Cationic [2,6-Bis(2′-oxazolinyl)phenyl]palladium(II) Complexes: Catalysts for the Asymmetric Michael Reaction

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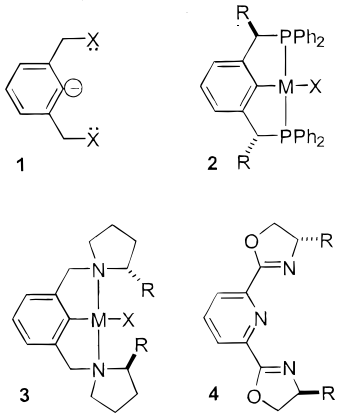
Reaction of 1,3-dicyanobenzene with β-amino alcohols (*S*)-$H_2NCHRCH_2OH$ (R = ^{i}Pr, ^{i}Bu, ^{t}Bu, CH_2Cy, CH_2Ph) and (*R*)-$H_2NCHPhCH_2OH$ gave new 1,3-bis(2′-oxazolinyl)benzenes (30−51%). These, together with 1,3-bis(4′,4′-dimethyl-2′-oxazolinyl)benzene, were treated with LDA/TMEDA followed by the addition of $PdBr_2$(1,5-COD) to give [2,6-bis(2′-oxazolinyl)phenyl]-palladium(II) bromide complexes (21−41%). In two cases no complexes were obtained (R = Ph, CH_2Ph) due to ring opening of the oxazolines by LDA/TMEDA. Treatment of the palladium complexes with $AgBF_4$, AgOTf, or $AgSbF_6$ in wet CH_2Cl_2 provided a series of cationic [2,6-bis(2′-oxazolinyl)phenyl]palladium complexes (28−87%) containing water coordinated to palladium, as established by an X-ray crystal structure analysis of (*S*,*S*)-[2,6-bis(4′-isopropyl-2′-oxazolinyl)phenyl]aquopalladium(II) trifluoromethanesulfonate. All of the cationic complexes proved to be efficient catalysts for the Michael reaction between α-cyanocarboxylates and methyl vinyl ketone and between acrylonitrile and activated Michael donors. Selectivities of up to 34% ee were obtained for the formation of (*R*)-ethyl 2-cyano-2-methyl-5-oxohexanoate.

Introduction

Transition-metal complexes derived from anionic terdentate ligands of general structure **1** (XCX) were first reported in 1976 with the synthesis of square-planar platinum group metal containing complexes with X corresponding to P^tBu_2.[1] More recently, there has been



a spate of interest in related PCP systems[2] and also in complexes containing SCS-,[3] OCO-,[4] NCN-,[5] and even PCN-based[6] ligands. These are finding widespread application, particularly as catalysts for reactions as varied as hydrocarbon activation,[7] dehydrogenation,[8] Kharasch addition,[9] and the Heck reaction.[10] In contrast, chiral variants of **1** are limited to PCP-containing complexes **2**[11] and proline-derived NCN complexes **3**;[12a] the former have been applied as catalysts for the asymmetric aldol reaction between aldehydes and methyl isocyanoacetate[11b,d] and the latter as catalysts for Kharasch addition.[12a] The modest enantioselectivities observed in these reactions contrast with the neutral

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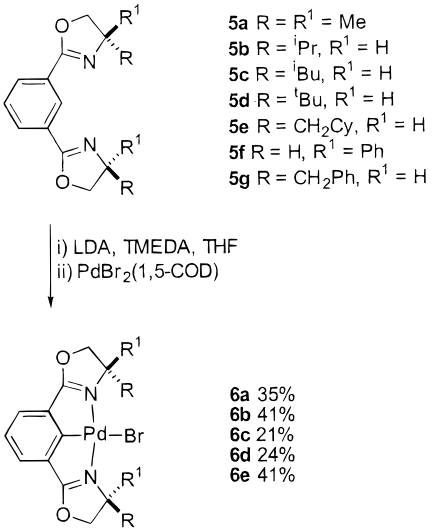
C_2-symmetric tridentate Pybox ligands **4**,[13] which in combination with Rh(III),[14] Pd(II),)[15] and Cu(II)[16] have been successfully applied in a variety of asymmetric transformations. These results, together with the ease of oxazoline synthesis, prompted our investigation into anionic terdentate ligands derived from 1,3-bis(2′-oxazolinyl)benzenes, and we now report in detail on the synthesis and application of the resulting palladium complexes.[17]During the course of this work two other groups reported on related palladium,[18,19] platinum,[20] and rhodium[19] complexes and application of the last group as catalysts for the enantioselective allylation of aldehydes.[21]

Results and Discussion

Synthesis of [2,6-Bis(2′-oxazolinyl)phenyl]palladium(II) Bromides. The known 1,3-bis(2′-oxazolinyl)-benzenes **5a**[22] and **5b** were prepared as previously described, the latter from a zinc chloride promoted condensation of (*S*)-valinol with 1,3-dicyanobenzene.[23] Using this same technique, the new bisoxazolines **5c**−**g** were prepared from the appropriate enantiomerically pure β-amino alcohols in moderate yield (30−51%).

Scheme 1



The large amount of literature reporting C−H bond activation through cyclometalation[24] includes the ortho palladation of 2-phenyl-4,4-dimethyloxazoline by heating this at reflux with palladium acetate in acetic acid.[25] Application of this method to **5a** gave a yellow solid displaying ν(C═N) at 1634 cm^{-1}, indicative of a palladium-coordinated oxazoline, but without the simple pattern expected in the ^{1}H NMR spectrum. In addition, no single compound could be isolated from the resultant complex mixture. Instead, our attention turned to the report that **5a** undergoes regioselective ortho/ortho lithiation on treatment with LDA/TMEDA,[22] a method that offered direct access to the desired complexes following transmetalation with a palladium(II) salt.[5b] Accordingly, a solution of lithiated **5a** was added to a solution of dibromo(1,5-cyclooctadiene)palladium in THF to yield **6a**, isolated by column chromatography as an air- and water-stable pale yellow crystalline solid (Scheme 1). This structure was verified by the absence from the ^{1}H NMR spectrum of the proton ortho to both oxazoline rings, the decrease in ν(C═N) by 33 cm^{-1} to 1618 cm^{-1} compared to **5a**, and the excellent agreement between the calculated and observed isotope pattern for the molecular ion in the EI-derived mass spectrum. Repetition of this method with the C_2-symmetric oxazolines **5b**−**g** successfully led to the isolation of complexes **6b**−**e** but conspicuously failed with the two oxazolines containing phenyl or benzyl substituents.

To investigate these anomalous results, **5f** was treated with LDA/TMEDA as before, followed by addition of

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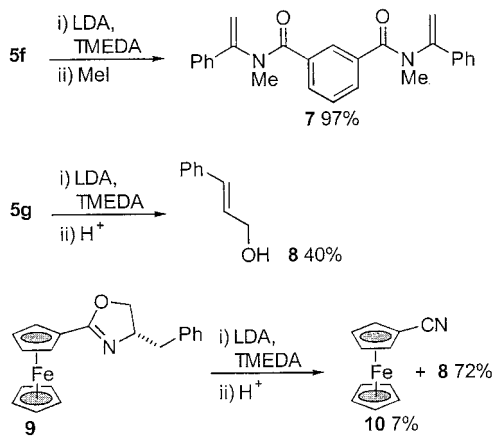
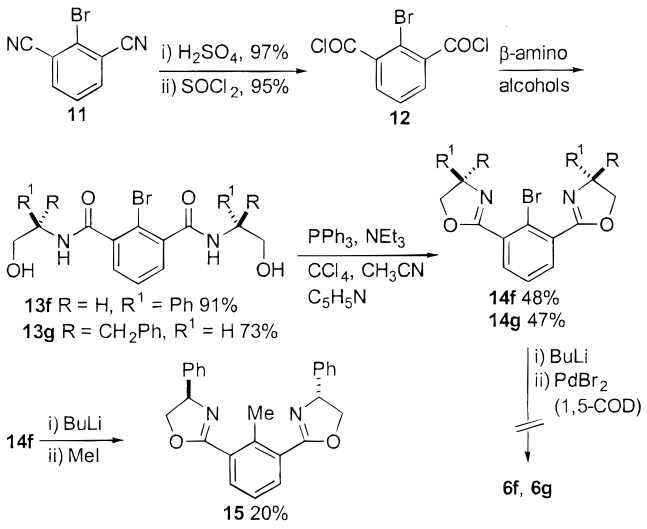
Scheme 2



Scheme 3



excess methyl iodide to give an excellent yield of enamide **7** (Scheme 2), most likely as a consequence of benzylic deprotonation and electrocyclic ring opening of the oxazoline. Similarly, **5g** was found to yield (*E*)-cinnamyl alcohol **8** as an elimination product from benzylic deprotonation, with concomitant formation of a nitrile. Although the other expected product, 1,3-dicyanobenzene, was not observed at the end of the reaction, application of this same procedure to ferrocenyloxazoline **9** did result in isolation of a small quantity of ferrocenyl cyanide **10** in addition to cinnamyl alcohol. The nitrile functionality produced in this ring opening appears to be readily consumed by the excess of LDA/TMEDA employed for the lithiation.

An alternative route to **6f**/**6g** began with 2-bromo-1,3-dicyanobenzene (**11**) (Scheme 3). When it was employed directly in a $ZnCl_2$-promoted cyclization with (*S*)-2-amino-3-phenyl-1-propanol, the two oxazoline rings were formed, though accompanied unsurprisingly by amino alcohol displacement of the halogen. Instead, the 2-bromo substituent was retained during conversion to the diacid chloride **12**, with subsequent amide formation and conversion of **13f**/**13g** to their corresponding bis-oxazolines **14f**/**14g** under Appel conditions.[26] Attempts to effect bromine/lithium exchange followed by addition

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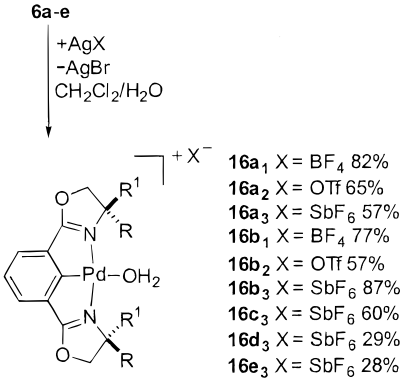
Scheme 4



of dibromo(1,5-cyclooctadiene)palladium again failed to yield any trace of the desired complexes, even though the validity of this approach was demonstrated by quenching of the reaction with methyl iodide to give **15**, albeit in low yield.[27] Methyl iodide has previously been employed for the methylation of the 2-lithio derivative of **5a**.[22] We speculate that the required transmetalations may have been prevented by arene−lithium interactions, of which there are many documented examples,[28] as there would appear to be no steric restriction to transmetalation (cf. formation of **6d**/**6e**). Since we carried out this work, Denmark et al. reported on the insertion of Pd(0) into the carbon−halogen bond of substrates, including **14g**,[18] and Nishiyama et al. described a Pd(II) transmetalation with 2-(trimethylstannyl)-1,3-bis(oxazolines), obtained from their corresponding 2-bromo derivatives by treatment with BuLi followed by Me_3SnCl.[19] Thus, our own work in this area sheds further light on the relative advantages and disadvantages of all three methods of synthesis.

Synthesis of Cationic [2,6-Bis(2′-oxazolinyl)-phenyl]palladium(II) Complexes. To investigate the catalytic properties of these complexes required replacement of the bromide ligand and occupation of a more labile neutral ligand at the exchangeable coordination site. Addition of 1.2 equiv of $AgBF_4$, AgOTf, or $AgSbF_6$ in wet CH_2Cl_2 gave the air-stable cationic complexes **16a$_1$**−**16e$_3$**, for which the yields quoted reflect the success of reprecipitation in providing analytically pure material (Scheme 4). Microanalysis revealed all of the complexes to contain 1 equiv of water, observed in the ^{1}H NMR spectrum as a broad peak between 2 and 3 ppm. That this neutral ligand is coordinated to palladium, as previously found for cationic palladium complexes derived from other NCN ligands,[5b] was confirmed by an X-ray structure analysis on crystals of the triflate salt **16b$_2$** formed by slow evaporation of an acetone solution.

The crystal structure consists of two independent cationic complexes $[Pd(C_{18}H_{23}N_2O_2)(H_2O)]^+$, both situated on 2-fold axes, and in each a triflate anion is hydrogen-bonded to water with water-oxygen to triflate-

(27) During the course of this work we also synthesized (*S*,*S*)-1,3-bis[4′-(cyclohexylmethyl)-5′,5′-dimethyl-2′-oxazolinyl]benzene but were unable to effect the lithiation and/or palladation of this material. Full details on the synthesis of this and related oxazolines will be reported elsewhere.

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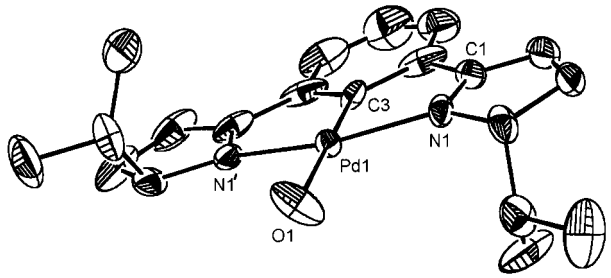
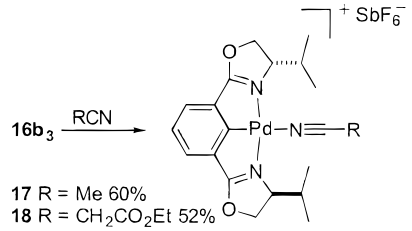


Figure 1. One of the two independent crystal structures of **16b$_2$**. Selected bond distances (Å) and angles (deg) are as follows (corresponding values for the unshown second structure are given in brackets): C(3)−Pd(1) = 1.85(3) [1.96(2)], C(1)−N(1) = 1.31(2) [1.298(14)], N(1)−Pd(1) = 2.060(10) [2.059], O(1)−Pd(1) = 2.16(2) [2.11(2)]; N(1)−Pd(1)−N(1′) = 160.4 (6) [158.6 (5)], C(1)−N(1)−Pd(1) = 112.1(9) [112.5(7)].

Scheme 5



oxygen distances of 2.702 and 2.673 Å. The rigid geometry of the terdentate ligand dictates a distorted-square-planar arrangement about palladium with C−Pd−N bond angles of 80.2 and 79.3° and, thus, N−Pd−N bond angles of 160.4 and 158.6°. The C−Pd bond distances of 1.85 and 1.96 Å are similar to that of the corresponding neutral complex (the chloride analogue of **6b**) determined at 1.928 Å,[19] other bond lengths and angles being also very similar. The isopropyl groups lie in neither a pronounced pseudoaxial nor a pseudoequatorial position, due to the relatively small deviation from planarity of the oxazoline rings. An ORTEP representation of **16b$_2$** and selected data are given in Figure 1.

The anions BF_4^- and SbF_6^- are reported to be weaker metal coordinators than triflate due to the presence of less basic sites on the periphery of the anion (F vs O),[29] and on this basis the other cationic complexes also contain coordinated water molecules. That a number of peaks arise in their IR spectra due to B−F and Sb−F stretching, indicating a loss of T_d and O_h symmetry, respectively, is a consequence of hydrogen bonding between these ions and coordinated H_2O.[30] The possibility of generating other neutral ligand adducts from **16** was briefly investigated by addition of either excess acetonitrile or excess ethyl cyanoacetate to **16b$_3$** followed by precipitation of complexes **17** and **18**, respectively (Scheme 5)

Asymmetric Catalysis with Cationic [2,6-Bis(2′-oxazolinyl)phenyl]palladium(II) Complexes. In a preliminary investigation of the catalytic potential of these complexes, we investigated their activity in the aldol reaction between benzaldehyde and methyl isocyanoacetate.[31] Use of 1 mol % of **16b$_3$** with 10 mol % of Hunig's base resulted in only a small increase in the rate of formation of the resulting oxazolines (trans:cis = 4:1), unlike related palladium-containing PCP cationic complexes, which are efficient catalysts for this reaction.[11b,d] Instead we examined the possibilities offered by nitrogen−metal coordination by swapping an isonitrile for a nitrile.[32−34] Thus, in the presence of 1 mol % of **16a$_3$** and 10 mol % of Hunig's base, ethyl cyanoacetate and methyl vinyl ketone cleanly gave the double Michael adduct **19** in 95% yield within 5 h in a reaction carried out at room temperature in CH_2Cl_2 (Scheme 6, reaction A: Table 1, entry 1). Significantly, in the absence of **16a$_3$**, essentially no reaction could be detected under the same conditions after 23 h (entry 2). To provide for the formation of a new stereogenic center, ethyl α-cyanopropionate was next employed as the Michael donor. When catalyzed by **16b$_1$**, again in the presence of 10 mol % of Hunig's base, the adduct **20a** was cleanly formed, albeit in a very modest 8% ee (reaction B, entry 3). Changing the counterion from BF_4^- to SbF_6^- resulted in little change in enantioselectivity (entry 4), although under the conditions and reaction times employed the competitive noncatalyzed background reaction is very slow (entry 5). A significant jump in selectivity was observed, however, on changing the solvent to toluene (entry 6), the ee of the product being essentially maintained on decreasing the amount of Hunig's base to just 1 mol % (entry 7). Further increases in ee were observed with increases in the size of the substituents attached to the oxazoline rings of the catalysts (entries 8 and 9), the best result of 34% ee being obtained with the cyclohexylmethyl substituents of catalyst **16e$_3$** (entry 10). This enantioselectivity was essentially unchanged when the reaction was

Scheme 6

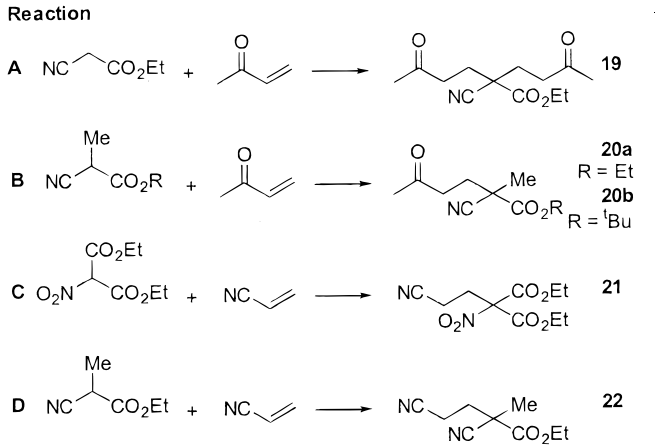


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Table 1. Results of the Catalysis of Michael Reactions with Cationic [2,6-Bis(2′-oxazolinyl)phenyl]palladium(II) Complexes

entry[a]	reacn/prod.	cat.[b]	solvent	time (h)	% yield[c] (% conversn[d])	% ee[e] (confign[f])
1	A/**19**[g]	**16a$_3$**	CH_2Cl_2	5	95	
2	A/**19**[g]		CH_2Cl_2	23	(<5)	
3	B/**20a**	**16b$_1$**	CH_2Cl_2	3.5	67	8 (*R*)
4	B/**20a**	**16b$_3$**	CH_2Cl_2	4	86	6 (*R*)
5	B/**20a**		CH_2Cl_2	4−50−95	(3)−(50)−(76)	
6	B/**20a**	**16b$_3$**	PhMe	4	73	22 (*R*)
7	B/**20a**[h]	**16b$_3$**	PhMe	7	73	20 (*R*)
8	B/**20a**[h]	**16c$_3$**	PhMe	143	78	29 (*R*)
9	B/**20a**[h]	**16d$_3$**	PhMe	97	80	27 (*R*)
10	B/**20a**[h]	**16e$_3$**	PhMe	120	86	34 (*R*)
11	B/**20a**[h,i]	**16e$_3$**	PhMe	143	66	33 (*R*)
12	B/**20a**[h]		PhMe	23−143−335	(7)−(29)−(38)	
13	B/**20b**	**16b$_3$**	CH_2Cl_2	1	90	17 (*R*)
14	B/**20b**	**16b$_3$**	PhMe	5	84	15 (*R*)
15	B/**20b**	**16e$_3$**	PhMe	70	70[j]	28 (*R*)
16	B/**20a**	**17**	PhMe	5	71	15 (*R*)
17	B/**20b**[h]	**17**	CH_2Cl_2	5	66	18 (*R*)
18	C/**21**	**16b$_3$**	CH_2Cl_2	3	79	
19	C/**21**		CH_2Cl_2	5−70−148	(0)−(23)−(42)	
20	D/**22**	**16e$_3$**	CH_2Cl_2	90	90	2[k]
22	D/**22**	**16e$_3$**	CH_2Cl_2	4−70−144	(0)−(11)−(21)	
22	D/**22**	**16e$_3$**	PhMe	46	74	8[k]

[a] Reactions were performed with 1.6 mmol of Michael acceptor, 2.4 mmol of activated esters, and 0.16 mmol of Hunig's base in 4 mL of solvent at room temperature. [b] 1 mol %. [c] After workup and bulb-to-bulb distillation. [d] Determined by ^{1}H NMR spectroscopy. [e] Determined by GC with CP-Chirasil-Dex CB. [f] Determined by optical rotation.[31b] [g] From 4.8 mmol of MVK. [h] 1 mol % Hunig's base. [i] 0 °C. [j] On the basis of 50% conversion, the reaction had ceased after 70 h. [k] Absolute configuration not determined.

carried out at 0 °C (entry 11). The bulkier oxazoline substituents also resulted in an increase in the time required for the reaction to complete, allowing some leakage in the potential selectivity due to a competitive noncatalyzed reaction (entry 12).

The influence of the size of the ester substituent was investigated with *tert*-butyl α-cyanopropionate, which on addition to methyl vinyl ketone resulted in the formation of **20b**. When the reaction was carried out in CH_2Cl_2, the product was formed with a higher ee than was observed with the corresponding ethyl ester (entry 13; compare to entry 4), but in this case a jump in selectivity was not observed on changing the solvent to toluene (entry 14). Neither did use of the cyclohexylmethyl-substituted catalyst **16e$_3$** promote a higher selectivity than previously observed in the ethyl ester series (entry 15). The two reactions leading to **20a** and **20b** were also efficiently catalyzed by the nitrile-containing complex **17**, confirming the lability of this functionality when attached to the exchangeable coordination site of these complexes (entries 16 and 17).

The possibility of activating the Michael acceptor through metal coordination was investigated by combining diethyl nitromalonate and acrylonitrile in the presence of Hunig's base. When **16b$_3$** was also present, the adduct **21** was readily formed (reaction C, entry 18), in contrast to its slow formation in the absence of this complex (entry 19). This result led us to investigate the addition of ethyl α-cyanopropionate to acrylonitrile catalyzed by **16e$_3$**, a reaction which offered the possibility of double asymmetric induction. Although these reactions produced adduct **22** in high yields (reaction D, entries 20 and 22) with comparatively little competitive noncatalyzed reaction (entry 21), only very low selectivities were observed. If this reaction proceeds via coordination of both nitriles to different palladium complexes, the interaction of the ligand frameworks in this instance is clearly not cooperative.

It is of note that in the absence of Hunig's base no reaction takes place, nor is any product observed when diethyl malonate is substituted for the α-cyanopropionates. These observations suggest the presence of a nitrogen-coordinated intermediate carrying a nitrile/palladium and ester-stabilized carbanion generated by Hunig's base. This subsequently undergoes partially selective addition of methyl vinyl ketone followed by protonation of the resulting enolate and regeneration of Hunig's base. This process differs slightly from the previous use of low-valent ruthenium[32] and rhodium[33,34a−f] complexes as catalysts for this reaction. These are rationalized by the oxidative addition of the metal into the α-C−H bond of the nitrile, leading via isomerization to an intermediate hydrido complex containing a nitrile-coordinated enolate. This is supported by the isolation and characterization by X-ray crystal structure analysis of the oxidative addition product of alkyl cyanoacetates to Ru(0) as *mer*-RuH(NCCHCO$_2$R)(NCCH$_2$CO$_2$R)(PPh$_3$)$_3$.[32b,35] For the Pd(II) systems described in this work, a similar mechanism not requiring a base would involve an intermediate cationic Pd(IV) intermediate. That reaction is only observed with Hunig's base present instead suggests a fixed Pd(II) oxidation level and activation of the α-C−H to deprotonation and/or enolate activation through nitrile−metal coordination. A fixed oxidation level is also consistent with activation of acrylonitrile, the palladium complex acting as a Lewis acid to this Michael acceptor. The kinetic lability of the palladium−nitrile bond, aided by the relatively high trans effect of the coordinated phenyl group, allows for the use of low catalyst loadings, as no significant level of product inhibition was observed. As the new stereogenic center is formed three bonds distant from palladium, the size and length of the oxazoline substituents are clearly important in determining the outcome of the reaction. In this context the rather open cleft defined

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by the N−Pd−N bond angle of 160.4° is a disadvantage, as it accentuates the distance between the oxazoline substituents and the newly forming stereogenic center.

Conclusion

In this work we have described the rapid synthesis of a series of enantiomerically pure 2,6-bis(2′-oxazolinyl)phenylpalladium(II) bromides, obtained directly from 1,3-bis(2′-oxazolinyl)benzenes, which are themselves easily synthesized from commercially available β-amino alcohols. The limitations of this approach have also been defined by both discovering the fate of bis(oxazolines) containing phenyl and benzyl substituents and attempting the lithiation/transmetalation sequence on a sterically congested bis(oxazoline) containing additional 5,5-dimethyl substituents. The palladium complexes are readily activated on treatment with a variety of silver salts to give analytically pure cationic complexes containing water in the exchangeable coordination site. The lability of ligands in this site was demonstrated by the low (1 mol %) loading required for the cationic complexes to efficiently catalyze the addition of α-cyanocarboxylates to Michael acceptors. Although the enantioselectivities described are modest, the efficiency of catalysis in these clean reactions and the potential for attachment of the catalysts to a solid support have maintained our interest in the design of related cationic palladium complexes.

Experimental Section

Tetrahydofuran was distilled from sodium benzophenone ketyl, and toluene, dichloromethane, chloroform, and TMEDA were distilled from calcium hydride. Methanol was distilled from activated 4 Å molecular sieves, and diisopropylamine was distilled from sodium hydroxide. Chlorobenzene was stored before use over activated 4 Å molecular sieves. Petroleum ether refers to that fraction boiling in the range 40−60 °C and hexane to the fraction boiling in the range 65.5−70 °C. Column chromatography was performed on SiO_2 (40−63 μm). Enantiomeric excesses were determined by GC using a CP-Chirasil-Dex CB column (25 m × 0.25 mm). Compound **5a** was prepared as previously described.[22] Chiral amino alcohols were obtained from Sigma-Aldrich Co. Ltd.

Preparation of 1,3-Bis(2′-oxazolinyl)benzenes 5c−g. The previously reported procedure for the synthesis of **5b**[23] was employed for the synthesis of the following new bis(oxazolines).

(*S*,*S*)-1,3-Bis(4′-isobutyl-2′-oxazolinyl)benzene (5c). Anhydrous zinc dichloride (0.15 g, 1.1 mmol), 1,3-dicyanobenzene (1.81 g, 14.1 mmol), and (*S*)-(+)-2-amino-4-methyl-1-pentanol (5.00 g, 42.7 mmol) were used. Column chromatography (CH_2Cl_2−EtOAc (95:5)) gave **5c** as a colorless crystalline solid (1.62 g, 35%). Mp: 48−49 °C. Anal. Found: C, 73.06; H, 8.35; N, 8.30. Calcd for $C_{20}H_{28}N_2O_2$: C, 73.14; H, 8.59; N, 8.53. $[\alpha]_D^{20}$ = −96 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1652 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 0.98 (12 H, d, *J* = 6.8 Hz, 4 × −C*H*$_3$), 1.36−1.41 (2 H, m, −C*H*(CH$_3$)$_2$), 1.68−1.74 (2 H, m, −CH*H*−), 1.81−1.87 (2 H, m, 2 × −C*H*H−), 3.99 (2 H, t, *J* = 8.0, −OC*H*H−), 4.30−4.38 (2 H, m, −C*H*N−), 4.51 (2 H, dd, *J* = 8.8, 7.6, −OCH*H*−), 7.44 (1 H, t, *J* = 7.8, 5-H), 8.05 (2 H, d, *J* = 7.6, 4- & 6-H), 8.47 (1 H, s, 2-H). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 22.7 (−*C*H$_3$), 22.8 (−*C*H$_3$), 25.4 (−*C*H(CH$_3$)$_2$), 45.6 (−*C*H$_2$−), 65.2 (−*C*HN−), 73.2 (−O*C*H$_2$−), 128.0 (Ph, 5-C), 128.2 (Ph, 4- & 6-C), 128.3 (Ph, 1- & 3-C), 130.7 (Ph, 2-C), 162.6 (C=N). MS (*m*/*z*; EI): 329 (M$^+$, 10%), 271 (100), 215 (20), 145 (12), 75 (12).

(*S*,*S*)-1,3-Bis(4′-*tert*-butyl-2′-oxazolinyl)benzene (5d). Anhydrous zinc dichloride (0.15 g, 1.1 mmol), 1,3-dicyanobenzene (1.81 g, 14.1 mmol), and (*S*)-(+)-2-amino-3,3-dimethylbutanol (5.00 g, 42.7 mmol) were used. Column chromatography (CH_2Cl_2−EtOAc (95:5)) gave **5d** as a colorless crystalline solid (1.40 g, 30%). Mp: 121−122 °C. Anal. Found: C, 73.18; H, 8.88; N, 8.58. Calcd for $C_{20}H_{28}N_2O_2$: C, 73.14; H, 8.59; N, 8.53. $[\alpha]_D^{20}$ = −168 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1651 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 0.89 (18 H, s, −C(C*H*$_3$)), 3.99 (2 H, dd, *J* = 10.1, 7.8 Hz, −OC*H*H−), 4.18 (2 H, t, *J* = 8.0, −C*H*N−), 4.29 (2 H, t, *J* = 9.9, −OCH*H*−), 7.38 (1 H, t, *J* = 7.8, 5-H), 7.99 (2 H, d, *J* = 7.8, 4- & 6-H), 8.44 (1 H, s, 2-H). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 26.3 (−*C*H$_3$), 34.5 (−*C*(CH$_3$)$_3$), 69.2 (−*C*HN−), 76.7 (−O*C*H$_2$−), 128.4 (Ph, 5-C), 128.6 (Ph, 4- & 6-C), 128.7 (Ph, 1- & 3-C), 131.3 (Ph, 2-C), 163.0 (*C*=N). MS (*m*/*z*; EI): 329 (M$^+$, 9%), 313 (10), 271 (94), 214 (11), 144 (41), 74 (5), 57 (100).

(*S*,*S*)-1,3-Bis(4′-cyclohexylmethyl-2′-oxazolinyl)benzene (5e). Anhydrous zinc dichloride (0.087 g, 0.64 mmol), 1,3-dicyanobenzene (0.82 g, 6.4 mmol), and (*S*)-(+)-2-amino-3-cyclohexyl-1-propanol (3.02 g, 19.2 mmol). Column chromatography (CH_2Cl_2−EtOAc (9:1)) gave **5e** as a colorless oil which solidified on standing (1.20 g, 46%). Mp: 57−58 °C Anal. Found: C, 76.71; H, 9.07; N, 7.04. Calcd for $C_{26}H_{36}N_2O_2$: C, 76.43; H, 8.89; N, 6.86. $[\alpha]_D^{20}$ = +144 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1652 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 0.97−1.83 (26 H, m, −C*H*$_2$*Cy*), 4.01 (2 H, t, *J* = 7.9 Hz, −OC*H*H−), 4.35−4.43 (2 H, m, −C*H*N−), 4.53 (2 H, t, *J* = 8.2, −OCH*H*−), 7.46 (1 H, t, *J* = 7.8, 5-H), 8.07 (2 H, d, *J* = 7.8, 4- & 6-H), 8.49 (1 H, s, 2-H). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 26.6 (−*C*H$_2$- × 2), 26.9 (−*C*H$_2$−), 33.8 (−*C*H$_2$−), 34.0 (−*C*H$_2$−), 35.3 (−CH$_2$*C*H−), 44.7 (−*C*H$_2$Cy), 65.1 (−*C*HN−), 73.7 (−O*C*H$_2$−), 128.4 (Ph, 5-C), 128.7 (Ph, 4- & 6-C), 128.7 (Ph, 1- & 3-C), 131.2 (Ph, 2-C), 163.1 (*C*=N). MS (*m*/*z*; EI): 407 (M$^+$, 91), 310 (71), 213 (19), 143 (100).

(*R*,*R*)-1,3-Bis(4′-phenyl-2′-oxazolinyl)benzene (5f). Anhydrous zinc dichloride (0.20 g, 1.5 mmol), 1,3-dicyanobenzene (1.56 g, 12.2 mmol), and (*R*)−(−)-2-amino-2-phenylethanol (5.00 g, 36.5 mmol) were used Column chromatography (CH_2Cl_2−EtOAc (95:5)) gave **5f** as a colorless crystalline solid (2.29 g, 51%). Mp: 129−130 °C Anal. Found: C, 78.46; H, 5.49; N, 7.43. Calcd for $C_{24}H_{20}N_2O_2$: C, 78.24; H, 5.47; N, 7.60. $[\alpha]_D^{20}$ = +100 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1652 (C=N) cm^{-1}; ^{1}H NMR (δ; $CDCl_3$): 4.32 (2 H, t, *J* = 8.4 Hz, −OC*H*H−), 4.83 (2 H, dd, *J* = 10.0, 8.5, −OCH*H*−), 5.42 (2 H, dd, *J* = 10.0, 8.3, −C*H*N−), 7.26−7.39 (10 H, m, Ph), 7.54 (1 H, t, *J* = 7.8, 5-H), 8.22 (2 H, d, *J* = 7.8, 4- & 6-H), 8.71 (1 H, s, 2-H). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 70.2 (−*C*HN−), 75.0 (−O*C*H$_2$−), 126.7 (Ph), 127.7 (Ph), 128.0 (Ph), 128.5 (Ph), 128.6 (Ph), 128.8 (Ph), 131.4 (Ph, 2-C), 142.2 (Ph, 1- & 3-C), 164.1 (*C*=N). MS (*m*/*z*; EI): 368 (M$^+$, 22%), 291 (5), 218 (11), 104 (24), 91 (68), 90 (97), 89 (100).

(*S*,*S*)-1,3-Bis(4′-benzyl-2′-oxazolinyl)benzene (5g). Anhydrous zinc dichloride (0.30 g, 2.2 mmol), 1,3-dicyanobenzene (2.82 g, 22.0 mmol), and (*S*)-(+)-2-amino-3-phenyl-1-propanol (10.00 g, 66.1 mmol). Column chromatography (CH_2Cl_2−EtOAc (9:1)) gave **5g** as a colorless crystalline solid (3.32 g, 38%). Mp: 107−109 °C Anal. Found: C, 78.55; H, 6.25; N, 7.31. Calcd for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. $[\alpha]_D^{20}$ = +52 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1649 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 2.88 (2 H, dd, *J* = 13.8, 8.2 Hz, −C*H*HPh−), 3.40 (2 H, dd, *J* = 13.8, 5.4, −CH*H*Ph), 4.31 (2 H, t, *J* 7.9, −OC*H*H−), 4.52 (2 H, t, *J* = 8.0, −OCH*H*−), 4.71−4.78 (2 H, m, −C*H*N−), 7.26−7.41 (10 H, m, Ph), 7.63 (1 H, t, *J* = 7.8, 5-H), 8.23 (2 H, d, *J* = 7.8, 4- & 6-H), 8.64 (1 H, s, 2-H). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 42.2 (−*C*H$_2$Ph), 68.4 (−*C*HN−), 72.4 (−O*C*H$_2$−), 127.0 (Ph), 128.6 (Ph), 128.9 (Ph), 129.0 (Ph), 129.7 (Ph), 131.4 (2-C), 138.3 (1- & 3-C), 163.7 (*C*=N). MS (*m*/*z*; EI): 397 (M$^+$, 9%), 305 (87), 213 (3), 143 (31), 90 (100).

General Procedure for the Preparation of 2,6-Bis(2′-oxazolinyl)phenylpalladium(II) Bromides 6a−e. A solution of diisopropylamine (3 equiv) in THF (3 mL/1 mL amine) was cooled under a nitrogen atmosphere to −78 °C. Butyl-

lithium (3.3 equiv) was added and the mixture stirred for 20 min at this temperature. The cooling bath was then removed and the solution warmed to room temperature for 30 min before replacing the cooling bath. This solution was transferred via a cannula into a flask containing a solution of the relevant 1,3-bis(2′-oxazolinyl)benzene (1 equiv) and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) (3 equiv) in THF (20 mL/g of oxazoline) under a nitrogen atmosphere at −78 °C. After the addition was complete, the cooling bath was removed and the resulting deep red solution was stirred at room temperature for 5−7 h. This was then added by cannula in small fractions to a stirred suspension of dibromo(1,5-cyclooctadiene)palladium(II) (1.5 equiv) in THF (20 mL/g) at 0 °C. After the addition was completed, the ice bath was removed and the reaction mixture stirred overnight at room temperature. The resulting black solution was filtered through Celite 520 and purified by column chromatography.

[2,6-Bis(4′,4′-dimethyl-2′-oxazolinyl)phenyl]palladium(II) Bromide (6a). LDA (3.3 mmol), **5a** (0.300 g, 1.10 mmol), TMEDA (0.385 g, 3.31 mmol) in THF (8 mL), and [$PdBr_2$(1,5-COD)] (0.45 g, 1.2 mmol) in THF (10 mL) followed by column chromatography [CH_2Cl_2-EtOAc (9:1)] gave **6a** as a pale yellow solid (0.176 g, 35%). Mp: 295−297 °C. Anal. Found: C, 42.28; H, 4.28; N, 6.27. Calcd for $C_{16}H_{19}BrN_2O_2Pd$: C, 41.99; H, 4.18; N, 6.12. IR (ν_{max}; Nujol): 1618 (C═N) cm^{-1}. ^1H NMR (δ; $CDCl_3$): 1.68 (12 H, s, −CH_3), 4.46 (4 H, s, −OCH_2−), 7.17 (1 H, t, J = 7.8 Hz, 4-H), 7.30 (2 H, d, J = 7.8, 3- & 5-H). $^{13}C\{^1H\}$ NMR (δ; $CDCl_3$): 28.1 (−*C*H_3), 66.2 (−*C*(CH_3)$_2$−), 82.8 (−O*C*H_2−), 124.0 (Ph, 4-C), 126.8 (Ph, 3- & 5-C), 130.0 (Ph, 2- & 6-C), 167.5 (Ph, 1-C), 172.6 (*C*═N). MS (*m*/*z*; EI): 462 (2%), 460 (7), 458 (10), 457 (5), 456 (7), 455 (4), 454 (2) [all M^+], 381 (34), 379 (75), 377 (88), 376 (67), 375 (32) [all M − Br], 41 (100).

(*S*,*S*)-[2,6-Bis(4′-isopropyl-2′-oxazolinyl)phenyl]palladium(II) Bromide (6b). LDA (5 mmol), **5b** (0.500 g, 1.66 mmol), TMEDA (0.590 g, 5.08 mmol) in THF (10 mL), and [$PdBr_2$(1,5-COD)] (0.94 g, 2.5 mmol) in THF (20 mL) followed by column chromatography (CH_2Cl_2) and further purification by precipitation from $CHCl_3$/hexane gave **6a** as a pale yellow solid (0.331 g, 41%). Mp: >290 °C. Anal. Found: C, 44.15; H, 4.77; N, 5.50. Calcd for $C_{18}H_{23}BrN_2O_2Pd$: C, 44.51; H, 4.78; N, 5.77. $[\alpha]_D^{20}$ = +128 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1620 (C═N) cm^{-1}. ^1H NMR (δ; $CDCl_3$): 0.81 (6 H, d, J = 6.9 Hz, −CH_3), 0.94 (6 H, d, J = 6.9, −CH_3), 2.85−2.94 (2 H, m, −CH(CH_3)$_2$), 4.34−4.39 (2 H, m, −CHN−), 4.60−4.69 (4 H, m, −OCH_2−), 7.18 (1 H, t, J = 7.6, 4-H), 7.32 (2 H, d, J = 7.4, 3- & 5-H). $^{13}C\{^1H\}$ NMR (δ; $CDCl_3$): 14.4 (−*C*H_3), 19.3 (−*C*H_3), 29.6 (−*C*(CH_3)$_2$), 67.5 (−*C*HN−), 71.5 (−O*C*H_2−), 124.5 (Ph, 4-C), 127.4 (Ph, 3- & 5-C), 129.7 (Ph, 2- & 6-C), 168.4 (Ph, 1-C), 174.4 (*C*═N). MS (*m*/*z*; EI): 490 (1%), 488 (5), 486 (8), 485 (5), 483 (2), 482 (1) [all M^+], 411 (5), 409 (21), 407 (14), 405 (47), 403 (53), 402 (56) [all M − Br], 361 (7), 257 (12), 43 (100).

(*S*,*S*)-[2,6-Bis(4′-isobutyl-2′-oxazolinyl)phenyl]palladium(II) Bromide (6c). LDA (4.6 mmol), **5c** (0.50 g, 1.5 mmol), TMEDA (0.53 g, 4.6 mmol) in THF (10 mL), and [$PdBr_2$-(1,5-COD)] (0.85 g, 2.3 mmol) in THF (15 mL) followed by column chromatography (CH_2Cl_2) gave **6c** as a pale yellow solid (0.16 g, 21%). Mp: >270 °C. Anal. Found: C, 46.75; H, 5.33; N, 5.21. Calcd for $C_{20}H_{27}BrN_2O_2Pd$: C, 46.76; H, 5.30; N, 5.45. $[\alpha]_D^{20}$ = +146 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1616 (C═N) cm^{-1}. ^1H NMR (δ; $CDCl_3$): 0.98 (6 H, d, J = 6.6 Hz, −CH_3), 1.01 (6 H, d, J = 6.6, −CH_3), 1.36−1.44 (2 H, m, −CH(CH_3)$_2$), 1.65−1.70 (2 H, m, −CHH−), 2.44−2.51 (2 H, m, −CHH−), 4.33−4.40 (2 H, m, −CHN−), 4.54 (2 H, dd, J = 8.6, 6.0, −OCHH−), 4.80 (2 H, t, J = 9.0, −OCHH−), 7.16 (1 H, t, J = 7.4, 4-H), 7.30 (2 H, d, J = 7.4, 3- & 5-H). $^{13}C\{^1H\}$ NMR (δ; $CDCl_3$): 21.7 (−*C*H_3), 23.7 (−*C*H_3), 25.5 (−*C*H(CH_3)$_2$), 43.8 (−*C*H_2−), 61.6 (−*C*HN−), 76.4 (−O*C*H_2−), 123.9 (Ph, 4-C), 126.7 (Ph, 3- & 5-C), 129.6 (Ph, 2- & 6-C), 168.3 (Ph, 1-C), 173.8 (*C*═N). MS (*m*/*z*; EI): 514 (M^+, 1%), 437 (42), 435 (83), 433 (100), 432 (77), 431 (37) [all M − Br], 376 (5), 327 (2), 271 (10), 57 (36), 55 (39).

(*S*,*S*)-[2,6-Bis(4′-*tert*-butyl-2′-oxazolinyl)phenyl]palladium(II) Bromide (6d). LDA (9.1 mmol), **5d** (1.00 g, 3.0 mmol), TMEDA (1.06 g, 9.1 mmol) in THF (20 mL), and [$PdBr_2$-(1,5-COD)] (1.71 g, 4.6 mmol) in THF (30 mL) followed by column chromatography (CH_2Cl_2−light petroleum (4:1)) gave **6d** as an orange solid (0.38 g, 24%). Mp: 258−260 °C. Anal. Found: C, 46.53; H, 5.77; N, 5.13. Calcd for $C_{20}H_{27}BrN_2O_2Pd$: C, 46.76; H, 5.30; N, 5.45. $[\alpha]_D^{20}$ = +600 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1610 (C═N) cm^{-1}. ^1H NMR (δ; $CDCl_3$): 1.10 (18 H, s, −C(CH_3)$_3$), 4.05 (2 H, dd, J = 8.4, 2.1 Hz, −OCHH−), 4.50 (2 H, t, J = 8.8, −CHN−), 4.76 (2 H, dd, J = 9.1, 2.2, −OCHH−), 7.12 (1 H, t, J = 7.8, 4-H), 7.24 (2 H, d, J = 7.5, 3- & 5-H). $^{13}C\{^1H\}$ NMR (δ; $CDCl_3$): 27.0 (−CH_3), 35.8 (−*C*(CH_3)$_3$), 70.8 (−*C*HN−), 74.1 (−O*C*H_2−), 124.5 (Ph, 4-C), 127.3 (Ph, 3- & 5-C), 129.7 (Ph, 2- & 6-C), 167.0 (Ph, 1-C), 175.1 (*C*═N). MS (*m*/*z*; EI): 514 (M^+, 2%), 438 (8), 437 (43), 435 (86), 433 (93), 432 (73), 431 (34) [all M − Br], 375 (8), 271 (32), 249 (7), 213 (8), 185 (6), 144 (13), 130 (7), 116 (15), 103 (7), 89 (12), 80 (8), 57 (100).

(*S*,*S*)-[2,6-Bis(4′-cyclohexylmethyl-2′-oxazolinyl)phenyl]palladium(II) Bromide (6e). LDA (7.4 mmol), **5e** (1.00 g, 2.5 mmol), TMEDA (0.85 g, 7.3 mmol) in THF (20 mL), and [$PdBr_2$(1,5-COD)] (1.50 g, 4.0 mmol) in THF (30 mL) followed by column chromatography (CH_2Cl_2−light petroleum (4:1)) gave **6e** as a pale yellow solid (0.60 g, 41%). Mp: 264−266 °C. Anal. Found: C, 52.71; H, 5.83; N, 4.63. Calcd for $C_{26}H_{35}BrN_2O_2Pd$: C, 52.58; H, 5.94; N, 4.72. $[\alpha]_D^{20}$ = +68 (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 1612 (C═N) cm^{-1}. ^1H NMR (δ; $CDCl_3$): 1.00−1.73 (24 H, m, −CHH*Cy*), 2.46 (2 H, brt, J = 8.3 Hz, −CHHCy), 4.29−4.35 (2 H, m, −CHN−), 4.46 (2 H, dd, J = 8.5, 6.0, −OCHH−), 4.72 (2 H, t, J = 8.9, −OCHH−), 7.08 (1 H, t, J = 7.8, 4-H), 7.22 (2 H, d, J = 7.6, 3- & 5-H). $^{13}C\{^1H\}$ NMR (δ; $CDCl_3$): 26.6 (−*C*H_2−), 32.5 (−*C*H_2−), 34.6 (−*C*H_2−), 35.3 (−CH_2*C*H−), 43.0 (−*C*H_2−), 61.6 (−*C*HN−), 76.9 (−O*C*H_2−), 124.3 (Ph, 4-C), 127.0 (Ph, 3- & 5-C), 130.0 (Ph, 2- & 6-C), 168.7 (Ph, 1-C), 174.2 (*C*═N). MS (*m*/*z*; EI): 519 (5%), 518 (18), 516 (37), 514 (40), 513 (29), 512 (13) [all M − Br], 408 (5), 81 (14), 79 (18), 55 (100).

Reaction of (*R*,*R*)-1,3-Bis(4′-phenyl-2′-oxazolinyl)benzene (5f) with LDA/TMEDA. (*R*,*R*)-1,3-Bis(4′-phenyl-2′-oxazolinyl)benzene **(5f**; 0.50 g, 1.4 mmol) was lithiated as described for the formation of **6a**−**e** (LDA, 4.1 mmol; TMEDA, 0.47 g, 4.0 mmol; THF, 20 mL) except that after stirring at room temperature for 5 h the reaction was quenched by the addition of MeI (1.93 g, 13.6 mmol). The resultant precipitate was removed by filtration and the filtrate diluted with EtOAc (25 mL), washed with water (2 × 20 mL), dried ($MgSO_4$), and filtered and the solvent removed in vacuo. Recrystallization from EtOAc/hexane gave enamide **7** (0.522 g, 97%) as a brown solid. Mp: 117−121 °C. IR (ν_{max}; Nujol): 1650 (C═O), 1635 (C═C) cm^{-1}. ^1H NMR (δ; $CDCl_3$): 3.13 (6 H, s, −CH_3), 4.69 (2 H, s, −C═CHH), 5.23 (2 H, s, −C═CHH), 6.93 (2 H, d, J = 7.5 Hz, 4- & 6-H), 7.19−7.30 (11 H, m, Ph and 5-H), 7.62 (1 H, s, 2-H). $^{13}C\{^1H\}$ NMR (δ; $CDCl_3$): 37.1 (−*C*H_3), 112.9 (−C═*C*H_2), 126.4 (4- & 6-C), 127.6 (−Ph), 127.8 (−Ph), 129.2 (−Ph), 129.4 (−Ph), 129.4 (−Ph), 136.2 (−Ph), 136.5 (1- & 3-C), 149.4 (−*C*═CH_2), 171.2 (*C*═O). MS (*m*/*z*; EI): 396 (M^+, 73%), 381 (12), 366 (80), 292 (45), 277 (10), 263 (68), 249 (32), 235 (91), 220 (20), 207 (40), 198 (44), 178 (100), 172 (58), 165 (42), 145 (70), 134 (64), 118 (88), 103 (90), 90 (69), 75 (68), 65 (81) High-resolution MS (*m*/*z*; EI): found for M^+, 396.1837; calcd for $C_{26}H_{24}N_2O_2$, 396.1838.

Reaction of (*S*,*S*)-1,3-Bis(4′-benzyl-2′-oxazolinyl)benzene (5g) with LDA/TMEDA. (*S*,*S*)-1,3-Bis(4′-benzyl-2′-oxazolinyl)benzene **(5g**; 0.54 g, 1.4 mmol) was lithiated and quenched as described for the formation of **7** (LDA, 4.08 mmol; TMEDA, 0.47 g, 4.0 mmol; THF, 20 mL; MeI, 1.93 g, 13.6 mmol). Identical workup and removal of the solvent in vacuo gave cinnamyl alcohol **8** (0.147 g, 40%) as a yellow oil which solidified on cooling, Mp: 35−36 °C (lit. mp 34 °C). IR (ν_{max}; Nujol): 3334 (O−H) cm^{-1}. ^1H NMR (δ; $CDCl_3$): 4.17 (2 H, d,

J = 5.4 Hz, −CH_2−), 6.21 (1 H, dt, J = 15.8, 5.9, −CH=CHCH$_2$−), 6.46 (1 H, d, J = 16.0, −CH=CHCH$_2$−), 7.14−7.23 (5 H, m, Ph).

Reaction of Ferrocenyloxazoline 9 with LDA/TMEDA. (*S*)-2-Ferrocenyl-4-benzyloxazoline **9**[36] (0.250 g, 0.72 mmol) was lithiated as described for the formation of **7** (LDA, 1.09 mmol; TMEDA 0.126 g, 1.08 mmol; THF, 2.5 mL) except that the reaction mixture was stirred at room temperature for only 30 min and then quenched with 1 M HCl(aq) (5 mL). After extraction with Et_2O (50 mL), the organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo and the residue chromatographed (EtOAc/petroleum ether) to give **10**[37] (0.01 g, 7%) and **8** (0.07 g, 72%).

***(R,R)*-Bis(2-hydroxy-1-phenylethyl)-2-bromo-1,3-benzenediamide (13f).** To a solution of (*R*)−(−)-2-amino-2-phenylethanol (1.95 g, 14.2 mmol) in dry chloroform (100 mL) cooled in an ice/water bath was added a solution of 2-bromo-1,3-benzene dichloride (1.00 g, 3.6 mmol) in dry chloroform (30 mL). The reaction mixture was removed from the cooling bath and stirred at room temperature for 24 h. The resultant colorless solid was collected by filtration, washed with Et_2O (3 × 100 mL), and recrystallized from hot methanol to give **13f** as a colorless crystalline solid (1.56 g, 91%). Mp: 257−259 °C. Anal. Found: C, 59.52; H, 4.96; N, 6.11. Calcd for $C_{24}H_{23}BrN_2O_4$: C, 59.61; H, 4.79; N, 5.80. $[\alpha]_D^{21} = -28$ (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 3278 (NH), 1652 (C=O) cm^{-1}. ^{1}H NMR (δ; d_6-DMSO): 3.59−3.67 (4 H, m, −OCH_2−), 4.90−4 95 (2 H, m, −OH), 5.00−5.05 (2 H, m, −CHN−), 7.20−7.50 (13 H, m, Ph), 8.85 (2 H, d, J = 8.2 Hz, −NH). ^{13}C{^{1}H} NMR (δ; d_6-DMSO): 55.5 (−CHN−), 64.5 (−OCH$_2$−), 116.0 (Ph), 126.7 (Ph), 127.0 (Ph), 127.4 (Ph), 127.9 (Ph), 128.7 (Ph), 140.1 (Ph), 140.7 (Ph, 1- & 3-C), 166.7 (*C*=O). MS (*m*/*z*; CI): 485/483 (M$^+$, 2%), 405 (7), 120 (100).

***(R,R)*-2-Bromo-1,3-bis(4′-phenyl-2′-oxazolinyl)benzene (14f).** To a suspension of **13f** (0.70 g, 1.4 mmol) in acetonitrile (30 mL) containing triethylamine (1.02 g, 10.15 mmol) and carbon tetrachloride (1.56 g, 10.1 mmol) was added dropwise a solution of triphenylphosphine (2.66 g, 10.1 mmol) in pyridine (40 mL) and acetonitrile (40 mL). The resulting yellow solution was stirred at room temperature overnight, concentrated in vacuo, diluted with EtOAc (100 mL), and washed with water (2 × 75 mL). The organic phase was dried ($MgSO_4$) and evaporated and the residue column-chromatographed (CH_2Cl_2−EtOAc (3:2)) to give **14f** as a pale yellow oil (0.31 g, 48%). $[\alpha]_D^{20} = +116$ (*c* 0.1, EtOH). IR (ν_{max}; liquid film): 1657 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 4.24 (2 H, t, J = 8.5 Hz, −OCHH−), 4.75 (2 H, dd, J = 10.1, 8.5, −OCHH−), 5.33 (2 H, dd, J = 10.2, 8.5, −CHN−), 7.22−7.32 (10 H, m, Ph), 7.34 (1 H, t, J = 7.7, 5-H), 7.71 (2 H, d, J = 7.9, 4- & 6-H). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 70.8 (−CHN−), 75.7 (−OCH$_2$−), 126.5 (Ph, 2-C), 127.2 (Ph), 127.6 (Ph), 128.1 (Ph), 129.2 (Ph), 132.4 (Ph), 133.5 (Ph), 142.3 (Ph, 1- & 3-C), 164.8 (*C*=N). MS (*m*/*z*; EI): 448 (M$^+$, 20%), 446 (5), 368 (3), 89 (100). High-resolution MS (*m*/*z*; EI): found for M$^+$, 446.0630; calcd for $C_{24}H_{19}BrN_2O_2$, 446.0630.

***(R,R)*-2-Methyl-1,3-bis(4′-phenyl-2′-oxazolinyl)benzene (15).** To a solution of **14f** (0.059 g, 0.132 mmol) in THF (5 mL) at −78 °C under nitrogen was added butyllithium (2.5 M, 0.05 mL, 0.13 mmol); the resulting mixture was stirred at −78 °C for 2 h and quenched with MeI (0.19 g, 1.3 mmol). After the mixture was warmed to room temperature, workup as described for **7** and column chromatography (CH_2Cl_2−EtOAc (7:3)) gave **15** as a colorless oil (0.01 g, 20%). IR ($\nu_{max;}$ liquid film): 1651 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 2.78 (3 H, s, −CH_3), 4.21 (2 H, t, J = 8.4 Hz, −OCHH−), 4.74 (2 H, dd, J = 10.2, 8.5, −OCHH−), 5.38 (2 H, dd, J = 10.2, 8.4, −CHN−), 7.20−7.30 (11 H, m, Ph), 7.83 (2 H, d, J = 7.8, 4- & 6-H). ^{13}C-{^{1}H} NMR (δ; $CDCl_3$): 19.4 (−CH$_3$), 70.9 (−CHN−), 74.9 (−OCH$_2$−), 125.8 (Ph), 127.0 (Ph), 127.2 (Ph), 128.0 (Ph), 129.2 (Ph), 129.6 (Ph), 132.8 (Ph), 142.7 (Ph, 1- & 3-C), 165.8 (*C*=N); MS (*m*/*z*; EI): 382 (M$^+$, 30), 235 (88), 220 (10), 89 (100) High-resolution MS (*m*/*z*): found for M$^+$, 382.1681; calcd for $C_{25}H_{22}N_2O_2$, 382.1681.

General Procedure for the Preparation of Cationic [2,6-Bis(2′-oxazolinyl)phenyl]aquopalladium(II) Salts 16a−e. To a stirred solution of [1,3-bis(2′-oxazolinyl)phenyl]-palladium(II) bromide (1 equiv) in CH_2Cl_2/H_2O (9.9:0.1 mL per 0.10 g of complex—a corresponding ratio of acetone to H_2O was used for the synthesis of the tetrafluoroborate complexes) in a foil-covered flask was added the appropriate silver salt (1.2 equiv) as a single portion. The reaction mixture was stirred for 3 h, and the resultant gray silver bromide precipitate was removed by filtration through Celite 520 and washed with additional CH_2Cl_2 (20 mL). The combined filtrate and washings were evaporated in vacuo to give a pale gray solid that was purified by repeated precipitation from CH_2Cl_2/hexane (acetone/Et_2O for the tetrafluoroborate complexes).

[2,6-Bis(4′,4′-dimethyl-2′-oxazolinyl)phenyl]aquopalladium(II) Tetrafluoroborate (16a$_1$). 6a (0.15 g, 0.3 mmol) in acetone/H_2O (14.85/0.15 mL) and silver tetrafluoroborate (0.07 g, 0.4 mmol) gave (0.13 g, 82%) of **16a$_1$** as a colorless solid. Mp: 267−270 °C Anal. Found: C, 39.84; H, 4.41; N, 5.91. Calcd for $C_{16}H_{21}BF_4N_2O_3Pd$: C, 39.83; H, 4.39; N, 5.81. IR (ν_{max}; Nujol): 3464 (OH), 1618 (C=N), 1109, 1058, 1007 (BF) cm^{-1}. ^{1}H NMR (δ; d_6-acetone): 1.40 (12 H, s, −CH_3), 2.90 (2 H, brs, −OH_2), 4.74 (4 H, s, −OCH_2−), 7.42 (1 H, t, J = 6.6 Hz, 4-H), 7.51 (2 H, d, J = 6.9, 3- & 5-H). ^{13}C{^{1}H} NMR (δ; d_6-acetone): 26.5 (−CH$_3$), 64.9 (−C(CH$_3$)$_2$), 82.5 (−OCH$_2$−), 125.8 (Ph, 4-C), 127.8 (Ph, 3- & 5-C), 130.1 (Ph, 2- & 6-C), 161.9 (Ph, 1-C), 172.8 (*C*=N).

***(S,S)*-[2,6-Bis(4′-isopropyl-2′-oxazolinyl)phenyl]aquopalladium(II) Trifluoromethanesulfonate (16b$_2$). 6b** (0.10 g, 0.2 mmol) in CH_2Cl_2/H_2O (9:1 mL) and $AgOSO_2CF_3$ (0.063 g, 0.25 mmol) gave 0.067 g (57%) of **16b$_2$** as a colorless solid. Mp: 208−210 °C. Anal. Found: C, 39.99; H, 4.29; N, 4.59. Calcd for $C_{19}H_{25}F_3N_2O_6PdS$: C, 39.84; H, 4.40; N, 4.89. $[\alpha]_D^{20} = +116$ (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 3490 (OH), 1620 (C=N), 1289 and 1033 (SO_3), 1242, 1161 (CF_3) cm^{-1}. ^{1}H NMR (δ; d_6-acetone): 0.88 (6 H, d, J = 6.9 Hz, −CH_3), 0.95 (6 H, d, J = 6.8, −CH_3), 2.14−2.21 (2 H, m, −CH(CH$_3$)$_2$), 3.13 (2 H, brs, −OH_2), 4.34−4.40 (2 H, m, −CHN−), 4.87−4.96 (4 H, m, −OCH_2−), 7.40 (1 H, t, J = 6.7, 4-H), 7.48 (2 H, d, J = 7.0, 3- & 5-H). ^{13}C{^{1}H} NMR (δ; d_6-DMSO): 14.7 (−CH$_3$), 18.6 (−CH$_3$), 29.9 (−CH(CH$_3$)$_2$), 66.4 (−CHN−), 72.2 (−OCH$_2$−), 125.9 (Ph, 4-C), 128.3 (Ph, 3- & 5-C), 129.5 (Ph, 2- & 6-C), 162.1 (Ph, 1-C), 173.7 (*C*=N), 202.0 (−CF$_3$).

***(S,S)*-[2,6-Bis(4′-isopropyl-2′-oxazolinyl]phenylaquopalladium(II) Hexafluoroantimonate (16b$_3$). 6b** (0.070 g, 0.14 mmol) in CH_2Cl_2/H_2O (9:1 mL) and $AgSbF_6$ (0.072 g, 0.21 mmol) gave 0.083 g (87%) of **16b$_3$** as a colorless solid. Mp: 176−179 °C. Anal. Found: C, 32.91; H, 3.71; N, 4.25. Calcd for $C_{18}H_{25}F_6N_2O_3PdSb$: C, 32.78; H, 3.82; N, 4.25. $[\alpha]_D^{20} = +248$ (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 3493 (OH), 1620 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 0.87 (6 H, d, J = 6.8 Hz, −CH_3), 0.98 (6 H, d, J = 6.8, −CH_3), 2.20−2.30 (2 H, m, −CH(CH$_3$)$_2$), 2.37 (2 H, br s, −OH_2), 4.36−4.41 (2 H, m, −CHN−), 4.64−4.73 (4 H, m, −OCH_2−), 7.23 (1 H, t, J = 6.6, 4-H), 7.31 (2 H, d, J = 6.9, 3- & 5-H). ^{13}C{^{1}H} NMR (δ; d_6-acetone): 14.2 (−CH$_3$), 17.5 (−CH$_3$), 30.2 (−CH(CH$_3$)$_2$), 66.7 (−CHN−), 72.4 (−OCH$_2$−), 125.9 (Ph, 4-C), 128.0 (Ph, 3- & 5-C), 129.6 (Ph, 2- & 6-C), 162.5 (Ph, 1-C), 174.1 (*C*=N).

***(S,S)*-[2,6-Bis(4′-isobutyl-2′-oxazolinyl)phenyl]aquopalladium(II) Hexafluoroantimonate (16c$_3$). 6c** (0.06 g, 0.1 mmol) in CH_2Cl_2/H_2O (4.9:0.1 mL) and silver hexafluoroantimonate (0.06 g, 0.2 mmol) gave **16c$_3$** as a colorless solid (0.048 g, 60%). Mp: 154−158 °C. Anal. Found**:** C, 35.85; H, 4.57; N, 3.97. Calcd for $C_{20}H_{29}F_6N_2O_3PdSb$: C, 34.94; H, 4.25; N, 4.07. $[\alpha]_D^{20} = +132$ (*c* 0.1, EtOH). IR (ν_{max}; Nujol): 3501 (OH), 1620 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 0.90 (12 H, d, J = 6.4 Hz,

(36) Sammakia, T.; Latham, H. A.; Schaad, D. R. *J. Org. Chem.* **1995**, *60*, 10.

−CH_3), 1.30−1.40 (2 H, m, −CH(CH_3)$_2$), 1.61−1.64 (2 H, m, −CHH−), 1.90−2.00 (2 H, m, −CHH−), 2.06 (2 H, brs, −OH_2), 4.30−4.40 (2 H, m, −CHN−), 4.47 (2 H, dd, J = 8.5, 6.3, −OCHH−), 4.80 (2 H, t, J = 9.0, −OCHH−), 7.14 (1 H, t, J = 6.7, 4-H), 7.23 (2 H, d, J = 7.6, 3- & 5-H). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 22.1 (−CH$_3$), 23.9 (−CH$_3$), 25.5 (−C(CH$_3$)$_2$), 44.2 (−CH$_2$−), 61.4 (−CHN−), 76.9 (−OCH$_2$−), 125.5 (Ph, 4-C), 128.0 (Ph, 3- & 5-C), 130.1 (Ph, 2- & 6-C), 171.0 (Ph, 1-C), 173.9 (C=N).

(*S,S*)-[2,6-Bis(4′-*tert*-butyl-2′-oxazolinyl)phenyl]aquopalladium(II) Hexafluoroantimonate (16d$_3$). 6d (0.10 g, 0.2 mmol) in CH_2Cl_2/H_2O (9.9:0.1 mL) and silver hexafluoroantimonate (0.08 g, 0.2 mmol) gave **16d$_3$** as a colorless solid (0.039 g, 29%). Mp: 238−240 °C. Anal. Found: C, 35.19; H, 4.36; N, 3.95. Calcd for $C_{20}H_{29}F_6N_2O_3PdSb$: C, 34.94; H, 4.25; N, 4.07. $[\alpha]_D^{20}$ = +204 (c 0.1, EtOH). IR (ν_{max}; Nujol): 3504 (OH) 1614 (C=N) cm^{-1}. ^{1}H NMR (δ; d_6-acetone): 0.98 (18 H, s, −CH_3), 2.93 (2 H, brs, −OH_2), 4.05 (2 H, dd, J = 9.0, 3.0 Hz, −CHN−), 4.90 (2 H, t, J = 9.3, −OCHH−), 5.13 (2 H, dd, J = 9.6, 3.0, −OCHH−), 7.44 (1 H, t, J = 6.8, 4-H), 7.52 (2 H, d, J = 7.2, 3- & 5-H). ^{13}C{^{1}H} NMR (δ; d_6-acetone): 25.8 (−CH$_3$), 35.7 (−C(CH$_3$)$_3$), 71.7 (−CHN−), 74.5 (−OCH$_2$−), 126.8 (Ph, 4-C), 128.9 (Ph, 3- & 5-C), 130.4 (Ph, 2- & 6-C), 162.5 (Ph, 1-C), 176 (C=N).

(*S,S*)-[2,6-Bis(4′-(cyclohexylmethyl)-2′-oxazolinyl)-phenyl]aquopalladium(II) Hexafluoroantimonate (16e$_3$). 6e (0.25 g, 0.4 mmol) in CH_2Cl_2/H_2O (19:1 mL) and silver hexafluoroantimonate (0.174 g, 0.51 mmol) gave **16e$_3$** as a colorless solid (0.090 g, 28%). Mp: 150−152 °C Anal. Found: C, 40.84; H, 4.76; N, 3.67. Calcd for $C_{26}H_{37}F_6N_2O_3PdSb$: C, 40.68; H, 4.86; N, 3.65. $[\alpha]_D^{20}$ = +176 (c 0.1, EtOH). IR (ν_{max}; Nujol): 3498 (OH), 1620 (C=N) cm^{-1}. ^{1}H NMR (δ; d_6-acetone): 0.95−1.98 (28 H, m, −CH_2*Cy* and −OH_2), 4.30−4.37 (2 H, m, −CHN−), 4.47 (2 H, dd, J = 8.5 Hz, 6.4, −OCHH−), 4.79 (2 H, t, J = 9.0, −OCHH−), 7.14 (1 H, t, J = 7.2, 4-H), 7.23 (2 H, d, J = 7.5, 3- & 5-H). ^{13}C{^{1}H} NMR (δ; d_6-acetone): 26.2 (−CH$_2$−), 26.4 (−CH$_2$−), 32.8 (−CH$_2$−), 34.3 (−CH$_2$−), 34.6 (−CH$_2$$C$H−), 42.9 (−$CH_2$−), 61.0 (−$C$HN−), 77.4 (−O$CH_2$−), 126.2 (Ph, 4-C), 128.2 (Ph, 3- & 5-C), 130.3 (Ph, 2- & 6-C), 168.0 (Ph, 1-C), 174.3 (C=N).

(*S,S*)-[2,6-Bis(4′-isopropyl-2′-oxazolinyl)phenyl](acetonitrile)palladium(II)Hexafluoroantimonate (17). Complex **16b$_3$** (0.030 g, 0.05 mmol) was dissolved in acetone (4 mL) and the solution degassed and placed under nitrogen. Acetonitrile (24 μL, 0.46 mmol) was added dropwise to the homogeneous solution and the mixture stirred overnight. The solution was concentrated in vacuo to ca. 1 mL, and addition of diethyl ether (20 mL) caused precipitation of an off-white solid (0.0185 g, 60%). Mp: 100−104 °C. Anal. Found: C, 35.37; H, 4.04; N, 5.89. Calcd for $C_{20}H_{26}F_6N_3O_2PdSb$: C, 35.19; H, 3.84; N, 6.16. $[\alpha]_D^{20}$ = +120 (c 0.1, EtOH). IR (ν_{max}; Nujol): 2320, 2292 (C=N), 1616 (C=N) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 0.89 (6 H, d, J = 7 Hz, −CH_3), 1.00 (6 H, d, J = 7, −CH_3), 2.10−2.20 (2 H, m, −CH(CH$_3$)$_2$), 2.40 (3 H, br s, −CH$_3$), 4.30−4.36 (2 H, m, −CHN−), 4.64−4.76 (4 H, m, −OCH$_2$−), 7.23 (1 H, t, J = 8, 4-H), 7.31 (2 H, d, J = 8, 3- & 5-H). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 12.5 (−CH$_3$), 14.9 (−CH$_3$), 18.4 (−CH$_3$), 30.4 (−CH-(CH$_3$)$_2$), 66.8 (−CHN−), 72.0 (−OCH$_2$−), 125.5 (Ph, 4-C), 127.8 (Ph, 3- & 5-C), 129.6 (Ph, 2- & 6-C), 142.5 (−C=N), 163.1 (Ph, 1-C), 174.4 (C=N).

General Procedure for Palladium-Catalyzed Michael Reactions. Under a nitrogen atmosphere, the catalyst (0.012 g, 0.01 equiv) was dissolved in either dry CH_2Cl_2 or dry toluene (4 mL). The cyano or nitro ester (1 equiv) was added dropwise via a syringe, followed by the neat Michael acceptor (1.5 equiv) and finally *N*-ethyldiisopropylamine (0.1 equiv. or 0.01 equiv). The homogeneous reaction mixture was stirred and monitored by ^{1}H NMR spectroscopy. After the ester had been consumed, the reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with 1 M HCl (20 mL). The organic layer was dried (Na_2SO_4), the solvent was removed in vacuo, and the resultant oil obtained was purified by Kugelrohr distillation.

Table 2. Crystallographic Data for Complex 16b$_2$

formula	$C_{19}H_{25}F_3N_2O_6PdS$
fw	572.87
temp, K	150(2)
wavelength, Å	0.71069
cryst syst	monoclinic
space group	*I*2 (No. 5)
a, Å	11.932(3)
b, Å	12.755(4)
c, Å	15.422(3)
β, deg	98.42(2)
V, Å^3	2321.8(10)
Z	4
d_{calcd}, g cm^{-3}	1.639
μ, mm^{-1}	0.893
F(000)	1160
cryst size, mm	0.25 × 0.20 × 0.15
θ range, deg	2.02−25.11
no. of rflns coll	5152
no. of indep rflns	3225 (R_{int} = 0.0691)
no. of data/restraints/params	3225/67/297
GOF on F^2	0.998
final R indices ($I > 2\sigma(I)$)	R1 = 0.0522, wR2 = 0.1281
R indices (all data)	R1 = 0.0647, wR2 = 0.1308

5-Cyano-5-(carboethoxy)nonane-2,8-dione (19).[34b] Colorless oil. IR (ν_{max}; liquid film): 2244 (C=N), 1745 (C=O), 1719 (C=O) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 1.31 (3 H, t, J = 7.1 Hz, −CH_3), 2.05−2.22 (4 H, m, −CH_2−), 2.15 (6 H, s, −COCH_3), 2.54−2.69 (4 H, m, −CH_2CO−), 4.24 (2 H, J = 7.1, q, −OCH_2−).

Ethyl 2-Cyano-2-methyl-5-oxohexanoate (20a).[34b] Colorless oil. IR (ν_{max}; liquid film): 2244 (C=N), 1744 (C=O), 1727 (C=O) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 1.29 (3 H, t, J = 7.1 Hz, −CH$_3$), 1.58 (3 H, s, −C(CN)CH_3), 1.96−2.21 (2 H, m, −CH$_2$−), 2.12 (3 H, s, −COCH_3), 2.54−2.64 (2 H, m, −CH_2−), 4.22 (2 H, q, J = 7.1, −OCH_2−).

***tert*-Butyl 2-Cyano-2-methyl-5-oxohexanoate (20b).**[34b] Colorless oil. IR (ν_{max}; liquid film): 2243 (C=N), 1741 (C=O), 1727 (C=O) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 1.49 (9 H, s, −C(CH_3)$_3$), 1.55 (3 H, s, −C(CN)CH_3), 1.99−2.21 (2 H, m, −CH_2−), 2.17 (3 H, s, −COCH_3), 2.56−2.68 (2 H, m, −CH_2−).

4,4-Bis(carboethoxy)-4-nitrobutanonitrile (21). Colorless oil. Anal. Found: C, 46.74; H, 5.70; N, 10.87. Calcd for $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.46; N, 10.85. IR (ν_{max}; liquid film): 2253 (C=N), 1753 (C=O), 1571 (NO$_2$) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 1.31 (6 H, t, J = 7 Hz, −CH_3), 2.72−2.75 (2 H, m, −CH$_2$−), 2.78−2.83 (2 H, m, −CH_2−), 4.36 (4 H, q, J = 7, −OCH_2−). ^{13}C{^{1}H} NMR (δ; $CDCl_3$): 12.99 (−CH$_2$−), 13.64 (−CH$_3$), 29.78 (−CH$_2$−), 64.38 (−OCH$_2$−), 95.11 (−C(NO$_2$)−), 117.56 (−C=N), 161.59 (C=O). MS (m/z; EI): 259 (M$^+$, 5%), 213 (7), 185 (5), 112 (100).

2-(Carboethoxy)-2-methylpentanedinitrile (22).[32b] Colorless oil. IR (ν_{max}; liquid film): 2241 (C=N), 1745 (C=O) cm^{-1}. ^{1}H NMR (δ; $CDCl_3$): 1.38 (3 H, t, J = 7 Hz, −CH_3), 1.70 (3 H, s, −C(CN)CH_3), 2.15 (1 H, ddd, J = 14, 9, 6, −CHHCN), 2.35−2.70 (3 H, m, −CH_2CHHCN), 4.30 (2 H, q, J = 7, −OCH_2−).

Crystal Structure Determination. The method employed for the crystal structure determination of **16b$_2$** was performed as previously described.[38] The noncentrosymmetric space group *I*2 (a nonstandard setting of *C*2) was confirmed by the successful solution and refinement of the structure. It is also consistent with only one-handed cationic complex species being present in the crystal. Initial attempts to solve the structure in the centrosymmetric space group *I*2/*m* were unsuccessful. Crystal data, details of data collection, and refinement are given in Table 2.

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Supporting Information Available: Text giving full characterization data for **16a$_2$**, **16a$_3$**, **16b$_1$**, **13g**, **14g**, **18**, and **12** and details of the X-ray structure determination of **16b$_2$**. This material is available free of charge via the Internet at http://pubs.acs.org.

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