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A NEW REGIOSPECIFIC SYNTHESIS OF ARYL KETONES FROM PALLADOCYCLES

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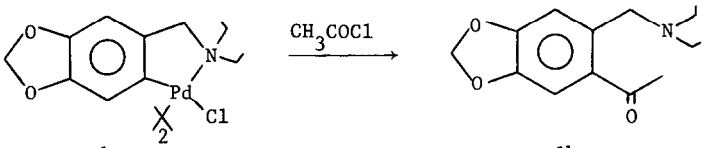
Abstract: Aromatic palladocycles undergo facile reaction with acid halides to regiospecifically provide aryl ketones in high yield.

Since their first preparation by Cope in 1968,[1] orthopalladated benzylic amines[2] have found some utility as synthetic intermediates. Thus far, orthopalladated materials have been found to react with nucleophiles to provide ortho alkylated or arylated aromatics,[3] and to undergo insertion reactions with olefins[4] and carbon monoxide.[5] Particularly important in each of these transformations is the complete regiochemical control afforded by the orthopalladation process.[6] We now wish to report the first example of the apparent reaction of orthochelated palladium(II) as a nucleophilic agent.

Treatment of a solution of complex 1a[6] in dichloroethane with acetyl chloride (5 mol equiv) at reflux for 12 h resulted in the isolation of aminoketone 1b[7,8] in 81% yield.[9]

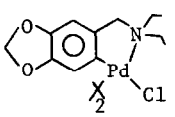
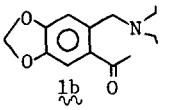
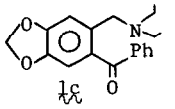
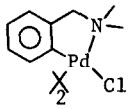
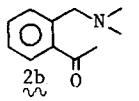
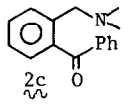
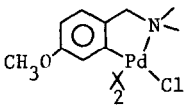
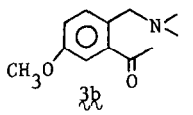
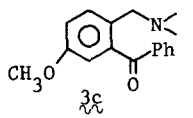
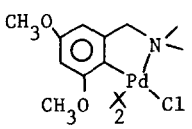
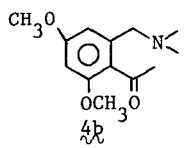
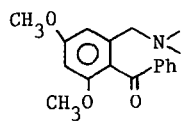
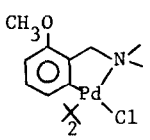
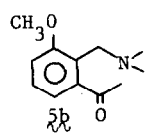
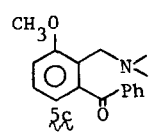


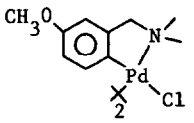
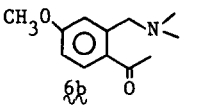
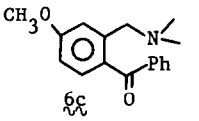
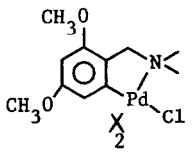
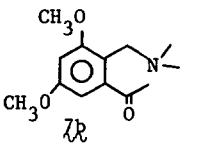
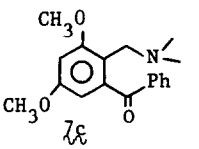
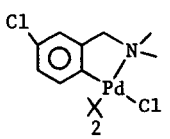
1a 1b

As the reaction proceeds, the initial yellow color due to 1 changes to an orange-red, indicative of the formation of uncomplexed palladium chloride which is removed upon aqueous workup.

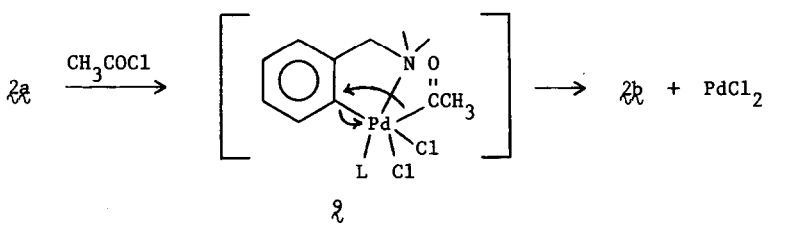
Other examples are listed in the table. Each of the acetylation reactions was run for 12 h at reflux in dichloroethane with 5 mol equiv of acetyl chloride. Benzoyl chloride was found to be less reactive with palladocycles; benzoylations listed in the table required 30 h at reflux in dichloroethane. Complexes in which the aromatic ring is unactivated, for example, 1a, react more slowly than do those bearing oxygen functionality. Electron withdrawing substituents on the aromatic ring appear to drastically retard the rate; complex 8a was recovered unchanged after three days at reflux in dichloroethane in the presence of either acetyl chloride or benzoyl chloride. Despite the large rate enhancement due to electron releasing substituents, the regiochemistry of the reaction appears not to change. In every case we have examined, the newly introduced acyl group is situated exclusively on the carbon previously bound to palladium. Thus, although electron releasing groups increase the rate of this reaction, they appear to have no effect on the orientation of the entering group.

Acylation of Aryl Palladium Complexes

Complex[7,10]	Electrophile	Product[7,8]	% Yield[9]
 1a	CH_3COCl	 1b	81
	PhCOCl	 1c	67
 2a	CH_3COCl	 2b	61
	PhCOCl	 2c	25
 3a	CH_3COCl	 3b	86
	PhCOCl	 3c	75
 4a	CH_3COCl	 4b	92
	PhCOCl	 4c	73
 5a	CH_3COCl	 5b	91
	PhCOCl	 5c	84

Complex[7,10]	Electrophile	Product[7,8]	% Yield[9]
 6a	CH_3COCl	 6b	88
	PhCOCl	 6c	81
 7a	CH_3COCl	 7b	93
	PhCOCl	 7c	75
 8a	CH_3COCl	No reaction	
	PhCOCl	No reaction	

Although we have no direct mechanistic evidence at this time, we postulate that this reaction proceeds via the intermediacy of a Pd(IV) species. Thus, oxidative addition of acetyl chloride to 2a might give rise to complex 9, possessing hexa- or pentacoordinate Pd(IV) acyl,



as a transient intermediate. Complex 9 could then simply collapse to the observed products via reduction elimination. Such a reductive elimination would almost certainly proceed rapidly from a Pd(IV) intermediate.

We believe that this mode of reactivity will prove to be important in both palladium chemistry and organic synthesis. To this end, we are exploring the reactivity of stable palladium complexes with a range of electrophilic agents.

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References and Notes:

1. A. C. Cope and E. C. Friedrich, J. Am. Chem. Soc., 90, 909 (1968).
2. For a review of cyclometallation reactions, see T. Dehand and M. Pfeffer, Coord. Chem. R 18, 327 (1976).
3. S. Murahashi, Y. Tanaba, M. Yamamura, and I. Moritani, Tetrahedron Lett., 3749 (1974).
4. R. A. Holton, ibid., 355 (1977).
5. J. M. Thompson and R. F. Heck, J. Org. Chem., 40, 2667 (1975).
6. R. A. Holton and R. G. Davis, J. Am. Chem. Soc., 99, 4175 (1977).
7. Characterized by C,H combustion analysis.
8. Spectral Data: 1b: IR ($CHCl_3$) 1715 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ0.97 (t,6), 2.45 (s,3) 2.47 (q,4), 3.68 (s,2), 5.95 (s,2), 6.98 (s,1), 7.07 (s,1). 1c: IR ($CHCl_3$) 1675 cm^{-1}; ^{1} NMR (90 MHz, $CDCl_3$) δ0.95 (t,6), 2.27 (q,4), 3.30 (s,2), 5.92 (s,2), 6.95 (s,1), 7.20-7. (m,6). 2b: IR ($CHCl_3$) 1700 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ2.08 (s,3), 2.15 (s,6), 3.32 (s,2), 7.08-7.31 (m,4). 2c: IR ($CHCl_3$) 1675 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ1.85 (s,6), 3.37 (s,2), 7.17-7.48 (m,9). 3b: IR ($CHCl_3$) 1710 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ2.20 (s, 2.47 (s,3), 3.67 (s,2), 3.85 (s,3), 6.82 (d,1,J=9Hz), 7.12 (dd,1,J=9,3Hz), 7.57 (d,1,J=3 3c: IR ($CHCl_3$) 1670 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.90 (s,6), 3.35 (s,2), 3.81 (s,3), 6 (d,1,J=9Hz), 6.88 (dd,1,J=9,3Hz), 7.21-7.48 (m,6). 4b: IR ($CHCl_3$) 1705 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ2.22 (s,6), 2.08 (s,3), 3.42 (s,2), 3.64 (s,6), 6.25 (d,1,J=3Hz), 6.38 (d,1 J=3Hz). 4c: IR ($CHCl_3$) 1690 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.80 (s,6), 3.32 (s,2), 3.76 (s,3), 3.81 (s,3), 6.21 (d,1,J=3Hz), 6.33 (d,1,J=3Hz), 7.21-7.43 (m,5). 5b: IR ($CHCl_3$) 1710 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ2.21 (s,6), 2.42 (s,3), 3.68 (s,2), 3.82 (s,3), 6.83-7.35 (m,3). 5c: IR ($CHCl_3$) 1670 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ1.70 (s,6), 3.30 (s,2), 3 (s,3), 6.60-6.80 (m,3), 7.07-7.33 (m,5). 6b: IR ($CHCl_3$) 1705 cm^{-1}; ^1H NMR (90 MHz, CDCl δ2.24 (s,6), 2.50 (s,3), 3.69 (s,2), 3.83 (s,3), 6.75 (dd,1,J=9,3Hz), 7.08 (d,1,J=3Hz), (d,1,J=9Hz). 6c: IR ($CHCl_3$) 1675 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ1.97 (s,6), 3.38 (s,2), (s,3), 6.80 (dd,1,J=9,3Hz), 6.93 (d,1,J=3Hz), 7.27-7.53 (m,6). 7b: IR ($CHCl_3$) 1700 cm^{-1} ^1H NMR (90 MHz, $CDCl_3$) δ2.44 (s,6), 2.53 (s,3), 3.82 (s,3), 3.88 (s,3), 3.98 (s,2), 6.57 (d,1,J=3Hz), 6.68 (d,1,J=3Hz). 7c: IR ($CHCl_3$) 1670 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ1.82 (s,6), 3.35 (s,2), 3.70 (s,3), 3.78 (s,3), 6.85 (d,1,J=3Hz), 6.98-7.23 (m,6).
9. All yields refer to isolated, spectrally and chromatographically homogeneous material.
10. Conveniently prepared as outlined in reference 6.

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