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Application of chiral dipyridylmethane ligands in the enantioselective palladium-catalyzed allylic alkylation

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Abstract

New chiral C_1-symmetric dipyridylmethane ligands have been prepared from naturally occurring monoterpenes according to a method based on two consecutive constructions of the pyridine rings. These ligands have been assessed in the enantioselective palladium catalyzed allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethylmalonate. Enantioselectivity up to 68% ee has been obtained.

Keywords: Chiral dipyridylmethane; Nitrogen heterocycles; Palladium complex; Allylic alkylation; Enantioselectivity

1. Introduction

In transition metal catalyzed reactions of organic substrates, the reactivity of a transition metal system can be modulated, among various factors [1–4], by varying the steric influence of the ligands coordinated to the metal. This goal can be achieved by changing the ligand bite-angle or, in other words, the chelate ring size of the metal-complex [5,6]. Accordingly, we have recently modified the structure of chiral 2,2′-bipyridines, which are finding increasing utility as ligands for metal complexes in asymmetric catalysis [7–9], by introducing an isopropylidene backbone between two chiral pyridine rings. In this way, the chiral C_2-symmetric dipyridines **1**–**3** (Scheme 1), in which the chirality has been introduced by the annulation of monoterpene moieties, have been prepared [10].

Although, the preliminary results obtained in the enantioselective palladium-catalyzed allylic alkylation with ligands **1**–**3** appeared to indicate that their Pd-complexes are poorly suitable catalysts for allylic alkylations, next findings prompted us to carry out a deeper investigation to determine the scope and limitations of this kind of ligands in this reaction.

Herein, we report on the preparation of the related chiral C_1-symmetric dipyridylmethane ligands **4a** and **b** (Scheme 2) and **5**–**8** (Scheme 3) and their application in the enantioselective palladium catalyzed allylic alkylation.

2. Results and discussion

Starting our investigation, as a model study of palladium-catalyzed allylic substitutions [7,11–16] we assessed the dipyridines **1**–**3** in the alkylation of 1,3-diphenylprop-2-enyl acetate (**18**) with dimethyl malonate, following a standard protocol which entails the use of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ as the procatalyst and the generation of the nucleophile by in situ treatment of dimethyl malonate, *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and potassium acetate in a methylene chloride solution at room temperature [17] (Table 1).

The dipyridine **1** gave a moderately reactive Pd-catalyst that required 60 h at room temperature to convert the starting material **18** to the dimethyl 1,3-diphenylprop-2-enylmalonate ((*S*)-**19**) in 88% yield and 53% enantiomeric excess (Table 1). A dramatic reduction of the catalytic activity was however observed when dipyridines substituted on both the benzylic positions of the tetrahydroquinoline rings were employed. Thus, with the ligand **2**, differing from **1** by the position of the dimethylmethylene bridge which in the former ligand is in close proximity to the nitrogen donor

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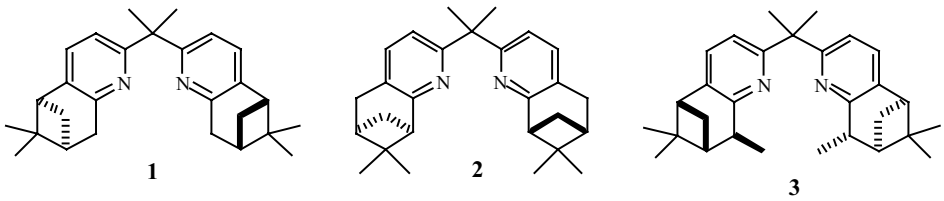
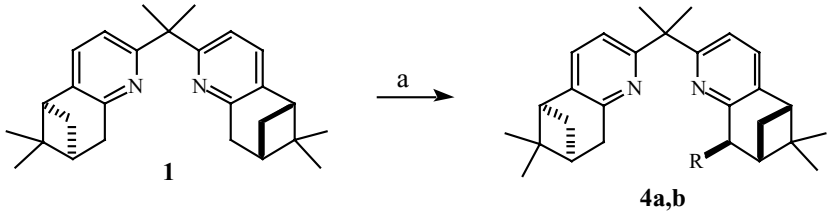


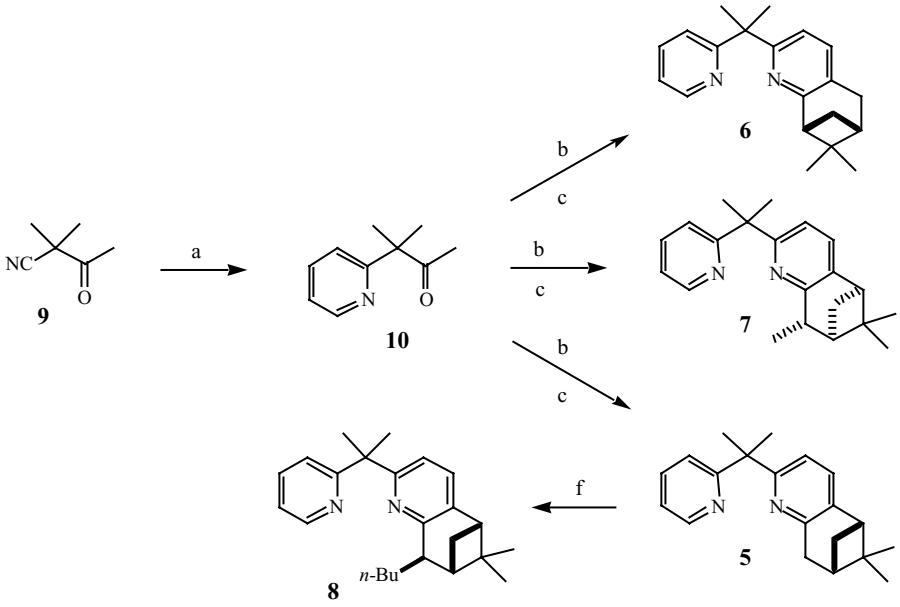
Scheme 1.



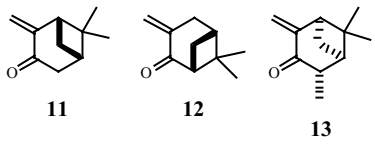
a: LDA, THF, -40 °C, 2h then MeI o BuI from -40 °C to r.t..

a: R= Me; **b**: R= *n*-Bu

Scheme 2.



a: CpCo(COD), acetylene, toluene, 100 °C;
b: LDA, THF, -40 °C, 2h; then **11** or **12** or **13** from -40 °C to slowly r.t.;
c: AcOH, NH_4OAc, THF, reflux, 2h;
d: LDA, THF, -40 °C, 2h, then BuI from -40 °C to slowly r.t.

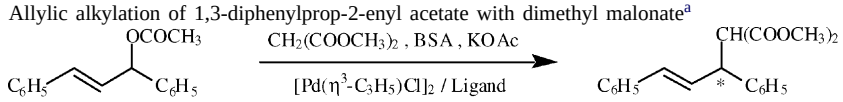


Scheme 3.

center, no reaction occurred after 168 h. The same outcome was obtained with the more sterically encumbered methyl analogue **3** [18].

A surprisingly result was however observed when the C_1-symmetric dipyridine **4a** which has an intermediate structure between the reactive ligand **1** and the unreactive ligand **3**, was assessed. In fact, **4a**, prepared by monoalkylation of 1 with methyl iodide (Scheme 2), afforded (*S*)-**19** in 68% ee, although a very long reaction time (156 h) was required for the complete conversion of the starting

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



18 **19**

Entry	Ligand	Reaction time (h)	Conversion (%)[b]	Yield (%)[c]	ee (%)[d]	Configuration[e]
1	**1**	60	100	84	53	*S*
2	**2**	168	–	–	–	–
3	**3**	168	–	–	–	–
4	**4a**	156	100	77	68	*S*
5	**4b**	168	19	n.d.	–	–
6	**5**	28	100	92	11	*S*
7	**6**	67	100	89	46	*S*
8	**7**	185	100	76	48	*S*
9	**8**	245	100	67	62	*R*

[a] Reaction of the ligand (0.04 mmol, 10 mol%) and $[Pd(\eta 3\text{-}C_3H_5)Cl]_2$ (4 mg, 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 (1.4 mg, 0.014 mmol, 3.5% mol) in CH_2Cl_2 (3 ml) at room 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 assignment is based on the sign of the optical rotation, see Ref [25].

material. Hoping to increase the enantioselectivity of the reaction, the more encumbered butyl analogue dipyridine **4b** was prepared (Scheme 2). This ligand however showed no catalytic activity after 168 h at room temperature.

The acquired data pointed out that the presence of C_2-symmetry is not a necessary requirement to achieve high enantiomeric excesses and the presence of encumbered substituents on both the pyridine rings of dipyridylmethane is detrimental for the catalytic activity [19].

On this basis we decided to prepare the new dipyridines **5**–**7** which are the C_1-symmetric analogue of **1**–**3**, respectively. Moreover, we prepared the dipyridine **8**, the structure of which is related to the ligand **4b** (note that **7** is related to **4a**).

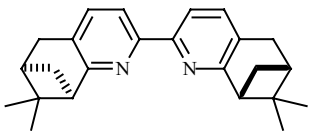
The synthesis of ligands **5**–**7** starts from the cyanoketone **9** which was submitted to Co-cyclotrimerization with acetylene in the presence of CpCoCOD as the catalyst [20,21] to give the pyridylketone **10** (Scheme 3). The conjugate addition of the lithium enolate of **10** (LDA, −40 °C, 2 h) with (−)-pinocarvone (**11**), prepared from α-pinene [22], followed by azaanellation of unisolated 1,5-dicarbonyl intermediate with the ammonium acetate/acetic acid system afforded the bipyridine **5**. The extension of this protocol to the more sterically hindered α-methylene ketones **12** and **13**, obtained from (−)-β-pinene [23] and (−)-isopinocampheol [24], yielded the dipyridylmethane ligands **6** and **7**, respectively. Finally, the preparation of **8** was easily obtained by introduction of a butyl group on the 8-position of the tetrahydroquinoline ring of **5** [7–9]. Thus, the red solution of lithiated **5** (LDA, −40 °C, 2 h) was quenched with *n*-butyl iodide to give in moderate yield (63%) the ligand **8** as a single epimer.

Under the general conditions for allylic alkylations, ligand **5** was able to provide an effective palladium catalyst giving (*S*)-**19** in good yield (92%), but with low enantioselectivity (11% ee). A considerable improvement of the selectivity (46% ee) was obtained with ligand **6** which however exhibited a reduced reaction rate. A further increment of the enantioselectivity was obtained by both the dipyridines **7** and **8** (48 and 62% ee, respectively), but in these cases, the complete conversion of the starting material required a very long reaction time (185 and 245 h, respectively).

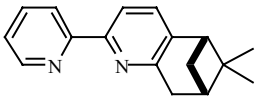
The results obtained using both C_1- and C_2-symmetric dipyiridines indicate that their Pd-complexes are poorly suitable catalysts for enantioselective allylic substitutions. With both this kind of ligands the catalytic activity decreases dramatically as the substituent close to the tetrahydroquinoline nitrogen becomes bulkier. The reduction of the reaction rate is very evident taking into account the two series of the C_1-symmetric dipyiridines **4a** and **5** versus **4b** and **8**, respectively. An extreme situation is achieved with the C_2-symmetric dipyiridines **1**–**3** where only the less encumbered ligand **1** turned out to be catalytically active.

The comparison between the related series of dipyridines (**2**, **5**–**8**) and bipryridines (**20**–**24**) shows that dipyridines provide less effective catalysts than the related bipryridines (Scheme 4 [26]). The two kinds of ligands differ from the chelate ring size of the metal-complex or, in other words, from the ligand bite-angle. In the case of dipyridines, in which these parameters result increased, the substituents on the two pyridine rings are pushed towards the substrate in the metal complex intermediate more than in the analogue bipryridines and so the interactions among the species that surround the metal in the chiral cavity increase.

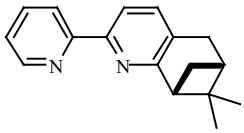
The shape of the chiral cavity is showed more clearly observing the face-on view of the ligand complexes



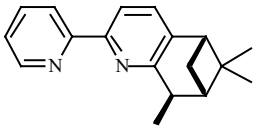
20 ((*S*)-**19**, 28%, 20% ee, unreported react.time)[18]



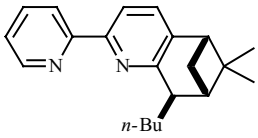
21 ((*R*)-**19**, 93%, 11% ee, 3 h react. time)[25]



22 ((S)-**19**, 60%, 26% ee, unreported react. time)[18]



23 ((*R*)-**19**, 95%, 74% ee, 12 h react. time)[25]

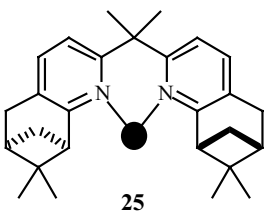


24 ((*R*)-**19**, 88%, 85% ee, 32 h react. time)[26]

Scheme 4.

(Scheme 5). Thus, the comparison of complexes **25** and **26**, derived from **2** and **20**, respectively, reveals a dramatic difference in the cone angle of the cavity created by the two substituted cycloalkeno-condensed frameworks in each complex. In the complex **26**, the cavity has a relatively wide "entrance door" which is much more narrow in the complex **25**. Therefore, it is reasonable to assume that the reduction of the space around the metal inhibits the ligand from form the Pd(η^3-1,3-diphenylallyl)-complex (probably preventing the oxidative addition process) [5] which is the intermediate on which the nucleophilic attack of the malonate anion occurs. This fact explains the low catalytic activity of the bipyridine **20** (28% yield and 20% ee) and the inertness to react of the dipyridine **2**. In spite of these differences, the enantioselective transition state for both these kinds of ligands is confidentially the same, because the configuration of the prevailing enantiomer **19** is strictly related to the configuration of their chiral framework (Scheme 4). The only exception is that of related dipyridine **5** and bipyridine **21** which afford **19** with the opposite configuration, but in this case the obtained enantiomeric excesses are very low.

In conclusion, a new kind of chiral C_1-symmetric dipyridylmethane ligands have been synthesized from the inexpensive chiral pool. The potentiality of their Pd-complexes to catalyze allylic substitutions has been demonstrated. Further applications in other asymmetric reactions will be considered.



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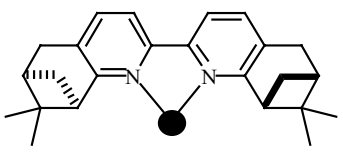

26

Scheme 5.

3. Experimental

3.1. General methods

The ^{1}H NMR spectra were obtained with a Varian VXR-300 spectrometer at 300 MHz and the chemical shifts are reported in ppm downfield from internal Me_4Si. 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. All reagents and solvents were purchased from Aldrich and used as received. THF was distilled from sodium-benzophenone ketyl and degassed thoroughly with dry nitrogen directly before use. 2-Bis[(5*S*,7*S*)-5,7-methano-6,6-dimethyl-5,6,7,8-tetrahydroquinolin-2yl]propane (**1**) [10], 2-bis[(6*R*,8*S*)-6,8-methano-7,7-dimethyl-5,6,7,8-tetrahydroquinolin-2yl]propane (**2**) [10], 2-bis[(5*R*,7*R*)-5,7-methano-6,6,8-trimethyl-5,6,7,8-tetrahydroquinolin-2yl]propane (**3**) [10] and 2,2-dimethyl-3-oxo-butyronitrile (**9**) [27] were prepared according to reported procedures. (−)-Pinocarvone (**11**) was obtained by oxidation of (+)-α-pinene (98% pure, 91% ee by GLC, Aldrich) [22]. (1*R*,5*R*)-6,6-Dimethyl-3-methylenebicyclo [3.1.1] heptan-2-one (**12**) and (1*R*,2*S*,5*R*)-2,6,6-trimethyl-4-methylenebicyclo[3.1.1]heptan-3-one (**13**) were prepared from (−)-β-pinene (99% pure, Aldrich) [23] and (−)-isopinocampheol (98% pure, 95% ee by GLC, Aldrich) [24], respectively.

3.2. (5S,7S,8R)-5,7-Methano-6,6,8-trimethyl-2-{1-[(5S,7S)-5,7-methano-6,6-dimethyl-5,6,7,8-tetrahydroquinolin-2yl]-1-methylethyl}-5,6,7,8-tetrahydroquinoline (4a)

A solution of the pyridine 1 (773 mg, 2.0 mmol) in anhydrous THF (2 ml) was added at −40 °C to a solution of lithium diisopropylamide (2.0 mmol) in anhydrous THF (10 ml). The resulting solution was stirred at −40 °C for 2 h and then a solution of methyl iodide (284 mg, 2.0 mmol) in

THF (2 ml) was added dropwise at −40 °C. After 0.5 h at −40 °C, the solution was allowed to reach slowly room temperature and then treated with H_2O. The organic phase was separated and the aqueous phase was extracted twice with diethyl ether. The combined organic phases were dried over anhydrous Na_2SO_4, the solvent was evaporated and the residue was purified by flash chromatography (petroleum ether/ethyl acetate = 10/1) to give **4a** as a pale yellow oil: 449 mg (56%); $[\alpha]_D^{25}$ +26.8 (*c* 1.09, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.05 (d, 1H, J = 7.8 Hz), 7.00 (d, 1H, J = 7.8 Hz), 6.77 (d, 1H, J = 7.8 Hz), 6.70 (d, 1H, J = 7.8 Hz), 3.09 (s, 2H), 2.73–2.60 (m, 1H), 2.54–2.45 (m, 1H), 2.38–2.32 (m, 1H), 2.14–2.08 (m, 1H), 1.79 (s, 3H), 1.78 (s, 3H), 1.39 (s, 6H), 1.31 (d, 3H, J = 7.7 Hz), 1.28 (d, 1H, J = 9.3 Hz), 1.27 (d, 1H, J = 9.3 Hz), 0.91 (t, 3H, J = 6.9 Hz), 0.64 (s, 3H), 0.63 (s, 3H). Anal. calcd. for $C_{28}H_{36}N_2$: C, 83,95; H, 9,06; N, 6,99. Found C, 83.76; H, 9.08; N, 6.95.

*3.3. (5S,7S,8R)-8-Butyl-5,7-methano-6,6-dimethyl-2-{1-[(5S,7S)-5,7-methano-6,6-dimethyl-5,6,7,8-tetrahydroquinolin-2yl]-1-methylethyl}-5,6,7,8-tetrahydroquinoline (**4b**)*

Compound **4b** was obtained as an oil following the procedure described for the preparation of **4a** and using *n*-butyl iodide: 398 mg (45%); $[\alpha]_D$25 +18.3 (*c* 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 7.05 (d, 1H, J = 7.8 Hz), 6.99 (d, 1H, J = 7.8 Hz), 6.78 (d, 1H, J = 7.8 Hz), 6.70 (d, 1H, J = 7.8 Hz), 3.09 (s, 2H), 2.95–2.86 (m, 1H), 2.73–2.60 (m, 2H), 2.52–2.42 (m, 1H), 2.40–2.32 (m, 1H), 2.30–2.22 (m, 1H), 2.20–2.32 (m, 1H), 1.79 (s, 3H), 1.78 (s, 3H), 1.48–1.18 (m, 8H), 1.39 (s, 6H), 0.91 (t, 3H, J = 6.9 Hz), 0.64 (s, 3H), 0.61 (s, 3H). Anal. calcd. for $C_{31}H_{42}N_2$: C, 84,11; H, 9,56; N, 6,33. Found C, 84.06; H, 9.58; N, 6.38.

*3.4. 3-Methyl-3-(pyridin-2-yl)butan-2-one (**10**)*

(π-Cyclopentadienyl)cobalt-1,5-cyclooctadiene (250 mg) was placed in a stainless-steel autoclave (200 ml). The autoclave was rocked and the air removed (0.1 atm). A solution of 2,2-dimethyl-3-oxo-butyronitrile (**9**) (11.11 g, 0.10 mol) in air-free toluene (100 ml) was introduced by suction. The reaction vessel was pressurized with acetylene up to 14 atm and then rocked and heated at 120 °C. After 72 h the autoclave was cooled and the residual gas released. The reaction mixture was taken up with diethyl ether and filtered. The solution was extracted with 10% aqueous hydrochloric acid. The aqueous phase was made alkaline with 10% sodium hydroxide solution and the organic products were extracted with diethyl ether. Drying on anhydrous sodium sulfate and evaporation of the solvent left a oil which was purified by flash chromatography (petroleum ether/ethyl acetate = 7/3) to give pure 10: 12.24 g (75%); oil; ^{1}H NMR ($CDCl_3$) δ: 8.58 (dd, 1H, J = 4.8, 0.9 Hz), 7.69 (dt, 1H, J = 7.8, 2.1 Hz), 7.30 (d, 1H, J = 7.8 Hz), 7.18 (ddd, 1H, J = 7.8, 4.8, 2.1 Hz), 1.97 (s, 3H), 1.53 (s, 6H). Anal. calcd. for $C_{10}H_{13}NO$: C, 73.59, H, 8.03, N, 8.58. Found: C, 73.65, H, 8.09, N, 8.46.

*3.5. (5S,7S)-(+)-5,7-Methano-6,6-dimethyl-2-[1-methyl-1-(pyridin-2-yl)ethyl]-5,6,7,8-tetrahydroquinoline (**5**)*

A solution of 3-methyl-3-(pyridin-2-yl)butan-2-one (**10**) (1.63 g, 10 mmol) in anhydrous THF (5 mL) was added dropwise at −78 °C to a solution of lithium diisopropylamide (10 mmol) in anhydrous THF (50 mL). The resulting solution was stirred at −40 °C for 2 h and then a solution of the α-methylene ketones 11 (10 mmol) in THF (5 mL) was added dropwise at −40 °C. After 15 min at −40 °C, the solution was allowed to reach slowly room temperature (overnight) and then poured into a mixture of ammonium acetate (7.7 g, 0.1 mol) and acetic acid (50 mL). The flask was connected with a distillation head and the THF was distilled off over a 3 h period. Most part of the acetic acid was removed under reduced pressure and the residue was taken up with H_2O and extracted with ethyl ether. The organic phase was separated, washed with a 5% NaOH solution and then dried on anhydrous Na_2SO_4. The solvent was evaporated and the residue was purified by flash chromatography (petroleum ether/ethyl acetate = 9/1): 0.555 g (19%); oil; $[\alpha]_D$25 + 35.5 (*c* 1.23, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.59–8.54 (m, 1H), 7.54 (dt, 1H, J = 7.8, 1.8 Hz), 7.13 (d, 1H, J = 7.8 Hz), 7.11–7.04 (m, 1H), 7.06 (d, 1H, J = 7.8 Hz), 6.78 (d, 1H, J = 7.8 Hz), 3.05 (d, 2H, J = 2.7 Hz), 2.74–2.58 (m, 2H), 2.38–2.30 (m, 1H), 1.79 (s, 6H), 1.38 (s, 3H), 1.27 (d, 1H, J = 9.3 Hz), 0.63 (s, 3H). Anal. calcd. for $C_{20}H_{24}N_2$: C, 82.15; H, 8.27; N, 9.58. Found C, 82.06; H, 8.08; N, 9.87.

*3.6. (6R,8R)-(−)-6,8-Methano-7,7-dimethyl-2-[1-methyl-1-(pyridin-2-yl)ethyl]-5,6,7,8-tetrahydroquinoline (**6**)*

Compound **6** was obtained as an oil following the procedure described for the preparation of 5 and using the α-methylene ketone 12: 0.438 g (15%); $[\alpha]_D$25 − 16.3 (*c* 1.16, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.59–8.53 (m, 1H), 7.52 (dt, 1H, J = 7.8, 1.8 Hz), 7.27 (d, 1H, J = 7.8 Hz), 7.11–7.04 (m, 2H), 6.88 (d, 1H, J = 7.8 Hz), 2.95 (t, 1H, J = 5.7 Hz), 2.88 (d, 2H, J = 2.7 Hz), 2.72–2.62 (m, 1H), 2.32–2.24 (m, 1H), 1.78 (s, 6H), 1.40 (s, 3H), 1.29 (d, 1H, J = 9.6 Hz), 0.65 (s, 3H). Anal. calcd. for $C_{20}H_{24}N_2$: C, 82.15; H, 8.27; N, 9.58. Found C, 82.06; H, 8.08; N, 9.87.

*3.7. (5R,7R,8S)-(−)-5,7-Methano-6,6,8-trimethyl-2-[1-methyl-1-(pyridin-2-yl)ethyl]-5,6,7,8-tetrahydroquinoline (**7**)*

Compound **7** was obtained as an oil following the procedure described for the preparation of **5** and using the α-methylene ketone **13**: 0.520 g (17%); $[\alpha]_D$25 − 14.5 (*c*

1.18, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.56 (d, 1H, $J = 5.4$ Hz), 7.53 (dt, 1H, $J = 7.8$, 2.1 Hz), 7.16 (d, 1H, $J = 7.8$ Hz), 7.08–7.04 (m, 1H), 7.02 (d, 1H, $J = 7.8$ Hz), 6.76 (d, 1H, $J = 7.8$ Hz), 3.15–3.07 (m, 1H), 2.71–2.62 (m, 1H), 2.54–2.44 (m, 1H), 2.11 (dt, 1H, $J = 6.0$, 2.4 Hz), 1.81 (s, 3H), 1.79 (s, 3H), 1.39 (s, 3H), 1.30 (s, 3H), 1.26 (d, 1H, $J = 9.6$ Hz), 0.63 (s, 3H). Anal. calcd. for $C_{21}H_{26}N_2$: C, 82.31; H, 8.55; N, 9.14. Found C, 82.44; H, 8.59; N, 9.33.

3.8. (5S,7S,8R)-(−)-8-Butyl-5,7-methano-6,6-dimethyl-2-[1-methyl-1-(pyridin-2-yl)ethyl]-5,6,7,8-tetrahydroquinoline (**8**)

A solution of **5** (0.24 g, 0.82 mmol) in anhydrous THF (2 mL) was added dropwise at −40 °C to a solution of lithium diisopropylamide (0.9 mmol) in anhydrous THF (13 mL). The resulting solution was stirred at −40 °C for 2 h and then a solution of *n*-butyl iodide (0.166 mg, 0.9 mmol) in THF (2 mL) was added dropwise. After 15 min at −40 °C, the solution was allowed to reach slowly room temperature (overnight) and then was taken up with water. The organic phase was separated and the aqueous phase was extracted with ethyl ether. The combined organic phase was dried on anhydrous Na_2SO_4 and the solvent was evaporated. The residue was purified by flash chromatography (petroleum ether/ethyl acetate = 9/1) to give pure: 0.183 g (63%); oil; $[\alpha]_D25$ − 2.2 (*c* 0.92, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 8.55 (d, 1H, $J = 3.9$ Hz), 7.53 (dt, 1H, $J = 7.8$, 1.8 Hz), 7.16 (d, 1H, $J = 8.1$ Hz), 7.06 (dd, 1H, $J = 7.2$, 4.8 Hz), 7.01 (d, 1H, $J = 7.8$ Hz), 6.75 (d, 1H, $J = 7.8$ Hz), 2.94–2.84 (m, 1H), 2.66 (t, 1H, $J = 5.7$ Hz), 2.52–2.42 (m, 1H), 2.25 (dt, 1H, $J = 6.3$, 3.0 Hz), 2.20–2.08 (m, 1H), 1.80 (s, 3H), 1.78 (s, 3H), 1.48–1.22 (overlapping, 5H), 1.39 (s, 3H), 1.26 (d, 1H, $J = 9.6$ Hz), 0.91 (t, 3H, $J = 8.7$ Hz), 0.60 (s, 3H). Anal. calcd. for $C_{24}H_{32}N_2$: C, 82.71; H, 9.25; N, 8.04. Found C, 82.66; H, 9.38; N, 8.33.

3.9. Allylic alkylation of 1,3-diphenylprop-2-enyl 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 1 h. 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 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 (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-enyl malonate. 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. If the right-hand peak of these two is larger, then this is typical of the (*S*)-enantiomer in excess, which was confirmed by comparing the specific rotation obtained with literature values [17].

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