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Chiral thienylpyridines as *N–S* ligands for asymmetric catalysis Palladium-catalyzed allylic alkylation and copper-catalyzed cyclopropanation reactions

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Abstract

Diastereomeric pure thienylpyridines were prepared and assessed in the enantioselective palladium-catalyzed allylic substitution of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate and copper-catalyzed cyclopropanation of styrene with ethyl diazoacetate. These ligands provided unreactive palladium catalysts but effective copper catalysts affording however low enantioexcesses.

Keywords: Chiral thienylpyridines; Palladium complex; Copper complex; Allylic substitution; Cyclopropanation; Enantioselectivity

1. Introduction

Since the design of chiral ligands plays a key role in the development of enantioselective reactions, many recent studies have been addressed on the development of novel chiral ligands for metal-catalyzed reactions [1,2].

Although thiophene is known to form complexes with a variety of metals [3,4], few attempts have been made to employ chiral thiophene derivatives as ligands for asymmetric catalysis. The most representative examples are those in which the thiophene sulphur is one of the donor atoms in bidentate or terdentate ligands such as thienyloxazolines **1**–**3** (Scheme 1) [5–7] (for other examples, see [8,9]).

Since it has been recently described an effective procedure for obtaining chiral thienylpyridines from naturally occurring monoterpenes [10], making available a new class of chiral ligands, we have now been intrigued to explore their potentiality as chiral controllers for asymmetric catalysis.

Here we report the synthesis of some new chiral thienylpyridines and the results obtained with this kind of ligands in two reactions frequently investigated as a probe for the effectiveness of new ligands, namely, the palladium-catalyzed allylic substitution of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate [11,12] and the copper-catalyzed cyclopropanation of styrene with ethyl diazoacetate [13].

2. Results and discussion

2.1. Synthesis of the ligands

We initially prepared the thienylpyridines **7** [10] and **8** [10] following the Kröhnke methodology [14] which demanded the reaction of the

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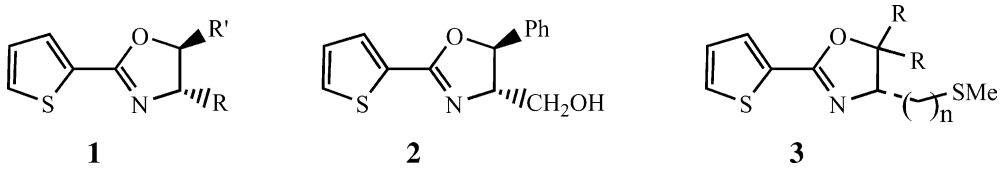
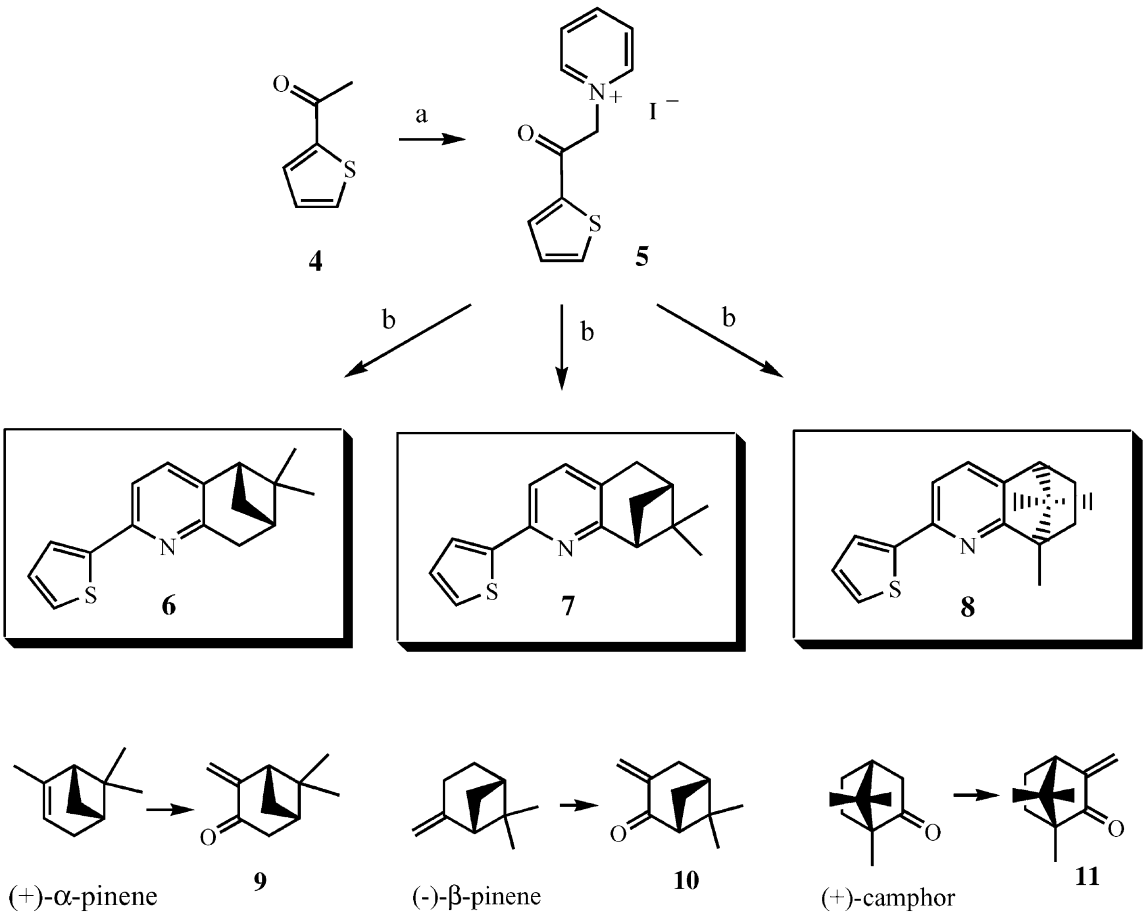


1 **2** **3**

Scheme 1.

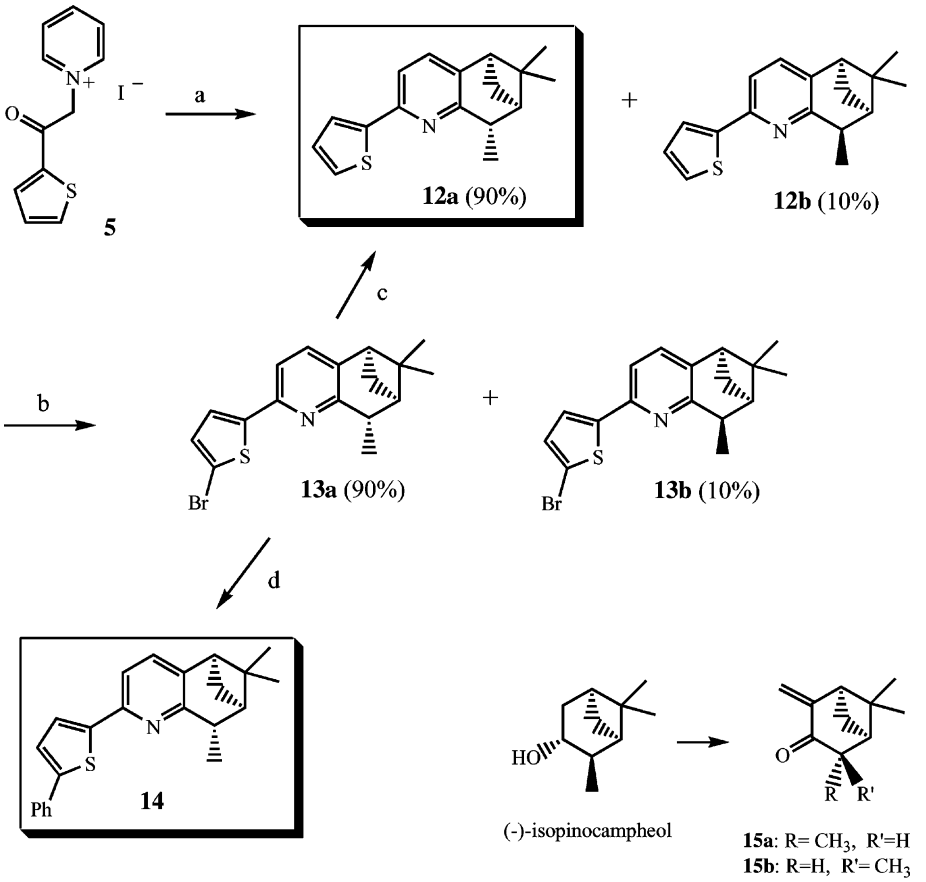
N-[2-oxo-(2-thienyl)ethyl]pyridinium iodide (**5**) [15] with the α-methylene ketones **10** and **11**. These were prepared from (−)-β-pinene [16] and (+)-camphor [10], respectively (Scheme 1). We next get ready, following this protocol, the new thienylpyridines **6** and **12** from the unsaturated ketones **9** and **15** obtained from (+)-α-pinene [10] and (+)-isopinocampheol [17], respectively (Schemes 2 and 3).

Thienylpyridines **6**–**8** were obtained as single diastereomers, while the thienylpyridine **12** was acquired



a: pyridine, I_2, reflux, 1.5 h; b: **9** or **10** or **11**, AcOH, $AcONH_4$, 120-140°C, 4-20h.

Scheme 2.



a: **15a** + **15b** in a 85/15 ratio, AcOH, $AcONH_4$, 120 °C, 4 h, 20%; b: Br_2, AcOH, reflux, 1h, 92%, then chromatographic separation; c: *n*-BuLi, Et_2O, -78 °C then AcOH, 100%; d: $PhB(OH)_2$, $Pd(PPh_3)_4$, DME, aqueous Na_2CO_3, 92%.

Scheme 3.

as a 9:1 mixture of epimers at the C8 of the tetrahydroquinoline ring (**12a** and **12b** in Scheme 3). This ratio was very close to that of the α-methylene ketone **15** [17] used as starting material (**15a** and **15b** in Scheme 2) as in the cyclization step the expected epimerization at the C8 in favour of the most stable diastereomer **12a** occurred only partially.

Since chromatographic separation of **12a** and **12b** was proven to be very problematic, precluding the effective isolation of the major diastereomer **12a**, we decided to follow an alternative approach. The mixture of **12a** and **12b** was treated with bromine in acetic acid to give almost quantitative yield a mixture of 5-bromothiophenes **13a** and **13b**. Fortunately, in this case the most abundant isomer **13a** was easily isolated by flash chromatography. The availability of diasteromeric pure **13a** opened a route to the parent thienylpyridine **12a**. Thus, halogen-metal exchange of **13a** with *n*-butyllithium, followed by treatment with aqueous acetic acid produced **12a** in 100% yield.

Moreover, the access to **13a** allowed to complete our program on the synthesis of thienylpyridines, namely the synthesis of a ligand with a substituent on the 5-position of the thiophene ring.

This aim stemmed from the consideration that in the case of chiral C1-symmetric bidentate ligands such as oxazolinylpyridines the presence of a substituent close to donor atom of the heterocycle not containing the chiral framework effects both catalytic activity and stereoselectivity of some asymmetric processes [18–21].

Thus, palladium(0)-catalyzed cross-coupling of bromothiophene **13a** with phenylboronic acid afforded the 5-phenylthiophene **14** in very high yield (Scheme 3).

2.2. Palladium-catalyzed allylic alkylation

Enantioselective reactions based on palladium-catalyzed allylic substitutions are currently an actively pursued research area [11,12]. In contrast to the great variety of ligands based on the pyridine framework, which have proven to give very good levels of enantioselectivity in the catalyzed asymmetric C–C bond forming reactions with allylic compounds [22], rare examples of application in this reaction of sulphur-containing pyridine ligands have been reported [23–27]. In order to define the scope and limitations of thienylpyridines as chiral controllers for asymmetric catalysis, we have first examined these *N*–*S* ligands in the enantioselective palladium catalysed allylic substitution of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate, which serve as model substrate and reagent to compare the outcome of different ligands.

Allylic substitution of *rac*-1,3-diphenylprop-2-enyl acetate was initially performed in CH_2Cl_2 at room temperature in the presence of (π-allyl)palladium-ligand complex generated in situ from 2.5 mol% of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and 10 mol% of the appropriate ligand (Scheme 4). The nucleophile was generated employing Trost's procedure which entails the use of dimethyl malonate in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and a catalytic amount of potassium acetate [28]. The reactions were run for 2 weeks. This reaction time was fixed as the time limit useful to compare the outcome of all ligands.

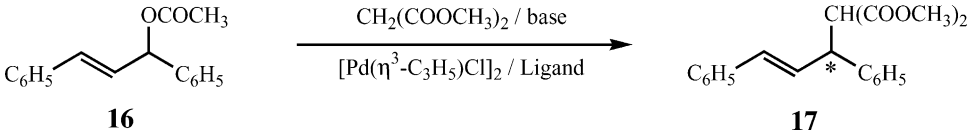
Under these conditions, thienylpyridines provided insufficiently reactive palladium catalysts affording only a very low conversion of the starting material (5–10%).

Though the protocol using the malonate anion obtained by Trost's procedure is generally the best way to carry out allylic substitution reactions, the use of preformed sodium dimethyl malonate, generated by the use of sodium hydride in THF, may in some cases offer best results [29]. Therefore, ligand **6** was employed to test the effectiveness of this procedure. Also under these conditions the reaction failed at room temperature, but partial conversion (53%) occurred after 4 days at reflux temperature. However, the reaction was not enantioselective.

The results obtained with thienylpyridines were rather disappointed in account of the satisfactory catalytic activity and good levels of asymmetric induction imparted in the palladium catalysed allylic substitution reaction by the related thienyloxazoline ligand **1** [5]. We were wondering whether the unexpected results could be ascribed to the possibility that the thienylpyridine behaves as a monodentate ligand binding to the palladium by the pyridine-*N* (in this case two molecules bind to the palladium by the pyridine-*N*) rather than as a bidentate ligand by the thiophene-*S* and pyridine-*N*.

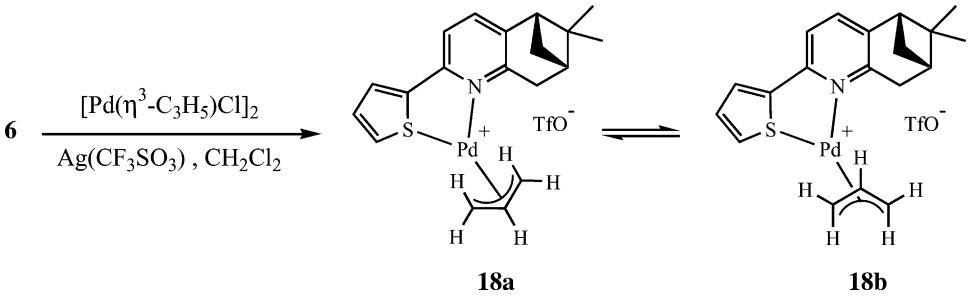
In order to obtain some information about the structure of the cationic palladium(II)-thienylpyridine complex, ligand **6** was treated with η^3-allylpalladium chloride dimer in the presence of $Ag(CF_3SO_3)$ in dichloromethane. The palladium complex **18** (Scheme 5) was obtained in high yield as white foamy solid. Since all attempts to crystallize it failed, structural assignment of this complex was performed by ^1H and ^{13}C NMR analysis.

Integration of the ^1H NMR spectrum indicated that there is one thienylpyridine molecule per allylpalladium complex fragment. The ^1H NMR spectrum of

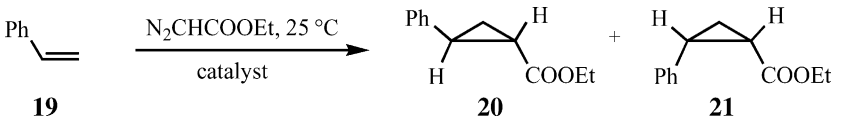


16 **17**

Scheme 4.



Scheme 5.



Scheme 6.

the complex showed that the resonances of both the pyridine and thiophene protons are shifted downfield with respect to those of the thienylpyridine itself. Coordination of the sp^2-hybridized electrons pair of the pyridine-*N* and thiophene-*S* causes a reduction of charge density on both the heterocycles determining the down field shift of ^{1}H NMR signals. Moreover, the spectrum of **18** showed the presence of a single diastereomer indicating that chemical exchange of the protons (**18a** $\rightleftharpoons$ **18b**) of the η^3-allyl moiety occurs quickly at room temperature.

Though these observations are consistent with a structure for the intermediate π-allyl palladium complex in which both pyridine and thiophene are coordinated to the palladium, at present the reasons why these ligands do not work in this catalytic process are obscure.

2.3. Copper-catalyzed cyclopropanation

To evaluate the efficiency of these ligands in the copper-catalyzed asymmetric cyclopropanation, we first examined the cyclopropanation of styrene using copper(II)-thienylpyridine catalysts prepared in situ from copper(II) triflate and the proper ligand. The reaction was carried out at room temperature by slow addition (2 h) of ethyl diazoacetate to a solution of styrene in CH_2Cl_2 containing the copper(II)-ligand adduct which was previously activated by stirring with a few equivalents of ethyl diazoacetate (Scheme 6). The results obtained in these runs are summarized in Table 1.

The copper(II)-thienylpyridine complexes exhibited high efficiency and afforded the *trans*- and *cis*-cyclopropanes **20** and **21** in good yields (83–93%). These diastereomeric cyclopropanes were however obtained with low *trans*:*cis* diastereoselectivity (about 65:35) and they did not show significant enantioexcesses (3–8%).

Then, we assessed thienylpyridines in the copper(I)-catalyzed asymmetric cyclopropanation of styrene.

Table 1
Enantioselective cyclopropanation of styrene with ethyl diazoacetate using $Cu(OTf)_2$[a]

Ligand	Yield[b] (%) (**20** + **21**)	*trans*:*cis*[c] (**20**:**21**)	% ee[c]	
			20	**21**
6	91	70:30	6	3
7	90	66:34	4	3
8	95	69:31	7	5
12a	83	68:32	5	3
14	93	65:35	8	5

[a] The ligand (35 μmol) in CH_2Cl_2 (1.5 ml) was added to a suspension of $Cu(OTf)_2$ (11.4 mg, 31 μmol) in CH_2Cl_2 (1.5 ml). After 2 h styrene (0.715 ml, 6.25 mmol) and ethyl diazoacetate (0.315 mmol) were added. After 30 min ethyl diazoacetate (2.5 mmol) in CH_2Cl_2 (2.5 ml) was added dropwise over a period of 2 h and then the mixture was stirred for 16 h.

[b] Isolated yield, based on the diazoacetate, for the mixture of *trans*- and *cis*-cyclopropanes.

[c] Determined by GC analysis on a chiral column.

Table 2
Enantioselective cyclopropanation of styrene with ethyl diazoacetate using Cu(OTf)[a]

Ligand	Yield[b] (%) (**20** + **21**)	*trans*:*cis*[c] (**20**:**21**)	% ee[c]	
			20	**21**
6	93	67:33	5	3
7	81	69:31	7	2
8	90	69:31	10	7
12a	91	68:32	8	5
14	79	69:31	6	3

[a] The ligand (34 μmol) in CH_2Cl_2 (2.5 ml) was added to a suspension of [Cu(OTf)(C_6H_6)0.5] (8 mg, 32 μmol) in CH_2Cl_2 (2.5 ml). After 30 min, the mixture was filtered through packed adsorbent cotton under argon and styrene (1.59 ml, 13.87 mmol) was added to the filtrate. Ethyl diazoacetate (2.5 mmol) in CH_2Cl_2 (2.5 ml) was added dropwise over a period of 2 h and then the mixture was stirred for 16 h.

[b] Isolated yield, based on the diazoacetate, for the mixture of *trans*- and *cis*-cyclopropanes.

[c] Determined by GC analysis on a chiral column.

The reaction was carried out at room temperature by slow addition (2 h) of ethyl diazoacetate to a solution of styrene in CH_2Cl_2 containing the copper(I)-ligand catalyst prepared in situ from copper(I) triflate and the ligand. The results obtained are reported in Table 2. The substitution of copper(II)-complexes with those of copper(I) did not change substantially neither yields, nor diastereoselectivities and enantioselectivities.

In conclusion, we have reported the synthesis of some new chiral thienylpyridines starting from compounds originating from the chiral pool and assessed their potentiality as chiral ligands for asymmetric catalysis.

The results reported in this paper demonstrate that thienylpyridines are poorly suitable catalysts for the enantioselective palladium-catalyzed allylic substitution. On the contrary, these ligands are good catalysts for the Cu-catalyzed cyclopropanation of styrene giving high yield of cyclopropanes though with low enantioexcesses.

3. Experimental

3.1. 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) and ^{13}H NMR (75.4 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. Gas chromatographic analyses were performed with a HP 5900 chromatograph using He (60 kPa) as the carrier gas. *N*-[2-Oxo-(2-thienyl)ethyl]pyridinium iodide **5** [15] was obtained according to a known method. (−)-Pinocarvone (**9**) was obtained by oxidation of (1*R*)-(+)-α-pinene (90% ee by GLC, Aldrich) [16]. (1*R*,5*R*)-6,6-Dimethyl-3-methylenebicyclo[3.1.1]heptan-2-one (**10**) [10], (1*R*,4*S*)-1,7,7-trimethyl-3-methylenebicyclo[2.2.1]heptan-2-one (**11**) [10], (1*R*,2*S*)-2,6,6-trimethyl-4-methylenebicyclo[3.1.1]heptan-3-one (**15**) [17] were prepared from (1*S*)-(−)-β-pinene ($[\alpha]_D^{25}$ −22.0 (neat) (99%, Aldrich), (1*R*)-(+)-camphor ($[\alpha]_D^{25}$ +44.1 (*c* 10, C_2H_5OH) (98%, Aldrich) and (−)-isopinocampheol ($[\alpha]_D^{22}$ −34 (*c* 20, C_2H_5OH) (97%, Aldrich), respectively, following published methods. (6*R*,8*R*)-7,7-Dimethyl-2-(thiophen-2-yl)-5,6,7,8-tetrahydro-6,8-methanoquinoline (**7**) [10] and (5*S*,8*R*)-8,9,9-trimethyl-2-(thiophen-2-yl)-5,6,7,8-tetrahydro-5,8-methanoquinoline (**8**) [10] were obtained following a reported procedure.

3.2. (5S,7S)-6,6-Dimethyl-2-(thiophen-2-yl)-5,6,7,8-tetrahydro-5,7-methanoquinoline (6)

A solution of *N*-[2-oxo-(2-thienyl)ethyl]pyridinium iodide (**5**) (7.28 g, 22 mmol), α-methylene ketone **9** (3.3 g, 22 mmol) and ammonium acetate (44 g, 0.57 mol) in glacial acetic acid (44 ml) was heated at 120 °C for 4 h under nitrogen. Then, most of the acetic acid was removed under reduced pressure and the residue was taken up with H_2O (600 ml) and extracted with ethyl ether (2 × 150 ml). The organic phase was washed with a 5% NaOH solution and then extracted with a 10% HCl solution. The acid solution was made alkaline with a 10% NaOH solution and extracted with ethyl ether (2 × 150 ml). The organic phase was dried on anhydrous Na_2SO_4, the solvent was evaporated and the residue was purified by flash chromatography (petroleum ether/ethyl acetate = 7/3) to afford pure **6** as a white solid: 4.1 g (73%); mp 72 °C; $[\alpha]_D^{25}$ +102.0 (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 750 (d, 1H, *J* = 3.6 Hz), 7.35–7.30 (m, 2H), 7.18

(d, 1H, $J = 7.8$ Hz), 7.08 (t, 1H, $J = 4.5$ Hz), 3.14 (d, 2H, $J = 2.7$ Hz), 2.74 (t, 1H, $J = 5.7$ Hz), 2.67 (dt, 1H, $J = 9.3$, 6.0 Hz), 2.39–2.34 (m, 1H), 1.39 (s, 3H), 1.27 (d, 1H, $J = 9.3$ Hz), 0.67 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 156.77, 149.84, 145.37, 140.37, 133.41, 127.77, 126.19, 123.43, 115.50, 46.26, 40.11, 39.47, 36.49, 31.88, 25.98, 21.28. Anal. Calcd. for $C_{16}H_{17}NS$: C, 75.25; H, 6.71; N, 5.48. Found: C, 75.36; H, 6.55; N, 5.55.

*3.3. (5R,7R,8S)-6,6,8-Trimethyl-2-(thiophen-2-yl)-5,6,7,8-tetrahydro-5,7-methanoquinoline (**12a**) and (5R,7R,8R)-6,6,8-trimethyl-2-(thiophen-2-yl)-5,6,7,8-tetrahydro-5,7-methanoquinoline (**12b**)*

Compound **12** was obtained as a diastereomeric mixture of **12a** (90%) and its epimer at the C8 **12b** (10%) following the procedure described for the preparation of **6** and using the α-methylene ketone **15**: 1.30 g (22%); oil; ^{1}H NMR ($CDCl_3$) (major isomer) δ: 7.51 (dd, 1H, $J = 3.9$, 0.9 Hz), 7.40–7.27 (m, 2H), 7.14 (d, 1H, $J = 8.1$ Hz), 7.06 (dd, 1H, $J = 8.1$, 1.5 Hz), 3.21 (dq, 1H, $J = 7.2$, 2.1 Hz), 2.74 (t, 1H, $J = 5.7$ Hz), 2.55 (dt, 1H, $J = 9.6$, 5.7 Hz), 2.15 (dt, 1H, $J = 6.0$, 3.2 Hz), 1.42 (d, 6H, $J = 8.4$ Hz), 1.29 (d, 1H, $J = 9.6$ Hz), 0.67 (s, 3H). ^{1}H NMR ($CDCl_3$) (minor isomer) δ: 7.51 (dd, 1H, $J = 3.9$, 0.9 Hz), 7.40–7.27 (m, 2H), 7.14 (d, 1H, $J = 8.1$ Hz), 7.06 (dd, 1H, $J = 8.1$, 1.5 Hz), 3.21 (dq, 1H, $J = 7.2$, 2.1 Hz), 2.74 (t, 1H, $J = 5.7$ Hz), 2.55 (dt, 1H, $J = 9.6$, 5.7 Hz), 2.29 (dt, 1H, $J = 6.0$, 3.2 Hz), 1.53 (d, 6H, $J = 8.4$ Hz), 1.29 (d, 1H, $J = 9.6$ Hz), 0.71 (s, 3H). Anal. Calcd. for $C_{17}H_{19}NS$: C, 75.79; H, 7.11; N, 5.20. Found: C, 75.67; H, 7.22; N, 5.29.

*3.4. (5R,7R,8S)-6,6,8-Trimethyl-2-(5-bromothiophen-2-yl)-5,6,7,8-tetrahydro-5,7-methanoquinoline (**13a**)*

A solution of bromine (0.72 g, 4.5 mmol) in acetic acid (12 ml) was added dropwise to a solution of **12a** and **12b** (0.807 g, 3.0 mmol) in acetic acid (12 ml). Then the mixture was heated under reflux for 1 h. After cooling, the mixture was poured into H_2O, neutralized with 10% NaOH and extracted with ethyl ether. The organic phase was washed with H_2O and dried on anhydrous sodium sulphate. Evaporation of the solvent left a residue whose ^{1}H NMR spectrum showed the presence of the two diastereomers **13a** and **13b** in a 9:1 ratio. Purification of this residue by flash chromatography (petroleum ether/ethyl acetate = 99/1) allowed to obtain pure **13a**: 0.85 g (81%); mp 102–103 °C; $[\alpha]_D^{25}$ −24.1 (*c* 2.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.17 (d, 1H, $J = 7.8$ Hz), 7.15 (d, 1H, $J = 3.9$ Hz), 7.09 (d, 1H, $J = 7.8$ Hz), 6.95 (d, 1H, $J = 3.9$ Hz), 3.35 (dq, 1H, $J = 6.6$, 2.1 Hz), 2.67 (t, 1H, $J = 6.0$ Hz), 2.50 (dt, 1H, $J = 9.9$, 6.0 Hz), 2.09 (dt, 1H, $J = 6.0$, 2.4 Hz), 1.36 (d, 6H, $J = 3.6$ Hz), 1.23 (d, 1H, $J = 9.9$ Hz), 0.62 (s, 3H). ^{1}H NMR ($CDCl_3$) (minor isomer **13b**) δ: 7.17 (d, 1H, $J = 7.8$ Hz), 7.15 (d, 1H, $J = 3.9$ Hz), 7.09 (d, 1H, $J = 7.8$ Hz), 6.95 (d, 1H, $J = 3.9$ Hz), 3.35 (dq, 1H, $J = 6.6$, 2.1 Hz), 2.67 (t, 1H, $J = 6.0$ Hz), 2.50 (dt, 1H, $J = 9.9$, 6.0 Hz), 2.23 (dt, 1H, $J = 6.0$, 2.4 Hz), 1.47 (d, 6H, $J = 3.6$ Hz), 1.23 (d, 1H, $J = 9.9$ Hz), 0.66 (s, 3H). Anal. Calcd. for $C_{17}H_{18}BrNS$: C, 58.62; H, 22.94; N, 4.02. Found: C, 58.77; H, 22.91; N, 4.13.

*3.5. (5R,7R,8S)-6,6,8-Trimethyl-2-(5-phenylthiophen-2-yl)-5,6,7,8-tetrahydro-5,7-methanoquinoline (**14**)*

A solution of **13a** (339 mg, 0.97 mmol) and tetrakis(triphenylphosphine)palladium[0] (33.6 mg, 0.39 mmol), in DME (1.8 ml) was stirred under argon atmosphere for 10 min. Phenylboronic acid (0.118 g, 0.97 mmol) in the minimum amount of EtOH was added. A 2 M solution of Na_2CO_3 (0.97 ml) was added and the solution was heated under reflux for 24 h. After cooling, the mixture was poured into H_2O and extracted with ethyl ether. The organic phase was dried on anhydrous sodium sulphate, the solvent was evaporated and the residue was purified by flash chromatography (petroleum ether/ethyl acetate = 95/5) to afford **14**: 0.309 g (92%); mp 87–89 °C; $[\alpha]_D^{25}$ −50.6 (*c*, 1.9 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.68 (dd, 2H, $J = 7.8$, 0.6 Hz), 7.48 (d, 1H, $J = 3.9$ Hz), 7.39 (t, 1H, $J = 7.2$ Hz), 7.33 (t, 1H, $J = 11.1$ Hz), 7.36–7.26 (m, 3H), 7.18 (d, 1H, $J = 7.8$ Hz), 3.23 (dq, 1H, $J = 7.2$, 2.4 Hz), 2.76 (t, 1H, $J = 5.7$ Hz), 2.56 (dt, 1H, $J = 9.6$, 5.4 Hz), 2.16 (dt, 1H, $J = 6.0$, 2.4 Hz), 1.42 (s, 6H), 1.31 (d, 1H, $J = 9.6$ Hz), 0.69 (s, 3H). Anal. Calcd. for $C_{23}H_{23}NS$: C, 79.96; H, 6.71; N, 4.05. Found: C, 79.77; H, 6.81; N, 4.14.

3.6. (5R,7R,8S)-6,6,8-Trimethyl-2-(thiophen-2-yl)-5,6,7,8-tetrahydro-5,7-methanoquinoline (**12a**)

A 2.5 M solution of *n*-butyllithium in hexane (0.396 ml, 0.99 mmol) was added dropwise to a solution of **13a** (314 mg, 0.99 mmol) in anhydrous ethyl ether (10 ml) cooled at −78 °C. After 1 h at −78 °C, acetic acid (1 ml) was added. The mixture was poured into H_2O and extracted with ethyl ether. The organic phase was dried on anhydrous sodium sulphate, the solvent was evaporated and the residue was purified by flash chromatography (petroleum ether/ethyl acetate = 95/5) to afford **12a**: 0.241 g (100%); oil; $[\alpha]_D^{25}$ −19.6 (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.51 (dd, 1H, J = 3.9, 0.9 Hz), 7.40–7.27 (m, 2H), 7.14 (d, 1H, J = 8.1 Hz), 7.06 (dd, 1H, J = 8.1, 1.5 Hz), 3.21 (dq, 1H, J = 7.2, 2.1 Hz), 2.74 (t, 1H, J = 5.7 Hz), 2.55 (dt, 1H, J = 9.6, 5.7 Hz), 2.15 (dt, 1H, J = 6.0, 3.2 Hz), 1.42 (d, 6H, J = 8.4 Hz), 1.29 (d, 1H, J = 9.6 Hz), 0.67 (s, 3H). Anal. Calcd. for $C_{17}H_{19}NS$: C, 75.79; H, 7.11; N, 5.20. Found: C, 75.89; H, 7.28; N, 5.33.

3.7. $[(\eta^3\text{-}C_3H_5)Pd(\mathbf{6})]^+CF_3SO_3^-$ (**18a** and **18b**)

A solution of **6** (127.5 mg, 0.5) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (91.5 mg, 0.25 mmol) in CH_2Cl_2 (13 ml) was stirred at room temperature for 4 h, then $Ag(CF_3SO_3)$ (128.5 mg, 0.5 mmol) was added. After stirring the mixture for additional 4 h, methanol (15 ml) was added. The white precipitate was filtered off with celite and the filtrate was concentrated to give **18a** and **18b** as white foamy solid (0.262 mg, 95%): ^{1}H NMR ($CDCl_3$) δ: 7.29 (dd, 1H, J = 3.6, 0.9 Hz), 7.48 (dd, 1H, J = 5.4, 1.5 Hz), 7.40 (AB, 2H, J = 7.8 Hz), 7.16 (dd, 1H, J = 5.1, 3.6 Hz), 5.46–5.34 (m, 1H, CH allyl), 4.01–3.91 (m, 2H, CH_2 allyl), 3.49–3.42 (m, 2H), 2.87 (t, 1H, J = 5.7 Hz), 2.78–2.61 (m, 3H, overlapping CH_2 allyl), 2.49–2.42 (m, 1H), 1.70 (s, 3H), 1.30 (d, 1H, J = 9.3 Hz), 0.67 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 158.87, 151.12, 143.13, 142.29, 135.49, 128.04, 127.40, 122.02, 119.06, 117.78, 112.40, 59.65, 46.19, 39.79, 39.44, 37.42, 31.49, 25.59, 21.12. Anal. Calcd. for $C_{20}H_{22}F_3NO_3PdS_2$: C, 43.52; H, 4.42; N, 2.54. Found: C, 43.66; H, 4.32; N, 2.43.

3.8. 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 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) and washed with ice-cold saturated aqueous ammonium chloride. The organic phase was dried on 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 by 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.

3.9. Asymmetric cyclopropanation of styrene using Cu(I)-complexes: typical procedure

A solution of the ligand (34 μmol) in CH_2Cl_2 (2.5 ml) was added to a suspension of $[Cu(OTf)(C_6H_6)_{0.5}]$ (8 mg, 32 μmol) in CH_2Cl_2 (2.5 ml). After 30 min, the mixture was filtered through packed adsorbent cotton under argon and styrene (1.59 ml, 13.87 mmol) was added to the filtrate. Then a solution of ethyl diazoacetate (2.5 mmol) in CH_2Cl_2 (2.5 ml) was added dropwise over a period of 2 h. The mixture was stirred for 16 h at room temperature and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 15/1) to afford a mixture of ethyl *trans*- and *cis*-2-phenyl-cyclopropane-1-carboxylates as colourless oil. The *trans*/*cis* ratio and the ee were determined by GC analysis on a diethyl *t*-butylsilyl β-cyclodextrin capillary column 25 m × 0.25 mm operated at 60 °C for 5 min, then programmed at 3 °C/min to 160 °C (retention times: 33.2 min

(1*S*,2*S*) and 33.5 min (1*R*,2*R*) for *trans* **20**; retention times: 31.4 min (1*R*,2*S*) and 31.8 min (1*S*,2*R*) for *cis* **21**].

3.10. Asymmetric cyclopropanation of styrene using Cu(II)-complexes: typical procedure

The ligand (35 μmol) in CH_2Cl_2 (1.5 ml) was added to a suspension of $Cu(OTf)_2$ (11.4 mg, 31 μmol) in CH_2Cl_2 (1.5 ml). After 2 h, styrene (0.715 ml, 6.25 mmol) and ethyl diazoacetate (0.315 mmol) were added. After 30 min, ethyl diazoacetate (2.5 mmol) in CH_2Cl_2 (2.5 ml) was added dropwise over a period of 2 h and then the mixture was stirred for 16 h. The solvent was evaporated under vacuo and the residue was then worked up as described above.

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References

[1] I. Ojiama (Ed.), Catalytic Asymmetric Synthesis, VCH, New York, 1993.
[2] R. Noyori, Asymmetric Catalysis in Organic Synthesis, Wiley, New York, 1994.
[3] M.J.H. Russell, C. White, A. Yates, P.M. Maitlis, J. Chem. Soc., Dalton Trans. (1978) 857.
[4] M.S. Loft, D.A. Widdowson, T.J. Mowlem, Synlett (1992) 135.
[5] C.G. Frost, J.M.J. Williams, Tetrahedron Lett. 34 (1993) 2015.
[6] J.V. Allen, C.G. Frost, J.M.J. Williams, Tetrahedron: Asymmetry 4 (1993) 649.
[7] J. Christoffers, A. Mann, J. Pickardt, Tetrahedron 55 (1999) 5377.
[8] C. Augier, L. Malara, V. Lazzeri, Tetrahedron Lett. 36 (1995) 8775.
[9] H. Brunner, R. Becker, G. Riepl, J. Organomet. Chem. 316 (1986) 1354.
[10] M. Gianini, A. von Zelewsky, Synthesis (1996) 702.
[11] G. Helmchen, J. Organomet. Chem. 576 (1999) 203.
[12] B.M. Trost, D.L. Van Vranken, Chem. Rev. 96 (1996) 395.
[13] M.P. Doyle, M.N. Protonova, Tetrahedron 54 (1998) 7919.
[14] F. Kröhnke, Angew. Chem., Int. Ed. Engl. 2 (1963) 386.
[15] E.C. Constable, R.P.G. Henney, D.A. Tocher, J. Chem. Soc., Dalton Trans. (1992) 2467.
[16] E.D. Mihelich, D.J. Eickhoff, J. Org. Chem. 48 (1983) 4135.
[17] Y. Bessière-Chrétien, C. Grison, Bull. Soc. Chim. Fr. (1970) 3103.
[18] G. Chelucci, S.P. Deriu, A. Saba, R. Valenti, Tetrahedron: Asymmetry 10 (1999) 145.
[19] G. Chelucci, S. Medici, A. Saba, Tetrahedron: Asymmetry 10 (1999) 543.
[20] G. Chelucci, S. Medici, A. Saba, Tetrahedron: Asymmetry 8 (1997) 3183.
[21] H. Brunner, P. Brandl, Tetrahedron: Asymmetry 2 (1991) 919.
[22] F. Fache, E. Schulz, M.L. Tommasino, M. Lemaire, Chem. Rev. 100 (2000) 2159.
[23] G. Chelucci, M.A. Cabras, Tetrahedron: Asymmetry 7 (1996) 965.
[24] G. Chelucci, D. Berta, A. Saba, Tetrahedron 53 (1997) 3843.
[25] G. Chelucci, D. Berta, D. Fabbri, G.A. Pinna, A. Saba, F. Ulgheri, Tetrahedron: Asymmetry 9 (1998) 1933.
[26] B. Koning, A. Meetsma, R.M. Kellogg, J. Org. Chem. 63 (1998) 5533.
[27] G. Chelucci, N. Culeddu, A. Saba, R. Valenti, Tetrahedron: Asymmetry 10 (1999) 3537.
[28] B.M. Trost, D.J. Murphy, Organometallics 4 (1985) 1143.
[29] C. Fiore, G. Martelli, M. Monari, D. Savoia, Tetrahedron: Asymmetry 10 (1999) 4803.