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New Pathway to C_2-Symmetric Atropoisomeric Bipyridine *N,N′*-Dioxides and Solvent Effect in Enantioselective Allylation of Aldehydes

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Dedicated to Milan Hájek on the occasion of his 65th birthday.

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

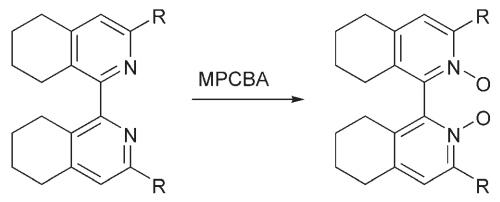
Abstract: The [2+2+2]cyclotrimerization of 1,7,9,15-hexadecatetrayne with nitriles catalyzed by dicarbonylcyclopentadienylcobalt(I) opened a new pathway for the synthesis of C_2-symmetrical bis(tetrahydroisoquinolines) that were used as starting material for the preparation of axially chiral bipyridine *N,N′*-dioxides. The *N,N′*-dioxides (1 mol%) were found to be highly catalytically active and enantioselective (up to 83% *ee*) for the asymmetric allylation of aldehydes with allyl(trichloro)silane in various solvents. In addition, a dramatic solvent effect was observed where the use of different solvents induced opposite chiralities of the product with the same enantiomer of the catalyst, e.g., 65% *ee* (*S*) in acetonitrile (MeCN) *vs.* 82% *ee* (*R*) in chlorobenzene.

Keywords: asymmetric catalysis; cobalt; cyclotrimerization; microwave heating; organocatalysis; solvent effect

Enantioselective organocatalysis is one of the fast growing areas in organic synthesis.[1] The main reason for its success lies in the high level of enantioselectivity that can usually be achieved by the use of rather simple substances. One such class of compounds are bipyridine *N,N′*-dioxides[2] that activate various substrates through a Lewis base reaction mechanism. Although a great deal of work has been done in this area by the groups of Nakajima,[3] Hayashi,[4] Kočovský,[5] Dennmark,[6] and others,[7] who prepared various catalysts and showed that they can catalyze a number of reactions, there are still issues that have not yet been clarified and are awaiting further exploration such as: i) the relationship between the structure of bipyridine *N,N′*-dioxides and degree of enantioselectivity, ii) the course of the reaction mechanism(s), and also iii) the development of simple synthetic approaches to new potential catalysts.

Since the bipyridine framework is accessible by [2+2+2]cyclotrimerization of alkynes with nitriles,[8,9] in our previous reports the effort was focused on the development of new synthetic procedures for the synthesis of unsymmetrically substituted bipyridine *N,N′*-dioxides *via* the cyclotrimerization pathway.[10] During the course of our study we found that a convenient method for the preparation of the bipyridine precursors of the bipyridine *N,N′*-dioxides is the $CpCo(CO)_2$-catalyzed cyclotrimerization under microwave irradition.[10,11] The prepared bipyridine *N,N′*-dioxides showed interesting enantioselectivity in the allylation of benzaldehydes.[12] In this communication we report: i) a new simple methodology for the synthesis of C_2-symmetric substituted bipyridines with the bis(tetrahydroisoquinoline) framework, ii) the synthesis of the corresponding chiral bipyridine *N,N′*-dioxides, and iii) a hitherto unreported solvent effect on the enantioselectivity of the benzaldehyde allylation.

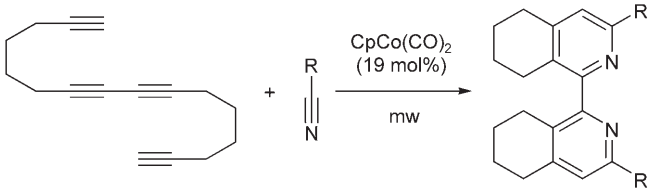
Initially, it was conceived that the partially hydrogenated isoquinoline units in a bipyridine compound would result in the following effects: i) by analogy with Binol and H_8-Binol,[13] the tetrahydroisoquino-



Scheme 1. Oxidation of **3** to **4**.

line moiety should be sterically bulkier than the isoquinoline unit, and the combination with itself should result in a larger dihedral angle,[14] ii) the presence of hydrogenated rings should increase its solubility in organic solvents. Although the cyclotrimerization of a tetrayne with nitriles can be envisioned as a simple approach to C_2-symmetrical bipyridines, only three syntheses of bipyridines with the 6,6′,7,7′-tetrahydro-1,1′-bis-5*H*-cyclopenta[*c*]pyridine framework were reported.[9] Interestingly, the use of this methodology for the preparation of bis(tetrahydroisoquinolines) has not yet been reported. We envisioned that the synthesis of the C_2-symmetrical bis(tetrahydroisoquinolines) could be accomplished by a cobalt complex-catalyzed co-cyclotrimerization of 1,7,9,15-hexadecatetrayne **1** with nitriles **2** (Scheme 1). The tetrayne **1** was prepared from the commercially available 1,7-octadiyne by Pd-catalyzed oxidative dimerization[15] in 15% isolated yield (the major side reaction was oligomerization of the starting material). Initial attempts to affect the catalytic cyclotrimerization of tetrayne **1** with nitriles **2** in the presence of $CpCo(CO)_2$ under thermal conditions (140 °C) did not meet with success and only complex reaction mixtures were obtained. Gratifyingly, the cyclotrimerization with an excess of nitriles **2** in the presence of a catalytic amount of $CpCo(CO)_2$ proceeded under microwave irradiation affording regioselectively the corresponding bipyridines **3** in reasonable isolated yields (Table 1). Thus the reaction with acetonitrile **2a** afforded bipyridine **3a** in 36% yield (entry 1). Also the reaction with benzonitrile **2b** gave the corresponding products in 51% yield (entry 2). Similarly, the cyclotrimerizations with substituted benzonitriles, 4-trifluoromethylbenzonitrile **2c**, 4-methoxybenzonitrile **2d**, and 3,4,5-trimethoxybenzonitrile **2e** afforded bipyridines **3c–e** in 47,

Table 1. Cocyclotrimerization of tetrayne **1** with nitriles **2** to symmetrical bipyridines **3**.



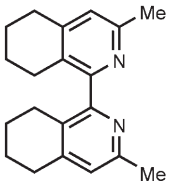
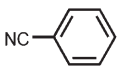
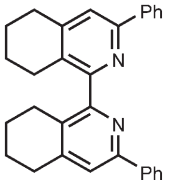
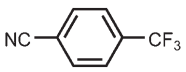
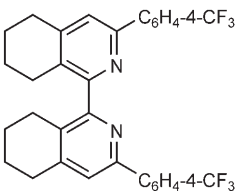
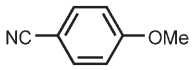
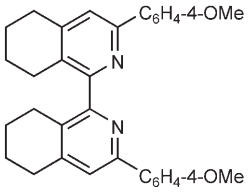
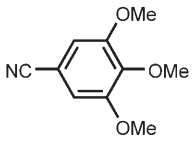
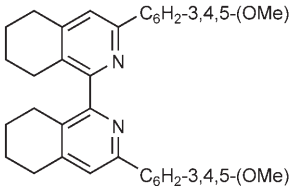
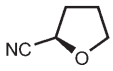
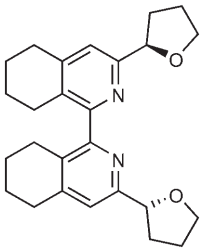
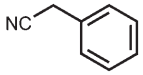
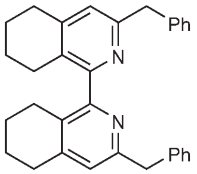
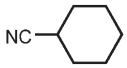
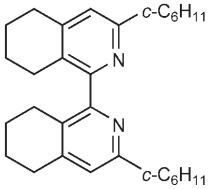
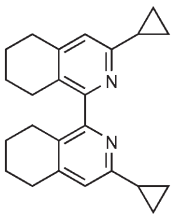
Entry	Nitrile **2**		Bipyridine **3**		Yield[a]
1	NC–Me	**2a**		**3a**	36%
2		**2b**		**3b**	51%
3		**2c**		**3c**	47%

Table 1. (Continued)

Entry	Nitrile **2**		Bipyridine **3**		Yield[a]
4		**2d**		**3d**	50%
5		**2e**		**3e**	46%
6		**2f**		**3f**	48%
7		**2g**		**3g**	34%
8		**2h**		**3h**	21%
9		**2i**		**3i**	9%

[a] Isolated yields.

50, and 46% yields (entries 3–5). Furthermore the cyclotrimerization with (*R*)-tetrahydrofuran-2-carbonitrile **2f** proceeded uneventfully to give bipyridine **3f** in good 48% isolated yield (entry 6). The reactions with alkyl nitriles such as benzyl cyanide **2g**, cyclohexanecarbonitrile **2h** and cyclopropanecarbonitrile **2i** proceeded as well, albeit in lower yields of 34, 21 and 9%, respectively (entries 6–9). The lower yields of the products in the latter entries could be attributed to a greater steric hindrance of the nitrile group located on the secondary carbon atom. In addition, using the recently reported catalytic system $CoCl_2 \cdot 6H_2O$/dppe/Zn[9c,16] for the cyclotrimerization of alkynes with nitriles was met with only partial success. After the reaction time of 24 h, an 8:1 mixture of 1-(1′,7′-octadiyn-1′-yl)-3-phenyl-5,6,7,8-tetrahydroisoquinoline and bipyridine **3b** was isolated in 50% combined yield, indicating that this procedure is not convenient for the straightforward synthesis of bis(tetrahydroisoquinolines).

Out of the prepared compounds, bipyridines **3b**, **3e**, and **3f** were selected for further oxidation by

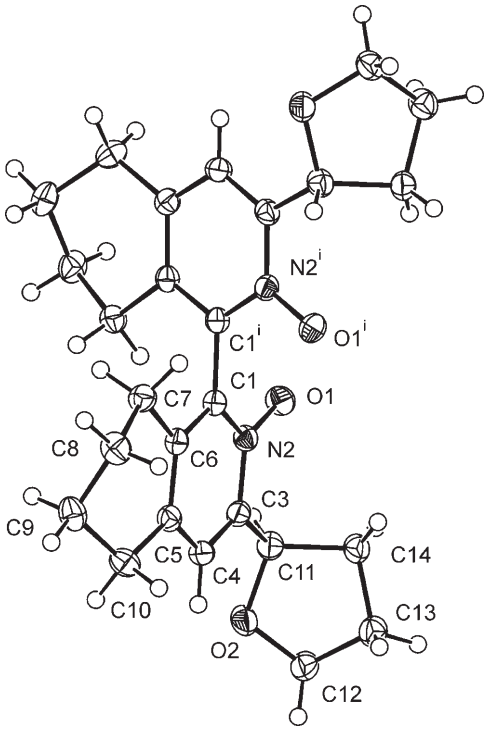


Figure 1. View on the molecule of (*R*,*R*,*R*)-**4c** with atom numbering schema. The displacement ellipsoids are drawn on 50% probability level. The second part of the molecule is generated *via* rotation of the two-fold axis passing perpendicularly on the C1–C1^{i} bond, symmetry code: (i) 1−*x*, −y,z.

MPCBA to the corresponding bipyridine *N,N′*-dioxides **4** (Scheme 1). Bipyridine *N,N′*-dioxides **4a** and **4b** were obtained in 41 and 22% yield, respectively, and were resolved into enantiomers by using HPLC with a chiral stationary phase (assignment of absolute configuration was similar as previously reported).[10b] Oxidation of **3f** afforded a mixture of diastereoisomers (*R*,*R*,*R*)-**4c** and (*S*,*R*,*R*)-**4c** that were isolated by using a simple column chromatography on alumina in 48 and 28% yields, respectively. The configuration and structure of (*R*,*R*,*R*)-**4c** was unequivocally assigned by X-ray crystallographic analysis (Figure 1).

The next target was to check the catalytic and enantioselective properties of the prepared chiral bipyridine *N,N′*-dioxides **4** in the addition of allyl(trichloro)silane to benzaldehydes (Sakurai–Hosomi reaction). Allylation of model compounds such as 4-trifluoromethylbenzaldehyde **5a**, benzaldehyde **5b**, and 4-methoxybenzaldehyde **5c** with 1 mol% of the catalyst was used as a standard procedure at −78 or −40 °C depending on the melting point of the solvent used. Although the allylation of benzaldehydes has usually been run only in acetonitrile, dichloromethane, and chloroform, we assumed that it would also be useful to study the course of the reaction in other solvents (Table 2). To the best of our knowledge, such a study has not been done yet, presumably because of the low solubility of the hitherto prepared catalysts in various solvents. At the outset we studied the allylation of benzaldehyde **5b** in commonly used solvents such as dichloromethane (entry 1) and acetonitrile (entry 2) with (*S*)-**4a**. It proceeded with full conversion to give product (*R*)-**6b** with average *ee* of 55 and 65%, respectively. The asymmetric induction proceeded as was previously observed: the (*S*)-catalysts gave (*R*)-products (and *vice versa*). As for diastereoisomer-

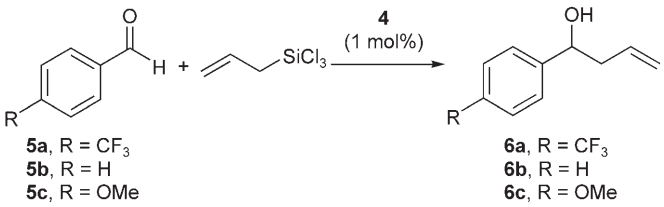
Table 2. Allylation of benzaldehyde **5b** in various organic solvents.

Entry	*T* [°C]	Solvent	Catalyst – *ee* [%][a] – (Yield [%][b])		
			(*S*)-**4a**	(*R*,*R*,*R*)-**4c**	(*S*,*R*,*R*)-**4c**
1	−78	CH_2Cl_2	55 (100), *R*	59 (50), *S*	37 (44), *R*
2	−40	MeCN	65 (100), *R*	48 (100), *S*	63 (82), *R*
3	−40	$CHCl_3$	36 (100), *R*		
4	−78	$EtNO_2$	53 (71), *R*		
5	−78	PhMe	83 (45), *S*	0 (0)	75 (10), *S*
6	−40	PhF	78 (100), *S*		
7	−40	PhCl	79 (100), *S*		
8	−40	*m*-$C_6H_4F_2$	73 (100), *S*		
9	−78	C_7F_8	50 (14), *S*		
10	−78	$CFCl_3$	40 (14), *S*		
11	−78	*n*-pentane	44 (1), *S*		
12	−78	THF	70 (100), *S*		
13	−78	EtOAc	74 (100), *S*		
14	−78	$MeOC_6F_5$/PhMe[c]	66 (10), S		
15	−78	MeCN/THF[d]	34 (100), *R*		

[a] Determined by GC.
[b] GC yields.
[c] 3/1 mixture.
[d] 1/1 mixture.

ic catalysts (*R*,*R*,*R*)-**4c** and (*S*,*R*,*R*)-**4c**, in dichloromethane the former afforded (*S*)-**6b** (59% *ee*) and the latter (*R*)-**6b** (37% *ee*) (entry 1), and in acetonitrile the former afforded (*S*)-**6b** (48% *ee*) and the latter one (*R*)-**6b** (63% *ee*) (entry 2). This clearly indicated that asymmetric induction was controlled by the axial chirality of the biaryl moiety.[17] Next, the allylation of benzaldehyde catalyzed by (*S*)-**4a** was carried out in chloroform (entry 3) and nitroethane (entry 4) to give the corresponding product (*R*)-**6b** with lower enantioselectivity (36 and 53% *ee*). The allylation catalyzed by (*S*)-**4a** in toluene (entry 5) proceeded to give the opposite enantiomer (*S*)-**6b** with good enantioselectivity (83%) and reasonable conversion (45%). Surprisingly, (*R*,*R*,*R*)-**4c** did not catalyze the allylation, but in the presence of (*S*,*R*,*R*)-**4c** was formed (*S*)-**6b** (75% *ee*), albeit in low yield (10%). Then the allylation catalyzed by (*S*)-**4a** was run in a number of other solvents (entries 6–15) and in all cases the product with the opposite stereochemistry (*S*)-**6b** was obtained in variable enantioselectivities and yields. Good enantioselectivity was obtained in fluorobenzene (entry 6, 78% *ee*), chlorobenzene (entry 7, 79% *ee*), and *m*-difluorobenzene (entry 8, 73% *ee*). Similar values were achieved also in polar aprotic solvents such as THF (entry 12, 70% *ee*) and ethyl acetate (entry 13, 74% *ee*). A combination of pentafluoroanisole with toluene did not have a positive effect either on enantioselectivity (66% *ee*) or on catalytic activity (10% yield) (entry 14). Finally, the allylation was carried out in a 1/1 mixture of MeCN and THF (entry 15), because in pure solvents (entries 2 and 12) it proceeded with similar *ee*s, but with the opposite enantioselectivity. In this instance (*R*)-**6b** was formed (34% *ee*), clearly showing that the effect of MeCN prevailed over that of THF.

Furthermore, the high catalytic activity of **4a** was reflected by the fact that the allylation of benzaldehyde **5b** (chlorobenzene, −40 °C) with 0.1 mol% of (*S*)-**4a** proceeded with full conversion within 1 h (TOF of >1000) and without loss of enantioselectivity (80% *ee*). The turnover frequency of (*S*)-**4a** was thus higher than that of the catalysts prepared by Hayashi.[4c]



Scheme 2. Enantioselective allylation of benzaldehydes **5**.

To assess the effect of the substituent on the aromatic ring of benzaldehyde on enantioselectivity, the allylation of benzaldehydes **5a**, **5b**, and **5c** was carried out in acetonitrile at −40 °C (Scheme 2, Table 3) (the reaction with benzaldehyde is presented for comparison). The allylation catalyzed by (*R*)-**4a** in MeCN of **5a**, **5b**, and **5c** gave the corresponding products (*S*)-**6a**, (*S*)-**6b**, and (*S*)-**6c** in good yields with 30, 65, and 80% *ee*s, respectively (entries 1–3). This trend is in accordance with previously published data showing an increase of enantioselectivity in the allylation of substituted benzaldehydes, when the substituents gradually change from electron-withdrawing to -donating ones.[3a,4,9b] A similar trend was also observed in the case of catalyst (*R*)-**4b** bearing trimethoxyphenyl substituents during the allylation in acetonitrile, albeit with lower enantioselectivity. This observation was rather surprising, because it was previously shown that the presence of electron-rich aromatic rings had a beneficial effect on enantioselectivity.[4c] The reactions catalyzed with (*R*,*R*,*R*)-**4c** in acetonitrile (entries 1–3) proceeded with a similar trend in enantioselectivity; however, the reaction with **5a** gave (*R*)-**6a** (15% *ee*) and those with **5b** and **5c** afforded (*S*)-**6b** (48% *ee*) and (*S*)-**6c** (60% *ee*). As for (*S*,*R*,*R*)-**4c** a different picture was observed: the reaction with **5a** and **5b** gave (*R*)-**6a** (16% *ee*) and (*R*)-**6b** (46% *ee*) (entries 1 and 2) but with **5c** chiral induction was not observed (entry 3).

Table 3. Allylation of benzaldehydes **5** to alcohols **6** in acetonitrile and chlorobenzene.

Entry	**5**	Solvent	Catalyst[a] – *ee* [%][b] – (Yield [%][c])			
			(*R*)-**4a**	(*R*)-**4b**	(*R*,*R*,*R*)-**4c**	(*S*,*R*,*R*)**4c**
1	**5a**	MeCN	30 (100), *S*	7 (32), *S*	15 (82), *R*	16 (100), *R*
2	**5b**	MeCN	65 (100), *S*	52 (61), *S*	48 (100), *S*	46 (100), *R*
3	**5c**	MeCN	80 (100), *S*	68 (24), *S*	60 (100), *S*	0 (100)
4	**5a**	PhCl	61 (83), *R*	73 (90), *R*	0 (0)	75 (40), *S*
5	**5b**	PhCl	82 (100), *R*	70 (100), *R*	0 (0)	62 (100), *S*
6	**5c**	PhCl	60 (78), *R*	33 (96), *R*	0 (0)	56 (47), *S*

[a] Reactions were run at −40 °C.
[b] Determined by GC.
[c] GC yields.

The allylations were then carried out in chlorobenzene under the same reaction conditions for comparison. As expected, catalysis by (*R*)-**4a** provided (*R*)-**6a–c**. The best enantioselectivity (82% *ee*) was observed in the reaction with simple benzaldehyde **5b** (entry 5). In the case of trifluoromethylbenzaldehyde **5a** and methoxybenzaldehyde **5c** the *ee*s were just 61 and 60% , respectively (entries 4 and 6). The reaction catalyzed by (*R*)-**4b** proceeded with a reversed enantioselectivity trend (entries 4–6); enantioselectivity decreased as the substituents changed from electron-withdrawing to electron-donating: **6a** (CF_3, 73% *ee*), **6b** (H, 70% *ee*), **6c** (OMe, 33% *ee*). Surprisingly, the reactions in the presence of (*R*,*R*,*R*)-**4c** did not proceed at all (entries 4–6). On the other hand, catalysis by (*S*,*R*,*R*)-**4c** provided the expected products with the stereochemistry and enantioselectivity trends reversed: 75% *ee* [(*S*)-**6a**], 62% *ee* [(*S*)-**6b**] and 56% *ee* [(*S*)-**6c**] (entries 4–6). It should be noted that the same solvent effect was observed also in the allylations of benzaldehydes catalyzed by the previously prepared *N*,*N*′-dioxides bearing one tetrahydroisoquinoline unit.[18]

Although the enantioselectivities realized are average, there are several issues worthy of mention. Firstly, it is the origin of the profound solvent effect. Although a similar phenomenon has been observed in several transition metal-catalyzed reactions,[19] its extent in organocatalysis, to the best of our knowledge, is rather unexpected. Not only could it effect stereochemistry reversion at the newly formed center of chirality, but it could also change the influence of electron-donating and electron-withdrawing groups attached to the aromatic ring of benzaldehydes on asymmetric induction. Secondly, in the case of diastereoisomeric catalysts **4c**, the change of solvent could completely hinder the transfer of chiral information [Table 2, (*S*,*R*,*R*)-**4c**, entry 3] or even totally inhibit the reaction [Table 2, (*R*,*R*,*R*)-**4c**, entries 4–6). Theoretically, the above mentioned effects are not impossible if the key enantiodifferentiating steps are influenced significantly by modified transition states or if entirely different mechanisms are involved. It can be reasoned that the solvent may have participated in enantiodifferentiating steps that are critical to the stereochemical outcome of the product, instead of serving merely as spectator molecules. Although, it has been shown that the allylation should proceed through a six-membered transition state,[20] and two reaction mechanisms have been proposed with respect to the catalyst used (dioxide[3a,5b] and monooxide[5c] mechanism), the true nature of the transition complex, its spatial arrangement and stoichiometry, is not exactly known.

In order to shed light on the above mentioned phenomena, we decided to study the interaction of allyl(trichloro)silane with an *N*,*N*′-dioxide catalyst by ^{1}H NMR spectroscopy in various solvents. Spectra of solutions containing various molar ratios of allyl(trichloro)silane and *N*,*N*′-dioxide **4a** ranging from ~1:10 to ~20:1 were recorded in CD_2Cl_2 at −73 °C and in C_6D_5Cl at −40 °C. The results of these measurements clearly indicated that in both solvents three types of allyl(trichloro)silane/**4a** complexes are generally formed depending on the *N*-oxide:bound silane ratio (only part of the added silane is bound). In low allyl(trichloro)silane/**4a** ratios (~1:2) 1:2 complexes were formed. Comparison of the obtained ^{1}H NMR spectra indicated that the structures of the two complexes were different. When the amount of allyl(trichloro)silane was increased to a 1:1 ratio with respect to **4a**, the formation of a 1:1 complex was observed. At high ratios (>10:1) formation of 2:1 complexes took place. (Detailed discussion and spectra supporting these assumptions can be found in the Supporting Information). Although it is difficult at the moment to determine the exact structure of these complexes and their relative reactivity with respect to aldehydes, it may be concluded that the change in enantioselectivity could be the result of the participation of complexes with different *N*-oxide:allyl(trichloro)silane stoichiometry. Obviously, in such cases an aldehyde could approach each species from a different side resulting in the formation of different enantiomers. Another issue is the reversal of the enantioselectivity trend observed in the case of catalysis by (*R*)-**4b** and (*S*,*R*,*R*)-**4c** in chlorobenzene (Table 2, entries 4–6), that is, reversal of enantioselectivity in allylation of the electron-rich and electron-poor substrate aldehydes (usually in the presence of bipyridine *N*,*N*′-dioxides higher enantioselectivity is observed in the allylation of electron-rich than electron-poor substrate aldehydes). This effect might be related to the presence of additional interactions prior to or during the reaction of the aldehyde with the complex. A similar trend was observed before in the allylation of benzaldehydes by pyridine mono-*N*-oxides.[5c] In view of the foregoing, it cannot be excluded that the allylation catalyzed by our bipyridine *N*,*N*′-dioxides could also proceed through the monooxide reaction mechanism in some solvents (chlorobenzene, etc.).

In conclusion, the presented results show that i) the $CpCo(CO)_2$ catalyzed cyclotrimerization of 1,7,9,15-hexadecatetrayne with nitriles under microwave irradiation represents the first general synthetic procedure for an efficient preparation of C_2-symmetrical bipyridines having the bis(5,6,7,8-tetrahydroisoquinoline) framework,[21,22] ii) these can serve as the starting material for the synthesis of chiral bis(5,6,7,8-tetrahydroisoquinoline) *N*,*N*′-dioxides, iii) the *N*,*N*′-dioxides can serve as highly active organocatalysts for allylation of aldehydes with good enantioselectivity and, iv) the appropriate choice of the solvent can control configuration at the newly created center of chirality by

changing the character of the catalytically active species. Further experiments to assess the scope of the bipyridine formation, clarify the reaction mechanism of allylation, as well as to increase enantioselectivity are under way and will be reported in due time.

Experimental Section

General Procedure for Cyclotrimerization of Hexadeca-1,7,9,15-tetrayne (1) with Nitriles

To a solution of hexadeca-1,7,9,15-tetrayne **1** (200 mg, 0.95 mmol) in a dry nitrile (15 mL) or a solution of a nitrile (20 mmol) in dry and degassed THF in a vial was added $CpCo(CO)_2$ (34 mg, 0.16 mmol) under an atmosphere of argon. Then the vial was placed into the microwave oven and irradiated for 30 min (300 W) (during the process temperature and pressure reached 200 °C and 20 barr). Then the nitrile was removed under reduced pressure and column chromatography of the residue on silica gel (solvent) afforded the respective product.

Bis-1,1′-(5,6,7,8-tetrahydro-3-phenylisoquinoline) (3b): Starting from benzonitrile (15 mL); column chromatography (3/1 hexane/Et_2O) afforded the title compound as a pale yellow solid; yield: 202 mg (51%); mp 193 °C (EtOAc); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 1.44$–1.48 (m, 8H), 2.48–2.52 (m, 4H), 2.64–2.72 (m, 4H), 7.16- 7.20 (m, 2H), 7.27–7.32 (m, 6H), 8.20–8.22 (m, 4H); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 23.3$ (2C), 24.1 (2C), 27.3 (2C), 30.6 (2C), 121.3 (2C), 128.6 (4C), 130.0 (2C), 130.2 (4C), 131.8 (2C), 141.8 (2C), 149.0 (2C), 154.8 (2C), 160.0 (2C); IR ($CHCl_3$): $\nu = 3059$, 2939, 2917, 2856, 2828, 1587, 1552, 1413, 1305, 1216, 1159, 1023, 859, 770, 688, 672, 612 cm^{-1} ; EI-MS: *m/z* (% relative intensity) = 416 (M^+, 100), 388 (20), 208 (22), 180 (7); HR-MS: *m/z* = 416.22416, calcd. for $C_{30}H_{28}N_2$: 416.22525.

Bis-1,1′-[5,6,7,8-tetrahydro-3-(tetrahydrofuran-2-yl)isoquinoline] (3f): Starting from hexadeca-1,7,9,15-tetrayne **1** (90 mg, 0.42 mmol), (*R*)-tetrahydrofuran-2-carbonitrile (1.0 g, 10.3 mmol), THF (3 mL), and $CpCo(CO)_2$ (16 mg, 0.08 mmol). Column chromatography (EtOAc) afforded the title compound as a pale yellow viscous liquid; yield: 90 mg (48%); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 1.44$–1.64 (m, 12H), 2.04–2.08 (m, 2H), 2.17–2.22 (m, 2H), 2.48- 2.50 (m, 6H), 2.51–2.66 (m, 2H), 3.72–3.78 (m, 2H), 3.92–3.98 m (2H) 5.18 (t, $J = 7.0$ Hz, 2H), 7.36 (s, 2H); ^{13}C NMR (100 MHz, C_6D_6): $\delta = 23.2$ (2C), 24.0 (2C), 26.6 (2C), 26.9 (2C), 30.4 (2C), 33.9 (2C), 69.5 (2C), 82.4 (2C), 120.2 (2C), 130.3 (2C), 147.8 (2C), 158.5 (2C), 160.0 (2C); IR ($CHCl_3$): $\nu = 2970$, 2936, 2860, 1590, 1555, 1448, 1432, 1394, 1324, 1299, 1220, 1159, 1061, 1001, 916, 871, 748 cm^{-1} ; EI-MS: *m/z* (% relative intensity) = 404 (M^+, 100), 376 (18), 359 (78), 348 (18), 292 (16), 256 (22), 213 (10), 185 (14), 167 (14), 149 (22), 129 (20), 111 (18), 97 (30); HR-MS: *m/z* = 404.24527, calcd. for $C_{26}H_{32}N_2O_2$: 404.24638.

General Procedure for Catalytic Enantioselective Allylation of Benzaldehydes with Allyl(trichloro)-silane

To a solution of **4** (0.01 mmol) in a solvent (1 mL) aldehyde (1 mmol), diisopropyl(ethyl)amine (155 mg, 208 μL, 1.2 mmol), and allyl(trichloro)silane (210 mg, 170 μL, 1.2 mmol) were added at −40 or −78 °C and the reaction mixture was stirred for 1 h. Then it was quenched with saturated aqueous $NaHCO_3$ (1 mL), the organic layer was separated and dried over $MgSO_4$. Yields and *ee*s of homoallyl alcohols **6** were determined by GC (HP-Chiral β, 30 m × 0.25 mm, oven: 80 °C for 15 min, then 1 °C min^{-1} to 150 °C, 5 min at that temperature).

Allylation of benzaldehyde 5b catalyzed by (*S*)-4a: In MeCN at −40 °C to afford (*R*)-(+)-1-phenyl-but-3-en-1-ol (**6b**); $t_R = 57.90$ min, $t_S = 58.33$ min, 65% *ee* (100% yield). In PhCl at −40 °C to afford (*S*)-(−)-**6b**, 79% *ee* (100% yield).

Experimental details of all procedures and compound charaterization data can be found in Supporting Information.

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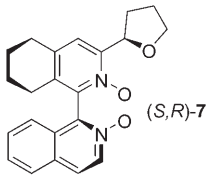
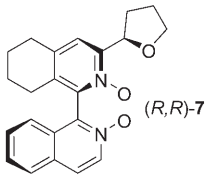
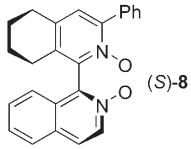




[18] Thus allylation of benzaldehyde catalyzed by (*S,R*)-**7**, (*R,R*)-**7** and (*S*)-**8** run in toluene (−78 °C) gave (*S*)-**6b** (20% *ee*), (*R*)-**6b** (36% *ee*), and (*S*)-**6b** (34% *ee*), respectively. For catalysis in CH_2Cl_2 by (*S,R*)-**7**, (*R,R*)-**7** see ref.[17]; catalysis by (*S*)-**8** gave (*R*)-**6b** (80% *ee*).



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