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Synthesis and Application of Cationic 2,6-Bis(2-oxazolinyl)phenylpalladium(II) Complexes

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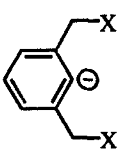
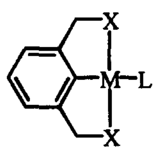
Abstract: Treatment of 1,3-bis(2-oxazolinyl)benzenes with LDA/TMEDA followed by the addition of $PdBr_2$(1,5-COD) gave 2,6-bis(2-oxazolinyl)phenylbromopalladium(II) complexes. Subsequent bromide abstraction with silver salts provided a series cationic 2,6-bis(2-oxazolinyl)-phenylpalladium(II) complexes that effectively catalyse the addition of α-cyano carboxylates to methyl vinyl ketone. © 1997 Elsevier Science Ltd.

Anionic terdentate ligands of general structure **1** form rigid square planar complexes of type **2** when combined with d^8 metals, with X as either a phosphorus,[1] nitrogen[2] or sulfur[3] containing donor group. Complexes with this general structure have been extensively employed as building blocks in the synthesis of a variety of supramolecular systems.[4] However, the difficulty of obtaining optically pure disymmetric variants of **2** has largely precluded investigations into their use as catalysts for asymmetric synthesis.[5] In contrast, neutral C_2-symmetric terdentate ligands of type **3** have been incorporated into Rh(III),[6] Pd(II)[7] and Cu(II)[8] complexes which have subsequently been applied to a variety of asymmetric transformations. Oxazoline ligands of this type are readily obtained from optically pure β-amino alcohols, and this provided sufficient incentive for an investigation into the synthesis of complexes containing anionic terdentate ligands derived from 1,3-bis(2-oxazolinyl)benzenes.



1 X = PR_2, NR_2, SR



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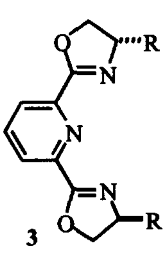
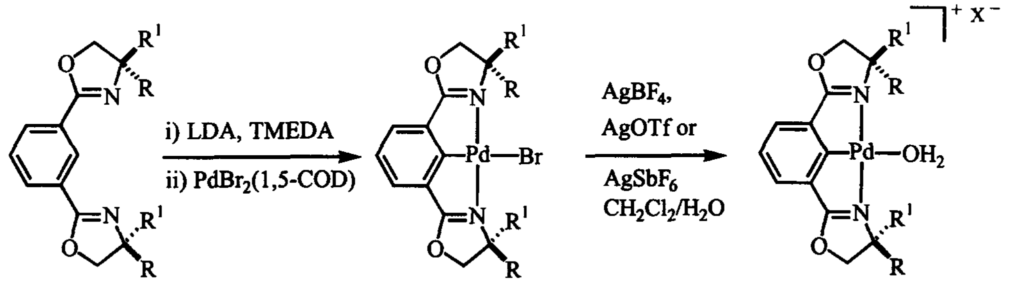


3

2-Phenyl-4,4-dimethyloxazoline has previously been shown to undergo regiospecific *ortho*-palladation when heated at reflux with palladium acetate in acetic acid,[9] a standard method for intramolecular cyclometallation of aromatic rings containing donor ligand substituents. When this method was repeated on the 1,3-bisoxazoline **4a**, a complex mixture resulted devoid of the required terdentate complex. Palladium-carbon bonds may also be generated by transmetallation of more electropositive metals such as lithium. It was noted that **4a** had been reported to undergo regioselective lithiation *ortho* to both oxazoline substituents when treated with LDA in the presence of TMEDA.[10] Repetition of this method followed by the addition of 1.2 equivalents of $PdBr_2(1,5\text{-}COD)$ resulted in a 41% yield of the pale yellow air-stable crystalline solid identified as the desired transmetallated terdentate complex **5a** (Scheme 1).[11] Of significance in this structural assignment was the absence from the ^1H NMR spectrum of a signal corresponding to the proton located *ortho* to both oxazoline substituents; the isotopic pattern in the mass spectrum due to the presence of both palladium and bromine; and a decrease by 34 cm^{-1} (compared to **4a**) of $\nu(C{=}N)$, indicative of nitrogen coordination to the metal. Extension of this reaction to a series of homochiral 1,3-bisoxazolines **4b-d** yielded their corresponding palladated complexes **5b-d** in moderate yields. The new 1,3-bisoxazolines **4c/d** were prepared as previously described for **4b**.[12]



4a	$R = R^1 = Me$	**5a**	41%	**6a**	$(X = BF_4)$	80%
4b	$R = {}^iPr, R^1 = H$	**5b**	29%	**7b**	$(X = OTf)$	60%
4c	$R = {}^tBu, R^1 = H$	**5c**	18%	**8b**	$(X = SbF_6)$	87%
4d	$R = CH_2Cy, R^1 = H$	**5d**	41%	**8c**	$(X = SbF_6)$	44%
				8d	$(X = SbF_6)$	28%

Scheme 1

Introduction of an exchangeable neutral ligand was achieved by bromide removal on treatment of the complexes with silver salts in wet dichloromethane. After filtration of silver bromide, the resulting cationic complexes precipitated from solution on addition of hexane, and all were found to contain coordinated water as revealed by microanalysis, ^1H NMR and IR spectroscopy.

Although Lewis acidic complexes of the late transition complexes have recently attracted some attention,[8b,d,e,13] we were unclear of the potential applications of these cationic palladium(II) species, especially as the metal is bound to an electron rich terdentate ligand. Indeed, addition of 1 mol% of **8b** to a mixture of cyclopentadiene and methacrolein barely increased the rate of Diels-Alder reaction and resulted in no change in the *exo* : *endo* ratio of **9** (Table 1, entry 1). A small rate increase was observed for the aldol reaction between benzaldehyde and methyl isocyanoacetate, yielding oxazolines **10** in the presence of 10 mol% Hunig's base (entry 2). However, when ethyl cyanoacetate was employed in a reaction with methyl vinyl ketone, the double Michael adduct **11** was obtained with essentially no competitive background reaction (entry 3), as was also the case when ethyl α-cyanopropionate was used for the formation of **12** (entry 4).

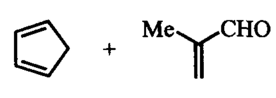
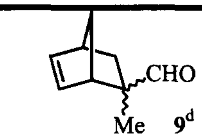
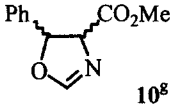
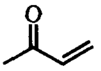
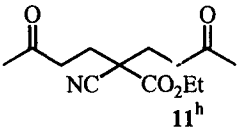
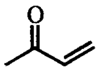
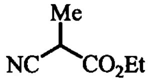
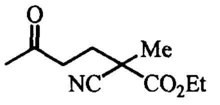
Entry	Substrates[a]	Product(s)	With 8b[b]		Without 8b	
			Time (h.)	% Con.[c]	Time (h.)	% Con.
1		 9[d]	10 30 110	25 63 88	35 104 –	18 40 –
2[e,f]	PhCHO + 	 10[g]	5 23 –	75 95 –	5 23 63	12 23 85
3[e]	 + 	 11[h]	3 20 –	88 100 –	6 23 –	0 <5 –
4[e]	 + 	 12	<5 – –	100 – –	4 25 95	3 32 76

Table 1. a) Reactions were performed with 1.6 mmol of electrophile (or methacrolein, entry 1) and 2.4 mmol of nucleophile (or cyclopentadiene, entry 1) in 4 ml of CH_2Cl_2 at room temperature under nitrogen. b) 1 mol% (0.010 g, 16 μm). c) Percentage conversions were determined by ^1H NMR spectroscopy. d) *Exo* : *endo* = 87 : 13 for both catalysed and uncatalysed runs. e) With 10 mol % Hunig's base. f) Reactions mixtures (both runs) heated at reflux. g) *Trans* : *cis* = 4 : 1 for catalysed run. h) From 4.8 mmol of methyl vinyl ketone.

The enantiomeric excess of **12** was determined (Table 2, entry 1), this figure improving on repetition of the reaction in toluene (entry 2). Further modest improvements were achieved with **8c** and **8d** (entries 3 and 4).

Entry[a]	Catalyst	Solvent	Yield of 12[b] %	e.e.[c] (config.)[d]
1	**8b**	CH_2Cl_2	88	6 (R)
2	**8b**	toluene	73	22 (R)
3[e]	**8c**	toluene	80	27 (R)
4[e]	**8d**	toluene	74	34 (R)

Table 2. a) Reactions performed as described in Table 1. b) After work-up and bulb to bulb distillation. c) Determined by GC with CP-Chirasil-Dex CB. d) Determined by optical rotation.[14b] e) With 1 mol% Hunig's base.

The reactions leading to the formation of **12** are thought to proceed *via* addition to the Michael acceptor of an enolate bound to palladium by the nitrile. The importance of the nitrile functionality was illustrated by the absence of any reaction between diethyl malonate and methyl vinyl ketone in the presence of **8b**. Furthermore, **12** is not formed when Hunig's base is omitted from the reaction. A similar nitrile enolate complex has been proposed for the asymmetric Michael reaction catalysed by Rh(I) complexes.[14] In our ongoing work we are attempting to increase the enantioselectivity of these efficient C-C bond forming catalysts.

Acknowledgements

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11. Analytical data for **5a**: m.p. 295 - 297 °C (Found: C, 42.28; H, 4.28; N, 6.27. $C_{16}H_{19}BrN_2O_2Pd$ requires C, 41.99; H, 4.18; N, 6.12%); ν_{max} (nujol)/cm^{-1} 1618 (C=N); δ_H (360 MHz, $CDCl_3$) 1.68 (12 H, s, -C*H*$_3$), 4.45 (4 H, s, -C*H*$_2$-), 7.17 (1 H, $\underline{A}B_2$, *J* 8, 4-H, 7.30 (2 H, $A\underline{B}_2$, *J* 8, 3- & 5-H); δ_C $\{^1H\}$ (90 MHz, $CDCl_3$) 28.13 (-*C*H$_3$), 66.17(-*C*(CH_3)$_2$-), 82.81 (-*C*H$_2$), 123.98 (4-C), 126.81 (3- & 5-C), 129.97 (2- & 6-C), 167.50 (1-C), 172.64 (*C*=N); *m/z* (EI) 462 (2%), 460 (7), 458 (10), 457 (5), 456 (7), 455 (4), 454 (2), 381 (34), 379 (75), 377 (88), 376 (67), 375 (32).
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