

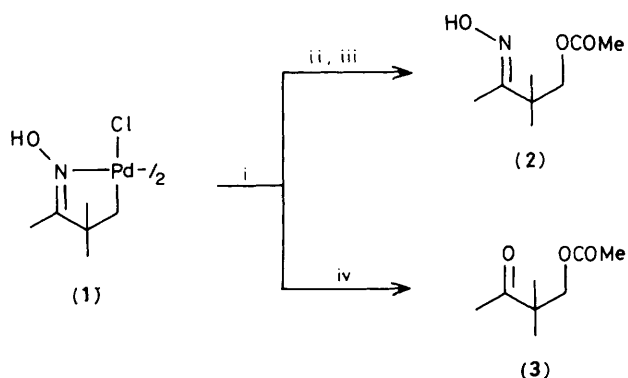
## Oxidation of Unactivated Methyl Groups via a Cyclopalladation Reaction

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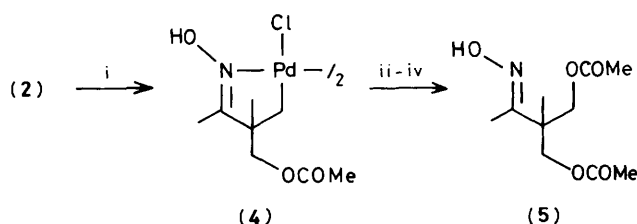
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The successive cyclopalladation-oxidation of *E*-pinacolone, *E*-2,2-dimethylcyclohexanone, 2,2,6,6-tetramethylcyclohexanone, and *E*-lupanone oxime led to the corresponding  $\beta$ -acetoxy derivatives; the second palladation in the case of the acetoxy compounds (2) and (8) takes place in one of the remaining methyl groups, being a regiospecific process, and in the case of the cyclic oximes the palladation occurs in the equatorial methyl group.

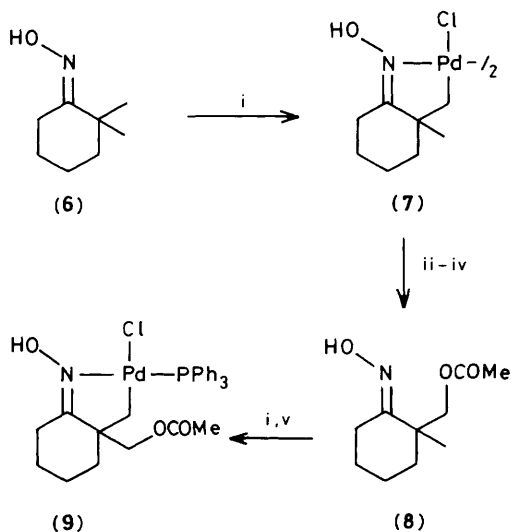
The cyclopalladation of *E*-pinacolone oxime leading to the dimeric organopalladium compound (1) has been described.<sup>1</sup>



Scheme 1. Reagents: i, pyridine; ii,  $\text{Pb}(\text{OAc})_4$ ; iii,  $\text{NaBH}_4$ ; iv, 2 equiv.  $\text{Pb}(\text{OAc})_4$ .



Scheme 2. Reagents: i,  $\text{Na}_2\text{PdCl}_4\text{-NaOAc}$ ; ii, pyridine; iii,  $\text{Pb}(\text{OAc})_4$ ; iv,  $\text{NaBH}_4$ .



Scheme 3. Reagents: i,  $\text{Na}_2\text{PdCl}_4$ ; ii, pyridine; iii,  $\text{Pb}(\text{OAc})_4$ ; iv,  $\text{NaBH}_4$ ; v,  $\text{PPh}_3$ .

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Very recently, the application of this reaction to the cyclopalladation of lanost-8-en-3-one oxime and its further deuteration or iodination has been published.<sup>2</sup> These results prompt us to report our independent findings in this field.

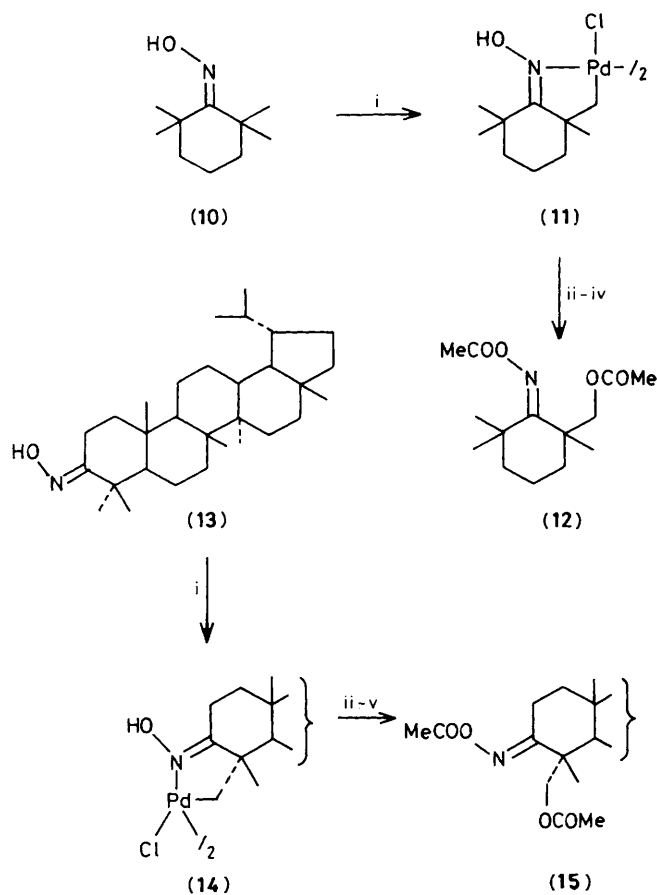
The oxidation of the pyridine complex derived from the compound (1) with lead tetra-acetate (1 equiv.) in acetic acid at room temperature led after reduction with sodium borohydride to the acetoxy oxime (2) (ca. 100% yield).§ In the absence of pyridine the reaction did not work. If the same process was carried out with double the stoichiometric amount of lead tetra-acetate the corresponding compound (3) was isolated (64% yield)§ (Scheme 1).

A second palladation-oxidation of compound (2) was done in order to study the regiochemistry of this process. Thus, when compound (2) was palladated the organopalladium dimer (4) was isolated (83% yield),§ and subsequent oxidation of this compound led to the diacetoxy oxime (5) (86% yield)§ (Scheme 2).

The palladation of *E*-2,2-dimethylcyclohexanone oxime (6) yielded the corresponding dimer (7) (85% yield)§ which was oxidized through its pyridine complex to give the compound (8) (96% yield).§ When this compound was again palladated the metallation took place on the remaining methyl group<sup>3</sup> affording the organopalladium compound (9) after treatment with triphenylphosphine (82% yield)§ (Scheme 3).

‡ When the reaction product bears the oxime group the reduction of  $\text{Pd}^{\text{II}}$  to  $\text{Pd}^0$  was carried out to avoid the trapping of the  $\text{Pd}^{\text{II}}$  by the oxime.

§ All new compounds have yielded satisfactory analytical and/or spectral data. Selected data: (2), m.p. 85–86°C;  $\nu$  1730  $\text{cm}^{-1}$  (C=O);  $\delta_{\text{H}}$  4.07 ( $\text{CH}_2\text{O}$ );  $\delta_{\text{C}}$  70.01 ( $\text{CH}_2\text{O}$ ) and 170.98 (C=O);  $m/z$  174 ( $M^+ + 1$ ). (3), b.p. 100°C (0.1 mmHg, Kugelrohr);  $\nu$  1750 and 1710  $\text{cm}^{-1}$  (C=O);  $\delta_{\text{H}}$  2.16 (MeCO) and 4.10 ( $\text{CH}_2\text{O}$ );  $\delta_{\text{C}}$  69.82 ( $\text{CH}_2\text{O}$ ), 170.66 ( $\text{CO}_2$ ), and 210.89 (C=O);  $m/z$  159 ( $M^+ + 1$ ). (4), m.p. 135–138°C;  $\delta_{\text{H}}$  2.34, 2.63 (2 d,  $J$  8.4 Hz,  $\text{CH}_2\text{Pd}$ ), 3.96, and 4.01 (2d,  $J$  11.3 Hz,  $\text{CH}_2\text{O}$ );  $\delta_{\text{C}}$  33.67 ( $\text{CH}_2\text{Pd}$ ) and 68.84 ( $\text{CH}_2\text{O}$ ). (5), m.p. 45–47°C;  $\delta_{\text{H}}$  4.18 ( $\text{CH}_2\text{O}$ );  $\delta_{\text{C}}$  65.70 ( $\text{CH}_2\text{O}$ ). (7), m.p. 182–185°C (decomp.);  $\delta_{\text{H}}$  2.51 and 2.57 (2d,  $J$  8.2 Hz,  $\text{CH}_2\text{Pd}$ );  $\delta_{\text{C}}$  26.48 (Me) and 40.40 ( $\text{CH}_2\text{Pd}$ );  $m/z$  562 ( $M^+$ ). (8), m.p. 125°C (0.1 mmHg, Kugelrohr);  $\nu$  1740  $\text{cm}^{-1}$  (C=O);  $\delta_{\text{H}}$  4.08 and 4.20 (2d,  $J$  11.0 Hz,  $\text{CH}_2\text{O}$ );  $\delta_{\text{C}}$  69.10 ( $\text{CH}_2\text{O}$ ) and 171.07 (C=O);  $m/z$  199 ( $M^+$ ). (9), m.p. 156–158°C (decomp);  $\delta_{\text{H}}$  1.40, 1.87 (2d,  $J$  10.0 Hz,  $\text{CH}_2\text{Pd}$ ), 3.81, 4.28 (2d,  $J$  10.8 Hz,  $\text{CH}_2\text{O}$ ), and 10.67 (d,  $J_{\text{HP}}$  3.0 Hz, OH);  $\delta_{\text{C}}$  42.30 ( $\text{CH}_2\text{Pd}$ ) and 68.29 ( $\text{CH}_2\text{O}$ );  $\delta_{\text{p}}$  30.49 p.p.m. (11), m.p. 177–179°C (decomp.);  $\delta_{\text{H}}$  2.33 and 2.46 (2d,  $J$  7.1 Hz,  $\text{CH}_2\text{Pd}$ );  $\delta_{\text{C}}$  41.22 ( $\text{CH}_2\text{Pd}$ ). (12), oil;  $\nu$  1745  $\text{cm}^{-1}$  (C=O);  $\delta_{\text{H}}$  2.06, 2.19 (2  $\times$  MeCO), 4.07, and 4.31 (2d,  $J$  10.7 Hz,  $\text{CH}_2\text{O}$ );  $\delta_{\text{C}}$  20.07, 20.87 (2  $\times$   $\text{CH}_3\text{CO}$ ), 71.34 ( $\text{CH}_2\text{O}$ ), 169.16, 170.78, and 172.85 (C=N and 2  $\times$  C=O). (14), m.p. > 210°C;  $\delta_{\text{H}}$  2.50 and 2.61 (br. s and d,  $J$  7.5 Hz,  $\text{CH}_2\text{Pd}$ );  $\delta_{\text{C}}$  43.15 ( $\text{CH}_2\text{Pd}$ ). (15), oil;  $\nu$  1740  $\text{cm}^{-1}$  (C=O);  $\delta_{\text{H}}$  2.06, 2.17 (2  $\times$  MeCO), 4.09, and 4.19 (2d,  $J$  11.0 Hz,  $\text{CH}_2\text{O}$ );  $\delta_{\text{C}}$  68.29 ( $\text{CH}_2\text{O}$ ), 169.65, and 170.84 (C=N and 2  $\times$  C=O);  $m/z$  542 ( $M^+ + 1$ ).



**Scheme 4.** Reagents: i,  $\text{Na}_2\text{PdCl}_4\text{-NaOAc}$ ; ii,  $\text{Ac}_2\text{O}$ ; iii, pyridine; iv,  $\text{Pb}(\text{OAc})_4$ ; v,  $\text{NaBH}_4$ .

The palladation of 2,2-dimethylcyclopentanone oxime fails owing to the difficulty in achieving planarity of the oxime and methyl groups necessary for palladation within the constraints applied by the five-membered ring.<sup>3</sup>

We have also studied the palladation-oxidation in a hindered ketone. Thus, when 2,2,6,6-tetramethylcyclohexanone oxime (10) was palladated the expected organopalladium dimer (11) was obtained (86% yield).§ In this case the oxime group must be acetylated in order to avoid its isomerization during the oxidation; the acetylation and further oxidation of compound (11) led to the product (12) (76% yield)§ (Scheme 4).

Finally, we have palladated lupanone oxime (13), isolating the expected dimer (14) (76% yield),§ which after acetylation and oxidation led to the expected 23-acetoxy derivative (15) (90% yield)§ (Scheme 4). The stereochemistry of (14), and hence the acetoxy derivative (15), was established by nuclear Overhauser effect (n.O.e.) studies at 500 MHz.

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