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Preliminary communication

Cyclopalladated 2-t-butyl-4,4-dimethyl-2-oxazoline: its preparation, and use in the functionalisation of a non-activated carbon–hydrogen bond

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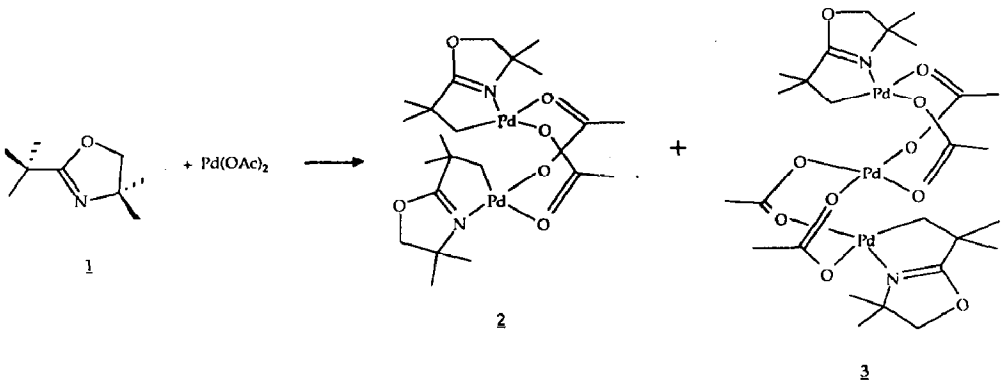
Abstract

Activation and functionalisation of one of the methyl groups of pivalic acid can be achieved through cyclopalladation of its 4,4-dimethyloxazoline derivative. This reaction gives a separable mixture of dinuclear and trinuclear species. The dimeric complex undergoes insertion of methyl vinyl ketone and of carbon monoxide, but is alkylated by aliphatic iodides, thereby providing a new route to homologated tertiary carboxylic acids.

The search for methods of regiospecific activation and functionalisation of carbon–hydrogen bonds by transition metal complexes remains a continuing challenge. Some major developments in this field are based on cyclometallation reactions. Since organopalladium compounds are valuable intermediates in organic synthesis, numerous examples of cyclopalladation reactions involving aromatic or benzylic C–H bonds have been reported [1,2], but only few cases involve non-activated aliphatic groups [3–6], and the reactions of the resulting complexes have been little studied [3,7,8].

We present here our findings on the cyclopalladation and functionalisation of the aliphatic oxazoline **1** (Scheme 1), a derivative of 2,2-dimethylpropanoic acid (pivalic acid). Oxazolines are useful substrates owing to their ready preparation from carboxylic acids, their transformations into esters, aldehydes, ketones, etc., as well as their efficiency as *ortho*-directing groups in aromatic lithiation [9] and palladation [10].

The reaction of 2-t-butyl-4,4-dimethyl-2-oxazoline (**1**) [11] with palladium acetate (1 eq) in acetic acid (95 °C, 1 h) readily afforded yellow crystals of the dimeric cyclopalladated complex **2** in 62% yield after crystallization (CH_2Cl_2/heptane). Interestingly, in addition to complex **2**, the trinuclear species **3** was isolated in 16% yield (Scheme 1). Such species have been occasionally observed in the cyclopallada-



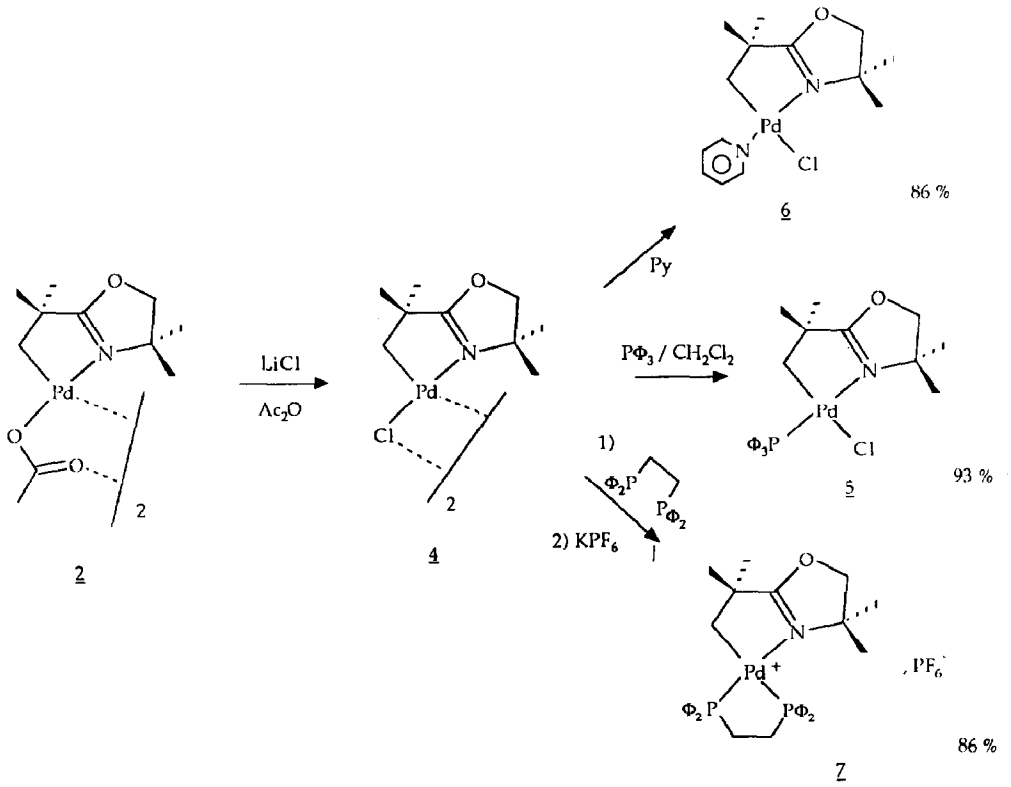
Scheme 1

tion of ligands containing nitrogen as the donor atom, and have been reported to be the sole product of the reaction [12].

The proposed structures for **2** and **3** are in good agreement with their analytical [13*] and spectroscopical data [14*]. Complex **2** is fluxional in solution on the NMR time scale at ambient temperatures, as shown by its ^{1}H NMR spectrum ($CDCl_3$, 250 MHz), which exhibits a sharp singlet (1.90 ppm, CH_3–COO) and four ill-resolved resonances. As is observed quite frequently for bis-μ-acetato palladium complexes [10], complex **2** is stereochemically rigid at low temperature. In particular, the spectrum at $-60\,^\circ$C displays a four-lines AB type pattern for each $-CH_2-$ moiety (CH_2–Pd 4.21 and 4.12 ppm; $J = 8.5$ Hz; CH_2–O: 2.07 and 2.01 ppm; $J = 8.5$ Hz), and two peaks for each $-CMe_2$ group (N–CMe_2: 1.38 and 1.16 ppm; Pd–CH_2–CMe_2: 1.26 and 1.24 ppm). Between $-25\,^\circ$C and $+30\,^\circ$C, the signals of the $-CH_2-$ and $-CMe_2$ protons broaden and coalesce, leading to four sharp singlets (4.06, 2.06, 1.28, 1.23 ppm) at $+60\,^\circ$C. A fast opening of the eight-membered ring formed by the metallic atoms and the acetato-bridging ligands (Scheme 1) is believed to be responsible for the fluxionality of **2**, as previously described in detail for the related cyclopalladated aryloxazolines [10]. From the coalescence temperature, $T_c = 293$ K, attributed to the N–CMe_2 moiety, the Eyring equation allows an activation barrier, ΔG^* of ca. 3.5 ± 0.4 kcal mol^{-1} for this process in complex **2**, significantly lower than that estimated for the cyclopalladated aryloxazolines ($\Delta G^* = 15.1 \pm 0.8$ kcal mol^{-1}) [10].

In the ^{1}H NMR spectrum of **3** (250 MHz, $CDCl_3$) at $25\,^\circ$C, the acetato methyl protons appear as four singlets, indicating that **3** contains both a *syn* and an *anti* isomer in a roughly 2/3 ratio. Both isomers give rise to two distinct acetate methyl resonances (Scheme 1). As for **2**, the two methyls of each $-CMe_2-$ moiety are diastereotopic, and these protons appear as four singlets for each isomer. Both isomers of the complex **3** are fluxional in solution at $25\,^\circ$C. Thus warming a solution of **3** leads to coalescence between $+50$ and $+70\,^\circ$C of the signals from the protons involved in the exchange. These signals partly coincide, to give six peaks of unequal height. The CH_2–Pd groups in **3** are displayed as a four line AB type pattern for

* Reference number with asterisk indicates a note in the list of references.

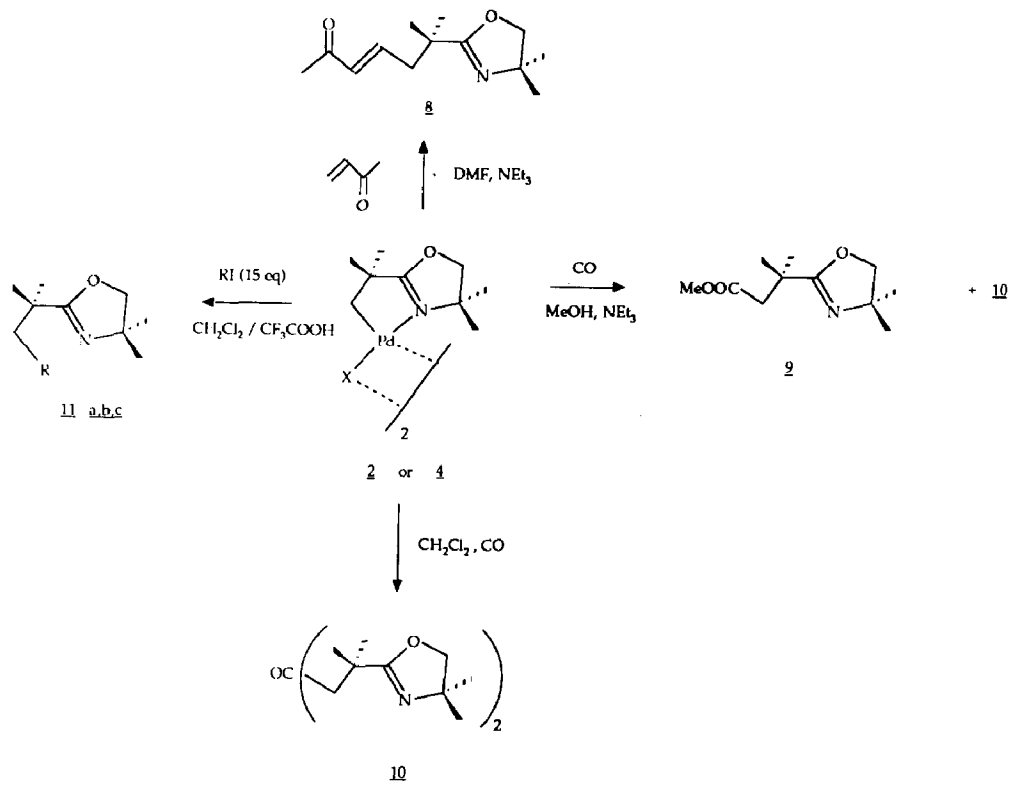


Scheme 2

each isomer. The conclusions drawn from these ^1H NMR studies are confirmed by further chemical transformations.

Thus, treatment of complex **2** with lithium chloride (1 eq) in acetic anhydride (20 °C, 12 h) gives the chloro-bridging dimer **4** as a yellow microcrystalline solid (92% yield) (Scheme 2). This same compound is obtained (96% yield), together with lithium tetrachloropalladate, when **3** is treated with an excess of lithium chloride in aqueous methanol [15*]. On treatment with triphenylphosphine or pyridine, complex **4** is converted into the crystalline monomers **5** and **6**. The cationic complex **7** can be isolated after successive reactions of **4** with 1,2-bis(diphenylphosphino)ethane (dppe) and an aqueous solution of potassium hexafluorophosphate.

When complex **4** in subjected to a Heck reaction with methyl vinyl ketone in DMF (75 °C, 24 h, 10 eq NEt_3) it gives the α,β-insaturated ketone **8** in 52% yield (Scheme 3). This vinylation represents an extension of a known process for aromatic cyclopalladated complexes [16]. Carbonylation of these species usually leads to the formation of esters, heterocycles, or acyl-palladium compounds according to both the structure of the complex and the experimental conditions [2]. However, Baldwin and coworkers [3] reported that no carbon monoxide insertion occurred during an attempted carbonylation of the aliphatic cyclopalladated pinacolone oxime. In contrast, we isolated the ester **9** (yield: 68%), together with the γ,γ'-dioxazolinylketone **10** (12%), from the reaction of **4** with CO in methanol (P_{CO} = 1 atm, 25 °C, 12 h). When the carbonylation was carried out in dry CH_2Cl_2 (P_{CO} = 20 atm) the ketone **10** was obtained in 78% yield (Scheme 3). These findings confirm our results



a : R = Me (72 %); b : R= allyl (62 %); c: R= n-butyl (46 %)

Scheme 3

concerning the reaction of cyclopalladated aryloxazolines with carbon monoxide [10].

Homologation of pivalic acid can be achieved through the alkylation of complex **2**. Thus, treatment of **2** with an excess of a 1-iodoalkane [17] in a CH_2Cl_2/CF_3COOH mixture provides an efficient route to the tertiary oxazolines **11a–c** (Scheme 3). To the best of our knowledge, this is the first example of the formation of a $C(sp_3)$–$C(sp_3)$ bond via cyclopalladated complexes.

The preparation of complex **2** and the carbonylation and alkylation reactions reported here, provide a synthetically useful method for selective "remote" functionalisation of aliphatic carboxylic acids. Furthermore, this is the first example of a metallation of a ligand containing a nitrogen as a donor atom by palladium acetate that yields both dinuclear and trinuclear species together.

References and notes

1 G.R Newkome, W.E. Puckett, V.K. Gupta and G.E. Kiefer, Chem. Rev., 86 (1986) 451.
2 A.D. Ryabov, Synthesis, (1985) 233.
3 J.E. Baldwin, R.H. Jones, C. Najera and M. Yus, Tetrahedron, 41 (1985) 699.
4 A.G. Constable, W.S. Mc Donald, L.C. Sawkins and B.L. Shaw, J. Chem. Soc., Dalton Trans., (1980) 1992.
5 B. Galli, F. Gasparini, B.E. Mann, L. Maresca, G. Natile, A.M. Manotti-Lanfreddi and A. Tiripicchio, J. Chem. Soc., Dalton Trans., (1985) 1155.

6 Y. Fuchita, K. Hiraki and Y. Matsumoto, J. Organomet. Chem., 280 (1985) C51; K. Hiraki, Y. Fuchita and Y. Matsumoto, Chem. Lett., (1984) 1947; Y. Fuchita, K. Hiraki and T. Uchimaya, J. Chem. Soc., Dalton Trans., (1983) 897.
7 K. Carr and J.K. Sutherland, J. Chem. Soc., Chem. Commun., (1984) 1227.
8 V. Rocherolle, J. Cristobal Lopez, A. Olesker and G. Lukacs, J. Chem. Soc., Chem. Commun., (1988) 513.
9 M. Reuman and A.I. Meyers, Tetrahedron, 41 (1985) 837.
10 G. Balavoine, J.C. Clinet, P. Zerbib and K. Boubekeur, J. Organomet. Chem., 389 (1990) 259 and references therein.
11 P. Allen and J. Ginos, J. Org. Chem., 28 (1963) 2759.
12 M. Pfeffer, E. Wehman and G. Van Koten, J. Organomet. Chem., 282 (1985) 127; Y. Fuchita, K. Hiraki and Y. Matsumoto, J. Organomet. Chem., 280 (1985) C51.
13 All new compounds gave satisfactory elemental analyses.
14 The structure of **2** was further confirmed by an X-ray diffraction study (G. Balavoine, J.C. Clinet and F. Theobald, to be published). The IR, ^{13}C NMR and MS spectra of **2** and **3** are in good agreement with the proposed structures.
15 Li_2PdCl_4 was characterized as $(Ph_3P)_2PdCl_2$ (89% yield).
16 L.S. Hegedus, Tetrahedron, 40 (1984) 2415.
17 S.J. Tremont and H. Ur Rahman, J. Am. Chem. Soc., 106 (1984) 5769.