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Tetrahedron: *Asymmetry* 17 (2006) 1853–1858

A P,N ligand with central and axial chiral elements: synthesis and application in allylic alkylation

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Received 22 May 2006; accepted 26 June 2006
Available online 25 July 2006

Abstract—Two epimers of 4-({5-[(diphenylphosphino)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}methyl)-4,5-dihydro-3*H*-dinaphtho[1,2-*e*:2′,1′-*c*]azepine were prepared starting from (2*S*,3*S*)-4-amino-2,3-*O*-isopropylidenebutane-1,2,3-triol and (*R*)- and (*S*)-binaphthol. These ligands, in association with Pd(0) gave enantioselectivities up to 89% (*S*) and 36% (*R*) ee for the (S_A,4*S*,5*R*) and the (R_A,4*S*,5*R*) ligands in the alkylation of racemic 1,3-diphenylprop-2-enyl acetate with dimethyl malonate, showing that the binaphthyl moiety is the most important structure in the enantioselective creation of the new stereogenic center.

1. Introduction

Asymmetric catalysis is one of the most powerful methods for the preparation of enantiomerically pure compounds.[1,2] An impressive number of chiral ligands have been prepared and employed with more or less success, among them P,P-, P,N-, and N,N-based ligands.[3] In recent years, chiral P,N-ligands have received a great deal of attention.[4] Amongst these, aminophosphines bearing a chiral dihydroazepine moiety have been prepared and have given very high enantiomeric excesses in allylic alkylation reactions.[5–14] Aminophosphine ligands containing axial and planar chiral elements have been described by Widhalm et al.[9–11]

We recently reported the synthesis of chiral aminophosphanes derived from tartaric acid and their use in asymmetric alkylation.[15,16] We were interested in the synthesis of chiral aminophosphanes bearing two types of stereogenic structures in the same molecule, namely a chiral dioxolanic skeleton and a binaphthyl unit, in order to study the influence of these elements on the enantioselectivity of allylic alkylation. The present paper deals with the synthesis of two epimeric P,N-ligands derived from tartaric acid and bearing effectively both chiral central and axial elements, and with some results concerning their applications in the palladium-catalyzed allylic alkylation reaction.

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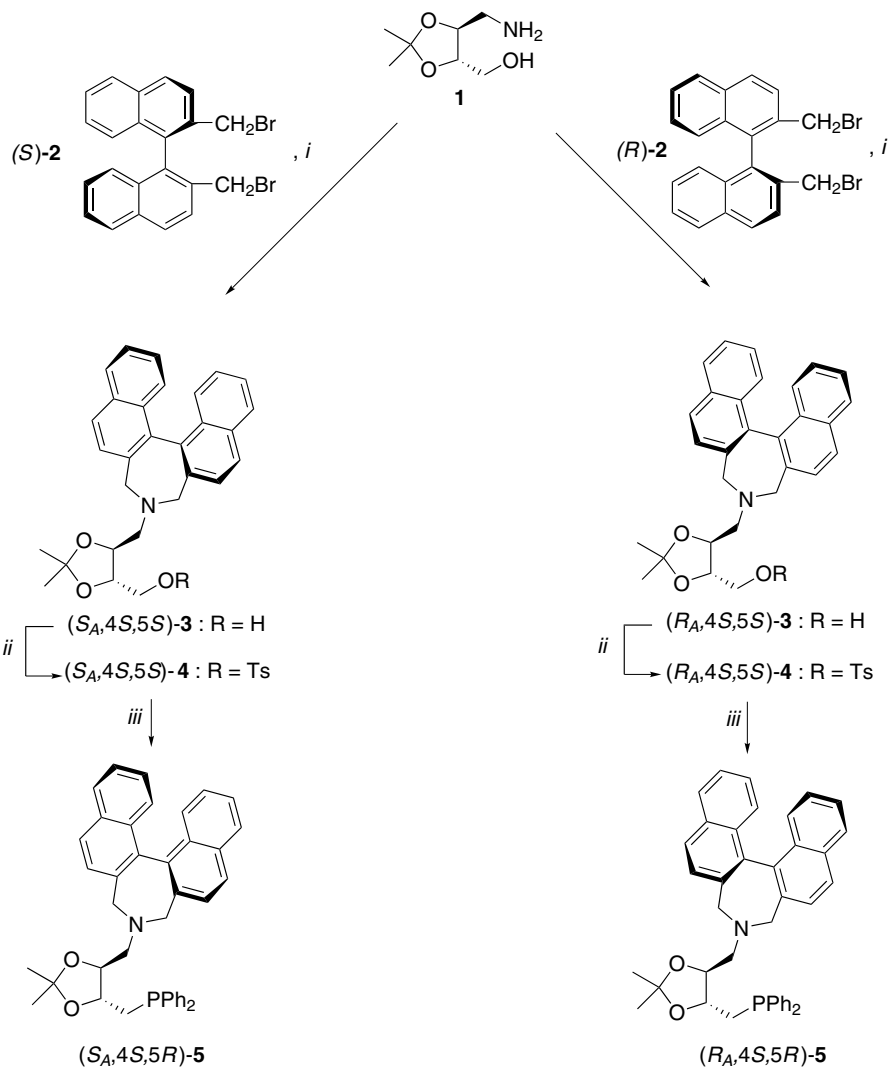
doi:10.1016/j.tetasy.2006.06.040

2. Results and discussion

Following on from our previous study on the synthesis of chiral 4-(diphenylphosphanyl)-1-(dialkylamino)butane ligands, we decided to introduce a second chiral element based upon a binaphthyl unit, more precisely the 3,5-dihydro-4*H*-dinaphathazepine unit. The starting enantiopure materials, namely (2*S*,3*S*)-4-amino-2,3-*O*-isopropylidenebutane-1,2,3-triol **1**[16] was prepared as previously described. (*S*)- and (*R*)-2,2′-di(bromomethyl)-1,1′-binaphthyl **2** were also obtained from commercially available (*S*)- and (*R*)-binaphthol according to the methodology of Zhang et al.[17]

The synthesis of the two chiral ligands, (R_A,4*S*,5*R*)-**5** and (S_A,4*S*,5*R*)-**5**, carrying the same two stereogenic centers, but differing in the absolute configuration of the binaphthyl unit, are described in Scheme 1. The reaction of amino alcohol **1** with (*S*)- and (*R*)-2,2′-di(bromomethyl)-1,1′-binaphthyl **2** in acetonitrile in the presence of K_2CO_3 as the base gave the corresponding (R_A,4*S*,5*S*)- and (S_A,4*S*,5*S*)-homopiperidine **3** in 42% and 56% yield, respectively. Subsequent reaction of amino alcohols **3** with tosyl chloride in C_5H_5N at 0 °C afforded amino tosylates (R_A,4*S*,5*S*)-**4** and (S_A,4*S*,5*S*)-**4** in 71% and 63% chemical yield, respectively.

Finally phosphination of these amino tosylates with lithium diphenylphosphide in THF gave the two amino phosphanes (R_A,4*S*,5*R*)-**5** and (S_A,4*S*,5*R*)-**5** in 67% and 73% yield, respectively.



Scheme 1. Reagents and conditions: (i) K_2CO_3, (*R*)-**5**, or (*S*)-**5**, CH_3CN, reflux; (ii) TsCl, C_5H_5N, 0 °C; (iii) PPh_2Li, THF, rt.

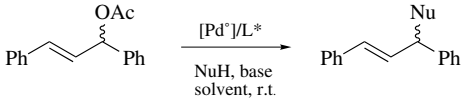
With these two epimeric phosphinamine ligands in hand, we choose to first explore their reactivity and enantioselectivity in the palladium-catalyzed allylic alkylation of *rac*-1,3-diphenyl-2-propenyl acetate with dimethyl malonate as the nucleophile in the presence of *N*,*O*-bis-(trimethylsilyl)acetamide (or BSA). The catalyst was generated in situ from $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and the ligand in a 1:1 ligand/palladium ratio.

With (S_A,4*S*,5*R*)-**5** as the ligand and in the presence of KOAc, conversion up to 96% was achieved after 2 h of reaction; however an enantiomeric excess of only 12% in favor of the (*S*)-enantiomer was obtained (Table 1, entry 1). It should be noted that no conversion was observed under exactly the same conditions when LiOAc was used instead of KOAc (Table 1, entry 2). When THF was replaced by CH_2Cl_2, quantitative conversion was observed in the presence of KOAc, with an ee up to 87% (*S*) obtained (Table 1, entry 3). Again the use of LiOAc instead of KOAc gave a very low conversion (10%), but with ee up to 89% (*S*) (Table 1, entry 4). It is noteworthy that ees of only 50% and 48% in favor of the (*S*)-enantiomer have been obtained when (2*R*,3*S*)-1-diphenylamino- and (2*R*,3*S*)-1-(dihydro-5*H*-dibenzo[*c*,*e*]azepin-6-yl)-4-diphenylphosphino-2,3-*O*-isopropylidene butane-2,3-diol,[16] bearing no axial chirality, were used as the ligand. With (R_A,*S*,*S*)-**5** as the ligand and in the presence of KOAc in CH_2Cl_2, total conversion was achieved after 2 h, with an ee of 36% in favor of the (*R*)-isomer (Table 1, entry 5). The ligands having the (S_A)- and (R_A)-configurations afforded products having the (*S*)- and (*R*)-configurations, albeit with a different degree of asymmetric induction.

For the reaction of dimethyl methylmalonate with 1,3-diphenylprop-2-ene-1-yl acetate, ligand (S_A,4*S*,5*R*)-**5**, under the above mentioned conditions, quantitatively gave the coupling product with quite similar enantioselectivities, 81% ee in favor of the (*R*)-enantiomer. When ligand (R_A,*S*,*S*)-**5** was used, the reaction was sluggish (only 63% conversion after 6 h), and the other enantiomer was obtained in 47% ee.

Diethyl acetamidomalonate quantitatively gave the coupling compound with an (*R*)-configuration in low

Table 1. Allylic alkylation of *rac*-(*E*)-1,3-diphenylpropenyl acetate with various nucleophiles catalyzed by palladium/ligand **5** complexes[a]



Entry	Nucleophile	Ligand	Base	Solvent	Conversion (%)[b]	ee (%)[c]
1	$CH_2(CO_2Me)_2$	(S_A,4*S*,5*R*)-**5**	BSA/KOAc	THF	96	12 (*S*)
2	$CH_2(CO_2Me)_2$	(S_A,4*S*,5*R*)-**5**	BSA/LiOAc	THF	—	—
3	$CH_2(CO_2Me)_2$	(S_A,4*S*,5*R*)-**5**	BSA/KOAc	CH_2Cl_2	100	87 (*S*)
4	$CH_2(CO_2Me)_2$	(S_A,4*S*,5*R*)-**5**	BSA/LiOAc	CH_2Cl_2	10	89 (*S*)
5	$CH_2(CO_2Me)_2$	(R_A,4*S*,5*R*)-**5**	BSA/KOAc	CH_2Cl_2	100	36 (*R*)
6	$CH_3CH(CO_2Me)_2$	(S_A,4*S*,5*R*)-**5**	BSA/KOAc	CH_2Cl_2	100	81 (*R*)
7	$CH_3CH(CO_2Me)_2$	(R_A,4*S*,5*R*)-**5**	BSA/KOAc	CH_2Cl_2	63	47 (*S*)
8	$AcNHCH(CO_2Et)_2$	(S_A,4*S*,5*R*)-**5**	BSA/KOAc	CH_2Cl_2	100	47 (*R*)
9	$AcNHCH(CO_2Et)_2$	(R_A,4*S*,5*R*)-**5**	BSA/KOAc	CH_2Cl_2	100	3 (*R*)
10	$CH_2(COCH_3)_2$	(S_A,4*S*,5*R*)-**5**	BSA/KOAc	CH_2Cl_2	100	20 (*R*)
11	$CH_2(COCH_3)_2$	(R_A,4*S*,5*R*)-**5**	BSA/KOAc	CH_2Cl_2	100	8 (*R*)

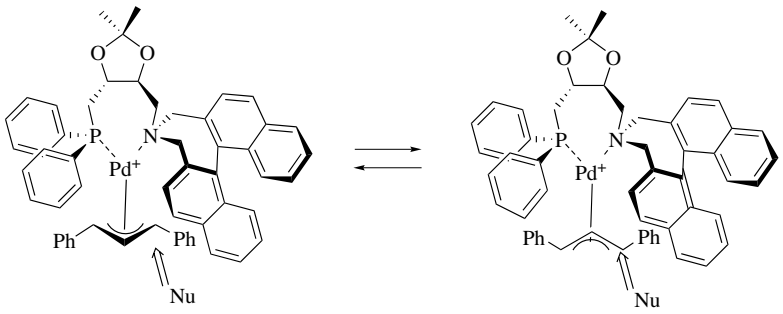
[a] [Nucleophile]/[acetate]/[$Pd_2(C_3H_5)_2Cl_2$]/[ligand]/[BSA]/[KOAc or LiOAc] = 150/50/1/2/150/1; 25 °C; 24 h.
[b] After purification.
[c] Determined by HPLC analysis with a chiral stationary column, daicel Chiracel OD-H.

enantioselectivities: 47% ee and 3% ee using ligands (S_A,4*S*,5*R*)-**5** and (R_A,4*S*,5*R*)-**5**, respectively.

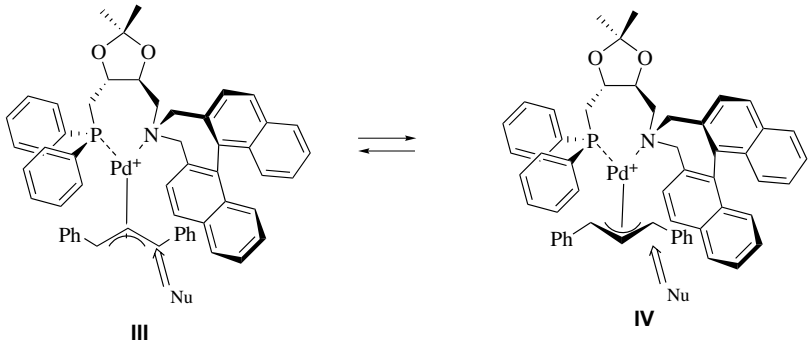
Finally, acetylacetone under these conditions gave quantitatively the coupling product with an (*R*)-configuration in 20% and 8% ee in the presence of ligands (S_A,4*S*,5*R*)-**5** and (R_A,4*S*,5*R*)-**5**, respectively.

Palladium-catalyzed coupling of 3-acetylcyclohex-1-ene with dimethyl malonate in the presence of (S_A,4*S*,5*R*)-**5** gave no reaction at all under these conditions.

These results show that the highest enantioselectivities were obtained using ligand (S_A,4*S*,5*R*)-**5**, demonstrating that the two chiral elements are matched. When (R_A,4*S*,5*R*)-**5** was



Scheme 2.



Scheme 3.

used as the chiral ligand, lower enantioselectivities, as well as a reversal of the chirality of the product obtained, were observed; in this case the two chiral elements are mismatching. It seems that this quite different behavior could be rationalized in terms of steric and electronic effects. Using ligand (S_A,4*S*,5*R*)-**5**, the reaction may proceed through the two diastereoisomeric intermediates **I** and **II** under equilibrium, if we assume a *syn–syn* geometry of the η^3-allyl system (Scheme 2). Molecular models show clearly that the formation of intermediate complex **I**, which presents the less steric interactions, is favored; attack of the nucleophile at the allylic terminus trans to the phosphine ligand[16] afforded the (*S*)-enantiomer. When ligand (R_A,4*S*,5*R*)-**5** was used, the two diastereoisomeric intermediates **III** and **IV** are in equilibrium, with complex **III** being less crowded (Scheme 3); the attack of the nucleophile on the η^3-allyl system would afford predominantly the (*R*)-enantiomer, albeit in lower enantioselectivity.

3. Conclusion

The two epimers (R_A,4*S*,5*R*) and (S_A,4*S*,5*R*) of 4-({5-[(diphenylphosphino)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}methyl)-4,5-dihydro-3*H*-dinaphtho[1,2-*e*:2′,1′-*c*]azepine have been prepared starting from (2*S*,3*S*)-4-amino-2,3-*O*-isopropylidenebutane-1,2,3-triol and (*R*)- and (*S*)-binaphthol. The (S_A,4*S*,5*R*)-ligand gave ee up to 89% in the palladium-catalyzed alkylation of *rac*-(*E*)-1,3-diphenyl-2-propenyl acetate with dimethyl malonate, when the (R_A,4*S*,5*R*)-ligand gave an ee of up to 36% in favor of the other enantiomer, showing clearly that the (S_A,4*S*,5*R*)- and the (R_A,4*S*,5*R*)-ligand are 'match pair' and the 'mismatch pair', respectively.

4. Experimental

4.1. General

Solvents were purified by standard methods and dried if necessary. All commercially available reagents were used as received. Reactions involving organometallic catalysis were carried out in a Schlenk tube under an inert atmosphere. Optical rotations were recorded using a Perkin–Elmer 241 polarimeter. The NMR spectra (^{1}H: 300 MHz, ^{13}C: 75.4 MHz, ^{31}P: 80 MHz) were recorded on a Brüker AM 300 spectrometer. (2*S*,3*S*)-4-Amino-2,3-*O*-isopropylidenebutane-1,2,3-triol **1**[16] and (*S*)- and (*R*)-2,2′-di(bromomethyl)-1,1′-binaphthyl **2**[17] were prepared according to literature procedures.

4.2. Preparation of amino alcohols 3

(*R*)- or (*S*)-2,2′-Di(bromomethyl)-1,1′-binaphthyl **2** (4.0 g, 10 mmol) was added at reflux over 30 min to a suspension of (2*S*,3*S*)-4-amino-2,3-*O*-isopropylidene butane-1,2,3-triol **1** (1.7 g, 10.5 mmol) and K_2CO_3 (4.0 g, 29 mmol) in CH_3CN (50 mL). The reaction mixture was refluxed for 24 h, then cooled at rt, and the solvent was removed under reduced pressure. Water (15 mL) was added to the residue and the organic product was extracted with CH_2Cl_2 (3×30 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate (1:1) as eluent. The product obtained was recrystallized from CH_2Cl_2/hexane to afford pure amino alcohol **3** as a solid.

4.2.1. (R_A,4*S*,5*S*)-5-(3,5-Dihydro-4*H*-dinaphtho[1,2-*e*:2′,1′-*c*]-azepin-4-ylmethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol (R_A,4*S*,5*S*)-3. Yield 42%; colorless solid; mp 186–189 °C; R_f 0.15 (petroleum ether/ethyl acetate 1:1). $[\alpha]_D^{20} = -275$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 2.85–2.92 (m, 2H, CH_2N), 3.33 (d, 2H, $J =$ 12.2 Hz, NCH_2Ar), 3.72 (d, 2H, $J = 12.2$ Hz, NCH_2Ar), 3.69–3.76 (m, 1H, CH_2O), 3.86 (ddd, 1H, $J =$ 8.2, 7.9, 3.2 Hz, >CH–), 3.93 (dd, 1H, $J = 10.2$, 3.2 Hz, CH_2O), 3.86 (ddd, 1H, $J = 8.4$, 8.2, 4.8 Hz, >CH–), 7.27 (dd, 2H, $J = 7.0$, 7.0 Hz, H_{arom}), 7.44–7.51 (m, 4H, H_{arom}), 7.55 (d, 2H, $J = 8.3$ Hz, H_{arom}), 7.93–7.99 (m, 4H, H_{arom}); ^{13}C NMR ($CDCl_3$) δ 26.7 (CH_3) and 26.9 (CH_3), 57.0 (NCH_2), 59.1 (NCH_2), 62.6 (OCH_2), 78.0 (OCH), 81.8 (OCH), 108.6 (*C*Me$_2$), 125.6–135.0 (C_{arom}). Anal. Calcd for $C_{29}H_{29}NO_3$: C, 79.24; H, 6.65. Found: C, 78.99; H, 6.68.

4.2.2. (S_A,4*S*,5*S*)-5-(3,5-Dihydro-4*H*-dinaphtho[1,2-*e*:2′,1′-*c*]-azepin-4-ylmethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol (S_A,4*S*,5*S*)-3. Yield 56%; colorless solid; mp 103–104 °C; R_f 0.17 (eluent: petroleum ether/ethyl acetate, 1:1); $[\alpha]_D^{20} = +250$ (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 2.36 (dd, 1H, $J = 13.0$, 9.8 Hz, CH_2N), 3.12 (dd, 1H, $J = 13.0$, 3.6 Hz, CH_2N), 3.30 (d, 2H, $J = 12.3$ Hz, NCH_2Ar), 3.55 (ddd, 1H, $J =$ 9.5, 9.5, 1.7 Hz, >CH–), 3.67 (d, 2H, $J = 12.3$ Hz, NCH_2Ar), 3.80–3.85 (m, 2H, >CH–, CH_2O), 3.88–4.2 (m, 1H, CH_2O), 7.26 (dd, 2H, $J = 8.3$, 8.3 Hz, H_{arom}), 7.42–7.50 (m, 4H, H_{arom}), 7.58 (d, 2H, $J = 8.3$ Hz, H_{arom}), 7.93 (d, 2H, $J = 8.3$ Hz, H_{arom}), 7.96 (d, 2H, $J = 8.3$ Hz, H_{arom}); ^{13}C NMR ($CDCl_3$) δ 27.3 (CH_3), 27.4 (CH_3), 55.5 (NCH_2), 55.6 (NCH_2), 62.9 (OCH_2), 79.5 (OCH), 82.8 (OCH), 109.3 (*C*Me$_2$), 126.0–135.5 (C_{arom}). HRMS (EI) calcd for $C_{29}H_{29}NO_3$ $[M+H]^+$: 440.2225, found: 440.2226.

4.3. Preparation of amino tosylates 4

A solution of $CH_3C_6H_4SO_2Cl$ (0.87 g, 4.56 mmol) in pyridine (3 mL) was added to amino alcohol **3** (1.95 g, 4.45 mmol) dissolved in pyridine (12 mL) at 0 °C. The mixture was stirred at rt for 6 h. The solution was then treated with cold water (20 mL), and the organic product was extracted with CH_2Cl_2 (3×20 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified by flash chromatography using petroleum ether/ethyl acetate (1:1) as the eluent to afford amino tosylate **4** as a solid.

4.3.1. (R_A,4*S*,5*S*)-5-(3,5-Dihydro-4*H*-dinaphtho[1,2-*e*:2′1′-*c*]-azepin-4-ylmethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methyl 4-methylbenzenesulfonate (R_A,4*S*,5*S*)-4. Yield 71%; colorless solid; mp 196 °C; R_f 0.80 (petroleum ether/ethyl acetate 1:1); $[\alpha]_D^{20} = -190$ (*c* 1.0, $CHCl_3$); ^{1}H NMR

($CDCl_3$) δ 1.38 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.64 (dd, 1H, $J = 13.0$, 6.2 Hz, CH_2N), 2.86 (dd, 1H, $J = 13.0$, 5.2 Hz, CH_2N), 3.23 (d, 2H, $J = 12.2$ Hz, NCH_2Ar), 3.71 (d, 2H, $J = 12.2$ Hz, NCH_2Ar), 3.98 (ddd, 1H, $J = 8.6$, 4.3, 4.0 Hz, >CH–), 4.12–4.22 (m, 1H, >CH–), 4.29 (dd, 1H, $J = 10.6$, 4.3 Hz, CH_2O), 4.32 (dd, 1H, $J = 10.6$, 4.1 Hz, CH_2O), 7.25–7.33 (m, 2H, H_{arom}), 7.49 (dd, 2H, $J = 7.5$, 7.5 Hz, H_{arom}), 7.57 (d, 1H, $J = 8.3$ Hz, H_{arom}), 7.86 (d, 2H, $J = 8.3$ Hz, H_{arom}), 7.97 (d, 2H, $J = 8.5$ Hz, H_{arom}); ^{13}C NMR ($CDCl_3$) δ 21.6 (CH_3), 26.6 (CMe_2), 27.2 (CMe_2), 56.5 (NCH_2), 58.2 (NCH_2), 69.3 (OCH_2), 75.7 (OCH), 77.5 (OCH), 109.9 (CMe_2), 125.4–144.9 (C_{arom}). Anal. Calcd for $C_{36}H_{35}NO_5S$: C, 72.83; H, 5.94. Found: C, 72.27; H, 5.92.

4.3.2. (S_A,4*S*,5*S*)-5-(3,5-Dihydro-4*H*-dinaphtho[1,2-*e*:2′,1′-*c*]azepin-4-ylmethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]-methyl 4-methylbenzenesulfonate (S_A,4*S*,5*S*)-4. Yield 63%; light yellow solid; mp 96–97.5 °C; R_f 0.80 (petroleum ether/ethyl acetate 1:1); $[\alpha]_D^{20} = +197$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.45 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.46 (dd, 1H, $J = 13.1$, 4.8 Hz, CH_2N), 2.93 (dd, 1H, $J = 13.1$, 6.8 Hz, CH_2N), 3.17 (d, 2H, $J = 12.2$ Hz, NCH_2Ar), 3.74 (d, 2H, $J = 12.2$ Hz, NCH_2Ar), 3.98 (ddd, 1H, $J = 8.9$, 4.2, 3.6 Hz, >CH–), 4.02–4.34 (m, 2H, >CH–, CH_2O), 4.31 (dd, 1H, $J = 10.5$, 3.6 Hz, CH_2O), 7.19 (d, 2H, $J = 8.1$ Hz, H_{arom}), 7.29 (ddd, 2H, $J = 7.3$, 7.0, 2.1 Hz, H_{arom}), 7.46–7.53 (m, 4H, H_{arom}), 7.61 (d, 2H, $J = 8.3$ Hz, H_{arom}), 7.78 (d, 2H, $J = 8.3$ Hz, H_{arom}), 7.97 (d, 2H, $J = 8.3$ Hz, H_{arom}); ^{13}C NMR ($CDCl_3$) δ 21.4 (CH_3), 26.7 (CMe_2), 27.2 (CMe_2), 55.5 (NCH_2), 57.0 (NCH_2), 69.3 (OCH_2), 76.0 (OCH), 77.8 (OCH), 110.0 (CMe_2), 125.4–144.8 (C_{arom}). Anal. Calcd for $C_{36}H_{35}NO_5S$: C, 72.83; H, 5.94. Found: C, 71.04; H, 5.85. HRMS (EI) calcd for $C_{36}H_{36}NO_5S$ $[M+H]^+$: 594.2314, found: 594.2313.

4.4. Synthesis of amino phosphanes 5

A solution of PPh_2Li, prepared under argon in THF (8 mL) at 0 °C from $ClPPh_2$ (1 mL) and Li (large excess), was slowly added to a solution of amino tosylate **4** (718 mg, 1.21 mol) in THF (35 mL), until the red color of the solution remained. The solution was stirred for 20 h, and then hydrolyzed with H_2O (2 mL). The solvent was evaporated under reduced pressure, the residue was treated with H_2O (8 mL), and extracted with CH_2Cl_2 (3×20 mL). The combined organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave a residue, which was purified by flash chromatography to afford amino phosphane **5** as a solid.

4.4.1. (R_A,4*S*,5*R*)-4-({5-[(Diphenylphosphino)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}methyl)-4,5-dihydro-3*H*-dinaphtho[1,2-*e*:2′,1′-*c*]azepine (R_A,4*S*,5*R*)-5. Yield 67%; colorless solid; mp 83–84 °C; R_f 0.34 (petroleum ether/ethyl acetate 6:1); $[\alpha]_D^{20} = -147$ (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.36 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 2.50–2.57 (m, 3H, CH_2N, CH_2P), 2.86 (dd, 1H, $J = 13.0$, 3.5 Hz, CH_2N), 3.21 (d, 2H, $J = 12.3$ Hz, NCH_2Ar), 3.72 (d, 2H, $J = 12.3$ Hz, NCH_2Ar), 3.87–3.91 (m, 1H, >CH–), 4.11–4.18 (m, 1H, >CH–), 7.24–7.38 (m, 8H, H_{arom}), 7.43–7.51 (m, 10H, H_{arom}), 7.92 (dd, 4H, $J = 8.3$, 8.3 Hz, H_{arom}); ^{13}C NMR ($CDCl_3$) δ 27.17 (CH_3), 27.26 (CH_3), 32.7 (PCH_2, $^1J_{C,P} = 14.8$ Hz), 56.2 (NCH_2), 57.5 (NCH_2, $^4J_{C,P} = 2.8$ Hz), 77.1 (OCH, $J_{C,P} = 14.8$ Hz), 80.3 (OCH, $J_{C,P} = 8.2$ Hz), 109.0 (CMe_2), 138.3 (PC_{arom}, $^1J_{C,P} = 13.7$ Hz), 138.5 (PC_{arom}, $^1J_{C,P} = 12.1$ Hz), 125.3–134.9 (C_{arom}); ^{31}P NMR ($CDCl_3$) δ −23.0. HRMS (EI) calcd for $C_{41}H_{39}NO_2P$ $[M+H]^+$: 608.2718, found: 608.2716.

4.4.2. (S_A,4*S*,5*R*)-4-({5-[(Diphenylphosphino)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}methyl)-4,5-dihydro-3*H*-dinaphtho[1,2-*e*:2′,1′-*c*]azepine (S_A,4*S*,5*R*)-5. Yield 73%; colorless solid; mp 86–88 °C; R_f 0.25 (eluent petroleum ether/ethyl acetate 6:1); $[\alpha]_D^{20} = +235$ (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.46 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 2.41–2.49 (m, 3H, CH_2N, CH_2P), 2.70 (dd, 1H, $J = 13.1$, 7.8 Hz, CH_2N), 3.09 (d, 2H, $J = 12.1$ Hz, NCH_2Ar), 3.75 (d, 2H, $J = 12.1$ Hz, NCH_2Ar), 4.05–4.13 (m, 2H, >CH–), 7.21–7.29 (m, 8H, H_{arom}), 7.32–7.44 (m, 4H, H_{arom}), 7.46–7.48 (m, 4H, H_{arom}), 7.56 (d, 2H, $J = 8.3$ Hz, H_{arom}), 7.94 (dd, 4H, $J = 8.3$, 8.3 Hz, H_{arom}); ^{13}C NMR ($CDCl_3$) δ 27.26 (CH_3), 27.29 (CH_3), 32.5 (PCH_2, $^1J_{C,P} = 15.4$ Hz), 55.5 (NCH_2), 57.3 (NCH_2, $^4J_{C,P} = 3.3$ Hz), 77.5 (OCH, $J_{C,P} = 16.5$ Hz), 80.7 (OCH, $J_{C,P} = 7.1$ Hz), 109.1 (CMe_2), 137.9 (PC_{arom}, $^1J_{C,P} = 13.2$ Hz), 138.4 (PC_{arom}, $^1J_{C,P} = 12.1$ Hz), 125.3–135.0 (C_{arom}); ^{31}P NMR ($CDCl_3$) δ −22.5. HRMS (EI) calcd for $C_{41}H_{39}NO_2P$ $[M+H]^+$: 608.2718, found: 608.2719.

4.5. Alkylation of *rac*-(*E*)-1,3-diphenyl-2-propenyl acetate

The catalyst was prepared in a Schlenk tube by stirring $[Pd(C_3H_5)Cl]_2$ (4.0 mg, 10.9 μmol) and ligand **5** (13.2 mg, 21.8 μmol) in the solvent (2.5 mL). To this solution was added *rac*-(*E*)-1,3-diphenylprop-2-enyl acetate (126 mg, 0.5 mmol) dissolved in the solvent (2.5 mL). This solution was then added to a Schlenk tube containing a mixture of the nucleophile (1.6 mmol), BSA (324 mg, 1.6 mmol), and KOAc (1.1 mg, 11 μmol) in the solvent (5 mL). The solution was stirred at rt for 24 h, and then quenched with a small amount of water. Evaporation of the solvent, followed by column chromatography gave the alkylated product. The conversion was determined by GC using a Quadrex OV1 column (30 m × 0.25 mm) and the enantioselectivity by HPLC on a chiral stationary phase (column: Daicel OD-H; eluent, hexane/*i*-PrOH). The absolute configurations of the enantiomers were determined by comparison of the retention times with those of authentic samples, and by measurement of the optical rotation of the product.

Acknowledgements

One of us (I.M.) thanks the CNRS for a fellowship.

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