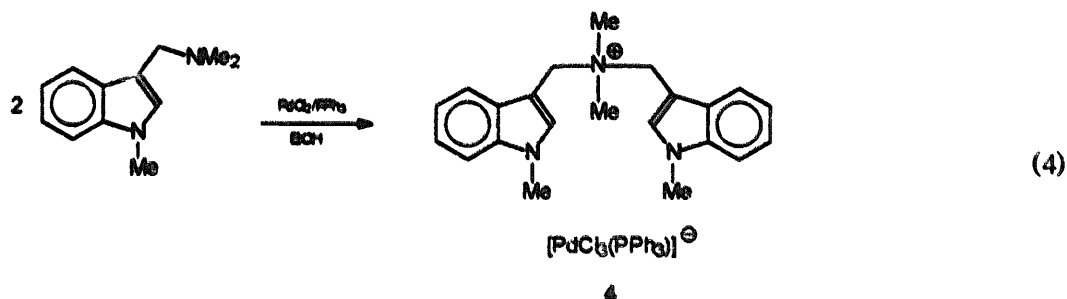
The structure of compound 4 was established by X-ray diffraction (vide infra) and its formation can be explained according to Scheme 1. The initial coordination of compound 2 to the metal is followed by cleavage of the C–N bond to give the transient 3-methylene-3H-indole. Nucleophylic trapping by the 1-methyl gramine 2 would ultimately lead to the cation 4 [14].

A similar reaction has been reported between gramine and carbon electrophiles, but, to our knowledge, this is the first example induced by metal complexation.

A crystal of 4 consists of a packing of [Pd(PPh$_3$)Cl$_3$]$^-$ anions and cations, and solvate CH$_2$Cl$_2$ molecules, separated by normal van der Waals contacts. A perspective view of the crystal packing is shown in Fig. 1; Fig. 2 shows an ORTEP drawing of the cation together with the atom numbering scheme. Selected interatomic distances and
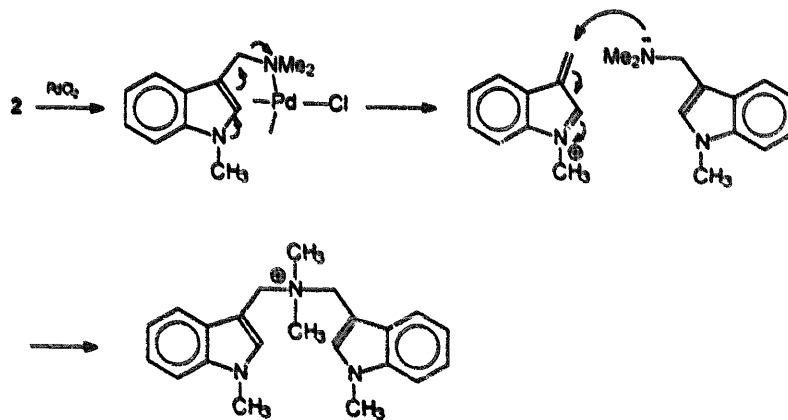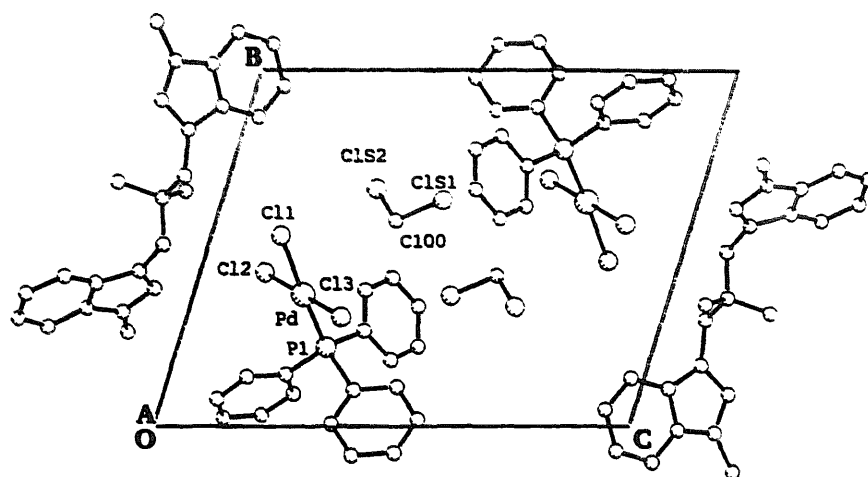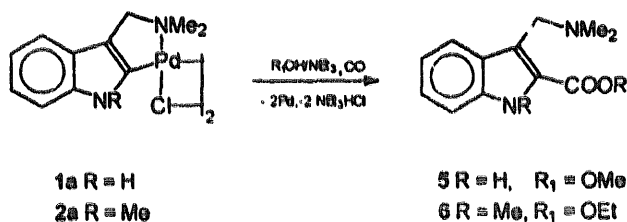

Scheme 1.

Fig. 1. Packing diagram of compound 4. Hydrogen atoms omitted for clarity.

angles are reported in Table 4. The geometrical parameters within the square planar anionic complex $[Pd(PPh_3)Cl_3]^-$ are essentially similar to those reported for the same anion by Bardi et al. [15], and the minor differences are probably due to a different packing environment. The pattern of bond distances and angles within the cation is comparable with that observed for other indoles. The C(8)–C(10)–N(2)–C(13)–C(14) system is essentially planar and almost orthogonal to the plane of the two indole moieties (dihedral angles 86.2(4) and 90.3(4)°).

One of the main aims of our work was to synthesise cyclopalladated complexes, which are useful for the functionalisation of the indole nucleus in the 2-position. Compounds 1a and 2a proved to be the appropriate derivatives. By carbonylating these compounds at atmospheric pressure in alcohols in the presence of Et_3N, the corresponding 2-carbalkoxy indole derivatives 5 and 6 were obtained in high yields (Eq. (5)):

$$\underset{\substack{\text{1a R = H}\\\text{2a R = Me}}}{\boxed{\text{indole-CH}_2\text{-NMe}_2\text{-Pd-Cl}}} \xrightarrow[\cdot \ 2Pd, \cdot 2\ NEt_3HCl]{R(OH)NEt_3, CO} \underset{\substack{\text{5 R = H, } R_1 = OMe\\\text{6 R = Me, } R_1 = OEt}}{\boxed{\text{indole-NMe}_2\text{-COOR}_1}} \tag{5}$$
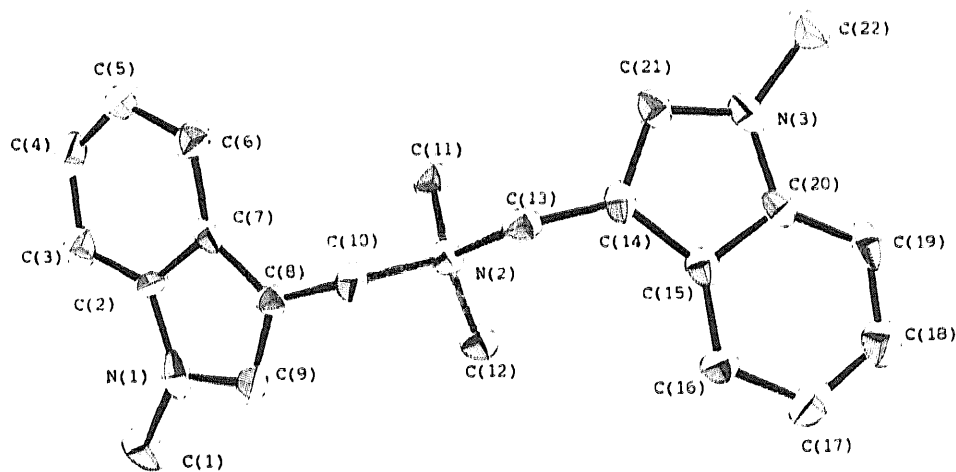

Fig. 2. Perspective drawing of the dimethyl-bis(3-methylene-1-methylindole)ammonium cation in the structure of 4. Thermal ellipsoids drawn at 30% probabilty.

Table 4
Interatomic distances (Å) and angles (deg) for (4)

Pd–Cl(1)	2.377(3)	Cl(1)–Pd–Cl(2)	90.7(1)
Pd–Cl(2)	2.300(2)	Cl(1)–Pd–Cl(3)	89.2(1)
Pd–Cl(3)	2.296(3)	Cl(1)–Pd–P(1)	176.3(1)
Pd–P(1)	2.228(3)	Cl(2)–Pd–Cl(3)	179.4(1)
P(1)–C(111)	1.818(9)	Cl(2)–Pd–P(1)	88.4(1)
P(1)–C(121)	1.825(8)	Cl(3)–Pd–P(1)	91.8(1)
P(1)–C(131)	1.833(8)		
N(1)–C(1)	1.523(10)	C(5)–C(6)	1.375(12)
N(1)–C(2)	1.384(10)	C(6)–C(7)	1.379(11)
N(1)–C(9)	1.416(11)	C(7)–C(8)	1.427(11)
N(2)–C(10)	1.528(9)	C(8)–C(9)	1.345(11)
N(2)–C(11)	1.491(9)	C(8)–C(10)	1.467(11)
N(2)–C(12)	1.491(9)	C(13)–C(14)	1.490(11)
N(2)–C(13)	1.538(10)	C(14)–C(15)	1.443(10)
N(3)–C(20)	1.386(10)	C(14)–C(21)	1.383(11)
N(3)–C(21)	1.366(10)	C(15)–C(16)	1.384(11)
N(3)–C(22)	1.449(11)	C(15)–C(20)	1.387(11)
C(2)–C(3)	1.394(12)	C(16)–C(17)	1.389(12)
C(2)–C(7)	1.405(11)	C(17)–C(18)	1.390(13)
C(3)–C(4)	1.367(13)	C(18)–C(19)	1.369(13)
C(4)–C(5)	1.383(13)	C(19)–C(20)	1.396(12)
C(1)–N(1)–C(2)	128.4(8)	C(6)–C(7)–C(8)	134.8(9)
C(1)–N(1)–C(9)	124.0(8)	C(7)–C(8)–C(9)	107.1(8)
C(2)–N(1)–C(9)	107.1(8)	C(7)–C(8)–C(10)	127.9(8)
C(10)–N(2)–C(11)	110.9(6)	C(9)–C(8)–C(10)	125.1(9)
C(10)–N(2)–C(12)	109.2(6)	N(1)–C(9)–C(8)	110.2(8)
C(10)–N(2)–C(13)	106.1(6)	N(2)–C(10)–C(8)	115.0(7)
C(11)–N(2)–C(12)	109.5(6)	N(2)–C(13)–C(14)	115.6(7)
C(11)–N(2)–C(13)	110.6(6)	C(13)–C(14)–C(15)	128.8(8)
C(12)–N(2)–C(13)	110.5(6)	C(13)–C(14)–C(21)	124.3(8)
C(20)–N(3)–C(21)	108.2(7)	C(15)–C(14)–C(21)	106.7(8)
C(20)–N(3)–C(22)	125.0(8)	C(14)–C(15)-1-C(16)	135.0(9)
C(21)–N(3)–C(22)	126.6(9)	C(14)–C(15)–C(20)	106.2(8)
N(1)–C(2)–C(3)	127.8(10)	C(16)–C(15)–C(20)	118.7(9)
N(1)–C(2)–C(7)	107.8(8)	C(15)–C(16)–C(17)	119.3(9)
C(3)–C(2)–C(7)	124.4(9)	C(16)–C(17)–C(18)	120.5(9)
C(2)–C(3)–C(4)	115.3(10)	C(17)–C(18)–C(19)	121.6(9)
C(3)–C(4)–C(5)	122.2(10)	C(18)–C(19)–C(20)	116.9(9)
C(4)–C(5)–C(6)	121.3(9)	N(3)–C(20)–C(15)	109.2(8)
C(5)–C(6)–C(7)	119.4(9)	N(3)–C(20)–C(19)	127.9(9)
C(2)–C(7)–C(6)	117.4(9)	C(15)–C(20)–C(19)	123.0(9)
C(2)–C(7)–C(8)	107.8(9)	N(3)–C(21)–C(14)	109.6(8)

This reaction probably proceeds via bridge splitting by NEt$_3$ of 1a and 2a, coordination and insertion of carbon monoxide into the Pd–C bond, and nucleophilic attack by alcohol to the carbonyl function of the acyl palladium(II) intermediate to give the final products.

3. Conclusions

The indole derivatives gramine 1 and its 1-methyl derivative 2 readily give cyclometallated complexes with platinum [5] and, as reported here, with palladium salts.

As in the case of the platination of gramine 1, the CH$_2$NMe$_2$ moiety is capable of directing cyclometallation to the 2-position, (SP-4-4) stereoisomer [16] being formed as the only organometallic product. This highly selective metallation reaction, and the easy reaction of the cyclopalladated complexes in alcohol with carbon monoxide at atmospheric pressure, allowed the synthesis of the 2-carbalkoxy derivatives of the indoles in excellent yields. It is worth mentioning here that the classical, organic synthesis of these organic compounds is not trivial.

Work is in progress in order to investigate the possibility of involving the palladium–carbon bond of the cyclopalladated complexes in other reactions, aimed at introducing other functional groups in the 2-position of the indole derivatives 1 and 2.

4. Experimental details

IR spectra were recorded as KBr disks on Perkin–Elmer 1310 and Nicolet MX-1FT-IR spectrophotometers. FAB[+] MS (+ve mode) were performed on a VG 7070/EQ instrument using *m*-nitrobenzyl alcohol (MNBA) as a matrix. ^{1}H, ^{31}P{^{1}H} and ^{13}C NMR spectra were respectively obtained using Varian XL-200 (200 MHz), Bruker WP-80SY (32.4 MHz) and Varian XL-200 (50.3 MHz) spectrometers.

4.1. Preparation of di-μ-chloro-{2-[(3-dimethylamino)methyl]-1H-indolyl-C²,N}dipalladium(II) 1a and di-μ-chloro-{1-methyl-2-[(3-dimethylamino)methyl]-1H-indolyl-C²,N}dipalladium(II) 2a

A suspension of PdCl$_2$ (135 mg, 0.76 mmol) and LiCl (46 mg, 1.52 mmol) in ethanol (5 ml) was heated under reflux conditions for 2 h to give a dark red solution of Li$_2$[PdCl$_4$]. The solution was cooled to room temperature and the corresponding ligand (0.63 mmol) in ethanol (2 ml) and sodium acetate trihydrate (52 mg, 0.63 mmol) were added. The resulting suspension was stirred at room temperature for 1 h. The insoluble, orange products **1a** and **2a** were filtered off, washed with ethanol (3 × 2 ml) and dried in vacuo.

4.2. Preparation of di-μ-bromo-{2-[(3-dimethylamino)methyl]-1H-indolyl-C²,N}dipalladium(II) 1b and di-μ-bromo-{1-methyl-2-[(3-dimethylamino)methyl]-1H-indolyl-C²,N}dipalladium(II) 2b

The corresponding ligand (0.5 mmol) was dissolved in dichloromethane (10 ml) degassed with dinitrogen. Pd(OAc)$_2$ (112 mg, 0.5 mmol) was added and the dark-orange solutions stirred for 1 h under dinitrogen and then concentrated in vacuo. The resulting residue was dissolved in ethanol (5 ml) and treated with LiBr (43 mg, 0.5 mmol) dissolved in ethanol (1 ml). The suspension was stirred at room temperature for 30 min. The insoluble, orange products were filtered off, washed with ethanol (2 × 2 ml) and dried in vacuo.

4.3. Synthesis of compounds 3a–d

A stirred suspension of the dimeric complexes **1a,b** or **2a,b** (0.4 mmol) in degassed dichloromethane (5 ml) was treated with PPh$_3$ (262 mg, 1 mmol) at room temperature for 1 h under a dinitrogen atmosphere. Addition of *n*-hexane

Table 5
Crystallographic data for (4)

Formula	C$_{41}$H$_{43}$Cl$_5$N$_3$PPd
F.w. (amu)	892.46
Crystal system	triclinic
Space group	P$\bar{1}$
a (Å)	11.572(2)
b (Å)	12.065(2)
c (Å)	15.403(1)
α (deg)	72.18(1)
β (deg)	83.80(1)
γ (deg)	85.40(1)
U (Å³)	2032.8(5)
Z	2
F(000)	912
D_{calc} (g cm^{-3})	1.458
μ(MoKα) (cm^{-1})	8.5
ω-scan width (deg)	1.2 + 0.35 tan θ
θ-range (deg)	3–23
Octants of reciprocal space explored	+ h, ± k, ± l
Measured reflections	5718
Unique reflections with $I > 3\sigma(I)$ (N_o)	2452
Final R and R_w indices [a]	0.039, 0.041
No. of variables (N_v)	460
ESD [b]	1.22

[a] $R = [\Sigma(F_o - k|F_c|)/\Sigma F_o]$; $R_w = [\Sigma(F_o - k|F_c|)^2/\Sigma wF_o^2]^{1/2}$.
[b] ESD = $[\Sigma(F_o - k|F_c|)^2/(N_o - N_v)]^{1/2}$.
$w = 1/[\sigma(F_o)]^2$; $\sigma(F_o) = [\sigma^2(I) + (0.04I)^2]^{1/2}/2F_o L_p$.

(15 ml) to the solution resulted in precipitation of the yellow solids. Recrystallisation of the crude products from dichloromethane–n-hexane gave the analytically pure yellow products 3a–d.

4.4. Preparation of compound 4

1-Methyl gramine 2b (0.5 mmol), PdCl$_2$ (85 mg, 0.5 mmol) and PPh$_3$ (262 mg, 1 mmol) were mixed in methanol (5 ml) in the presence of AcONa (41 mg, 0.5 mmol), and the suspension was kept under a dinitrogen atmosphere. After stirring overnight, the resulting pink solution was evaporated in vacuo. The residue was taken up in

Table 6
Fractional atomic coordinates with e.s.d.s for (4)

Atom	x	y	z
Pd	0.22851(7)	0.36978(6)	0.23260(5)
Cl(1)	0.1181(2)	0.5353(2)	0.1491(2)
Cl(2)	0.3929(2)	0.4323(2)	0.1373(2)
Cl(3)	0.0637(2)	0.3068(2)	0.3266(2)
P(1)	0.3372(2)	0.2222(2)	0.3149(2)
N(1)	0.4234(7)	0.3207(6)	−0.1358(5)
N(2)	0.1952(5)	0.6403(5)	−0.1253(4)
N(3)	0.0597(6)	1.0221(6)	−0.1850(5)
C(1)	0.5438(7)	0.2648(8)	−0.1138(7)
C(2)	0.3654(7)	0.3304(7)	−0.2120(5)
C(3)	0.3975(9)	0.2791(8)	−0.2813(6)
C(4)	0.3228(9)	0.3032(8)	−0.3484(6)
C(5)	0.2220(8)	0.3727(8)	−0.3470(6)
C(6)	0.1917(8)	0.4211(7)	−0.2771(6)
C(7)	0.2640(7)	0.4015(7)	−0.2078(6)
C(8)	0.2610(7)	0.4360(7)	−0.1269(5)
C(9)	0.3570(8)	0.3875(7)	−0.0851(6)
C(10)	0.1721(7)	0.5104(7)	−0.0933(5)
C(11)	0.2177(8)	0.6834(8)	−0.2269(5)
C(12)	0.2983(7)	0.6595(7)	−0.0824(6)
C(13)	0.0854(7)	0.7025(8)	−0.0930(6)
C(14)	0.0902(7)	0.8310(7)	−0.1134(5)
C(15)	0.1305(7)	0.8957(7)	−0.0587(6)
C(16)	0.1758(7)	0.8664(7)	0.0254(5)
C(17)	0.2030(8)	0.9545(8)	0.0593(6)
C(18)	0.1850(8)	1.0708(8)	0.0094(7)
C(19)	0.1373(8)	1.1026(7)	−0.0728(7)
C(20)	0.1102(7)	1.0127(7)	−0.1053(6)
C(21)	0.0464(8)	0.9121(7)	−0.1887(6)
C(22)	0.021(1)	1.1305(9)	−0.2490(7)
C(111)	0.4307(7)	0.1464(7)	0.2464(6)
C(112)	0.5386(8)	0.0911(8)	0.2741(6)
C(113)	0.6039(8)	0.0314(8)	0.2208(6)
C(114)	0.5669(8)	0.0237(8)	0.1412(6)
C(115)	0.4606(8)	0.0765(8)	0.1159(6)
C(116)	0.3941(8)	0.1391(8)	0.1651(6)
C(121)	0.4331(7)	0.2681(7)	0.3827(5)
C(122)	0.4821(8)	0.1859(8)	0.4557(6)
C(123)	0.5615(9)	0.223(1)	0.5029(7)
C(124)	0.5894(9)	0.336(1)	0.4775(6)
C(125)	0.5384(9)	0.4165(9)	0.4067(7)
C(126)	0.4593(8)	0.3818(7)	0.3590(6)
C(131)	0.2594(7)	0.1028(7)	0.3982(6)
C(132)	0.2313(8)	0.0075(8)	0.3744(6)
C(133)	0.1700(8)	−0.0796(8)	0.4366(8)
C(134)	0.137(1)	−0.072(1)	0.5218(8)
C(135)	0.163(1)	0.020(1)	0.5485(8)
C(136)	0.2231(9)	0.1112(9)	0.4846(7)
Cl(s1)	0.0661(3)	0.6341(3)	0.4613(2)
Cl(s2)	0.2511(3)	0.6653(4)	0.3174(2)
C(100)	0.138(1)	0.5772(9)	0.3760(7)

dichloromethane (5 ml), filtered and n-hexane (20 ml) added. Colourless, needle-shaped crystals of the complex 4 (48 mg, 11.8%) separated after 1 week by low evaporation of the solvents at ca. 4°C.

^{1}H NMR (DMSO-d_6): 2.90 (s, 6H, N-Me_2), 4.39 (s, 3H, N-Me), 4.80 (s, 4H, CH_2N), 7.0–8.0 (m, 10H, aromatic); FAB-MS m/z 332 [(L – NMe$_2$)L]$^+$; Anal. Calc. (found) for $C_{40}H_{41}Cl_3N_3PPd$: C, 59.49 (59.53); H, 5.12 (5.03); N, 5.2 (5.29%).

4.5. Preparation of 5 [N,N-dimethyl-2-methoxycarbonyl-1H-indole-3-methanamine]) and 6 [N,N,1-trimethyl-2-ethoxycarbonyl-1H-indole-3-methanamine]

Carbonylation of the μ-dichloro complexes 1a and 2a (0.5 mmol) in alcohol (10 ml) at room temperature with CO at atmospheric pressure was carried out in the presence of triethylamine (2 mmol) for 3 h. The precipitated palladium was separated by filtration and the solvent was evaporated to dryness. The residues were purified on a silica-gel column, eluting with dichloromethane–methanol (19:1) to give 5 (92% yield) and 6 (79%).

5: (CDCl$_3$): 2.35 (s, 6H, NMe_2), 3.89 (s, 3H, OMe), 4.05 (s, 2H, CH_2N), 6.62 (brs, 1H, NH), 7.0–7.58 (m, 3H, aromatic), 7.83 (d, 1H, J = 8.2 Hz, H-7); EI-MS (70 eV) m/z 232 (M$^+$, 51%), 217 (22%), 201 (15%), 174 (55%), 130 (100%), 117 (39%).

6: (CDCl$_3$): 1.41 (t, 3H, CH_3CH_2O), 2.42 (s, 6H, NMe_2), 4.05 (s, 2H, CH_2N), 4.11 (qt, 2H, CH_3CH_2O), 4.49 (s, 3H, NMe), 7.0–7.47 (m, 3H, aromatic), 7.79 (d, 1H, J = 8.3 Hz, H-7); EI-MS (70 eV) m/z 260 (M$^+$, 63%), 245 (100%), 231 (86%), 216 (94%), 202 (43%), 188 (92%), 172 (26%), 144 (72%).

5. X-ray data collection and refinement

Crystals of compound 4 suitable for the X-ray structural determination were obtained as described in Section 4.4. Details of the data collection and refinement of the structure of compound 4 are reported in Table 5. Preliminary examination of a crystal, mounted on a glass fibre in a random orientation, and data collection were performed with graphite monochromatised MoKα radiation (0.71073 Å) on an Enraf–Nonius CAD4 diffractometer. Cell constants and an orientation matrix for data collection were obtained from least squares refinement, using the setting angles of 25 reflections, measured by the computer-controlled diagonal slit method of centring. The data were collected at room temperature using a variable scan rate. As a check on crystal and electronic stability, three representative reflections were measured every 2 h and showed no decay of the scattering power of the crystals during the data collection.

Lorentz, polarisation and a semi-empirical absorption correction [17] were applied to the data. The structure was solved by Patterson and Fourier methods and refined with full-matrix least squares minimising the function $\Sigma w(|F_o| - |F_c|)^2$. Scattering factors were taken from Cromer and Waber [18]. Anomalous dispersion effects were included in F_c; the values for $\delta f'$ and $\delta f''$ were taken from Cromer [19]. All the hydrogen atoms, with the exception of those on atoms C(1) and C(22), bonded to sp^2 centres, were placed at calculated positions (C–H = 0.95 Å); for the remainder the conformational arrangement was derived from a ΔF map and, subsequently, their idealised positions were recalculated. No refinement of the hydrogen atoms was carried out. Calculations were performed on an 80486/33 computer using Personal SDP software [20]. The final atomic coordinates are reported in Table 6.

Acknowledgements

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