ChemPubSoc Europe

DOI: 10.1002/chem.201704800

CHEMISTRY
A European Journal
Communication

Diphosphane Chemistry

Reducing Diastereomorphous Bis(phosphane oxide) Atropisomers to One Atropisomerically Pure Diphosphane: A New Ligand and a Novel Ligand-Preparation Design

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Abstract: 1,1′-Biphenyl-2,2′-diphosphanes with an achiral bridge spanning C-5 and C-5′ form atropisomers that are enantiomers. Accessing them in an atropisomerically pure form requires resolving a racemic mixture thereof or of a bis(phosphane oxide) precursor. 1,1′-Biphenyl-2,2′-diphosphanes with a homochiral bridge spanning C-5 and C-5′ form atropisomers that are diastereomers. We synthesized the first compound of this kind 1) atropselectively and 2) under thermodynamic control—seemingly a first-time exploit in diphosphane synthesis. The selectivity-inducing step was a high-temperature reduction of two non-interconverting bis(phosphane oxide) atropisomers (60:40 mixture). It furnished the desired diphosphane atropisomerically pure (and atropconvergently because the yield was 67 %). This diphosphane proved worthwhile in Tsuji–Trost allylations, the Hayashi addition of phenylboronic acid to cyclohexenone, and the asymmetric hydrogenation of methyl acetoacetate (up to 95 % yield and 95 % *ee*).

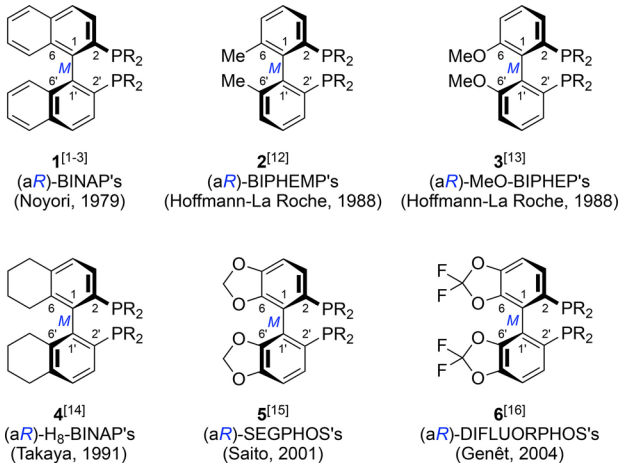

Figure 1. 1,1′-Biaryl-2,2′-diphosphanes for transition-metal mediated asymmetric catalysis (usually, R is for aryl, occasionally, for alkyl). In order to perform their role these ligands must be atropisomerization-stable. This is guaranteed by being 6,6′-disubstituted.

In 1980 Noyori et al. enriched the early field of asymmetric synthesis by introducing (a*R*)- and (a*S*)-1,1′-binaphthyl-2,2′-bis(diphenylphosphane) (BINAP, **1**; Figure 1) as a ligand for transition-metal-mediated asymmetric catalysis.[1] Accessing enantiomerically pure BINAP was studied in detail[2] and re-optimized.[3] This allowed the two enantiomers to become the most important ligand for establishing stereocenters with a single configuration 1) by additive control and 2) in catalytic amounts.[4] BINAP revolutionized synthesis, continues to be a gold standard for the performance of asymmetric catalysis, and has shaped these fields so profoundly that its originator gained the Nobel Prize in Chemistry in 2001.[5] The structure and virtues of BINAP have inspired the development of a considerable variety of related 1,1′-biaryl-2,2′-bis(diarylphosphanes) for almost 30 years.[6,7] We have designed, synthesized, and tested a novel bis(diarylphosphane) of this kind (**16**) as described from here onward.

Most 1,1′-biaryl-2,2′-bis(diaryl- or dialkylphosphanes) known to date form atropisomers that are enantiomers. Obtaining them in an atropisomerically pure form—as required for any application in asymmetric catalysis—almost always[8–11] includes the resolution of a racemic precursor (e.g., for obtaining the diphosphanes **1**–**6** shown in Figure 1[1–3,12–16]). We found how such a resolution can be avoided while an enantiomerically pure 1,1′-biaryl-2,2′-bis(diphenylphosphane) results nevertheless: if its atropisomers are diastereomers.

Figure 2 shows two 1,1′-biaryl-2,2′-bis(diaryl- or dialkylphosphane) designs of the last-mentioned kind, namely the structures **7** and **8**. They are 6,6′-unsubstituted compounds—that is, a priori atropisomerization-labile—yet 5,5′-disubstituted. The placement of one homochiral substituent at C-5 or the placement of two homochiral substituents at both C-5 and C-5′ de-

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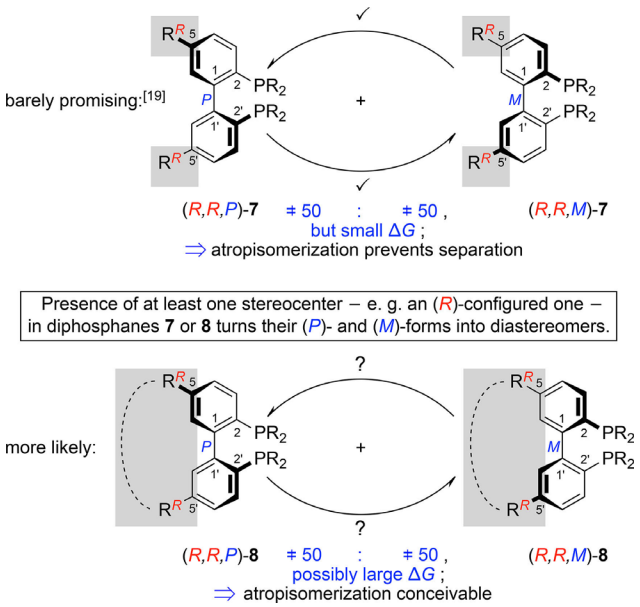
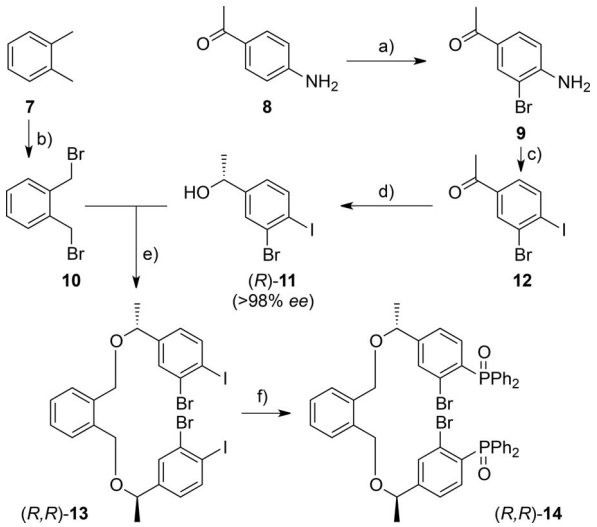


Figure 2. 1,1′-Biaryl-2,2′-diphosphanes which are 6,6′-unsubstituted but 5,5′-disubstituted by at least one homochiral substituent. The latter uplifts 1) the mirror symmetry between the respective atropisomers and thus 2) their energetic degeneracy. The involvement of two stereocenters is shown here (like in our proof-of-principle compound **16**), but one stereocenter or more than two stereocenters might act similarly.

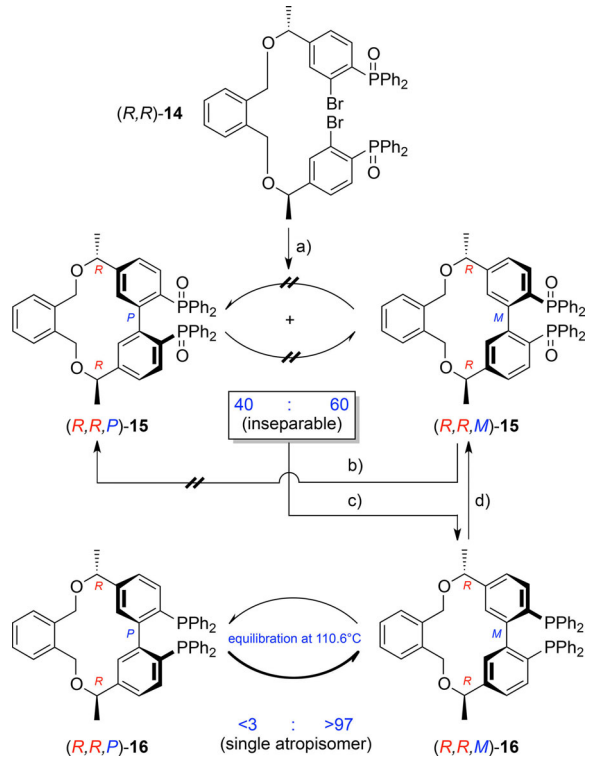
fines diphosphane **7**. Alternatively, a single homochiral substituent between C-5 and C-5′ characterizes diphosphane **8**. Unbridged diphosphane **7** should atropisomerize readily[17] without delivering atropisomerically pure material. This is because the Gibbs free-energy difference between (*R,R,P*)-**7** and (*R,R,M*)-**7** is expected to be relatively small.[18–20] A 5,5′-bridged diphosphane **8** might (!) be atropisomerization-labile, too. If so, it looks more likely that **8** occurs as a single atropisomer under thermodynamic control—because $\Delta\Delta G_f$ is sufficiently large ("case 1")—than a type-**7** diphosphane would. Such a preference might result from the differential restraints, which a bridge between C-5 and C-5′ imposes.[21] On the other hand, a bridged diphosphane (*R,R,P*)-**8** or (*R,R,M*)-**8** might be atropisomerization-stable ("case 2"). If so, even a synthesis of **8** lacking atropselectivity might provide atropisomerically pure material(s) after standard purifications (like crystallization or flash-chromatography on silica gel[22]). Finally ("case 3"), an appropriate preparation protocol might furnish an atropisomerization-stable diphosphane **8** atropselectively right away. This would be due to kinetic control and to $\Delta\Delta G_f^{\neq}$ being sufficiently large. Any of these "cases 1–3" would work without resolving a racemic intermediate. This is worth noting, since exactly this is indispensable for reaching any of the diphosphanes **1**–**6** shown in Figure 1 in an atropisomerically pure form.

We are interested in atropisomerically unique type-**8** 1,1′-biaryl-2,2′-bis(diaryl- or dialkylphosphanes) corresponding to any of the three "cases". The first compound of this kind that we identified—diphosphane (*R,R,M*)-**16** (formula: Scheme 2)—represents an "in-between type": It is conformationally labile at around 150 °C ("case-1" diphosphane) and conformationally stable below 100 °C ("case-2" diphosphane; details: below).

The diphosphane (*R,R*)-**16** was obtained as a pure (*M*)-atropisomer in seven steps (Schemes 1 and 2). 4-Aminoacetophenone (**8**) was monobrominated in 97% yield (Scheme 1). The resulting aminobromoacetophenone **9**[23] was transformed into



Scheme 1. Reagents and conditions: a) NBS, NH_4OAc (5 mol-%), MeCN, RT, 60 min; 97%. b) Br_2, *hν*, no solvent, reflux, 90 min; 58% (ref. [30]: 45–55%). c) $NaNO_2$, conc. HCl, 0 °C, 45 min; KI, 0 °C→RT, 16 h; 72%. d) Concomitant addition of 12 and BH_3·THF to (3a*S*)-1-Methyl-3,3-diphenyltetrahydro-3*H*-pyrrolo[1,2-*c*][1,3,2]oxazaborole[27] (20 mol%) in THF, 0 °C, 3 h; RT, 2 h; 98%. e) NaH, THF, RT, 20 h; 81%. f) (i) *i*PrMgCl·LiCl, THF, −30 °C, 45 min; $ClPPh_2$; → RT, 6 h; 94%; (ii) H_2O_2, 15 min; 96%.



Scheme 2. Reagents and conditions: a) Cu (100 mesh), DMF, 140 °C, 20 h; 80%. b) DMF, 127 °C, 24 h. c) $HSiCl_3$ (10 equiv), NEt_3 (10 equiv), toluene, reflux, 5 h; 67%. d) H_2O_2, THF, RT, 30 min; 98%.

the bromoiodoacetophenone **12**[24] by diazotation and treatment with KI. A Corey–Itsuno reduction[25–27] ensued. It provided the (*R*)-enantiomer[28] of carbinol **11** in 90% yield with 98% *ee*.[29] Successive exposures to NaH and *ortho*-bis(bromomethyl)benzene (**10**; from a double bromination of *ortho*-xylene[30]) furnished the diether **13**. It was purified by flash-chromatography on silica gel[22] as a seemingly pure[31] (*R,R*)-isomer. A Br-tolerating I→Mg exchange with *i*PrMgCl·LiCl at −30 °C,[32] quenching the resulting mixture with $ClPPh_2$, and an H_2O_2 oxidation performed in situ gave 90% of the bis(phosphane oxide) (*R,R*)-**14**.[31]

Exposing the bis(phosphane oxide) (*R,R*)-**14** (0.01 M solution in DMF) to vacuum-dried copper powder (100 mesh) at 140 °C induced an Ullmann cyclization (Scheme 2). It led to up to 80% of an inseparable mixture of the atropisomers (*R,R,P*)-**15** (ca. 40%) and (*R,R,M*)-**15** (ca. 60%).[31] Reduction of this mixture with $HSiCl_3/NEt_3$ in refluxing toluene furnished 67% of the diphosphane (*R,R,M*)-**16**. It was obtained as a single atropisomer and possessed the (*M*)-configuration according to X-ray crystallography.[33] This finding implies that a near-complete[34] (*P*)→(*M*) atropisomerization occurred during[35] the reduction. It became feasible after the bulky $P(=O)Ph_2$ groups had given way to the smaller PPh_2 groups.[36]

The uniqueness of our ligand design and its variability—as the "ligand cases 1–3" above—called for a thorough analysis. We performed it by DFT calculations on the B3LYP-D3/cc-pVDZ level of theory. The environment was taken into account by means of a dielectric continuum (PCM). Figure 3 summarizes the essence of our insights.[37] Diphosphane (*R,R*)-**16** possesses two $E_{pot\,at\,0K}$ minima both for its (*P*)- and its (*M*)-atropisomer. Both (*P*)-atropisomers are less stable ($E_{rel\,at\,0K}$ = 2.94 and 5.52 kcal mol^{-1}) than both (*M*)-atropisomers ($E_{rel\,at\,0K}$ = 0.00 and 0.86 kcal mol^{-1}). The (*P*)-atropisomer is more stable when C_1- rather than C_2-symmetric, whereas the opposite holds true for the (*M*)-atropisomer. Equaling these E_{rel} values with Gibbs free energies, atropisomerically equilibrated (*R,R*)-**16** should consist of (*R,R,M*)-**16**$_{C_2\text{-symmetric}}$ (mainly), (*R,R,M*)-**16**$_{C_1\text{-symmetric}}$ (secondarily), and (*R,R,P*)-**16**$_{C_1\text{-symmetric}}$ (a little). At 110.6 °C, this should give rise to a 73.1:25.3:1.6 mixture[34] and thus an atropisomeric excess of 96.7% of the (*M*)-atropisomers.

We also identified four transition structures (Figure 3 alludes to them). The most stable ($E_{rel\,at\,0K}$ = 9.61 kcal mol^{-1}) belongs to the interconversion of the (*P*)-atropisomers and the second-most stable ($E_{rel\,at\,0K}$ = 11.00 kcal mol^{-1}) to that of the (*M*)-atropisomers. A third transition structure ($E_{rel\,at\,0K}$ = 32.01 kcal mol^{-1}) allows the C_1-symmetric atropisomers to interconvert. The least stable transition structure ($E_{rel\,at\,0K}$ = 48.53 kcal mol^{-1}) prevents a one-step interconversion of the C_2-symmetric atropisomers. The *combined* atropisomerizations (*R,R,P*)-**16**$_{C_1\text{-symmetric}}$ →(*R,R,M*)-**16**$_{C_1\text{-symmetric}}$ and (*R,R,M*)-**16**$_{C_1\text{-symmetric}}$ ⇄(*R,R,M*)-**16**$_{C_2\text{-symmetric}}$ should proceed with a half-lifetime of 56 min at 110.6 °C (details: Supporting Information, Section 14). Its shortness explains the atropconvergence of the phosphane oxide reduction of Scheme 2.[35]

At 110 °C the 5,5′-bridged 1,1′-biaryl-2,2′-bis(diphenylphosphane) **16** atropisomerizes—that is, diastereomerizes—within a few hours, whereas the analogous compounds **17a-e**[38] and

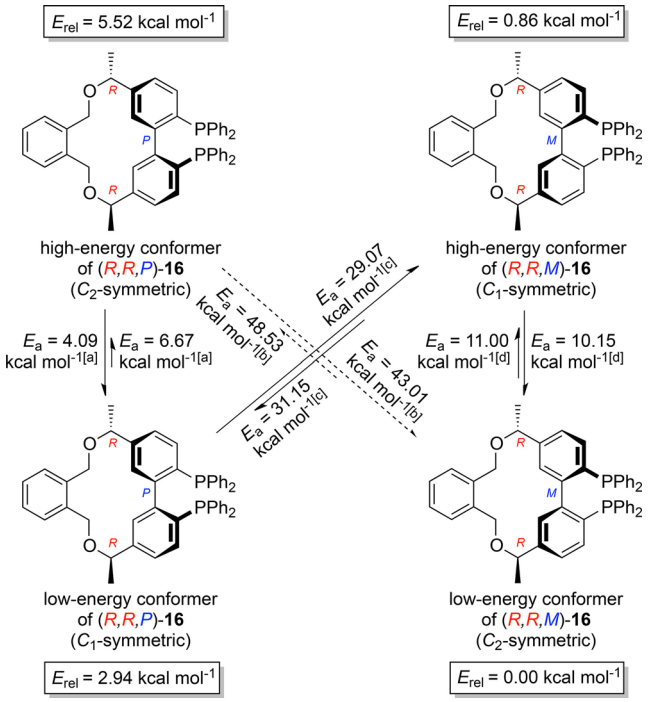


Figure 3. The four most stable stereostructures of the 5,5′-bridged 1,1′-biaryl-2,2′-diphosphane (*R,R*)-**16** in toluene and three ways to interconvert them, all by DFT calculations [B3LYP-D3/cc-pVDZ]. The differences between a) (*R,R,P*)-**16**$_{C_2\text{-symmetric}}$ and (*R,R,P*)-**16**$_{C_1\text{-symmetric}}$ or b) (*R,R,M*)-**16**$_{C_1\text{-symmetric}}$ and (*R,R,M*)-**16**$_{C_2\text{-symmetric}}$ are hard to visualize. [a] $E_{transition\,state}$ = 9.61 kcal mol^{-1}. [b] $E_{transition\,state}$ = 48.53 kcal mol^{-1} [not competitive for realizing (*P*)/(*M*) interconversions]. [c] $E_{transition\,state}$ = 32.01 kcal mol^{-1}. [d] $E_{transition\,state}$ = 11.00 kcal mol^{-1}.

19a–g[39] do not atropisomerize—that is, racemize—within as much as 12 h[38–40] (Figure 4). That is, our diphosphane **16**, which contains a 14-membered ring, atropisomerizes faster

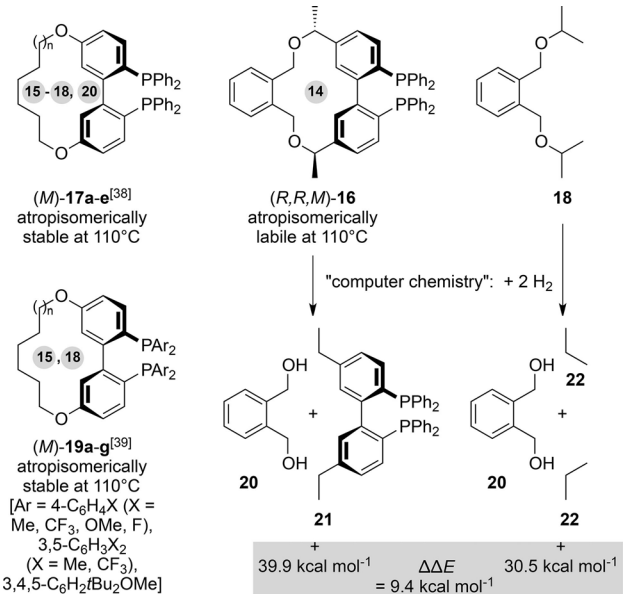
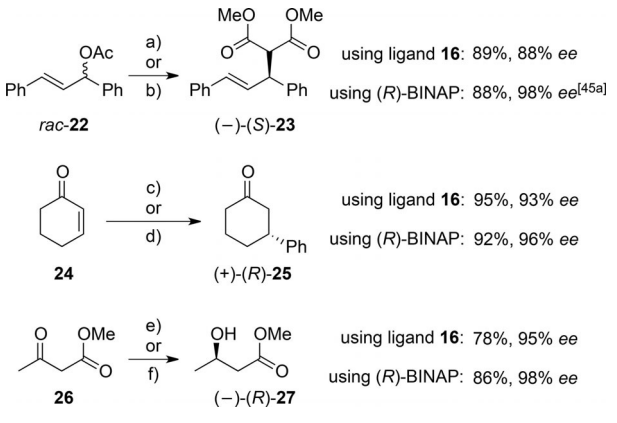


Figure 4. The 5,5′-bridged 1,1′-biaryl-2,2′-diphosphanes (*M*)-**17a–e**[38] and (*M*)-**19a–g**[39] from Wanbin Zhang's laboratories and (*R,R,M*)-**16** from ours.

than the diphosphanes **17** or **19**, which contain 15- to 18- and 20-membered rings. Perhaps the shorter and stiffer 5,5′-bridge in the diphosphane **16** imposes a greater resemblance to the transition structure of atropisomerization than the longer and more flexible bridges in the diphosphanes **17** and **19** do. Suspecting such an effect to pair with more strain in the diphosphane **16** than in **17** or **19**, we estimated the strain in the former as 9.4 kcal mol^{-1}. This value equals the extra-energy liberated when ligand **16** is ring-opened by hydrogenolysis ($\rightarrow$**20** + **21**; $\Delta E_{\text{pot at 0 K}} = -39.9$ kcal mol^{-1}) compared to when its backbone model **18** is hydrogenolyzed ($\rightarrow$**20** + 2 × **22**; $\Delta E_{\text{pot at 0 K}} = -30.5$ kcal mol^{-1}), both in silico (B3LYP-D3/cc-pVDZ).

Diphosphane (*R*,*R*)-**16** acts sufficiently as an (*M*)-atropisomer for behaving like Noyori's (*M*)-configured ligand (a*R*)-BINAP (**1**)[1–3] in typical transition-metal-catalyzed transformations, although not quite as well (Scheme 3). Pd-complexed (*R*,*R*)-**16** catalyzed a Tsuiji–Trost allylation[41] at 0 °C—at which fully equilibrated (*R*,*R*)-**16** would have approximately 99.3 % atropisomeric excess[42,43]—and provided 89 % of the malonate (−)-**23**[44] with 88 % *ee*. (a*R*)-BINAP (**1**) delivered the same product in 88 % yield and with 98 % *ee* in our group[45a] and in 84 % yield and with 99 % *ee* using the corresponding zinc enolate.[45b] Rh-complexed (*R*,*R*)-**16** catalyzed the phenylborylation of cyclohexenone[46] at 100 °C—at which the fully equilibrated (*R*,*R*)-**16** would have approximately 97.2 % atropisomeric excess[42,43]—and provided 95 % of the 1,4-adduct (+)-**25**[47] with 93 % *ee*. (a*R*)-BINAP (**1**) delivered the same product in 83 % yield and with 99 % *ee* according to reference [48] and in 92 % yield and with 96 % *ee* in own hands. Ru-complexed (*R*,*R*)-**16** catalyzed the asymmetric hydrogenation of the β-ketoester[49] **26** at room temperature—at which the fully equilibrated (*R*,*R*)-**16** would have approximately 98.9 % atropisomeric excess[42,43]—and provided 78 % of the hydroxyester (−)-**27**[50] with 95 % *ee*. (a*R*)-BINAP (**1**) delivered the same product in 86 % yield and with 98 % *ee* in our hands.



Scheme 3. Reagents and conditions: a) Dimethyl malonate (1.2 equiv), bis(trimethylsilyl)acetamide (2.2 equiv), NaOAc (5.0 mol %), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.50 mol %), **16** (1.0 mol %), CH_2Cl_2, 0 °C, 1 h. b) Similarly as (a) but using (*R*)-BINAP at −40 °C.[45a] c) $PhB(OH)_2$ (2.5 equiv), $[Rh(acac)(C_2H_4)_2]$ (1.0 mol %), **16** (1.2 mol %), dioxane:H_2O = 9:1, 100 °C, 5 h. d) Same as (c) but using (*R*)-BINAP. e) H_2 (5 bar), $[Et_2NH_2]^{\oplus}$ $\{[ClRu(\mathbf{16})]_2(\mu\text{-}Cl)_3\}^{\ominus}$ (0.5 mol %), EtOH, RT, 20 h. f) Same as (e) but using $[Et_2NH_2]^{\oplus}$ $\{[ClRu((R)\text{-BINAP})]_2(\mu\text{-}Cl)_3\}^{\ominus}$ (0.5 mol %).

In summary we designed and gained an enantiopure 1,1′-biaryl-2,2′-bis(diphenylphosphane) (*R*,*R*)-**16** of diastereomorphic atropisomers. Under equilibrating conditions (!) the (*M*)-atropisomer(s) dominated over their (*P*)-counterpart(s) approximately 60-fold. This allowed (*R*,*R*)-**16** to be employed in asymmetric catalyzes and to achieve up to 95 % *ee*. The design principle behind diphosphane **16** appears highly variable. This nourishes hopes that **16** might represent a lead structure for a novel type of "privileged ligands[51]". These are adoptable for several if not many applications.

Acknowledgements

This research was supported by the DFG (IRTG 1038 "CCROS"). F.S. is thankful to the *Stiftung der Deutschen Wirtschaf*t for a fellowship. We are indebted to Prof. Dr. Bernd Engels (Institut für Physikalische und Theoretische Chemie, Julius-Maximilians-Universität Würzburg) for providing C.B. the time and the computational capacity for joining this cooperation. We thank Dr. Daniel Kratzert (Institut für Anorganische Chemie, Albert-Ludwigs-Universität Freiburg) for the single-crystal X-ray analysis.

Conflict of interest

The authors declare no conflict of interest.

Keywords: asymmetric catalysis · asymmetric induction · atropisomerism · biaryls · diphosphanes

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devoid of phosphorus were transformed into atropisomerically pure 1,1′-biaryl-2,2′-diphosphanes in 3 steps—by liberating two aryl-bound OH groups, making their bis(triflate), and coupling with $HPAr_2$.[10c]

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[11] The cyclizations to which reference [8] alludes or which underlie the studies of reference [10] were atropselective and gave 5,5′-di-unsubstituted 6,6′-disubstituted 1,1′-biaryl-2,2′-diphosphanes in the end. In stark contrast the cyclization giving bis(phosphane oxide) **15** is not atropselective. Irrespective thereof, it sets the stage for reaching the 5,5′-bridged 6,6′-di-unsubstituted 1,1′-biaryl-2,2′-diphosphane **16** atropconvergently. This makes our ligand design fundamentally distinct from literature precedence.

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[19] The diphosphane design **7** can have some potential for asymmetric catalysis nevertheless. This was shown impressively in reference [18].

[20] An atropisomerization-labile 1,1′-biaryl-2,2′-bis(diphenylphosphane), the "atropisomers" of which would be enantiomers, converged to an atropisomerically pure Pd^{II} complex in the presence of an enantiopure diamine ligand. The complex stayed atropisomerically pure even after removal of this diamine by protonation: a) K. Mikami, K. Aikawa, Y. Yusa, M. Hatano, *Org. Lett.* **2002**, *4*, 91; for an insightful contextualization of the concept behind the findings of reference [20a]—which is very different from ours—see: b) K. Mikami, K. Aikawa, Y. Yusa, J. J. Jodry, M. Yamanaka, *Synlett* **2002**, 1561.

[21] Potential energy differences of -3.7 to $+6.8$ kcal mol^{-1} between the (*P*)- vs. (*M*)-atropisomer were calculated (B3LYP/6-31G*) for biaryls in which a homochiral tetralactame links C-5 to C-5′ and the C-2- and C-2′-substituents are H, OH, OMe, Me or Br: G. Haberhauer, C. Tepper, C. Wölper, D. Bläser, *Eur. J. Org. Chem.* **2013**, 2325. It was assumed but not proved that these biaryls are atropisomerically labile.

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[27] (3a*S*)-1-Methyl-3,3-diphenyltetrahydro-3*H*-pyrrolo[1,2-*c*][1,3,2]oxazaborole[26] was obtained from BASF Corporation.

[28] Alcohol **11** was dextrorotatory. It should be (*R*)-configured because its (*R*)-debromo and its (*R*)-deiodo analogs are dextrorotatory, too (details: Supporting Information).

[29] This *ee* value was determined by HPLC analysis using an enantiomerically pure stationary phase (details: Supporting Information).

[30] Procedure: a) R. Brückner, S. Braukmüller, H.-D. Beckhaus, J. Dirksen, D. Goeppel, M. Oestreich, *Praktikum Präparative Organische Chemie—Organisch-Chemisches Grundpraktikum*, Spektrum, Heidelberg, **2008**, pp. 83; analytical data: b) R. P. Kreher, J. Kalischko, *Chem. Ber.* **1991**, *124*, 645.

[31] Alcohol (*R*)-**11** (98% *ee*) and dibromide **10** should have afforded a 98:2 mixture of diether (*R,R*)-**13** (99.98% *ee*) and its *meso* diastereomer. We observed neither the latter nor the *meso* isomer of any of the follow-up products. It is possible that we removed the *meso* compund(s) flash-chromatographically (reference [22]).

[32] Br(!)/Mg exchange reactions with this reagent: A. Krasovskiy, P. Knochel, *Angew. Chem. Int. Ed.* **2004**, *43*, 3333; *Angew. Chem.* **2004**, *116*, 3396.

[33] 8% of the P atoms of diphosphane (*R,R,M*)-**16** had been oxidized (inadvertently) in the crystals, which we studied after months of storage: They pertained to $P(=O)Ph_2$ units. It is noteworthy that this left the C, O, and P atom sites unaffected throughout the crystal. Therefore, refinement was possible as if the material had been homogeneous. Details and ORTEP plots: Supporting Information. CCDC 1475863 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[34] At equilibrium in toluene solution of 110.6 °C the diphosphanes (*R,R,M*)-$\mathbf{16}_{C_2\text{-symmetric}}$ and (*R,R,P*)-$\mathbf{16}_{C_1\text{-symmetric}}$ should represent a 97.9:2.1 mixture ($K_{eq}=47.4$; details: Supporting Information, Section 10.1). The diphosphanes (*R,R,M*)-$\mathbf{16}_{C_2\text{-symmetric}}$ and (*R,R,M*)-$\mathbf{16}_{C_1\text{-symmetric}}$ combined should prevail over (*R,R,P*)-$\mathbf{16}_{C_1\text{-symmetric}}$ in a 98.4:1.6 ratio ($K_{eq}=59.7$; details: Supporting Information, Section 10.3).

[35] At 110.6 °C in toluene solution, a 60:40 mixture of a mixture of the diphosphanes (*R,R,M*)-$\mathbf{16}_{C_2\text{-symmetric}}$ and (*R,R,M*)-$\mathbf{16}_{C_1\text{-symmetric}}$ combined vs. pure (*R,R,P*)-$\mathbf{16}_{C_1\text{-symmetric}}$ should provide a 96.4:3.6 mixture within 4 h (details: Supporting Information, Section 13). This alone may have left (*R,R,P*)-**16** undetected. Assistance by having decreased its proportion during purification by flash-chromatography[22] is conceivable.

[36] Oxidation of the diphosphane (*R,R,M*)-**16** with H_2O_2 gave 98% of the bis(phosphane oxide) **15** (Scheme 2). It was pure (*R,R,M*)-**15**, without a trace of (*R,R,P*)-**15**, and remained atropisomerically pure while heating a DMF solution thereof at 127 °C for 24 h. This inertness could be due to an insurmountable atropisomerization barrier and/or to a lack of driving force.

[37] Detailed representations of all minimum and transition structures, atomic coordinates, bond angles, dihedral angles, distortion parameters, and paralleling results obtained with other functional/basis set combinations: Supporting Information.

[38] a) C. Wang, G. Yang, J. Zhuang, W. Zhang, *Tetrahedron Lett.* **2010**, *51*, 2044; corrigendum: C. Wang, G. Yang, J. Zhuang, W. Zhang, *Tetrahedron Lett.* **2011**, *52*, 5196; these ligands were named "C_n-BridgePHOSs" by b) J. Chen, D. Liu, D. Fan, Y. Liu, W. Zhang, *Tetrahedron* **2013**, *69*, 8161.

[39] a) W. Zhang, J. Shen, D. Liu, *Faming Zhuanli Shenqing*, CN 105481684 A 20160413, **2016**; b) W. Zhang, J. Li, J. Shen, D. Liu, *Faming Zhuanli Shenqing*, CN 105384623 A 20160309, **2016**; c) W. Zhang, Z. Zhang, J. Chen, Y. Bao, J. Dong, Y. Jing, Y. Li, *Faming Zhuanli Shenqing*, CN 105254474 A 20160120, **2016**; d) W. Zhang, Z. Zhang, J. Chen, Y. Bao, Y. Zhang, Y. Li, *Faming Zhuanli Shenqing*, CN 105218335 A 20160106, **2016**.

[40] The diphosphanes (*M*)-**17a–e** or **−19a–g** and their (*P*)-atropisomers are pairs of enantiomers. Thus, accessing them atropisomerically pure required resolving racemic specimens by chiral HPLC.[38,39] These properties liken **17** and **19** to the diphosphanes **1–6** (Figure 1), but differentiate them from (*M*)- vs. (*P*)-**16** which are a pair of diastereomers.

[41] Recent reviews: a) R. Ferraccioli, L. Pignataro, *Curr. Med. Chem.* **2015**, *19*, 106; b) B. M. Trost, D. R. Fandrick, *Aldrichimica Acta* **2007**, *40*, 59; c) B. M. Trost, M. R. Machacek, A. Aponick, *Acc. Chem. Res.* **2006**, *39*, 747; d) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921.

[42] Diphosphane (*R*,*R*)-**16** need not assume the same (*M*):(*P*) equilibrium ratio in a Pd-, Rh- or Rh-complex as if unbound (cf. reference [18]).

[43] Calculation: see the Supporting Information, Section 10.3.

[44] a) (−)-**23** exhibited $[\alpha]_D^{20} = -9.0$ ($c = 0.85$, $CHCl_3$); b) (−)-**23** is (*S*)-configured according to V. G. Albano, M. Bandini, M. Monari, E. Marcucci, F. Piccinelli, A. Umani-Ronchi, *J. Org. Chem.* **2006**, *71*, 6451 {$[\alpha]_D^{20} = -8.8$ ($c = 0.6$, $CHCl_3$)}.

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[47] a) (+)-**25** exhibited $[\alpha]_D^{20} = +18.3$ ($c = 1.13$, $CHCl_3$); b) (+)-**25** is (*R*)-configured according to A. G. Schultz, R. E. Harrington, *J. Am. Chem. Soc.* **1991**, *113*, 4926 {$[\alpha]_D^{22} = +20.5$ ($c = 0.58$, $CHCl_3$)}.

[48] T. Hayashi, M. Takahashi, Y. Takaya, M. Ogasawara, *Org. Synth.* **2002**, *79*, 84.

[49] Reviews: a) M. Kitamura, R. Noyori in *Ruthenium in Organic Synthesis* (Ed.: S.-I. Murahashi,) Wiley-VCH, Weinheim, **2004**, pp. 3–52; b) T. Ohkuma, M. Kitamura, R. Noyori in *Catalytic Asymmetric Synthesis, 2nd ed.* (Ed.: I. Ojima), Wiley-VCH, Weinheim, **2000**, p. 1.

[50] a) (−)-**27** exhibited $[\alpha]_D^{20} = -41.2$ ($c = 0.98$, $CHCl_3$); b) (−)-**27** is (*R*)-configured according to D. A. Evans, J. Bartroli, T. L. Shi, *J. Am. Chem. Soc.* **1981**, *103*, 2127 {$[\alpha]_D = -45.8$ ($c = 1.7$, $CHCl_3$)}.

[51] a) T. P. Yoon, E. N. Jacobsen, *Science* **2003**, *299*, 1691; b) *Privileged Chiral Ligands and Catalysts* (Ed.: Q.-L. Zhou), Wiley-VCH, Weinheim, **2011**.

Manuscript received: June 15, 2017
Revised manuscript received: October 11, 2017
Version of record online: ■■ ▮▮, 0000

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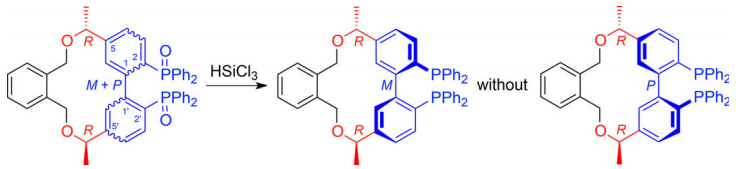

Atropconvergence: A 1,1′-biaryl-2,2′-diphosphane with a "homochiral bridge" between C-5 and C-5′ defines a pair of atropisomers that are diastereomers. This suggests that the synthesis of such a compound as a pure atropisomer may be achieved by a unilaterally biased atropisomerization. The first diphosphane synthesis of this kind is reported—the reduction of a 60:40 mixture of atropisomeric bis(phosphane oxides) at 110 °C provided 67 % of a single diphosphane atropisomer.

Diphosphane Chemistry

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Reducing Diastereomorphous Bis(phosphane oxide) Atropisomers to One Atropisomerically Pure Diphosphane: A New Ligand and a Novel Ligand-Preparation Design