Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron 62 (2006) 6700–6706
Tetrahedron

Ligand effects in aluminium-catalyzed asymmetric Baeyer–Villiger reactions

Jean-Cédric Frison, Chiara Palazzi and Carsten Bolm*

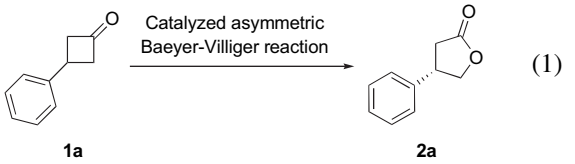
Insitut für Organische Chemie der RWTH Aachen, Landoltweg 1, 52074 Aachen, Germany

Received 1 December 2005; revised 28 December 2005; accepted 29 December 2005
Available online 26 May 2006

Abstract—Asymmetric Baeyer–Villiger oxidations of racemic and prochiral cyclobutanones can be performed with chiral aluminium-based Lewis acids resulting in products with good enantioselectivities in high yields. By employing substituted BINOL derivatives as ligands, remarkable catalyst efficiencies have been achieved and γ-butyrolactones with up to 84% ee were obtained. The relation between the electronic properties of the ligand and the enantioselectivity of the reaction has been investigated, leading to a better understanding of the requirements for achieving a good enantioselectivity in this aluminium-catalyzed oxidative transformation.

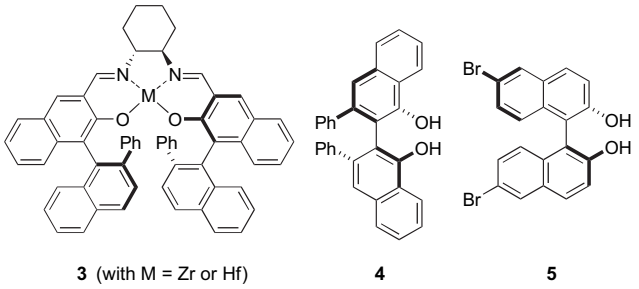
1. Introduction

The Baeyer–Villiger reaction is a highly useful oxidative transformation in synthetic organic chemistry, which allows the conversion of ketones into esters and lactones.[1] The latter represents core structures of a number of biologically active compounds and, in particular, γ-butyrolactones have proven to be useful intermediates for the synthesis of complex target molecules. Since the first reports on metal-catalyzed asymmetric Baeyer–Villiger reactions in 1994,[2] numerous chiral catalysts have been developed for this transformation.[3] To date, however, only very few of them allow the conversion of simple substrates such as 1-phenylcyclobutanone (**1a**) into the corresponding γ-butyrolactone **2a** with more than 80% ee (Eq. 1). For example, Katsuki utilizes chiral salen metal complexes **3** (with M=Zr or Hf) as catalysts for asymmetric transformations of **1a** (ee_{max}=87%).[4] Another system stems from our group and is based on chiral BINOL-type ligands in combination with aluminium reagents. For example, we found that VANOL (**4**)[5] or 6,6′-dibromo-BINOL (**5**)[6] when treated with equimolar amounts of Me_2AlCl promoted the Baeyer–Villiger oxidation of cyclobutanone **1a** to give lactone **2a** with good enantioselectivity (83 and 77% ee, respectively) in excellent yield.



(1)

1a **2a**



3 (with M = Zr or Hf) **4** **5**

Several optimization studies have already been conducted and the appropriate choice of reagents and reaction parameters such as the solvent, the oxidant, the aluminium source and the temperature proved to be essential for achieving an efficient catalysis.[6] In order to further improve the promising result obtained with simple BINOL derivative **5**, we decided to determine the influence of the ligand structure on the catalyst activity and the enantioselectivity in more detail. The results of this study are presented here. Unless noted otherwise, all enantioselectivities and yields mentioned in this article refer to the Baeyer–Villiger reaction of 3-phenylcyclobutanone (**1a**) to give γ-butyrolactone **2a** (Eq. 1), which we used as standard test. In cases, where incomplete reactions are reported, prolongations of the reaction time did not lead to higher conversions. Thus, the indicated reaction time corresponds to the point at which maximum conversion was reached.

2. Results and discussion

2.1. Effects of substituted ligands

Our previous studies had shown that axially chiral BINOL-type ligands gave high enantioselectivities. However, in the

Keywords: Aluminium; Baeyer–Villiger oxidation; BINOL; Catalysis; Oxidation.
* Corresponding author. Tel.: +49 241 8094675; fax: +49 241 8092391; e-mail: carsten.bolm@oc.rwth-aachen.de

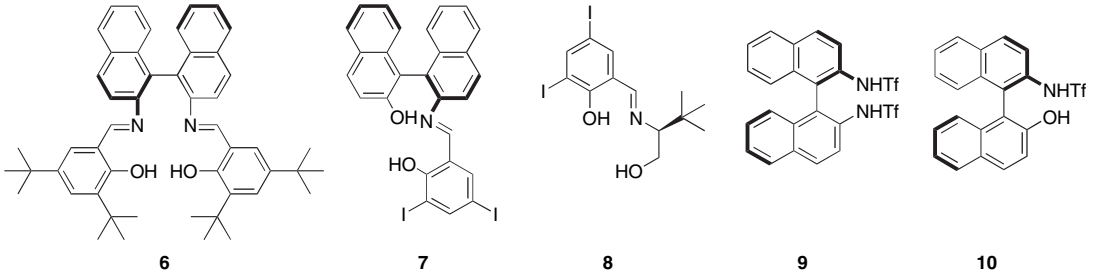
0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.12.080

light of the successful applications of other chelating molecules in metal-catalyzed oxidations, the current optimization study was started by investigating the effect of Schiff-bases **6**,[7] **7**[8] and **8**[9] on the transformation shown in Eq. 1. Whereas the former two compounds are axially chiral as **5**, the latter has only a stereogenic centre. Unfortunately, however, the presence of none of these compounds (in combination with Me_2AlCl) allowed the oxidations of **1a** with cumene hydroperoxide (CHP) as oxidant under standard reaction conditions. Since additives such as amines or phosphine oxides can inhibit the oxidation, we hypothesized that the presence of multiple coordination sites in **6–8** was responsible for this low catalyst activity. Consequently, the use of axially chiral *N*,*N*- and *N*,*O*-chelates **9**[10] and **10**[11] was attempted. Those compounds resemble BINOLs, but distinguish themselves by the presence of one or two triflated amino groups. Also the presence of these compounds had a detrimental effect on the catalyst activity, which was now attributed to the electronic properties of the ligand.

Table 1. Application of steroidal BINOLs in Baeyer–Villiger oxidations of **1a**[a]

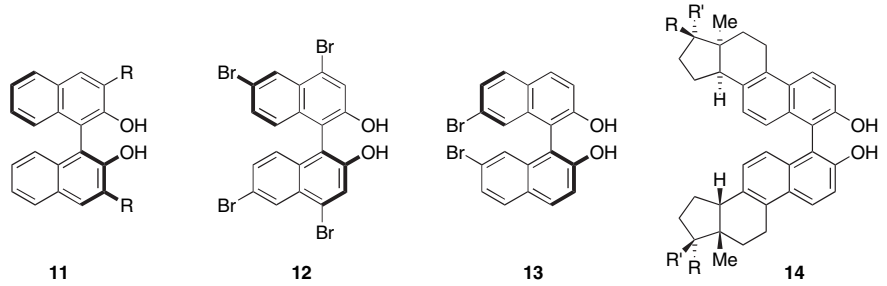
Entry	Ligand[b]	R	R′	Conv. (%) of **1a**	Abs config. of **2a**	ee (%) of **2a**[c]
1	(S_a)-**14a**	H	H	100	(+)	67
2	(R_a)-**14a**	H	H	100	(−)	68
3	(S_a)-**14b**	N–NH_2		60	(+)	8
4	(R_a)-**14b**	N–NH_2		40		*rac*
5	(R_a)-**14c**	N–NHTos		100	(−)	67
6	(S_a)-**14d**	SCH_2CH_2S		100	(+)	60
7	(R_a)-**14d**	SCH_2CH_2S		100	(−)	68
8	(S_a)-**14e**	OH	H	100	(+)	69
9	(R_a)-**14e**	OH	H	100	(−)	69
10	(R_a)-**14f**	O		100	(−)	73

[a] Reaction conditions: **1a** (0.5 mmol), **14** (50 mol %), Me_2AlCl (50 mol %), CHP (1.5 equiv), toluene, −25 °C to rt.
[b] Only the axial chirality is indicated. The stereogenic centres relate to the natural steroid skeleton.
[c] Determined by GC using a chiral column: Lipodex B (25×0.25 mm), 60 kPa N_2, at 140 °C; 140 °C, 15 min, 2 °C/min, 160 °C, 50 min; t_R=65.0 min (*S*), 66.6 min (*R*).



6 **7** **8** **9** **10**

Based on these observations we decided to focus our attention on the use of substituted BINOLs.[12] Previous studies had revealed that BINOLs **11** with substituents at the 3- and 3′-positions were less efficient compared to their 6,6′-disubstituted counterparts (such as **5**) giving lactones with very low enantioselectivity.[6] To our surprise it was now found that 4,4′,6,6′-tetrabromo-BINOL **12**[13] gave racemic **2a**. BINOL **13** having bromo substituents at the 7,7′-positions[14] afforded **2** in good ee of 64%.

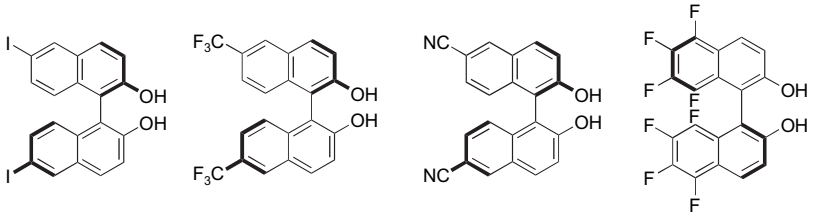


11 **12** **13** **14**

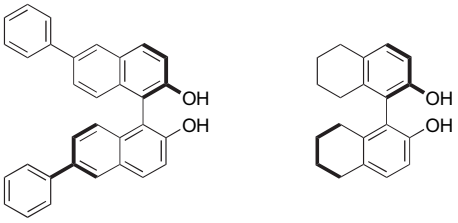
Steroidal BINOLs **14**[15] have previously been applied in various enantioselective metal-catalyzed reactions including the asymmetric oxidation of sulfides.[15b] There, use of such BINOL derivatives resulted in higher enantioselectivities than with BINOL. In contrast, no major improvement in ee was found, when steroidal BINOLs **14** were applied in the Baeyer–Villiger reaction of **1a**, and out of a range of derivatives only a single compound (**14f**) performed better than BINOL leading to **2a** with 73% ee (Table 1). As revealed by the similar ee-values of products obtained in reactions with diastereomeric ligands, the additional stereogenic centres in the ligand backbone had only a minor influence on the enantioselectivity of the oxygen insertion. Only with the two diastereomeric ligands of **14d** a difference of 8% ee (60 vs 68% ee; entries 6 and 7, respectively) in the formation of product **2a** was detected. In all cases the absolute configuration of lactone **2a** was determined by the chiral axis. Again, the presence of an additional coordinating group (such as the hydrazone moiety in **14b**; Table 1, entries 3 and 4) was detrimental to both catalytic activity and enantioselectivity.

Since at this stage BINOL derivative **5** with two bromo substituents at the 6,6′-positions had led to the best enantioselectivity, this type of substitution pattern was investigated in more detail. Assuming that the bromo substituents exhibited an electronic effect on the ligand, the application of other BINOLs with electronically modified arenes was studied. A particular emphasis was put on BINOLs

with electron-withdrawing substituents, since those were expected to positively affect the catalytically active metal centre by increasing its Lewis acidity. Starting point was the synthesis and use of **15**, **16**[16] and **17**[17] with iodo, trifluoromethyl and nitrilo substituents, respectively, in the 6- and 6′-positions of the BINOL skeleton. Furthermore, octafluoro derivative **18**[18] was tested.



15 **16** **17** **18**

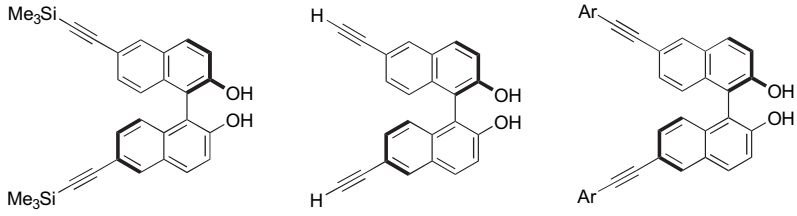


19 **20**

To our delight we found that Baeyer–Villiger oxidation of **1a** with 10 mol % of a catalyst derived from diiodo BINOL **15** (and equimolar amounts of Me_2AlCl in combination with CHP as oxidant) showed improved properties compared to the previous systems affording **2a** with 82% ee (at −30 °C). In an attempt to further improve the stereoselectivity, the reaction was conducted at lower temperatures, but unfortunately, only a decrease in activity and enantioselectivity was observed (59% ee at −50 °C and only 54% conversion after 48 h). In contrast to our expectations, however, use of **16**, **17** and **18** led to catalysts with very low activity, and lactone **2a** was formed either as a racemate (as with a catalyst derived from **16**) or with low ee in only small quantities (best result with 10 mol % of the catalyst obtained from **17**: 45% conversion of **1a**, formation of **2a** with 34% ee after 48 h in toluene at −30 °C).

In order to further investigate the impact of the ligand structure on the performance of the catalyst, 6,6′-diphenyl-BINOL **19**[19] and octahydro-BINOL **20**[20] were applied in the Baeyer–Villiger reaction of **1** next. Compared to unsubstituted BINOL, **19** and **20** possess a larger torsion angle between the naphthyl moieties induced by the two phenyl substituents at the 6,6′-positions and the sp^3 hybridized carbons in the ligand framework, respectively. Presumably, due to these steric effects in combination with the lack of activating substituents the catalysts bearing **19** and **20** showed only a moderate efficiency (with full conversions of **1a** after 24 and 16 h, respectively) affording lactone **2a** with 76 and 73% ee, respectively.

Since Shibasaki had demonstrated that BINOLs with acetylenic substituents in the 6,6′-positions were excellent ligands for Lewis acid catalyzed processes,[21] we decided to extend our studies on the use of BINOL derivatives **21**–**25**.



21 **22**

23 Ar = *p*-MeO-Ph
24 Ar = Ph
25 Ar = 3,5-$(CF_3)_2$Ph

Gratifyingly, BINOL **21** bearing two trimethylsilylalkynyl groups at positions 6 and 6′ was also highly efficient in the Baeyer–Villiger reaction, and conversion of **1a** afforded **2a** with 84% ee. Both the catalyst loading (25 mol %) and the temperature (−30 °C) were critical for achieving this enantioselectivity at a reasonable reaction rate. Conducting the reaction with only 5 mol % of the catalyst furnished the lactone with a slightly reduced ee (83%), and the reaction did not go to completion even after 7 days. As with **15**, the enantioselectivity dropped when the catalysis was performed at another temperature (81 and 57% ee at −20 and −50 °C, respectively; in the latter case <10% conversion). Removal of the trimethylsilyl group of **21** to give BINOL **22**[17] proceeded smoothly (K_2CO_3 in MeOH, 98% yield), but unfortunately, use of the resulting catalyst (prepared from BINOL **22** and Me_2AlCl) did not lead to any improvement of the enantioselectivity in the formation of **2a** (82% ee). We therefore concluded that the alkynyl moiety itself and not its terminal substituent were of importance for the catalyst performance

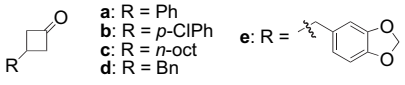
in the Baeyer–Villiger reaction. In order to confirm this hypothesis, BINOLs **23**–**25** with aryl-substituted alkynyl groups were prepared and applied in the catalysis. Using **22** as starting material all three BINOLs could be obtained by Sonogashira coupling with the corresponding aryl bromides. By selecting the appropriate aryl moiety the electronic properties of the alkynyl group (as well as the entire BINOL) could be varied. Due to the remote position of the electronic modification we did not expect a major impact by the inherent steric alternation. Application of BINOLs **23**–**25** in the Baeyer–Villiger oxidation of **1a** revealed that the best result was obtained with *p*-methoxy-substituted ligand **23**. In this case, a full conversion of **1a** was observed after 18 h (at −30 °C in toluene with 20 mol % of **23**, an equimolar amount of Me_2AlCl and CHP as oxidant) leading to lactone **2a** with 82% ee. Bis(trifluoromethyl)-substituted BINOL **25** gave the worst result in this series. Even after 48 h only 54% of ketone **1a** was converted and the resulting product had only 45% ee. After the same period of reaction time the catalysis with phenyl-substituted **24** led to full conversion of **1a** yielding lactone **2a** with 76% ee. These results are remarkable since they indicate that catalysts prepared with these types of BINOLs require electron-rich ligands, which appear to contradict the first assumption that electron-poor BINOLs might be more efficient due to the resulting increased Lewis acidity at the metal centre. Apparently, a well-balanced electronic tuning of the ligand is essential for the success of the reaction, and the background of this key issue will be discussed below taking mechanistic aspects into consideration.

2.2. Substrate scope

Using the catalyst derived from BINOL derivative **21** (in conjunction with 1 equiv of Me_2AlCl), the substrate scope of the asymmetric Baeyer–Villiger oxidation was investigated. Cyclobutanones **1a**–**e** served as test substrates. The results are summarized in Table 2.

Compared to the (so far best) catalyst derived from VANOL (**4**), the system with **21** as ligand proved about equal or less enantioselective for aryl and alkyl substituted cyclobutanones (Table 2, entries 1–3 vs catalyses with 20 mol % of VANOL, which gave **2a**, **2b** and **2c** with 83, 84 and 69% ee, respectively).[5] However, the conversion of benzyl-substituted substrates occurred in a more enantioselective manner (Table 2, entries 4 and 5 vs catalyses with 20 mol % of VANOL, which gave **2d** and **2e** with 41 and 37% ee, respectively).[5]

Table 2. Substrate scope of the asymmetric Baeyer–Villiger reaction (in analogy to Eq. 1)[a]

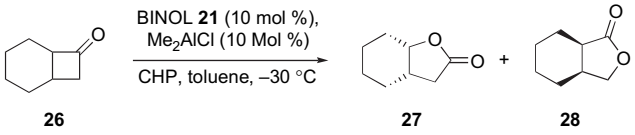


Entry	Substrate	mol % of **21**	ee (%) of **2**[b]
1	**1a**	25	84
2	**1b**	10	72
3	**1c**	10	70
4	**1d**	10	65
5	**1e**	10	56

[a] Reaction conditions: **1** (0.5 mmol), ratio of **21** and Me_2AlCl=1:1, CHP (1.25 equiv), toluene, −30 °C; in all cases the conversion of **1** was complete.

[b] Determined by GC using chiral columns.

Finally, the oxidation of racemic ketone **26** was investigated. As in previous studies,[3] this cyclobutanone gave two regioisomeric lactones **27** and **28** upon Baeyer–Villiger reaction (83% conversion of **26**). Again, the enantioselectivities (34% ee for **27** and 99% ee for **28**) were better than those obtained before with analogous systems (e.g., BINOL-based ones[6]), albeit the ratio between the two products was similar (**27**:**28**=6.7:1).



Cycloalkanones with larger ring sizes could not be converted with the BINOL **21**/Me_2AlCl catalyst system.

2.3. Mechanistic considerations

For a rational design and targeted search of new ligands it was considered desirable to get insight into the mechanistic scenario and to identify relevant intermediates. As a first step, we probed the existence of nonlinear effects (NLEs),[22] and determined the relationship between the ee of the ligand and the ee of product **2**. At the outset of this investigation, the following observations were made. Upon addition of Me_2AlCl to a solution of BINOL in toluene, the mixture turned into a milky suspension with a white precipitate. This mixture became clearer after the addition of the ketone, which we interpreted as indication for a modification of the catalyst structure. The NLE studies were then done with BINOL derivative **21**. The positive deviation from linearity [(+)-NLE] revealed the presence of nonmonomeric species and their relevance in the stereochemistry-determining step.

Since throughout the catalysis the composition of the reaction media changes with time, we had to ensure that the (enantiomerically enriched) product (here **2a**) as well as the (achiral) ketone (here **1a**) did not affect the ongoing reaction. Therefore a control experiment was performed, which unequivocally showed that the product was formed with the same level of enantioselectivity throughout the entire process. Phenomena such as autocatalysis, autoamplification or product inhibition/poisoning were thereby excluded.

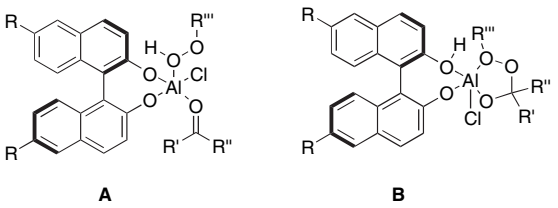
Next, NMR studies were undertaken. A very complex ^1H NMR spectrum was obtained from a 1:1 mixture of BINOL **21** and Me_2AlCl in toluene-d_8.[23] Upon addition of 5 equiv of 3-phenylcyclobutanone (**1a**) two singlets appeared at 0.24 and 0.33 ppm, replacing the broad coalescent signal corresponding to the TMS groups. Furthermore, clear peaks resulted in the aromatic region. Although a detailed interpretation of (the spectra and) this behaviour is impossible at the present stage, it is hypothesized that the sharpening of the

signals indicates a change from oligomeric to more low-molecular associates upon addition of the substrate. Treatment of this mixture with CHP at −30 °C gave lactone **2a** with 80% ee, which is close to the 84% ee obtained under more diluted conditions.

As demonstrated in other aluminium-catalyzed processes,[24] an ageing of the reaction mixture can be crucial for achieving high enantioselectivities, and presumably, this process involves the conversion of multiple (mostly unselective) catalysts into species presenting high enantioselectivities. In the attempt to make use of this effect, a 1:1 mixture of BINOL (**11** with R=H) and $(i\text{-Bu})_2AlCl$ was stirred at room temperature for 30 min prior to the addition of the ketone. Unfortunately, however, under those conditions both conversion (80%) and enantioselectivity (68% ee) were low. Apparently, the ageing of the catalyst mixture had a negative effect in this case and presumably more oligomeric species were formed, which were neither active nor enantioselective. As a consequence, the conversion of the substrate was slowed down rendering the overall catalysis inefficient.

With the goal to achieve a break-up of the oligomers and to utilize this deoligomerization in the formation of more active low-molecular species, we decided to submit the initial reagent mixture to higher temperatures and, furthermore, to use the Lewis-basic substrate (ketone **1a**) to support this cleavage process. Thus, after BINOL (**11** with R=H) was treated with the aluminium reagent (20 mol % each), the ketone was added, and the resulting mixture was heated at 70 °C for a period of 30 min. After cooling to −30 °C and addition of the oxidant, the reaction proceeded smoothly to full conversion of **1a** (after 24 h), and lactone **2a** was obtained with remarkable 75% ee. A comparable experiment without this pretreatment at elevated temperature led to product **2a** with only 68% ee. A higher temperature (90 °C) or prolonged heating times (2–16 h) resulted in a lower catalyst activity. The same procedure was applied in a catalysis with **19** as ligand, and also in this case, product **2a** was formed with an improved enantioselectivity (80% ee). Catalysts prepared from VANOL (**4**) and BINOL derivative **21** behaved differently, and no increase in ee was found.

The formation of aggregates might also explain the required electronic fine-tuning of the ligand, which is a key for achieving high activity and enantioselectivity. On one hand, a certain level of Lewis acidity is essential for the conformational fixation and activation of the substrate. Thus, we assume that the ketone is coordinated to the metal site of an intermediately formed chiral aluminium reagent, and upon oxygen transfer and stereoselective rearrangement the observed Baeyer–Villiger product is formed. Such process could proceed via the intermediacy of a pentacoordinated aluminium complex **A**, which would show structural analogies to other known organoaluminium reagents. If, on the other hand, the Lewis acidity is (too) high, two other points become relevant. First, the (spectroscopically observed) aggregates of the chiral aluminium reagent are difficult to break, which slows down the catalysis, and second, the Criegee adduct formed during the reaction might act as bidentate ligand and thereby block turnover of the catalyst by chelation. Arrangement **B** would then be a critical intermediate, from which the product needs to be liberated for further catalysis. The more Lewis acidic the metal is, the more difficult this step will be, and even a lack of turnover (as observed with catalysts derived from **16** and **18**) can result.



3. Conclusion

In conclusion, we described ligand effects in the aluminium-catalyzed asymmetric Baeyer–Villiger reaction of cyclobutanones. The careful choice of the ligand in combination with appropriate reaction conditions allows the preparation of lactones in excellent yields with enantioselectivities that are among the highest ever obtained in this reaction.

4. Experimental

4.1. General

Details of the asymmetric Baeyer–Villiger reaction protocol as well as the analytical data (including ee determinations) have been reported previously.[5,6]

4.1.1. (*R*)-6,6′-Bis-(4-methoxyphenylethynyl)-[1,1′]binaphthalenyl-2,2′-diol (23). In a Schlenk tube filled with argon were successively added $PdCl_2$ (9 mg, 0.05 mmol), PPh_3 (55 mg, 0.2 mmol), CuI (11 mg, 0.06 mmol), **22** (334 mg, 1 mmol) and NEt_3 (10 mL). 4-Bromoanisole (470 mg, 2.5 mmol) was then added, and the mixture was heated at 70 °C for 8 h. When the reaction was complete (controlled by TLC), the solution was diluted with ethyl acetate and filtered through Celite. The volatiles were removed and the crude mixture redissolved in ethyl acetate, washed with 1 M HCl, brine and dried ($MgSO_4$). Column chromatography (silica gel; acetone/pentane 1:4) furnished 498 mg of a yellow solid (91% yield); mp=147–149 °C; ^{1}H NMR (400 MHz) δ 7.99 (s, 2H), 7.86 (d, J=8.8 Hz, 2H), 7.35–7.25 (m, 8H), 6.98 (d, J=8.7 Hz, 2H), 6.80 (d, J=8.8 Hz, 2H), 5.06 (br s, 2H), 3.74 (s, 6H); ^{13}C NMR (100 MHz) δ 159.6, 153.3, 133.1, 132.7, 131.6, 131.4, 130.2, 129.2, 124.3, 119.3, 118.5, 115.4, 114.1, 110.9, 89.8, 88.2, 55.4; IR (KBr): ν=3000 cm^{-1}; MS (EI, 70 eV): *m*/*z* 546 (100), 273 (50); Anal. Calcd for $C_{38}H_{26}O_4$: C, 83.50; H, 5.21. Found: C, 83.01; H, 5.14.

4.1.2. (*R*)-6,6′-Bis-(phenylethynyl)-[1,1′]binaphthalenyl-2,2′-diol (24).[21] In analogy to the synthesis of **23** but with bromobenzene (425 mg, 2.5 mmol) instead of 4-bromoanisole. Column chromatography (silica gel; acetone/pentane 1:4) furnished 498 mg of a white solid (91% yield). ^{1}H NMR (400 MHz) δ 8.04 (d, J=1.4 Hz, 2H), 7.88 (d, J=9.0 Hz, 2H), 7.51–7.46 (m, 4H), 7.37 (m, 10H), 7.04 (d, J=8.5 Hz, 2H), 5.06 (br s, 2H); ^{13}C NMR (100 MHz)

δ 153.4, 132.9, 131.9, 131.6, 131.5, 130.2, 129.1, 128.4, 128.3, 124.3, 123.3, 119.0, 118.6, 110.8, 89.8, 89.3.

4.1.3. (*R*)-6,6′-Bis-(3,5-bis-trifluoromethylphenylethynyl)-[1,1′]binaphthalenyl-2,2′-diol (25). In analogy to the synthesis of **23** but with 3,5-bis(trifluoromethyl)-bromobenzene (732 mg, 2.5 mmol) instead of 4-bromoanisole. Column chromatography (silica gel; acetone/pentane 1:4) furnished 728 mg of a yellow solid (96% yield); mp=117–119 °C; ^{1}H NMR (400 MHz) δ 8.18 (d, *J*=1.6 Hz, 2H), 8.00 (s, 6H), 7.86 (s, 2H), 7.59–7.42 (m, 4H), 7.16 (d, *J*=8.6 Hz, 2H), 4.94 (br s, 2H); ^{13}C NMR (100 MHz) δ 154.0, 133.9, 133.4, 131.8, 131.4, 130.3, 129.0, 127.0, 124.5, 121.5, 119.0, 117.5, 110.9, 93.0, 86.7; IR (KBr): ν=3188 cm^{-1}; MS (EI, 70 eV): *m*/*z* 758.2 (100), 379.2 (22), 351.1 (18); Anal. Calcd for $C_{40}H_{20}F_{12}O_2$: C, 63.34; H, 2.69. Found: C, 63.21; H, 3.01.

4.1.4. (*R*)-2,2′-Dihydroxy-[1,1′]binaphthalenyl-6,6′-dicarbonitrile (17).[21] Step 1 (synthesis of (*R*)-2,2′-bis-methoxymethoxy-[1,1′]binaphthalenyl-6,6′-dicarbonitrile): In a Schlenk tube filled with argon were successfully added $Pd(dba)_2$ (23 mg, 0.04 mmol), DPPF (44 mg, 0.08 mmol), (*R*)-2,2′-bis-methoxymethoxy-[1,1′]binaphthalenyl-6,6′-dibromide (532 mg, 1 mmol), CuCN (540 mg, 5 mmol), *n*-Bu_4I (369 mg, 1 mmol) and dioxane (2 mL). The solution was heated at 100 °C for 3 h, then cooled to rt, diluted with ethyl acetate and filtered through Celite. The organic layer was successively washed with 1 M NaOH, saturated $NaHCO_3$, brine and dried (Na_2SO_4). The solvents were removed, and the crude product was flash chromatographed with pentane/diethyl ether 1:1 to afford 348 mg of a white solid (82% yield). ^{1}H NMR (300 MHz) δ 8.20 (d, *J*=1.5 Hz, 2H), 7.95 (d, *J*=9.2 Hz, 2H), 7.64 (d, *J*=9.2 Hz, 2H), 7.28 (dd, *J*=1.5, 8.9 Hz, 2H), 7.07 (d, *J*=8.9 Hz, 2H), 5.06 (d, *J*=6.9 Hz, 2H), 4.97 (d, *J*=6.9 Hz, 2H), 3.11 (s, 6H); ^{13}C NMR (75 MHz) δ 155.2, 135.4, 134.4, 130.6, 128.5, 127.1, 126.2, 119.8, 119.4, 118.0, 107.6, 94.6, 56.1. This product was utilized in the subsequent step without further analysis.

Step 2 (synthesis of (*R*)-2,2′-dihydroxy-[1,1′]binaphthalenyl-6,6′-dicarbonitrile (**17**)):[21] To 2,2′-bis-methoxymethoxy-[1,1′]binaphthalenyl-6,6′-dicarbonitrile (212 mg, 0.5 mmol) in CH_2Cl_2 (1 mL) was added at 0 °C a saturated methanolic HCl solution (2 mL). The mixture was stirred for 2 h at rt, and then treated with saturated $NaHCO_3$. Subsequently, the solution was diluted with CH_2Cl_2, extracted with brine and the organic layer dried (Na_2SO_4). After removal of the solvents, the crude product was recrystallized from CH_2Cl_2/pentane to afford 320 mg of **17** as a white solid (95% yield). ^{1}H NMR (300 MHz) δ 8.15 (s, 2H), 7.94 (d, *J*=8.9 Hz, 2H), 7.42 (d, *J*=8.9 Hz, 2H), 7.31 (d, *J*=8.7 Hz, 2H), 7.05 (d, *J*=8.7 Hz, 2H), 5.93 (br s, 2H); ^{13}C NMR (75 MHz) δ 154.5, 134.4, 133.4, 131.0, 127.2, 127.0, 124.3, 119.0, 118.0, 110.4, 106.1.

Acknowledgements

This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft (DFG) within the Schwerpunktprogramm 1118. We thank Dr. M. Schneider, Schering AG, Berlin, and Professor Dr. A. K. Yudin, University of Toronto, for providing samples of BINOL derivatives **14** and **18**, respectively.

References and notes

1. (a) Krow, G. R. *Org. React.* **1993**, *43*, 251; (b) Hassal, C. H. *Org. React.* **1957**, *9*, 73; (c) Krow, G. R. *Comprehensive Organic Synthesis*; Trost, B. M., Fliming, I., Eds.; Pergamon: Oxford, 1991; Vol. 7, p 671; (d) Bolm, C. *Advances in Catalytic Processes*; Doyle, M. P., Ed.; JAI: Greenwich, 1997; Vol. 2, p 43; (e) Renz, M.; Meunier, B. *Eur. J. Org. Chem.* **1999**, 737.
2. (a) Bolm, C.; Schlinghoff, G.; Weickhardt, K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1848; (b) Gusso, A.; Baccin, R.; Pinna, F.; Strukul, G. *Organometallics* **1994**, *13*, 3442.
3. (a) Bolm, C.; Luong, T. K. K.; Beckmann, O. *Asymmetric Oxidation Reactions*; Katsuki, T., Ed.; University Press: Oxford, 2001; p 147; (b) Bolm, C. *Peroxide Chemistry*; Adam, W., Ed.; Wiley-VCH: Weinheim, 2000; p 494; (c) Kelly, D. R. *Chim. Oggi* **2000**, *18,* 33 and 52; (d) Bolm, C.; Beckmann, O. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Stuttgart, 1999; Vol. 2, p 803; (e) Strukul, G. *Angew. Chem., Int. Ed.* **1998**, *37*, 1199; (f) Bolm, C. *Med. Res. Rev.* **1999**, *19*, 348; (g) ten Brink, G.-J.; Arends, I. W. C. E.; Sheldon, R. A. *Chem. Rev.* **2004**, *104*, 4105; (h) Bolm, C.; Le Paih, J.; Frison, J. C. *Modern Oxidation Methods*; Bäckvall, J. E., Ed.; Wiley-VCH: Weinheim, 2004; p 253; (i) Bolm, C.; Palazzi, C.; Beckmann, O. *Transition Metals for Organic Synthesis*, 2nd ed.; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, p 267.
4. (a) With Zr see: Watanabe, A.; Uchida, T.; Ito, K.; Katsuki, T. *Tetrahedron Lett.* **2002**, *43*, 4481; (b) Watanabe, A.; Uchida, T.; Irie, R.; Katsuki, T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5737; (c) With Hf see: Matsumoto, K.; Watanabe, A.; Uchida, T.; Ogi, K.; Katsuki, T. *Tetrahedron Lett.* **2004**, *45*, 2385.
5. Bolm, C.; Frison, J.-C.; Zhang, Y.; Wulff, W. D. *Synlett* **2004**, 1516.
6. (a) Bolm, C.; Beckmann, O.; Palazzi, C. *Can. J. Chem.* **2001**, *79*, 1593; (b) Bolm, C.; Beckmann, O.; Kühn, T.; Palazzi, C.; Adam, W.; Rao, P. B.; Saha-Möller, C. R. *Tetrahedron: Asymmetry* **2001**, *12*, 2441.
7. For the aluminium complex, see: Evans, D. A.; Janey, J. M.; Magomedov, N.; Tedrow, J. S. *Angew. Chem., Int. Ed.* **2001**, *40*, 1884.
8. (a) Yuan, Y.; Li, X.; Sun, J.; Ding, K. *J. Am. Chem. Soc.* **2002**, *124*, 14866; (b) Yuan, Y.; Long, J.; Sun, J.; Ding, K. *Chem.—Eur. J.* **2002**, *8*, 5033 and references therein.
9. For successful applications of this ligand in sulfide oxidations, see: (a) Pelotier, B.; Anson, M. S.; Campbell, I. B.; Macdonald, S. J. F.; Priem, G.; Jackson, R. F. W. *Synlett* **2002**, 1055; (b) Legros, J.; Bolm, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 4225; (c) Legros, J.; Bolm, C. *Angew. Chem., Int. Ed.* **2003**, *42*, 5487; (d) Legros, J.; Bolm, C. *Chem.—Eur. J.* **2005**, *11*, 1086.
10. Ooi, T.; Ohmatsu, K.; Uraguchi, D.; Maruoka, K. *Tetrahedron Lett.* **2004**, *45*, 4481.
11. Belokon, Y. N.; Bespalova, N. B.; Churkina, T. D.; Cisarova, I.; Ezernitskaya, M. G.; Harutyunyan, S. R.; Hrdina, R.; Kagan, H. B.; Kocovsky, P.; Kochetkov, K. A.; Larionov, O. V.; Lyssenko, K. A.; North, M.; Polasek, M.; Peregudov, A. S.; Prisyazhnyuk, V. O. V.; Vyskocil, S. *J. Am. Chem. Soc.* **2003**, *125*, 12860.

12. Chen, Y.; Yekta, S.; Yudin, A. K. *Chem. Rev.* **2003**, *103*, 3155.
13. Gong, L. Z.; Hu, Q. S.; Pu, L. *J. Org. Chem.* **2001**, *66*, 2358.
14. Bandin, M.; Casolari, S.; Cozzi, P. G.; Proni, G.; Schmohel, E.; Spada, G. P.; Tagliavini, E.; Umani-Ronchi, A. *Eur. J. Org. Chem.* **2000**, 491.
15. (a) For the preparation of substituted steroidal BINOL-type ligands, see: Schneider, M. F.; Harre, M.; Pieper, C. *Tetrahedron Lett.* **2002**, *43*, 8751. For applications of such ligands in asymmetric catalyses, see: (b) Enev, V. S.; Mohr, J.; Harre, M.; Nickisch, K. *Tetrahedron: Asymmetry* **1998**, *9*, 2693; (c) Bolm, C.; Dabard, O. *Synlett* **1999**, 360; (d) Kostova, K.; Genov, M.; Philipova, I.; Dimitrov, V. *Tetrahedron: Asymmetry* **2000**, *11*, 3253; (e) Hodgson, D. M.; Stupple, P. A.; Pierard, F. Y. T. M.; Labande, A. H.; Johnstone, C. *Chem.—Eur. J.* **2001**, *7*, 4465.
16. Ishitani, H.; Ueno, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 8180.
17. (a) Sasai, H.; Tokunaga, T.; Watanabe, S.; Suzuki, T.; Itoh, N.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 7388; (b) For the synthetic method, see: Sakamoto, T.; Ohsawa, K. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2323.
18. Yudin, A. K.; Martyn, L. J. M.; Pandiaraju, S.; Zheng, J.; Lough, A. *Org. Lett.* **2000**, *2*, 41.
19. (a) Chen, R.; Qian, C.; de Vries, J. G. *Tetrahedron Lett.* **2001**, *42*, 6919; (b) Chen, R.; Qian, C.; de Vries, J. G. *Tetrahedron* **2001**, *57*, 9837; (c) Kumaraswamy, G.; Sastry, M. N. V.; Jena, N.; Ravi Kumar, K.; Vairamani, M. *Tetrahedron: Asymmetry* **2003**, *14*, 3797.
20. (a) For a review, see: Au-Yeung, T. T.-L.; Chan, S.-S.; Chan, A. S. C. *Adv. Synth. Catal.* **2003**, *345*, 537; (b) For the use of this ligand with aluminium, see: Lin, Y.-M.; Fu, I.-P.; Uang, B.-J. *Tetrahedron: Asymmetry* **2001**, *12*, 3217.
21. (a) See Ref. 17; (b) Morita, T.; Arai, T.; Sasai, H.; Shibasaki, M. *Tetrahedron: Asymmetry* **1998**, *9*, 1445.
22. (a) Blackmond, D. G. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5732; (b) Kagan, H. B. *Adv. Synth. Catal.* **2001**, *343*, 227; (c) Girard, C.; Kagan, H. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 2922; (d) Kagan, H. B.; Luukas, T. O. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Stuttgart, 1999; Vol. 1, p 101; (e) Bolm, C. *Advanced Asymmetric Catalysis*; Stephenson, G. K., Ed.; Chapman and Hall: London, 1996; p 9.
23. Arai, T.; Sasai, H.; Yamagushi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 441.
24. Ketter, A.; Glahsl, G.; Herrmann, R. *J. Chem. Res., (S)* **1990**, 278; *J. Chem. Res., (M)* **1990**, 2118.