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Enantioselective addition of dimethylzinc to aldehydes: assessment of optimal *N*,*N*-substitution for 2-dialkylamino-1,1,2-triphenylethanol ligands

Noemí García-Delgado, Montserrat Fontes, Miquel A. Pericàs,*,† Antoni Riera and Xavier Verdaguer*

Unitat de Recerca en Síntesi Asimètrica (URSA-PCB), Parc Científic de Barcelona and Departament de Química Orgànica, Universitat de Barcelona, c/Josep Samitier, 1-5, E-08028 Barcelona, Spain

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Abstract—A general methodology for the synthesis of 2-dialkylamino-1,1,2-triphenylethanol has been developed. Novel ligands **3**, **4**, and **5**, bearing flexible alkyl chains on nitrogen have been synthesized by epoxide-ring opening of the encumbered (*S*)-triphenyloxirane. These ligands along with 2-piperidino-1,1,2-triphenyl ethanol **1** have been tested in the addition of dimethylzinc to aldehydes. This allowed for the assessment of the structural features that favor the catalytic activity and selectivity of the ligands with respect to nitrogen substitution.

1. Introduction

Since its early reports, the catalytic enantioselective addition of dialkylzinc species to aldehydes has been studied extensively. A large variety of ligands have been reported to yield the corresponding chiral secondary alcohols in excellent enantiomeric excess.[1] For the past decade, our group has been working on the development of synthetic chiral amino alcohol ligands derived from epoxides that are readily accessible from the Sharpless and Jacobsen epoxidation reactions (Fig. 1).[2] The main feature of these ligands is that they are modular in nature, which allows for the fast optimization of the catalytic properties in any application.

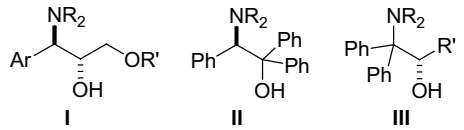

Figure 1.

Because of its decreased reactivity, asymmetric dimethylzinc addition has attracted much less attention than the corresponding Et_2Zn additions. However, the chiral 1-hydroxyethyl moiety resulting from the enantioselective addition of a methyl group to an aldehyde is widespread in nature and makes this process highly attractive from a synthetic point of view.[3] Soai et al. reported that *N*,*N*-dialkyl derivatives of norephedrine work as efficient ligands for the asymmetric addition of both Et_2Zn and Me_2Zn.[4] In particular, *N*,*N*-di-*n*-butylnorephedrine (DBNE) bearing a conformationally flexible *N*,*N*-dibutylamino fragment provided excellent selectivities for the addition of dimethylzinc to aliphatic aldehydes. Ligands of general structure **II** (Fig. 1) represent an excellent choice among other ligands reported in the literature when performing asymmetric Et_2Zn and Ph_2Zn additions.[5] In particular, 2-piperidino-1,1,2-triphenylethanol **1** provides excellent enantioselectivities (up to 99% ee). In addition, the two enantiomers are readily available in a two step reaction pathway starting from triphenylethylene.[6]

We have previously reported the synthesis of several ligands of general structure **II** bearing cyclic alkyl groups on nitrogen. Here we report on the synthesis of

* Corresponding authors: Tel.: +34-977920-211; fax: +34-977920-224 (M.A.P.); tel.: +34-934037093; fax: +34-934037095 (X.V.); e-mail addresses: mapericas@iciq.es; xverdaguer@pcb.ub.es
† Present address: Institute of Chemical Research of Catalonia, Avgda. Països Catalans s/n, E-43007 Tarragona, Spain.

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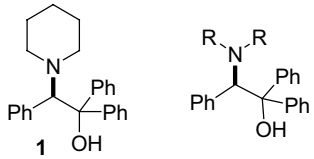
new ligands of general structure **II** with distinct flexible alkyl groups on nitrogen. This would allow for the correct assessment of the structural features that favor the catalytic activity of type **II** ligands with respect to nitrogen substitution. In a second stage, the novel ligands were tested in the enantioselective addition of dimethylzinc to benzaldehyde and heptanal along with (*R*)-2-piperidino-1,1,2-triphenylethanol **1**.

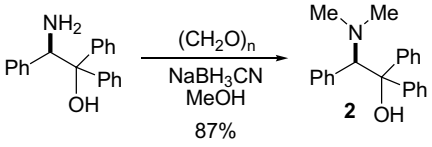


1

2, R = Me
3, R = Et
4, R = *n*-Pr
5, R = *n*-Bu

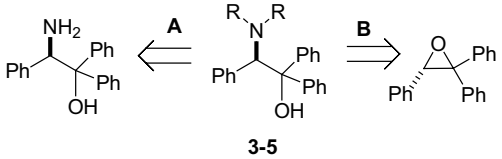
2. Synthesis of the ligands

The presence of a trisubstituted amine in the 1,2-amino alcohol ligand is crucial to attain good catalytic activities in the enantioselective alkylation of aldehydes.[7] With this in mind, we planned the synthesis of ligands **2**–**5**, which bear a straight chain *N*,*N*-dialkylamino groups of increasing length. Ligand **2** was synthesized from the commercially available (*R*)-2-amino-1,1,2-triphenylethanol by means of reductive amination with formaldehyde and sodium cyanoborohydride[8] (Scheme 1). Attempts to prepare **2**, by means of an Eschweiler–Clark reaction (CH_2O, HCO_2H)[9] as previously reported in the literature,[10] led to the isolation of the corresponding *N*-methyl cyclic aminal. Alternatively, alkylation of the corresponding primary amine with MeI in K_2CO_3/MeOH produced the desired compound in a 58% yield. However, reproducibility of this procedure was poor, probably because of the partial formation of the quaternary amine.



Scheme 1.

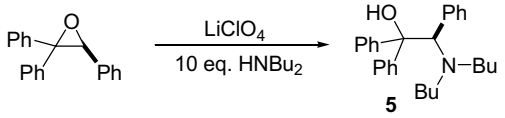
The synthesis of ligands **3**–**5** was attempted following synthetic routes A and B (Scheme 2). With the (*R*)-2-amino-1,1,2-triphenylethanol in hand route A was first examined. Soai et al. reported the dialkylation of norephedrine with several primary alkyl halides under K_2CO_3/MeOH conditions.[4] Under the same conditions, reaction with (*R*)-2-amino-1,1,2-triphenylethanol with EtBr provided exclusively monoalkylation compounds. This reaction is very sensitive to steric hindrance around the amino group, since a similar behavior has been reported with the regioisomeric 2-amino-1,2,2-triphenylethanol. [2e] On the other hand, it is known that reductive amination ($RCHO/Pt/H_2$) of structurally related 2-amino-1,2-diphenylethanol affords again monoalkylation products. The double alkylation has been accomplished, albeit with low yields, by using stoichiometric amounts of aluminum trichloride as activator during the reductive amination process.[11]



Scheme 2.

To find a reliable process for the synthesis of ligands **3**–**5**, route B was next examined. The nucleophilic ring opening of (*S*)-triphenyloxirane under Crotti conditions (amine/$LiClO_4$/82 °C, acetonitrile)[12] with cyclic secondary amines led to the convenient synthesis of a number of β-amino alcohols. However, initial experiments with straight chain di-*n*-butylamine in refluxing acetonitrile did not provide any of the desired epoxide ring-opening product, probably because of its increased steric hindrance with respect to cyclic amines. To check whether the ring opening with di-*n*-butylamine was feasible, the reaction temperature was raised to 155 °C in the absence of solvent (Table 1). Under these conditions **5** was detected as a minor product in the reaction mixture. Further efforts to optimize the reaction temperature and the equivalents of lithium perchlorate to increase the yield of amino alcohol **5** is summarized in Table 1.

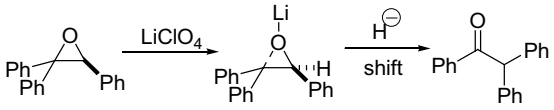
Table 1. Ring opening of (*S*)-triphenyloxirane with di-*n*-butylamine



T (°C)	Time	Equiv. $LiClO_4$	Yield (%)[a]
155	8.5 h	2	Minor
140	8 h	2	36
140	12 h	2	Minor
140	2.5 days	2	Minor
120	2 days	4	17
120	1.5 days	4	45[b]

[a] Yields refer to isolated crystalline compounds of >95% purity as determined by elemental analysis.
[b] Yield estimated by ^1H NMR analysis of the final reaction mixture was 70%.

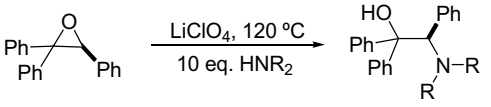
Optimal conditions required 2–4 equiv of $LiClO_4$ and 120 °C. Increasing the amount of the Lewis acid promoter and the temperature resulted in a faster reaction. However, higher temperatures and addition of an excess of $LiClO_4$ (over 4 equiv) produced the undesired lithium epoxide rearrangement that generates a ketone byproduct (Scheme 3) with the consequent decrease in yield.[13] The use of other Lewis acid salts [$CaCl_2$, $Mg(ClO_4)$] did not produce any of the desired ring-opening product.



Scheme 3.

Preparation of novel ligands **3**, **4**, and **5** was accomplished in practical yields by running the reactions with 10 equiv of the corresponding amine without solvent at 120 °C (Table 2). Reactions with low-boiling amines were conducted in a pressure tube. Conveniently, all the new isolated ligands were crystalline solids. The enantiomeric excess of the final compounds isolated was >95% ee by ^{19}F NMR analysis of the corresponding diastereomeric Mosher's acid salts.

Table 2. Synthesis of amino alcohols **3**–**5** from (*S*)-triphenyloxirane



R	Equiv. $LiClO_4$	Time (days)	Product	Yield (%)[a]	Rotation
Et	2	5 days	**3**	40	(−)
Pr	4	2 days	**4**	57	(−)
Bu	4	1.5 days	**5**	45	(−)

[a] Yields refer to isolated crystalline compounds of >95% purity as determined by elemental analysis.

3. Catalysis

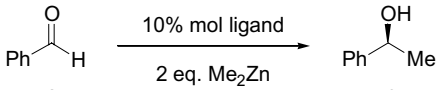
3.1. Results

As the starting point to examine the efficiency of these ligands **1**–**5** in catalysis, benzaldehyde was chosen as substrate. In this set of experiments the active catalysts were prepared by mixing 2 equiv of Me_2Zn and 10 mol% of the corresponding amino alcohol in hexane or toluene at room temperature. After 30 min the reaction was cooled to the desired temperature and the aldehyde was then added. The reactions were analyzed by GC, the results are summarized in Table 3.

Ligands **1**–**2** were clearly superior to **3**–**5** in terms of conversion and enantioselectivity. Thus, using 10 mol% of **1** the resulting 1-phenylethanol was obtained in greater than 90% ee. When the reaction temperature was reduced to 0 °C (Table 3, entry 1) the best enantiomeric excess was obtained (94% ee), but with slightly lower conversion numbers in comparison with the reaction performed at room temperature. With respect to solvents, hexane behaved slightly better than toluene when **1** or **5** were used (Table 3, entries 1–2 and 11–12). As a general trend, open chain *N*-alkyl substituents (in ligands **2**–**5**) had a deleterious effect on enantioselectivity and conversion. While the *N*,*N*-dimethyl substituted amino alcohol **2** showed only slightly decreased enantioselectivity (85% ee), a sharp decrease was observed when the homologous *N*,*N*-diethylamino derivative **3** was used (21% ee). From this point on, an increase in the chain length of the substituents on nitrogen had practically no effect on either selectivity or conversion.

The catalytic efficiency of ligands **1**–**5** for the addition of Me_2Zn to aliphatic substrates was also examined. Heptanal was chosen as a standard straight chain aldehyde. Reactions were run using 2 equiv of Me_2Zn and 10 mol% of the corresponding β-amino alcohol ligand. Again, 2-piperidino-1,1,2-triphenylethanol **1** was a superior catalyst and provided 2-octanol in 69% ee (Table 4). Solvent had an important influence in the enantiomeric excess of the product alcohol, again hexane provided better selectivities than toluene (Table 4, entries 1–4). On the other hand, the reaction

Table 3. Enantioselective addition of Me_2Zn to benzaldehyde catalyzed by ligands **1**–**5**

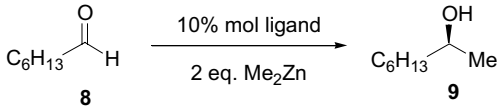


8 **9**

Entry	Ligand	Solvent	*T* (°C)	Time (h)	Conversion (%)[a]	Ee (%)[b]
1	**1**	Hexane	0	24	87	94
2	**1**	Toluene	0	48	65	93
3	**1**	Hexane	rt	24	98	91
4	**1**	Toluene	rt	27	95	90
5	**2**	Hexane	0	24	38	85
6	**2**	Toluene	rt	24	55	81
7	**3**	Hexane	0	24	61	21
8	**3**	Toluene	rt	24	63	13
9	**4**	Hexane	0	24	67	30
10	**4**	Toluene	rt	24	66	22
11	**5**	Hexane	0	24	60	25
12	**5**	Toluene	rt	24	26	18

[a] Conversion was determined by GC.
[b] Enantiomeric excess was determined by GC on a β-DEX 120 column.

Table 4. Catalytic enantioselective addition of Me_2Zn to heptanal mediated by ligands **1**, **2**, and **5**



8 **9**

Entry	Ligand	Solvent	*T* (°C)	Time (h)	Conversion (%)[a]	Ee (%)[b]
1	**1**	Toluene	22	36	85	57
2	**1**	Hexane	22	36	83	69
3	**1**	Toluene	0	22	67	35
4	**1**	Hexane	0	22	80	69
5	**2**	Hexane	0	24	56	42
6	**5**	Hexane	0	24	60	9

[a] Conversion was determined by GC.
[b] Determined by GC upon analysis of the corresponding acetate on a β-DEX 120 column.

temperature had only a limited effect on the reaction enantioselectivity (Table 4, entries 2 and 4). As in the reaction with benzaldehyde, switching the piperidino group for a noncyclic *N*,*N*-dialkylamino group resulted in a sharp decrease in enantiomeric excess, down to 9% ee in the case of **5** (Table 4, entry 6).

3.2. Discussion

In a similar fashion to Et_2Zn, addition of Me_2Zn catalyzed by **1**–**5** provides the product alcohols with *S* configuration in agreement with the Noyori rule.[14] Theoretical calculations show that the stereochemical outcome of the dialkylzinc addition to aldehydes can be predicted on the basis of four diastereomeric transition state structures [*anti*-(*S*), *anti*-(*R*), *syn*-(*S*), *syn*-(*R*)].[15] In the case of Et_2Zn addition to benzaldehyde catalyzed by **1**, the *anti*-(*S*) TS was calculated to have the lowest energy barrier by means of a quantum mechanics/molecular mechanics (IMOMM) procedure.[16] A model structure of the *anti*-(*S*) TS for 2-dialkylamino-1,1,2-triphenylethanol ligand **IV** and for *N*,*N*-dialkylephedrine derivatives **V** is depicted in Figure 2. According to this model, bulky alkyl groups on nitrogen may produce the destabilization of **IV** because of an unfavorable steric interaction with the *gem*-diphenyl moiety, as would occur for ligands **3**–**5**. Conversely, smaller dialkyl groups on nitrogen (ligands **1**–**2**) lead to tolerable interactions in the transition state. In this case, the corresponding TS's are not perturbed and better conversions and selectivities could be recorded.

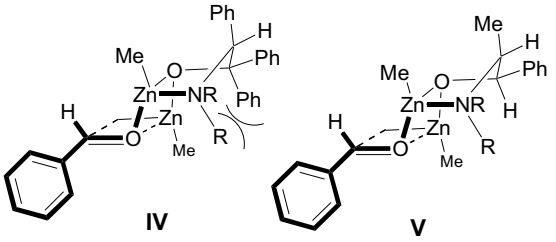


Figure 2.

It is interesting to note that the same model may serve to explain why ligands with an ephedrine backbone exhibit differential behavior. There are several examples in the literature of highly effective ephedrine derived ligands containing a *N*,*N*-di-*n*-butyl moiety (DBNE, and η^6-arene-chromium complex of DBNE).[3,4] In the case of ephedrine (model structure **V**) a much smaller hydrogen atom replaces the axial –Ph group in **IV**. In this scenario, there is room enough to accommodate a larger *n*-Bu group on nitrogen with no energy penalization for the corresponding transition states.

4. Conclusions

In summary, a general methodology for the synthesis of 2-dialkylamino-1,1,2-triphenylethanol has been developed. The ring opening of the sterically hindered (*S*)-triphenyloxirane with 2–4 equiv of $LiClO_4$ and a straight chain dialkyl amine in the absence of solvent allows the synthesis of novel ligands **3**, **4**, and **5** in one step. The nucleophilic ring opening shown proceeds in a stereospecific manner. The effectiveness of **1**–**5** ligands toward dimethylzinc addition to both aromatic and aliphatic aldehydes has been examined. Up to 94% and 69% ee has been achieved in the asymmetric addition to benzaldehyde and heptanal, respectively, when using 2-piperidino-1,1,2-triphenyl ethanol **1**. Comparison of the results obtained for the series of piperidino, dimethyl, diethyl, di-*n*-propyl and di-*n*-butyl ligands has allowed us to ascertain that small alkyl groups on the chelating nitrogen provide far better enantiocontrol for type **II** catalysts. This finding stresses once again the importance and advantages of a modular ligand design for the optimization of ligand architecture.

5. Experimental

5.1. Instruments and materials

Dimethylzinc reactions were carried out on a Radley's Metz Syn-10 Reaction Station under argon. Hexane was distilled under nitrogen and stored over sodium. Toluene was distilled over sodium prior to use. Aldehydes were distilled and stored under argon. All reactions were performed under argon. Enantiomerically pure (*S*)-

triphenyloxirane was prepared as described by Jacobsen et al., followed by recrystallization on hexane. Optical rotations were measured at room temperature on a Perkin–Elmer 241 MC polarimeter. Melting points were determined by differential scanning calorimetry (DSC) using a Mettler Toledo DSC. Infrared spectra were recorded on a Fourier Thermo Nicolet Nexus FT-IR using NaCl film or KBr pellet techniques. NMR spectra were acquired on a Varian Unity-300 or a Mercury 400 instrument. ^{1}H chemical shifts are quoted relative to TMS and ^{13}C, ^{19}F shifts relative to solvent signals. Carbon multiplicities have been assigned by distortionless enhancement polarization transfer (DEPT) experiments. Mass spectra (MS) were measured by the Servei d'Espectrometria de Masses of the Universitat de Barcelona and elemental analysis (EA) by the Servicios Xerais de Apoio á Investigación of the Universidade de A Coruña. Gas chromatography (GC) analyses were carried out on a Agilent 6890N chromatograph.

5.2. Synthesis of (*R*)-2-dimethylamino-1,1,2-triphenylethanol 2[10]

To a stirred solution of 0.1 g (0.35 mmol) of (*R*)-2-amino-1,1,2-triphenylethanol in 1 mL of methanol, paraformaldehyde (62 mg, 0.11 mmol) and a 20% HCl solution in ethanol (26 μL) were added. Next, 43 mg (0.69 mmol) of $NaBH_3CN$ in 1 mL of methanol was added via canulae. The reaction mixture was stirred at room temperature for 3.5 days. The crude reaction was quenched with 1 mL of water and filtered over Celite. The organic solvents were removed under vacuum and the aqueous solution was acidified with a HCl (1 M), washed with Et_2O. NaOH (1 M) solution was then added to the resulting aqueous solution until a white solid formed. The aqueous solution was then extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and removed under vacuum. The desired product (95 mg) was obtained as a white solid in 87% yield.

^{1}H NMR: δ ($CDCl_3$) 7.63 (m, 2H), 7.15–6.95 (m, 13H), 5.11 (d, $J = 2$ Hz, 1H), 4.18 (d, $J = 2$ Hz, 1H), 4.15 (s, 1H), 2.12 (s, 3H).

5.3. Preparation of (*R*)-2-dialkylamino-1,1,2-triphenylethanols

General procedure. (*S*)-Triphenyloxirane, $LiClO_4$, and the appropriate dialkylamine were placed in a pressure tube. The mixture was heated at 120 °C until the reaction was completed (TLC). The crude reaction mixture was then poured over a H_2O/CH_2Cl_2 biphasic mixture. The organic layer was dried ($MgSO_4$) and removed under vacuum. The excess amine was removed by filtration on SiO_2 to yield the crude amino alcohol.

5.3.1. (*R*)-2-Diethylamino-1,1,2-triphenylethanol 3. Following the general procedure, 0.50 g (1.84 mmol) of (*S*)-triphenyloxirane, 0.39 g (3.67 mmol) of $LiClO_4$, and 1.92 mL (18.4 mmol) of diethylamine were used. The reaction mixture was heated for 5 days. The product was filtered on silica using hexane/EtOAc 10% to remove the excess amine. The product was recrystallized from a 2-propanol/H_2O mixture to obtain **3** as a white crystalline solid (254 mg, overall yield 40%). Mp = 104–105 °C. ^{1}H NMR ($CDCl_3$): δ 7.64 (d, $J = 7$ Hz, 2H), 7.30–6.90 (m, 13H), 4.76 (s, 1H), 2.45 (m, 2H), 2.24 (m, 2H), 1.54 (s, 1H, OH), 0.89 (t, $J = 7$ Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 149.2 (Cq), 145.9 (Cq), 137.6 (Cq), 131.5 (CH), 127.8 (CH), 127.4 (CH), 127.1 (CH), 126.9 (CH), 126.8 (CH), 126.2 (CH), 125.8 (CH), 125.7 (CH), 78.2 (Cq), 73.8 (CH), 44.9 (CH_2), 12.5 (CH_3). IR (KBr): ν_{max} 2967, 1493, 1165, 1078, 702 cm^{-1}. MS (CI, NH_3): m/z 345 (M^+, 100%). EA (calculated for $C_{24}H_{27}NO$, found): C (83.44, 83.27), H (7.88, 7.74), N (4.05, 3.94). $[\alpha]_D = -121.2$ (c 1.01, $CHCl_3$).

5.3.2. (*R*)-2-Dipropylamino-1,1,2-triphenylethanol 4. Following the general procedure, 50 mg (0.18 mmol) of (*S*)-triphenyloxirane, 78 mg (0.73 mmol) of $LiClO_4$, and 0.25 mL (1.83 mmol) of di-*n*-propylamine were used. The reaction mixture was heated for 2 days. The product was extracted and filtered on silica using hexane/EtOAc 10% to remove the excess amine. The crude product was solved in CH_2Cl_2 and was submitted to acid-basic extraction to yield **4** as a white solid in 56% yield (38 mg). Mp = 74.6 °C. ^{1}H NMR ($CDCl_3$): δ 7.62 (d, $J = 7$ Hz, 2H), 7.35–6.95 (m, 13H), 6.00 (br s, 1H), 4.72 (s, 1H), 2.32 (m, 2H), 2.13 (m, 2H), 1.35 (m, 4H), 0.68 (t, $J = 7$ Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 149.0 (Cq), 145.8 (Cq), 137.4 (Cq), 131.6 (CH), 127.8 (CH), 127.4 (CH), 127.1 (CH), 126.9 (CH), 126.2 (CH), 125.9 (CH), 125.8 (CH), 78.4 (Cq), 74.5 (CH), 53.9 (CH_2), 20.7 (CH_2), 11.5 (CH_3). IR (KBr): ν_{max} 2957, 1449, 704 cm^{-1}. MS (CI, NH_3): m/z 373 (M^+, 100%). EA (calculated for $C_{26}H_{31}NO$, found): C (83.60, 83.82), H (8.37, 8.05), N (3.75, 3.52). $[\alpha]_D = -118.2$ (c 0.6, $CHCl_3$).

5.3.3. (*R*)-2-Dibutylamino-1,1,2-triphenylethanol 5. Following the general procedure, 0.50 g (1.84 mmol) of (*S*)-triphenyloxirane, 0.78 g (7.34 mmol) of $LiClO_4$, and 3.1 mL (18.4 mmol) of di-*n*-butylamine were used. The reaction was heated for 1.5 days. Next, the product was filtered on SiO_2 using hexane/EtOAc 5% to eliminate the excess amine, the yellow solid was recrystallized in methanol. Compound **5** was obtained as a white crystalline solid in 45% yield (0.33 g). Mp = 97.8 °C. ^{1}H NMR ($CDCl_3$): δ 7.62 (dd, $J = 8$ Hz, $J' = 1$ Hz, 2H), 7.35–6.95 (m, 13H), 6.05 (br s, 1H), 4.73 (s, 1H), 2.36 (m, 2H), 2.14 (m, 2H), 1.31 (m, 4H), 1.06 (m, 4H), 0.78 (t, $J = 7$ Hz, 6H). ^{13}C NMR: ($CDCl_3$) δ 149.2 (Cq), 145.9 (Cq), 137.4 (Cq), 131.6 (CH), 127.8 (CH), 127.3 (CH), 127.1 (Cq), 127.0 (CH), 126.9 (CH), 126.2 (CH), 125.9 (CH), 125.7 (CH), 74.5 (CH), 51.7 (CH_2), 29.7 (CH_2), 20.3 (CH_2), 13.9 (CH_3). IR (KBr): ν_{max} 2927, 1597, 1449, 1161, 1030, 696 cm^{-1}. MS (CI, NH_3): m/z 400 (M^+, 100%). EA (calculated for $C_{28}H_{34}NO$,

found): C (83.74, 83.65), H (8.78, 9.06), N (3.49, 3.46). $[\alpha]_D = -115.5$ (c 1.08, $CHCl_3$). Enantiomeric excess was determined by ^{19}F NMR upon mixing a stoichiometric amount of Mosher's acid. Enantiomeric excess was determined to be >95%. ^{19}F NMR ($CDCl_3$): δ (Mosher R) = −70.915, δ (Mosher S) = −71.084.

5.4. Enantioselective amino alcohol-catalyzed addition of dimethylzinc to aldehydes

General procedure. In a reaction tube flushed with argon and equipped with a magnetic stirring bar, a solution of the chiral catalyst (10 mol%) in 2 mL of anhydrous solvent was added. 2 M dimethylzinc (0.5 mL, 1 mmol) in toluene was added via syringe and the reaction mixture was stirred at room temperature for 30 min. The reaction was then cooled to the desired temperature and the aldehyde (0.5 mmol) was added dropwise. The reacting mixture was stirred for the designated time.

5.4.1. Addition of dimethylzinc to benzaldehyde. *Work-up and analysis conditions*: The reaction was quenched by the addition of a saturated NH_4Cl solution (1 mL). The solution was then extracted with Et_2O and the combined organic extracts were washed with a 1 M HCl solution, followed by saturated $NaHCO_3$ solution. Conversion and enantiomeric purity of the resulting alcohols were determined by GC analysis.

GC analysis: Supelco β-DEX 120 column, 30 m length, 130 °C isotherm, t_R aldehyde 6.0 min, t_R R isomer 12.7 min, t_R S isomer 13.1 min.

5.4.2. Addition of dimethylzinc to heptanal. *Work-up and analysis conditions*: A reaction aliquot was quenched by the addition of a saturated NH_4Cl solution (1 mL). The solution was then extracted with Et_2O and the combined organic extracts were washed with a 1 M HCl solution followed by saturated $NaHCO_3$ solution. Conversion to the resulting alcohols was determined from the crude mixture by GC analysis of the organic extract.

GC analysis: Supelco β-DEX 120 column, 30 m length, 100 °C isotherm, t_R aldehyde 7.6 min, t_R alcohol 15.9 min.

To the remaining reaction mixture, 70 μL of acetyl chloride was added. The reaction was stirred for 5 h at room temperature. The mixture was extracted with Et_2O and the organic layers were washed with 1 M NaCl solution. Enantiomeric purity of the resulting alcohols was determined from the organic extract by GC analysis.

GC analysis: Supelco β-DEX 120 column, 30 m length, 100 °C isotherm, t_R S isomer 18.4 min, t_R R isomer 20.9 min.

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