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Steric effects of the ligand in the enantioselective palladium-catalyzed allylic alkylation using chiral oxazolinylpyridines

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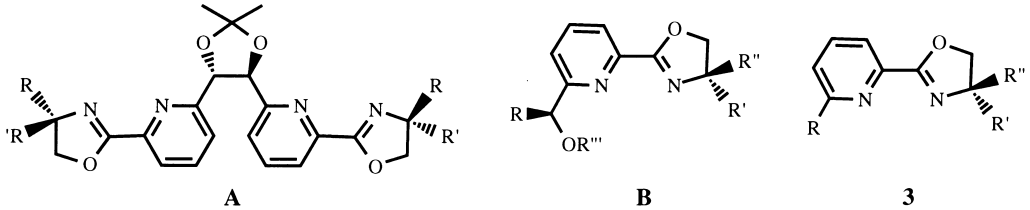
Abstract

Eight new chiral oxazolinylpyridines were prepared and assessed in the enantioselective palladium-catalyzed allylic substitution of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate. Catalytic activity and enantioselectivity were found to be highly dependent upon the steric requirement of the substituent on the pyridine ring: enantioselectivity up to 92% has been obtained. © 1999 Elsevier Science Ltd. All rights reserved.

1. Introduction

Recently, we and Moberg's group introduced the use of chiral oxazolinylpyridines as ligands for enantioselective palladium-catalyzed allylic substitutions,[1] obtaining nearly absolute enantiomeric excess in the alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate.[2,3] In both these studies oxazolinylpyridines with at least two stereocenters were used (A and B, Scheme 1).



A **B** **3**

Scheme 1.

More recently, we have prepared and assessed chiral oxazolinylpyridines in this catalytic process (3, Scheme 1) with a single stereocenter in the 4-position of the oxazoline ring.[4] This preliminary investigation stressed the dramatic effect on stereoselectivity of the reaction produced by the introduction of a methyl group in the 6-position of the pyridine. Thus, the low stereoselectivity (24% ee) obtained

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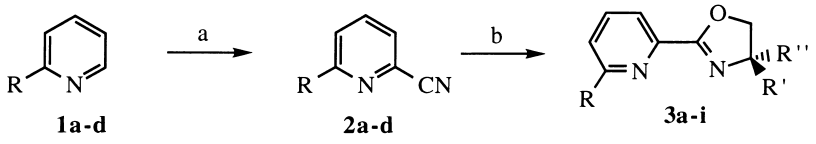
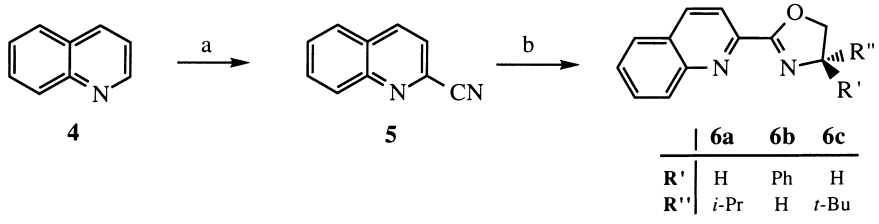
with 4-(isopropyl-2-oxazolinyl)pyridine **3a** (Scheme 2 and Table 1) increased to 70% with the use of the corresponding 6-methyl substituted **3c**.



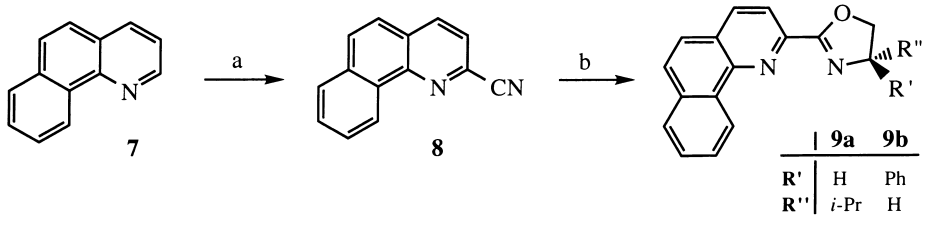
1a : R= H
1b: R= Me
1c R= *p*-Tol
1d: R= *t*-Bu

2a : R= H
2b: R= Me
2c : R= *p*-Tol
2d: R= *t*-Bu

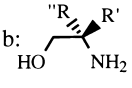
	3a	3b	3c	3d	3e	3f	3g	3h	3i
R	H	H	Me	Me	Me	Me	*p*-Tol	*p*-Tol	*t*-Bu
R'	H	Ph	H	Ph	H	H	H	Ph	H
R''	*i*-Pr	H	*i*-Pr	H	Bn	*t*-Bu	*i*-Pr	H	*i*-Pr



	6a	6b	6c
R'	H	Ph	H
R''	*i*-Pr	H	*t*-Bu



	9a	9b
R'	H	Ph
R''	*i*-Pr	H

a: MCPA, CH_2Cl_2, rt, 24 h then Me_3SiCN, Me_2NCOCl, CH_2Cl_2, rt, 6 d; b:  , $ZnCl_2$, C_6H_5Cl, reflux.

Scheme 2.

These observations prompted us to prepare new chiral oxazolinylpyridines with different substituents in the pyridine ring and in the 4-position of the oxazoline moiety in order to disclose their cross effects on the catalytic activity and stereoselectivity of the palladium-catalyzed asymmetric allylic alkylation.

2. Results and discussion

2.1. Synthesis of the ligands

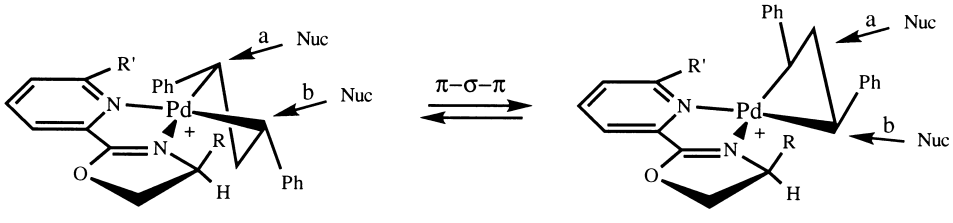
The synthesis of ligands started from cyanopyridines **2** and cyanoquinolines **5** and **8** which were obtained in good yields from the corresponding heterocycles following a conventional protocol. This required the oxidation of compounds **1**, **4**, and **7** with 3-chloroperbenzoic acid in CH_2Cl_2 at room temperature for 24 h and then treatment of the obtained oxide with dimethylcarbamyl chloride and trimethylsilylcyanide in CH_2Cl_2 at room temperature for 6 days.[5] Oxazolinylpyridines **3**, **6** and **9** were

obtained in 22–76% yields by heating a chlorobenzene solution of cyanoderivatives **2**, **5**, **8** under reflux with the appropriate aminoalcohol in the presence of a catalytic amount of zinc chloride[6] (Scheme 2).

2.2. Palladium-catalyzed allylic alkylation

Allylic substitutions were carried out employing Trost's procedure which used $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ as procatalyst and a mixture of dimethyl malonate, *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and potassium acetate.[7] The reactions were carried out in methylene chloride at room temperature and at reflux temperature when the ligand provided an insufficiently reactive palladium catalyst. The results obtained under control of the new ligands are summarized in Table 1 from which the following considerations can be made: (i) the enantioselectivity of the substitution reaction increases in the series of ligands **3a**, **3b** (entries 1, 7), **3e**, **3c**, **3d**, **3f** (entries 11, 2, 8, 12) and **6a**–**6c** (entries 13–15) containing the same substituent in the pyridine ring and substituents of increasing steric bulk in the oxazoline moiety; (ii) the enantioselectivity of the substitution reaction increases in the two groups of ligands **3a**, **3c** (entries 1, 2), **3b**, **3d** (entries 7, 8), **3a**, **6a** (entries 1, 13), and **3b**, **3d** (entries 7, 8) containing the same substituent in the oxazoline ring and in which a methyl group or a benzo-fused ring replace the hydrogen atom in the 6-position of the pyridine ring; (iii) the introduction of a bulk substituent in the 6-position of the pyridine ring is detrimental for the catalytic activity; this effect is independent of the substituent in the oxazoline ring. With some of these unreactive ligands (**3g**, **3h**) the reaction carried out at reflux temperature (40°C) gives total conversion of the starting material in less than 14 h and a surprisingly high level of enantioselectivity (entry 3 versus 4 and entry 9 versus 10).

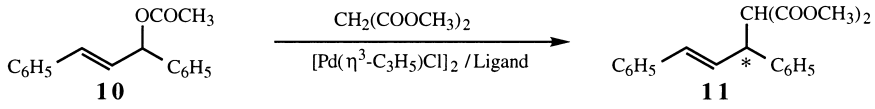
The obtained results can be explained as follows. The accepted mechanism for palladium-catalyzed allylic substitutions which proceed through a meso η^3-allyl intermediate, foresees that the nucleophile attacks the allylic termini of two alternative diastereomeric π-allyl palladium complexes (for instance **12** and **13** for ligands with (*S*) configuration). As a consequence, there are in principle four reaction pathways, of which two lead to the preferred product of (*S*) configuration (a in **12** and b in **13**) and the remainder to the other enantiomer. The regioselectivity and stereoselectivity of the nucleophilic attack are determined by the steric and electronic properties of the ligand but in this case, since the two ligand nitrogens are electronically very similar, only steric factors should be considered.[8]



12 **13**

The two diastereomeric π-allyl palladium complexes **12** and **13** which interconvert through a π–σ–π mechanism, are present at the equilibrium in a different ratio. Of the two, **12** should be more stable than **13** on account of the steric repulsion in this diastereomer between the phenyl group of the π-allyl moiety and the substituent on the oxazoline ring. Moreover, the percentage of the sterically favoured diastereomer **12** would increase for those ligands with a bulkier substituent than hydrogen in the 6-position of the pyridine ring. In fact, in both diastereomers **12** and **13**, interaction of the pyridine bulky group with the phenyl group of the π-allyl moiety forces the other phenyl group against the substituent in the oxazoline, but this effect is more relevant in diastereomer **13** than **12**. The stereochemical outcome implys that the nucleophile predominantly attacks the allylic terminus *trans* to the oxazoline nitrogen in the preferred

Table 1
Allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate[a]



10 **11**

Entry	Ligand	Temperature	React. time, h	Conv.[b]	Yield[c]	% Ee[d]	Conf.[e]
1	**3a**	r.t.	1	100	84	24	S[f]
2	**3c**	r.t.	2	100	93	70	S
3	**3g**	r.t.	48	trace	-	-	-
4	**3g**	reflux	14	100	81	60	S
5	**3i**	r.t.	168	-	-	-	-
6	**3i**	reflux	96	trace	n.d.	n.d.	-
7	**3b**	r.t.	2.5	100	86	55	R[f]
8	**3d**	r.t.	4.5	100	81	74	R[f]
9	**3h**	r.t.	168	trace	-	-	-
10	**3h**	reflux	3	100	77	70	R[f]
11	**3e**	r.t.	7.5	100	88	62	S[f]
12	**3f**	r.t.	2.3	100	92	91	S[f]
13	**6a**	r.t.	4.5	100	88	62	S
14	**6b**	r.t.	15	100	85	68	R
15	**6c**	r.t.	17	100	93	92	S
16	**9a**	r.t.	168	22	n.d.	28	R
17	**9b**	r.t.	168	trace	n.d.	n.d.	-

[a]Reaction of the ligand (10 mol %) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2.5 mol %) with 1,3-diphenylprop-2-enyl acetate (0.4 mmol), $CH_2(COOMe)_2$ (1.2 mmol), N,O-bis(trimethylsilyl)acetamide (BSA) (1.2 mmol) and KOAc (3.5 % mol) in CH_2Cl_2 (2 ml) at room or reflux temperature. [b]Determined by ^{1}H-NMR of the crude reaction mixture. [c]Isolated yields. [d]Determined by ^{1}H-NMR using $Eu(hfc)_3$ as chiral shift reagent. [e]The assignement is based on the sign of the optical rotation: Leutenegger, U.; Umbricht, G.; Fahrni, C.; Matt, P.V.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143. [f]These data are taken from ref. 4

(major) diastereomer (a in **12**) or *cis* in the less stable (b in **13**). We prefer the former explanation for a variety of reasons. Firstly, the increase of the product enantioselection is parallel to the increase of the steric bulk of the substituent in the oxazoline moiety which in turn stabilizes conformation **12**. Further improvement of the stereoselectivity obtained with the ligands bearing a substituent in the pyridine ring is closely related to an increase in the percentage of the diastereomer **12**. These results comply with the observation that the reaction product comes from the most abundant complex.[9] Secondly, reaction rate of the alkylation is inversely proportional to both the improvement of the percentage of diastereomer **12** and the enantioselection. This effect is more important when changing the substituent in the pyridine (**3c** versus **3g**; **3d** versus **3h**) than in the oxazoline moiety (**3c** versus **3d**; **3d** versus **3f**). This agrees with the supposition that the diastereomer is preferentially attacked by the nucleophile, obviously taking into account that the equilibration of isomeric complexes **12** and **13** is faster than the nucleophilic attack on the complex.[10] Thirdly, if the reaction proceeds through a nucleophilic attack to the allylic terminus *cis* to the oxazoline nitrogen of the less stable intermediate (b in **13**) and perhaps the more reactive, the reaction rate would be faster as the destabilization of this species becomes higher and higher. In fact, taking into account the rapid equilibration of isomeric complexes **12** and **13**, the reduction of the steric strain correlated to the cleavage of this Pd–C bond would not only lead to an improvement of the stereodifferentiation but also to a faster reaction rate. If so, in the series of ligands **3a**, **3c** (entries 1, 2), **3b**, **3d** (entries 7, 8), **3a**, **6a** (entries 1, 13) and **3b**, **3e** (entries 7, 11) the reaction rate would be faster for

the latter. Instead, experimental data shows that the former react quicker, thus indicating that this is not the preferred pathway for the enantioselection.

Finally, it should be noted that using unreactive ligands, reactions carried out at 40°C gave unexpectedly high levels of enantiodifferentiation and, since the prevailing configuration of the products was the same as expected by the configuration of the oxazoline stereocenter, it is reasonable to assume that in this case also the transition states are the same as those observed previously.

3. Conclusions

The catalytic activity and stereoselectivity in the palladium-catalyzed allylic substitution of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate using simple chiral oxazolinylpyridines as ligands was found highly dependent upon the steric requirements of the substituents both in the pyridine and in the oxazoline ring. The cross-effects reach the best compromize in oxazolinylpyridine **6c** bearing the *t*-butyl group in the oxazoline and a benzo-fused ring in the pyridine with which a 92% ee have been obtained. The stereochemical results have been rationalized on the basis of considerations concerning the transition states and the related reaction rates.

We now address our efforts to prepare chiral oxazolinylpyridines bearing electron-donating and withdrawing groups in the pyridine ring in order to optimize their use in this asymmetric process.

4. Experimental

4.1. General methods

Boiling points are uncorrected. Melting points were determined on a Buchi 510 capillary apparatus and are uncorrected. The ^{1}H NMR (300 MHz) spectra were obtained with a Varian VXR-300 spectrometer. Optical rotations were measured with a Perkin–Elmer 241 polarimeter in a 1 dm tube. Elemental analyses were performed on a Perkin–Elmer 240 B analyser.

4.2. Starting material

2-[4,5-Dihydro-4-(1-methylethyl)oxazol-2-yl]pyridine **3a** and 2-(4,5-dihydro-4-phenyloxazol-2-yl)-pyridine **3b** were prepared following a literature procedure.[11] 2-[4,5-Dihydro-4-(1-methylethyl)oxazol-2-yl]-6-methylpyridine **3c**, 2-[4,5-dihydro-4-phenyloxazol-2-yl)]-6-methylpyridine **3d**, 2-[4,5-dihydro-4-phenylmethyloxazol-2-yl]-6-methylpyridine **3e**, and 2-[4,5-dihydro-4-(1,1-dimethylethyl)oxazol-2-yl]-6-methylpyridine **3f** were prepared according to Chelucci et al.[4] 2-Quinolinecarbonitrile **5** was purchased from Aldrich A.G.

2-Cyano-6-(4-methylphenyl)pyridine **2c**, 2-cyano-6-(1,1-dimethylethyl)pyridine[12] **2d** and 2-cyano-benzo[*h*]quinoline **8**[13] were synthesized in good yields following a general procedure from 2-(4-methylphenyl)pyridine **1c**, 2-(1,1-dimethylethyl)pyridine **1d** and benzo[*h*]quinoline **7**, respectively. This procedure requires the oxidation of **1**, **4**, and **7** with 3-chloroperbenzoic acid in CH_2Cl_2 at room temperature for 24 h[2] and then treatment with the obtained oxide, dimethylcarbamyl chloride and trimethylsilylcyanide in CH_2Cl_2 at room temperature for 6 days.[5] Compound **2c**, bp 115°C (1 mmHg); ^{1}H NMR ($CDCl_3$) δ: 7.92 (m, 3H), 7.85 (dd, 1H, J=8.4, 7.2 Hz), 7.58 (dd, 1H, J=7.2, 0.9), 7.30 (d, 2H,

J=8.1 Hz), 2.42 (s, 3H). Compound **2d**, mp 144–146°C; ^{1}H NMR ($CDCl_3$) δ: 7.83 (t, 1H, J=7.8 Hz), 7.69 (d, 1H, J=8.4 Hz), 7.55 (d, 1H, J=7.5 Hz), 1.37 (s, 9H).

4.3. General procedure for the preparation of oxazolinylpyridines

In a 25 ml two-necked flask, zinc chloride (14 mg, 0.10 mmol) was melted under high vacuum and cooled under argon. After cooling to room temperature, chlorobenzene (30 ml) was added followed by the nitrile (2 mmol) and the amino alcohol (2.5 mmol). The resulting mixture was heated under reflux for the appropriate time (vide infra) and then the solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (6 ml) and the resulting solution was washed with water (3×4 ml). The aqueous solution was extracted with CH_2Cl_2 (6 ml), the combined organic phases dried over anhydrous Na_2SO_4 and the solvent evaporated. The residue was purified by chromatography on a silica gel column with the indicated eluent.

*4.3.1. (S)-2-[4,5-Dihydro-4-(1-methylethyl)oxazol-2-yl)]-6-(4-methylphenyl)pyridine **3g***

Reaction time: 48 h; chromatographic eluent: benzene:acetone=8:2; 0.358 g (64%); mp 88–90°C; $[\alpha]_D^{25}$ −56.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.98 (t, 1H, J=4.1 Hz); 7.94 (d, 2H, J=8.4 Hz), 7.74 (dd, 2H, J=5.1, 1.5 Hz), 7.25 (d, 2H, J=7.2 Hz), 4.50 (t, 1H, J=8.5 Hz), 4.25–4.11 (m, 2H), 2.37 (s, 3H, CH_3), 1.89 (m, 1H), 1.05 (d, 3H, J=6.9), 0.94 (d, 3H, J=6.9 Hz). Anal. calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.31; H, 7.05; N, 9.96.

*4.3.2. (R)-2-(4,5-Dihydro-4-phenyloxazol-2-yl)-6-(4-methylphenyl)pyridine **3h***

Reaction time: 32 h; chromatographic eluent: benzene:acetone=2:1; 0.333 g (53%); mp 99–100°C; $[\alpha]_D^{25}$ +91.62 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.11 (t, 1H, J=4.5 Hz), 7.97 (d, 2H, J=7.8 Hz), 7.84 (d, 2H, J=4.5), 7.43–7.26 (m, 7H), 5.48 (dd, 1H, J=9.6, 9.0 Hz), 4.93 (dd, 1H, J=9.6, 9.0 Hz), 4.42 (t, 1H, J=8.7 Hz), 2.41 (s, 3H, CH_3). Anal. calcd for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91. Found: C, 80.42; H, 5.69; N, 8.89

*4.3.3. (S)-2-[4,5-Dihydro-4-(1-methylethyl)oxazol-2-yl]-6-(1,1-dimethylethyl)pyridine **3i***

Reaction time: 48 h; chromatographic eluent: benzene:acetone=9:1; 0.130 g (27%); oil; $[\alpha]_D^{25}$ −55.8 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.95 (d, 1H, J=7.7 Hz), 7.76 (t, 1H, J=7.8 Hz), 7.48 (d, 1H, J=7.8 Hz), 4.51 (dd, 1H, J=8.1, 0.9 Hz), 4.26–4.10 (m, 2H), 1.89 (m, 1H), 1.05 (d, 3H, J=6.9), 0.94 (d, 3H, J=6.9 Hz),1.38 (s, 9H, *t*-but). Anal. calcd for $C_{15}H_{22}N_2O$: C, 73.13; H, 9.00; N, 11.37. Found: C, 73.10; H,9.08 N,11.40.

*4.3.4. (S)-2-[4,5-Dihydro-4-(1-methylethyl)oxazol-2-yl]quinoline **6a***

Reaction time: 48 h; chromatographic eluent: benzene:acetone=8:2; 0.290 g (61%); mp 75–76°C; $[\alpha]_D^{25}$ −67.3 (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.28 (d, 1H, J=8.4 Hz), 8.23 (s, 2H), 7.85 (d, 1H, J=8.1 Hz), 7.75 (dt, 1H, J=7.2, 1.2 Hz), 7.60 (dt, 1H, J=7.6, 0.9 Hz), 4.60 (dd, 1H, J=9.3, 8.1 Hz), 4.35–4.17 (m, 2H), 1.94 (m, 1H), 1.09 (d, 3H, J=6.9 Hz), 0.98 (d, 3H, J=6.6 Hz). Anal. calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.91; H, 6.65; N, 11.58.

*4.3.5. (R)-2-(4,5-Dihydro-4-phenyloxazol-2-yl)quinoline **6b***

Reaction time: 31 h; chromatographic eluent: benzene:acetone=8:2; 0.120 g (22%); mp 141–143°C; $[\alpha]_D^{25}$ +144.7 (*c* 1.3 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.32–8.23 (m, 3H), 7.87 (d, 1H, J=8.1 Hz), 7.78 (dt, 1H, J=8.2, 1.2 Hz), 7.63 (t, 1H, J=7.5 Hz), 7.41–7.24 (m, 5H), 5.52 (dd, 1H, J=9.9, 8.4 Hz), 4.99 (dd, 1H,

J=10.2, 8.4 Hz), 4.48 (t, 1H, J=8.4 Hz). Anal. calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.61; H, 5.05; N, 10.46.

*4.3.6. (*S*)-2-[4,5-Dihydro-4-(1,1-dimethylethyl)oxazol-2-yl]quinoline* ***6c***

Reaction time: 24 h; chromatographic eluent: benzene:acetone=8:2; 0.384 g (76%); mp 92–93°C; $[\alpha]_D^{25}$ −116.5 (*c* 1.2 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.30–8.20 (m, 3H); 7.85 (d, 1H, J=9 Hz); 7.75 (dt, 1H, J=7.5, 0.6 Hz), 7.60 (t, 1H, J=7.5 Hz), 4.55 (dd, 1H, J=9.9, 9.0 Hz), 4.40 (dd, 1H, J=8.7, 8.4 Hz), 4.19 (dd, 1H, J=10.2, 8.4 Hz), 1.01 (s, H, *t*-but). Anal. calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.61; H, 7.11; N, 10.98.

*4.3.7. (*S*)-2-[4,5-Dihydro-4-(1-methylethyl)oxazol-2-yl]benzo[*h*]quinoline* ***9a***

Reaction time: 72 h; chromatographic eluent: benzene:acetone=8:2 and then benzene:acetone=9.5:0.5; 0.40 g (69%); mp 102–103°C; $[\alpha]_D^{25}$ −87.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 9.40 (d, 1H, J=8.1 Hz); 8.28 (d, 1H, J=8.1 Hz); 8.11 (d, 1H, J=8.4 Hz); 7.81 (d, 1H, J=8.1), 7.76–7.60 (m, 3H), 7.55 (d, 1H, J=9.0), 4.59 (dd, 1H, J=9.0, 7.8 Hz), 4.33–4.18 (m, 2H), 1.93 (m, 1H), 1.10 (d, 3H, J=6.6 Hz, CH_3), 0.97 (d, 3H, J=6.6, CH_3). Anal. calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.65; H, 6.21; N,9.70.

*4.3.8. (*R*)-2-(4,5-Dihydro-4-phenyloxazol-2-yl)benzo[*h*]quinoline* ***9b***

Reaction time: 96 h; chromatographic eluent: benzene:acetone=8:2; 0.447 g (58%); mp 148°C; $[\alpha]_D^{25}$ +5.93 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 9.42 (d, 1H, J=8.7 Hz); 8.42 (d, 1H, J=8.4 Hz), 8.26 (d, 1H, J=8.4 Hz), 7.90 (m, 2H), 7.74 (m, 3H), 7.37 (m, 5H), 5.54 (dd, 1H, J=10.2, 8.7 Hz), 5.02 (dd, 1H, J=9.9, 8.7 Hz), 4,50 (t, 1H, J=8.4 Hz). Anal. calcd for $C_{22}H_{16}N_2O$: C, 81.46; H, 4.97; N, 8.64. Found: C, 81.40; H, 5.01; N, 8.61.

4.4. Allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethyl malonate: general procedure

A solution of ligand (0.04 mmol, 10 mol%) and $[\{Pd(\eta^3\text{-}C_3H_5)Cl\}_2]$ (4 mg, 2.5 mol%) in dry CH_2Cl_2 (2 ml) was stirred at room temperature for 15 min. This solution was treated successively with a solution of *rac*-(*E*)-1,3-diphenyl-2-propenyl acetate (0.4 mmol) in CH_2Cl_2 (1 ml), dimethyl malonate (1.2 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (1.2 mmol) and anhydrous potassium acetate (3.5 mol%). The reaction mixture was stirred at room or reflux temperature for the appropriate time (see Table 1) until conversion was complete as shown by TLC analysis (light petroleum:ether, 3:1). The reaction mixture was diluted with ether (25 ml) then washed with ice-cold saturated aqueous ammonium chloride. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography (light petroleum:ether, 3:1) to afford dimethyl 1,3-diphenylprop-2-enylmalonate. The enantiomeric excess was determined from the ^{1}H NMR spectrum in the presence of enantiomerically pure shift reagent Eu(hfc)$_3$; splitting of the signals for one of the two methoxy groups was observed.

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