[12] (*E*)-1-[3-(*tert*-Butyldimethylsilyl)oxy-1-propenyl]-1,3,2-benzodioxaborole could be used instead of the boronic acid for this reaction.
[13] **2**: Oil; $R_f = 0.34$ (EtOAc/hexane, 5/95); IR (KBr): $\tilde{\nu} = 1677, 1580\ cm^{-1}$; UV (EtOH): $\lambda_{max} = 379, 243$ nm; ^1H NMR (300 MHz, C_6D_6): $\delta = 1.11$ (6H, s), 1.44 – 1.50 (2H, m), 1.53 – 1.63 (2H, m), 1.72 (3H, s), 1.76 (3H, d, $J = 1.0$ Hz), 1.95 (2H, br t, $J = 6.5$ Hz), 5.79 (1H, m), 6.01 (1H, dd, $J = 15.1$, 7.7 Hz), 6.27 (1H, d, $J = 16.1$ Hz), 6.35 – 6.47 (3H, m), 7.12 (1H, dd, $J = 15.1$, 12.0 Hz), 9.42 (1H, d, $J = 7.7$ Hz); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 12.4$, 19.6, 21.9, 29.1 (2C), 33.3, 34.5, 39.8, 124.8, 126.2, 130.1, 130.4, 132.2, 133.8, 137.9, 138.0, 141.0, 144.8, 192.2; FAB-MS: *m/z*: 271 (M^++H); HR-MS calcd for $C_{19}H_{27}O$ (M^++H): 271.2062; found: 271.2068.
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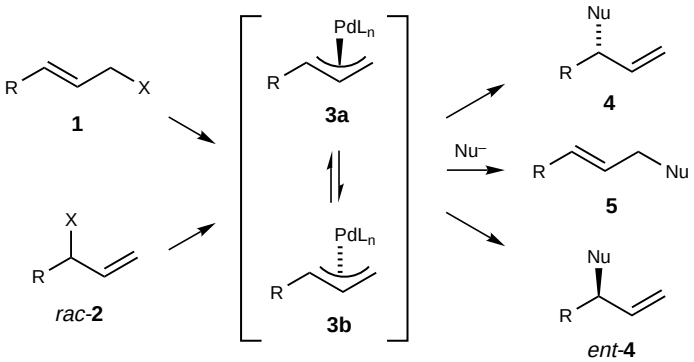
[15] **3**: Oil; $R_f = 0.23$ (EtOAc/hexane, 15/85); IR (KBr): $\tilde{\nu} = 2160, 1659, 1584\ cm^{-1}$; UV (EtOH): $\lambda_{max} = 370, 252$ nm; ^1H NMR (300 MHz, C_6D_6): $\delta = 1.04$ (6H, s), 1.35 – 1.45 (2H, m), 1.50 – 1.60 (2H, m), 1.61 (3H, s), 1.63 (3H, s), 1.89 (2H, br t, $J = 6.5$ Hz), 5.16 (1H, d, $J = 10.5$ Hz), 6.20 (1H, d, $J = 16.0$ Hz), 6.36 (1H, br d, $J = 16.0$ Hz), 6.62 (1H, dd, $J = 12.1$, 10.5 Hz), 6.78 (1H, d, $J = 12.1$ Hz), 8.91 (1H, d, $J = 1.2$ Hz); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 15.6$, 19.6, 21.8, 29.1 (2C), 33.2, 34.5, 39.8, 91.9, 96.5, 104.6, 127.0, 130.8, 131.4, 137.6, 137.7, 142.9, 143.1, 175.4; MS (70 eV): *m/z* (%): 268 (M^+); HR-MS calcd for $C_{19}H_{24}O$ (M^+): 268.1826; found: 268.1814.

New Ligands for Regio- and Enantiocontrol in Pd-Catalyzed Allylic Alkylations

Roger Prétôt and Andreas Pfaltz*

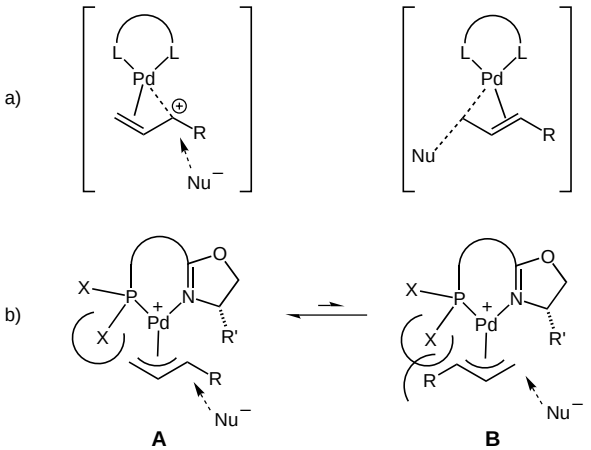
During the last few years dramatic progress has been made in the enantiocontrol of palladium-catalyzed allylic alkylations. New chiral ligands have been developed which can induce impressive levels of enantioselectivity in reactions with stabilized carbanions and various N-, O-, and S-nucleophiles.[1] However, the lack of regiocontrol is often a problem. For example, monosubstituted allylic substrates such as **1** and **2** (R = aryl) generally react predominantly at the unsubstituted allyl terminus (Scheme 1).[2] Consequently, the achiral, linear product **5** is formed rather than the chiral, branched isomer **4** or its enantiomer *ent*-**4**, which are the preferred products for applications in asymmetric synthesis. Although predominant formation of the branched isomers has been observed with achiral catalysts derived from other metals[3] (most notably W and Ir), the development of enantioselective catalysts for this class of substrate remains a challenge.



Scheme 1. Pd-catalyzed allylic alkylations generally produce the same products, regardless of whether substrate **1** or **2** is employed.

In 1995 we reported on the conversion of (*E*)-3-aryl-2-propenylphosphates **1** (R = aryl, X = OP(O)(OEt)$_2$) into chiral malonic acid derivatives **4** (Nu = CH(CO$_2$Me)$_2$).[4] High enantiomeric excesses and moderate to good regioselectivities were achieved with a tungsten catalyst prepared from the chiral (phosphanyloaryl)dihydrooxazole ligand **6a**[5] (see Scheme 3). The corresponding (*Z*) isomers and racemic substrates **2**, on the other hand, afford low enantioselectivities, in contrast with analogous Pd-catalyzed reactions, which generally proceed via rapidly equilibrating allyl intermediates and, therefore, in most cases give identical results with these three types of substrates.

Here we describe a new class of palladium catalysts that afford good enantio- and regioselectivities with both achiral and racemic aryl-substituted substrates **1** and **2**. The design of these catalysts was based on the following considerations: 1) Nucleophilic attack by an S_N2-type process should take place preferentially at the less substituted allyl terminus, whereas the opposite regioselectivity would be expected in an S_N1-like reaction via a cationic transition state (Scheme 2a).



Scheme 2. Nucleophilic attack in the Pd-catalyzed allylic alkylation. a) Transition states in S_N1- (left) and S_N2-like (right) processes. b) Steric encumbrance introduced by bulky substituents X on the P atom of the ligand favors attack of the substituted allyl terminus.

In order to enhance the S_N1 character, we decided to introduce electronegative substituents at the coordinating P atom that render the Pd center more electrophilic. 2) Steric factors affecting the equilibrium between allyl intermediates **A** and **B** also can play an important role (Scheme 2b). Bulky groups at the P atom are expected to destabilize isomer **B** as well as the transition states of the reaction pathways leading from **B** to the corresponding substitution products. Therefore, a pathway via **A** should be preferred and, assuming that nucleophilic attack at the allyl terminus *trans* to the Pd – P

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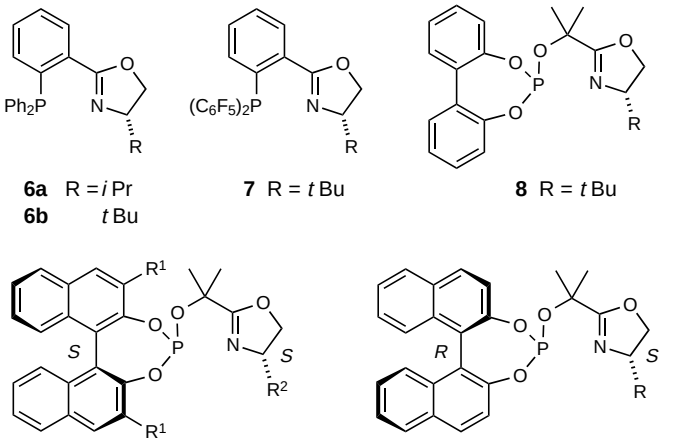
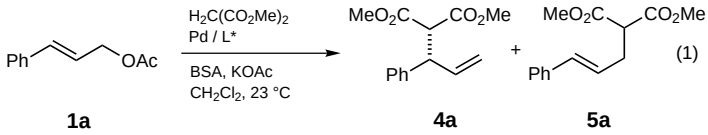
bond is electronically favored,[6] reaction at the substituted allyl end should be facilitated. Although there are certainly other factors affecting the regioselectivity, these straightforward concepts put us on the right track.

Replacement of the phenyl groups at the P atom of **6b** by electron-withdrawing pentafluorophenyl groups (→**7**, Scheme 3)[7] shifted the regioselectivity in the desired direction from 4:96 to 48:57 (Table 1). A similar effect was observed when ligand **8** was used, which has a biphenylphosphite group in place of the diphenylphosphane substituent.



6a R = *i* Pr
6b *t* Bu
7 R = *t* Bu
8 R = *t* Bu
9a R^1 = H R^2 = *t* Bu
9b H *i* Pr
9c H Ph
9d Me *t* Bu
10 R = *t* Bu

Scheme 3. Chiral ligands L* tested in the Pd-catalyzed allylic alkylation.



1a **4a** **5a**

Table 1. Results of enantioselective allylic alkylation [Eq. (1)] using different ligands L*.[a]

L*	Yield [%][b]	*ee* of **4a** [%][c]	**4a**:**5a**[d]
6b	90	78	4:96
7	87	84	47:53
8	75	81	63:37
9a	84	86	69:31
9a	86	90	76:24[e]
10	80	79	46:54
9b	92	77	68:32
9c	84	91	39:61
9d	88	92	55:45

[a] 1 mol% $[Pd(C_3H_5)Cl]_2$, 2.4 mol% L*, 50°C, CH_2Cl_2, 2 h; 2 equiv of $CH_2(CO_2Me)_2$ and *N*,*O*-bis(trimethylsilyl)acetamide (BSA), 4 mol% KOAc, 23°C, 18 h.[12] [b] Total yield of purified (*S*)-**4a** and (*E*)-**5a** after chromatography. [c] Determined by HPLC (Chiralcel OJ).[4] All reactions gave the (*S*)-(−) enantiomer. [d] Determined by GC analysis of the crude reaction mixture and ^{1}H NMR analysis after chromatography. [e] Reaction in benzene.

The regio- and enantioselectivities could be further improved by introduction of a second stereogenic unit derived from binaphthol. The best results were obtained with ligand (*S*,*S*)-**9a**; the (*R*,*S*) diastereomer **10**, derived from (*R*)-binaphthol, gave lower regio- and enantioselectivities. Apparently, the enantioselectivity is determined largely by the chiral dihydrooxazole ring. The chiral binaphthol unit has a minor, but still significant effect. The analogous isopropyldihydrooxazole ligand **9b** gave a somewhat lower *ee* value; the phenyldihydrooxazole ligand **9c**, on the other hand, was inferior in terms of regioselectivity. Introduction of two *ortho*-methyl groups in the binaphthol system (→**9d**) improved the enantioselectivity, but the regioselectivity decreased. The best results were achieved with ligand **9a** in benzene at 23°C (90% *ee*, **4a**:**5a** 76:24; Table 1) and in dichloromethane at −35°C (88% *ee*, 79:21).

Even better regio- and enantioselectivities were obtained with 1-naphthyl-substituted allylic acetates **1b** and **2b** (Table 2). The achiral substrates **1a**–**1c** afforded essentially the same regio- and enantioselectivities as the corresponding racemic isomers **2**. Apparently, the intermediate allyl complexes undergo rapid isomerization before they react with the nucleophile in the slower selectivity-determining step. The limitations of these catalysts become apparent with substrates **1d** and **2e**, which react with distinctly lower selectivities.

Table 2. Allylic alkylation of various substrates **1** and *rac*-**2** using ligand **9a** (Scheme 1; X = OAc, Nu = $CH(CO_2Me)_2$).[a]

	R	Yield [%][b]	*ee* of **4** [%][c]	**4**:**5**[d]
1b	1-naphthyl	87	94(*S*)	95:5
2b	1-naphthyl	91	96(*S*)	96:4
1c	2-naphthyl	72	88	77:23
2c	2-naphthyl	71	89	74:26
2a	phenyl	82	88(*S*)	66:34
1d	methyl	75	41[e]	30:70
2e	$(CH_3)_2C{=}CH$	72	51	75:25[f]

[a] For experimental conditions see Table 1. [b] Total yield of **4** and **5** after chromatography. [c] Determined by HPLC analysis (Chiralcel OJ and OD-H). Configurations of **4a** and **4b** were assigned by comparison to ref. [4]. [d] Determined by GC analysis of the crude reaction mixture and ^{1}H NMR analysis after chromatography. [e] Determined by GC analysis (Chiraldex G-TA). [f] Reaction in benzene.

A comparison of 3-phenyl-2-propenyl acetate **1a** with the corresponding *p*-methoxyphenyl- and *p*-cyanophenyl-2-propenyl acetates confirms that the regioselectivity is strongly affected by electronic factors. While the electron-donating *p*-methoxy substituent enhances the regioselectivity from 69:31 to 76:24 in favor of the chiral isomer (76% *ee*), the cyano group has the opposite effect, resulting in a reversed product ratio of 13:87 with the linear isomer **5** as the main product.

The synthesis of ligands **9** is straightforward (Scheme 4). Starting from various amino alcohols, hydroxy acids, and diols, a wide range of analogues can be readily prepared in this way. Libraries of ligands that are accessible by this route could be used to further optimize the selectivities obtained so far.

Our results demonstrate how the regioselectivity of allylic alkylations can be changed by systematic modification of the electronic and steric properties of the ligand attached to the

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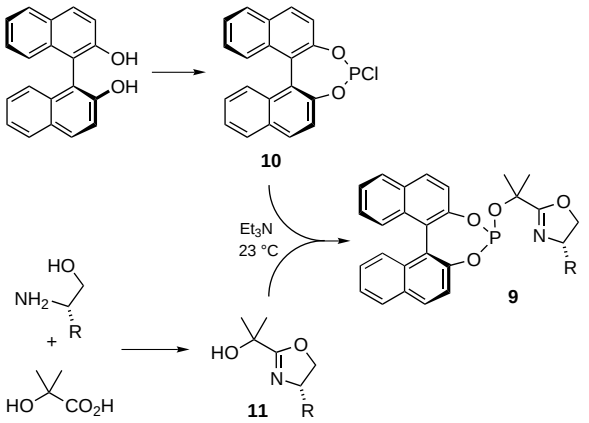

Scheme 4. Synthesis of ligands **9**. The preparation of compounds **10**[10] and **11**[11] is described elsewhere.

palladium catalyst. By using a new type of chiral P,N ligand, practically useful enantio- and regioselectivities have been obtained in the reaction with 1- and 3-aryl-2-propenyl acetates.[8] Although at present the range of substrates that afford good selectivities is limited to aryl-substituted derivatives, the concepts used for the design of ligands **9** may serve as guidelines for the development of new catalysts for different classes of substrates. In addition, these ligands have other possible applications in asymmetric catalysis.[9]

Experimental Section

9a: All reactions were performed under argon in degassed solvents. A solution of **10**[10] (1.1 g, 3.2 mmol) in toluene (10 mL) was added dropwise to Et_3N (2.6 g, 25.7 mmol) in toluene (20 mL) at $-78^\circ C$. This solution was stirred for 5 min at $-78^\circ C$ before a solution of **11**[11] (0.6 g, 3.2 mmol) in toluene (5 mL) was added quickly. The solution was allowed to gradually warm up to room temperature and stirred for 12 h. The white precipitate was removed by filtration. Evaporation of the solvent afforded a yellow oil, which was purified by column chromatography (silica gel, 3.0×20 cm; *n*-hexane/EtOAc 4/1, $R_f = 0.4$) to afford (*S*,*S*)-**9a** (890 mg, 56%) as an amorphous solid. $[\alpha]_{589} = +269$ ($CHCl_3$, $c = 3.1$, 23°C); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.96$ (s, 9H; *t*Bu), 1.65 (s, 3H; Me), 1.75 (s, 3H; Me), 3.95–4.00 (m, 1H; HCN), 4.20–4.35 (m, 2H; CH_2O), 7.22–7.52 (m, 8H; arom. CH), 7.89–7.96 (m, 4H; arom. CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 25.8$ (*t*Bu), 28.1 (d, $J = 7.9$ Hz; Me), 28.2 (d, $J = 5.7$ Hz; Me), 33.9 (*t*Bu), 69.7 (CH_2O), 75.7 (CHN), 77.2 (C), 121.9/122.4 (arom. CH), 123.2 (arom. C), 124.5 (d, $J =$ 3.1 Hz; arom. C), 124.6/124.8/125.8/126.0/126.9/127.0/128.1/128.2/129.3/130.0 (arom. CH), 131.1/131.4/132.7/132.8 (arom. C), 147.9 (d, $J = 2.3$ Hz; arom. C), 148.0 (d, $J = 3.7$ Hz; arom. C), 168.3 (C=N); ^{31}P NMR (100 MHz, $CDCl_3$): $\delta = 151.5$.

Catalytic reactions (Tables 1 and 2) were carried out according to the literature procedure.[12] Purification and analytical data of the products are described elsewhere.[3b, 4].

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Synthesis of a New Class of Solvent-Sensitive Fluorescent Labels

James J. La Clair*

Charge transfer (CT) labels such as 5-(dimethylamino)-naphthalene-1-sulfonyl (dansyl) chloride have been used extensively for the detection, characterization, and localization of carbohydrates, phospholipids, proteins, oligonucleotides, and numerous other synthetic and natural substances.[1] These materials typically experience shifts in their UV/Vis absorption and/or fluorescence bands depending on the nature of their solvent shells.[2] This effect together with modifications of fluorescence lifetimes, extent of intersystem crossing, and fluorescence quantum yield have encouraged

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