Nickel-accelerated addition of dialkylzinc reagents to aldehydes. Application to enantioselective synthesis

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Dedicated to Professor Armand Lattes on his 50th years of teaching and research

Abstract

The reaction of several dialkylzinc reagents with aromatic aldehydes **1** in the presence of a catalytic amount of nickel(II) acetylacetonate (5 mol%) at 0 ºC gave the expected addition products **2** in 1 h in very good yields. Aliphatic aldehydes **1** required stirring at room temperature for 24 h to afford the addition products in good yields. In comparison with non-catalyzed reactions this process represents a great improvement in reaction rate and selectivity for the formation of addition products. The enantioselective addition of diethylzinc to benzaldehyde **1a** in the presence of the nickel catalyst and chiral aziridino alcohols **3** results in an interesting switch of the sense of the asymmetric induction in comparison with the nickel-free process.

Keywords: Dialkylzinc reagents, nickel-accelerated addition, enantioselective synthesis, aldehydes

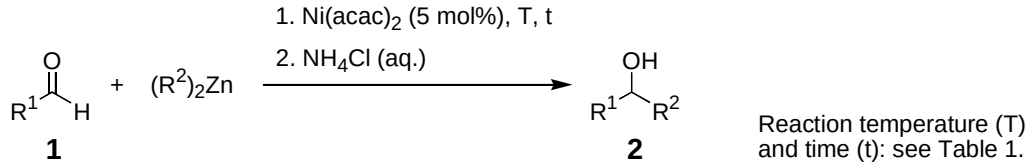
Introduction

The formation of carbon-carbon bonds is one of the fundamental operations in organic synthesis. The addition of organometallic reagents to carbonyl compounds is among the most common reactions to achieve this goal.[1] Among organometallic reagents, dialkylzinc reagents are very useful nucleophiles because organozinc reagents[2] bearing several functional groups can be easily prepared,[3] which upon addition reaction to electrophiles afford polyfunctionalized organic compounds. However, the addition reaction of dialkylzinc compounds to aldehydes is very slow, and ketones have been shown to be unreactive.[4] Moreover, dialkylzinc compounds with β-hydrogen atoms tend to complicate the addition reactions by forming reduction products.[5] The rate of the addition reaction and the selectivity of the addition product can be improved by

activation of the aldehyde by Lewis acids (such as magnesium or zinc bromides, trimethylsilyl halides, titanium tetrachloride or tetraisopropoxide)[6] or by activation of the organozinc compound with Lewis bases (such as tetrabutylammonium halides, amino alcohols, diols and diamines).[6a,7] The use of a catalytic amount of a chiral β-amino alcohol as an additive has rendered the addition reaction into an enantioselective process, and addition products with excellent optical purities can easily be obtained nowadays.[3b,8] Titanium(IV) complexes have been shown to be very efficient catalysts for the enantioselective addition to both aromatic and aliphatic aldehydes.[8d,9,10] Cobalt(II) and palladium(II) complexes are also able to catalyze the addition of diethylzinc to aromatic aldehydes with moderate enantioselectivities.[11] Continuing our studies on the use of organometallic reagents in organic synthesis, we decided to explore the utility of nickel catalysts for the addition of dialkylzinc reagents to aldehydes, because, to the best of our knowledge, there was only one previous report in the literature using nickel complexes derived from α-amino amides and $Ni(OAc)_2$.[12] According to the success reported on conjugate addition reactions,[13] we considered that $Ni(acac)_2$ would be a good candidate to promote the addition of dialkylzinc reagents to aldehydes.[14,15] In this paper we show that a catalytic amount of $Ni(acac)_2$ greatly accelerates the addition reaction to both aromatic and aliphatic aldehydes. We also report our results on the enantioselective addition of diethylzinc to benzaldehyde in the presence of chiral aziridino alcohols.

Results and Discussion

The reaction of benzaldehyde **1a** with an excess of diethylzinc (1:2.2 molar ratio) in the presence of a catalytic amount of $Ni(acac)_2$ (1:0.05 molar ratio) at 0 ºC for 1h led, after hydrolysis, to the expected addition product **2ab** (92%; Scheme 1 and Table 1, entry 2). Benzyl alcohol, resulting from the reduction of benzaldehyde, was obtained as a minor by-product (7%). In the absence of the nickel catalyst, the reaction was found to be very slow: it was not complete after 48 h at room temperature and yielded benzyl alcohol as major product with a small amount of addition product **2ab** (^{1}H NMR: ratio **1a**:**2ab**:$PhCH_2OH$ = 1:0.32:0.89). The reaction with our method is also much faster than the only nickel-catalyzed process previously reported,[12] which uses 10 mol% of the nickel complex and needs 24 h at room temperature to reach completion. In our case, the reaction was finished after 1 h at 0 ºC using only 5 mol% of $Ni(acac)_2$.



Scheme 1

Two more nickel complexes were also tested as catalysts. $NiCl_2(PPh_3)_2$ efficiently promoted the addition of diethylzinc to benzaldehyde giving the addition product at 0 ºC in 1 h, although in lower yield than with $Ni(acac)_2$ (Table 1, entry 3). However, the nickel(0) complex $Ni(COD)_2$ did not show any catalytic activity. After 24 h at room temperature, only 4% of the addition product **2ab** was obtained (Table 1, entry 4), which was probably formed via the non-catalyzed reaction. From these results it becomes clear that a nickel(0) species is not involved in the catalytic cycle, nickel(II) being the active catalyst.

Table 1. $Ni(acac)_2$-catalyzed addition of dialkylzinc reagents to aldehydes **1**. Preparation of alcohols **2**

	Aldehyde					Product		
Entry	No.	R^1	$(R^2)_2Zn$	T [ºC]	Time [h]	No.	R^2	Yield [%][a,b]
1	**1a**	Ph	Me_2Zn	0	1	**2aa**	Me	82 (75)
2	**1a**	Ph	Et_2Zn	0	1	**2ab**	Et	92[c] (71)
3	**1a**	Ph	Et_2Zn	0	1	**2ab**	Et	75[c,d]
4	**1a**	Ph	Et_2Zn	0–20	24	**2ab**	Et	8[c,e]
5	**1a**	Ph	*i*-Pr_2Zn	0	1	**2ac**	*i*-Pr	48 (44)
6	**1a**	Ph	*n*-Bu_2Zn	0	1	**2ad**	*n*-Bu	85 (70)
7	**1b**	4-ClC_6H_4	Et_2Zn	0	1	**2b**	Et	96 (80)
8	**1c**	4-BrC_6H_4	Et_2Zn	0	1	**2c**	Et	98 (81)
9	**1d**	4-$Me_2NC_6H_4$	Et_2Zn	0–20	24	**2d**	Et	---[f]
10	**1e**	2,5-$Me_2C_6H_3$	Et_2Zn	0	1	**2e**	Et	74 (64)
11	**1f**	2,4-$(MeO)_2C_6H_3$	Et_2Zn	0–20	24	**2f**	Et	46 (40)
12	**1g**	3,5-$(MeO)_2C_6H_3$	Et_2Zn	0	1	**2g**	Et	94 (83)
13	**1h**	*n*-C_6H_{13}	Et_2Zn	0–20	24	**2h**	Et	68 (52)
14	**1i**	$PhCH_2CH_2$	Et_2Zn	0–20	24	**2i**	Et	83 (70)
15	**1j**	*c*-C_6H_{11}	Et_2Zn	0–20	24	**2j**	Et	66 (42)

[a] Yield determined by ^1H NMR using commercially available diphenylmethane as internal standard.

[b] In parentheses: isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on starting material **1**. All isolated compounds **2** were ≥ 95% pure (GC and/or 300 MHz ^1H NMR).

[c] Yield determined by quantitative GC, using commercially available **2ab** and *n*-hexadecane (internal standard) in the determination of response factors.

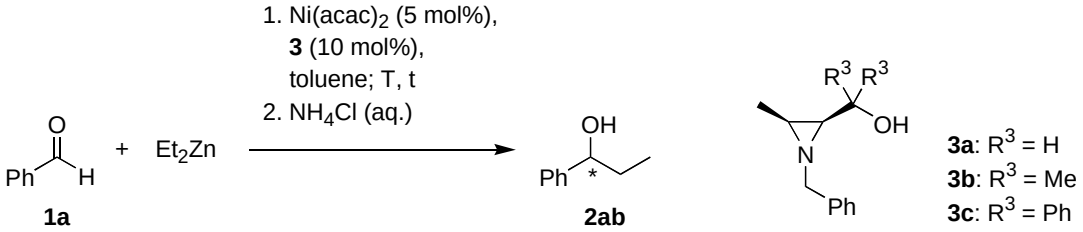
[d] $NiCl_2(PPh_3)_2$ was used instead of $Ni(acac)_2$.

[e] $Ni(COD)_2$ was used instead of $Ni(acac)_2$.

[f] No reaction was observed after 24 h at room temperature. Aldehyde **1d** was recovered unchanged.

The process was extended to a few representative dialkylzinc reagents and aldehydes (Table 1). The reaction of benzaldehyde **1a** with dimethyl-, diisopropyl- and dibutylzinc was also quite fast giving the addition products **2aa**, **2ac** and **2ad**, respectively, in moderate to very good yields after 1 h at 0 ºC (Table 1, entries 1, 5 and 6). Activated aromatic aldehydes **1b**, **1c** and **1g** afforded within 1 h the expected addition products **2b**, **2c** and **2g**, respectively, in excellent yields (Table 1 entries 7, 8 and 12). Electron-releasing groups at the aromatic ring of the aldehyde caused a decrease of the reaction rate (entries 9–11 in Table 1). No reaction was observed with aldehyde **1d** bearing a dimethylamino group at the *para* position of the aromatic ring even after 24 h at room temperature (Table 1, entry 9). The addition of diethylzinc to aliphatic aldehydes **1h**–**1j** was also successful, although the reaction was slower: the reaction mixture had to be stirred for 24h at room temperature in order to get almost complete conversion of the starting materials (Table 1, entries 13–15). Increasing the amount of the nickel catalyst up to 10 mol% did not improve the reaction rate. Reduction by-products of type R^1CH_2OH were obtained in very small amounts (≤ 10%), unless there was steric hindrance in either the dialkylzinc reagent (Table 1, entry 5, 34% of reduction product) or the aldehyde (Table 1, entries 10, 11, and 15: 12%, 30% and 31%, respectively, of reduction products). These by-products were easily removed from the desired addition products by column chromatography.

α,β-Unsaturated aldehydes were tested with disappointing results. (*E*)-Cinnamaldehyde gave an intractable mixture of products when reacted with diethyl- or dimethylzinc. On the other hand, (*E*)-2-octenal reacted slowly with diethylzinc at room temperature: after 24 h the starting material (29%) and a mixture of 1,2- and 1,4-addition products (7 and 36%, respectively) were detected (GC-MS and ^{1}H NMR).



1a **2ab**

Scheme 2

The enantioselective addition of diethylzinc to benzaldehyde was investigated using aziridino alcohols **3** as chiral ligands (Scheme 2). Compounds **3** were chosen in order to compare the results with those reported on the same addition reaction in the absence of the nickel catalyst.[16] The reactions were performed at different temperatures using 5 mol% of $Ni(acac)_2$ and 10 mol% of ligand **3** (Table 2). For ligands **3a**,**b** ee increased when changing from 0 to –23ºC and a slight decrease was observed when the temperature was further lowered to –30ºC (cf. entries 1–3 and 4–6 in Table 2). However, the best ee with ligand **3c** was obtained at –30ºC (cf. entries 7–9 in Table 2). When these results are compared with those reported for the same addition reactions in the absence of the nickel catalyst [reaction time: 24 h at room temperature;

ligand (ee, absolute configuration of the major enantiomer): **3a** (38%, *S*), **3b** (30%, *S*), **3c** (17%, *S*)],[16] some aspects are worthy of comment. The nickel-catalyzed reactions are much faster: the reactions are completed within 3 h. In the nickel-catalyzed process, a switch in the enantioselectivity is observed when passing from ligand **3a** (R^3 = H) to **3b** (R^3 = Me) and again from **3b** to **3c** (R^3 = Ph), whereas the same *S* configuration has been reported for all three ligands in the absence of the nickel catalyst.[16] Aziridino alcohols **3a** and **3c** gave a different configuration of the major enantiomer in the nickel-catalyzed and the nickel-free processes (compare entries 1–3 and 7–9 in Table 2 with the aforementioned data for the reaction without nickel). It is interesting to note that with ligands **3a** and **3c** the sense of the asymmetric induction can be changed by performing the reaction in the presence (major enantiomer: *R*) or the absence (major enantiomer: *S*) of the nickel catalyst. The ee obtained with ligand **3b** at –23 ºC in our procedure (Table 2, entry 5) was slightly higher than the one previously reported,[12] with a much shorter reaction time in our case (1.5 h instead of 24 h). From all these results, it can be deduced that different catalytically active species are involved in the nickel-catalyzed and the nickel-free processes and there is no general trend for the stereochemical outcome of the reaction in relation with the substituents on the hydroxyl group bearing carbon atom of the ligand.

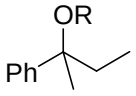
Table 2. Formation of 1-phenyl-1-propanol **2ab** by $Ni(acac)_2$–catalyzed enantioselective addition of diethylzinc to benzaldehyde in the presence of aziridino alcohols **3**

Entry	Ligand	T [ºC]	Time [h]	Yield [%][a]	ee [%][b]	Config.[c]
1	**3a**	0	1	60	6	*R*
2	**3a**	–23	1.5	73	16	*R*
3	**3a**	–30	3	50	13	*R*
4	**3b**	0	1	59	24	*S*
5	**3b**	–23	1.5	73	33	*S*
6	**3b**	–30	3	73	31	*S*
7	**3c**	0	1	63	10	*R*
8	**3c**	–23	1.5	64	12	*R*
9	**3c**	–30	3	47	20	*R*

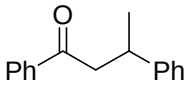
[a] Isolated yields after column chromatography (silica gel, hexane/ethyl acetate), based on **1a**.
[b] Determined by HPLC analysis using a chiral column (ChiralCel OD-H) and 5% *i*-PrOH in hexane as eluent.
[c] Absolute configuration of the major enantiomer determined by comparison of the optical rotation with the data given in the literature (see experimental part).

We also tried to apply this method to ketones. When acetophenone reacted with diethylzinc in the presence of 10 mol% of $Ni(acac)_2$ at room temperature, only traces of the expected addition product, 2-phenylbutan-2-ol (**4a**) were detected (GC-MS) after 24 h. The major product was 1,3-diphenylbutan-1-one (**5**), in accordance with previously described results.[17] When the

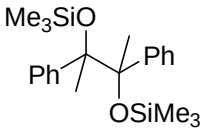
reaction was repeated in the presence of trimethylsilyl chloride (1 equiv.), the silylated addition product trimethyl(1-methyl-1-phenylpropoxy)silane (**4b**) was obtained (11%) together with the silylated pinacols **6**. Compound **5** was not formed under the latter reaction conditions. We are currently studying the effect of different additives on the course of the reaction.



4a: R = H
4b: R = $SiMe_3$



5



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Conclusions

In conclusion, we report a very efficient procedure to effect the addition of dialkylzinc reagents to aldehydes under mild reaction conditions and shorter reaction times. The use of 5 mol% of $Ni(acac)_2$ as a catalyst greatly accelerates the reaction affording the expected addition products in very good yields. The process is applicable to both aromatic and aliphatic aldehydes at room temperature with reaction times of 1 h for the former and 24 h for the latter. This procedure represents a great improvement in comparison with the non-catalyzed reaction and is much faster than the only nickel-catalyzed reaction previously reported.[12] This method is applicable to the enantioselective addition of diethylzinc to benzaldehyde **1a** when chiral aziridino alcohols **3** (10 mol%) are used as ligands. When the nickel-catalyzed and the nickel-free processes are compared, similar levels of enantioselectivity are obtained with one of the ligands and an interesting switch in the absolute configuration of the major enantiomer is observed with other two ligands. The nickel-catalyzed reactions are always much faster.

Experimental Section

General Procedures. All moisture sensitive reactions were carried out under an argon atmosphere. Commercially available anhydrous THF (99.9%, water content ≤0.006%, Acros) and toluene (≥99.7%, water content ≤0.005%, Fluka) were used as solvents in the reactions. All starting aldehydes **1** were commercially available and the liquid aldehydes were distilled before use. Solid aldehydes and commercially available $Ni(acac)_2$ were used without further purification. Toluene or heptane solutions of dialkylzinc reagents were used as commercially available (Aldrich, Fluka). Aziridino alcohols **3** were prepared as described in the literature.[18] All glassware was dried in an oven at 100 ºC and cooled to room temperature under argon before use. Column chromatography was performed with Merck silica gel 60 (0.040–0.063 μm, 240–400 mesh). Thin layer chromatography (TLC) was performed on precoated silica gel plates

(Merck 60, F254, 0.25 mm). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AC-300 spectrophotometer using $CDCl_3$ as solvent; internal references were tetramethylsilane (TMS) for ^1H NMR and $CDCl_3$ for ^{13}C NMR. Mass spectra (EI) were obtained at 70 eV on a Hewlett Packard HP-5890 GC/MS instrument equipped with a HP-5972 selective mass detector. Infrared (FT-IR) spectra were obtained on a Nicolet 510 P-FT spectrophotometer. Optical rotations were measured on a Perkin-Elmer 341 polarimeter. HPLC analyses were performed at 25ºC on a Shimadzu LC-10 AD apparatus.

Nickel-catalyzed addition of dialkylzinc reagents to aldehydes 1. Preparation of products alcohols 2. General procedure. The commercially available solution of the dialkylzinc reagent in toluene (for dimethyl-, diethyl- and diisopropylzinc) or heptane (for dibutylzinc) [4.4 mmol of $(R^2)_2Zn$] was added dropwise at 0 ºC during approximately 5 min to a stirred mixture of aldehyde **1** (2.0 mmol) and $Ni(acac)_2$ (26 mg, 0.1 mmol) under argon. After stirring at 0 ºC for 1 h (for aldehydes **1a**–**1c**, **1e** and **1g**) or for 24 h allowing the temperature to rise to room temperature (for aldehydes **1d**, **1f** and **1h**–**1j**), the reaction was hydrolyzed with aqueous saturated NH_4Cl solution (5 mL). The mixture was acidified with 2M HCl until a clear solution was obtained, which was then extracted with ethyl acetate (3 × 20 mL). The organic layers were combined, successively washed with a saturated solution of $NaHCO_3$ (5 mL), water (5 mL) and brine (5 mL), and dried (Na_2SO_4). After filtration, diphenylmethane (84 mg, 0.5 mmol, internal standard) was added, solvents were evaporated and yield from the resulting residue was determined by 1H NMR by comparing the integrals of the methine proton signal of the secondary alcohol **2** with that of the methylene protons of diphenylmethane. For product **2ab**, yields were determined by quantitative GC, using commercially available **2ab** and *n*-hexadecane (internal standard) in the determination of response factors. When applicable (Table 1, entries 1, 2, 5–8 and 10–15), the crude residue was purified by column chromatography (silica gel, hexane/ethyl acetate), giving products **2** in the yields indicated in parentheses in Table 1. Compounds **2aa** and **2ab** (commercially available, Aldrich) were characterized by comparison of their physical and spectroscopic data with authentic samples. For products **2ac**–**2j** the corresponding physical and spectroscopic data follow.

2-Methyl-1-phenyl-1-propanol (2ac).[19] Yellow oil; R_f 0.53 (hexane/ethyl acetate 1:1). IR (film): $\tilde{\nu}$ 3388 (OH), 3088, 3060, 3028, 1602, 1498 (HC=C), 1028 cm^{-1} (CO). δ_H 0.78, 0.99 (3H each, 2d, J = 6.7 Hz each, 2×Me), 1.82–2.15 (1H, m, C*H*Me), 4.33 (1H, d, J = 6.9 Hz, CHO), 7.13–7.45 (5H, m, ArH). δ_C 18.3, 19.1 (2×Me), 35.3 (*C*HMe), 80.1 (CO), 126.7 (2C), 127.5, 128.3 (2C), 143.7 (ArC). EI-MS: *m/z* (%) 150 (8) [M^+], 107 (100), 79 (46), 77 (24).

1-Phenyl-1-pentanol (2ad).[20] Colorless oil; R_f 0.49 (hexane/ethyl acetate 1:1). IR (film): $\tilde{\nu}$ 3355 (OH), 3093, 3066, 3033, 1607, 1498 (HC=C), 1034 cm^{-1} (CO). δ_H 0.87 (3H, t, J = 7.1 Hz, Me), 1.12–1.45, 1.57–1.85 (4H and 2H, respectively, 2m, 3×CH_2), 2.27 (1H, s, OH), 4.59 (1H, dd, J = 7.0, 6.3Hz, CHO), 7.17–7.41 (5H, m, ArH). δ_C 13.9 (Me), 22.5, 27.9, 38.7 (3×CH_2), 74.5 (CO), 125.8 (2C), 127.3, 128.3 (2C), 144.9 (ArC). EI-MS: *m/z* (%) 165 (<1) [M^++1], 164 (8) [M^+], 107 (100), 79 (38), 77 (18).

1-(4-Chlorophenyl)-1-propanol (2b).[21] Yellow oil; R_f 0.40 (hexane/ethyl acetate 1:1). IR (film): $\tilde{\nu}$ 3361 (OH), 3082, 3055, 3028, 1602, 1493 (HC=C), 1094 cm^{-1} (CO). δ_H 0.86 (3H, t, *J* = 7.4 Hz, Me), 1.55–1.83 (2H, m, CH_2), 2.43 (1H, br s, OH), 4.51 (1H, t, *J* = 6.0 Hz, CHO), 7.08–7.38 (4H, m, ArH). δ_C 10.0 (Me), 31.8 (CH_2), 75.2 (CO), 127.4 (2C), 128.4 (2C), 132.9, 143.0 (ArC). EI-MS: *m/z* (%) 172 (4) [M^++2], 171 (1) [M^++1], 170 (11) [M^+], 143 (32), 141 (100), 113 (19), 77 (49).

1-(4-Bromophenyl)-1-propanol (2c).[22] Yellow oil; R_f 0.43 (hexane/ethyl acetate 1:1). IR (film): $\tilde{\nu}$ 3366 (OH), 3088, 3060, 3011, 1596, 1493 (HC=C), 1072 cm^{-1} (CO). δ_H 0.82 (3H, t, *J* = 7.2 Hz, Me), 1.92–2.24 (2H, m, CH_2), 3.19 (1H, br s, OH), 4.41 (1H, t, *J* = 6.1 Hz, CHO), 7.10, 7.40 (2H each, 2d, *J* = 8.2 Hz each, ArH). δ_C 9.9 (Me), 31.7 (CH_2), 75.1 (CO), 121.0, 127.7 (2C), 131.3 (2C), 143.5 (ArC). EI-MS: *m/z* (%) 216 (13) [M^++2], 215 (1) [M^++1], 214 (13) [M^+], 187 (91), 185 (100), 159 (16), 157 (19), 78 (25), 77 (49).

1-(2,5-Dimethylphenyl)-1-propanol (2e).[23] Colorless oil; R_f 0.58 (hexane/ethyl acetate 1:1). IR (film): $\tilde{\nu}$ 3366 (OH), 3055, 3022, 1613, 1460 (HC=C), 1094 cm^{-1} (CO). δ_H 0.95 (3H, t, *J* = 7.3 Hz, *Me*CH_2), 1.59–1.80 (2H, m, CH_2), 2.26, 2.31 (3H each, 2s, 2×*Me*Ar), 4.79 (1H, t, *J* = 6.5 Hz, CHO), 6.95, 7.00 (1H each, 2d, *J* = 7.9 Hz each, 2×ArH), 7.25 (1H, s, 1×ArH). δ_C 10.3, 18.5, 21.0 (3×Me), 30.9 (CH_2), 71.9 (CO), 125.8, 127.7, 130.2, 131.3, 135.5, 142.5 (ArC). EI-MS: *m/z* (%) 165 (3) [M^++1], 164 (21) [M^+], 136 (10), 135 (100), 107 (92), 105 (23), 91 (47), 77 (11).

1-(2,4-Dimethoxyphenyl)-1-propanol (2f).[24] Yellow oil; R_f 0.49 (hexane/ethyl acetate 1:1). IR (film): $\tilde{\nu}$ 3443 (OH), 3071, 3006, 1618, 1509 (HC=C), 1208, 1045 cm^{-1} (CO). δ_H 0.93 (3H, t, *J* = 7.3 Hz, *Me*CH_2), 1.62–1.91 (2H, m, CH_2), 2.47 (1H, br s, OH), 3.79, 3.81 (3H each, 2s, 2×MeO), 4.72 (1H, t, *J* = 6.8 Hz, CHO), 6.39–6.53 (2H, m, 2×ArH), 7.19 (1H, d, *J* = 8.9 Hz, 1×ArH). δ_C 10.5 (*Me*CH_2), 30.1 (CH_2), 55.2, 55.3 (2×MeO), 71.9 (CHO), 98.6, 103.9, 124.9, 127.6, 157.7, 159.9 (ArC). EI-MS: *m/z* (%) 196 (5) [M^+], 167 (100), 151 (12), 137 (17).

1-(3,5-Dimethoxyphenyl)-1-propanol (2g).[25] Yellow oil; R_f 0.29 (hexane/ethyl acetate 1:1). IR (film): $\tilde{\nu}$ 3421 (OH), 3088, 3060, 1607, 1471 (HC=C), 1208, 1055 cm^{-1} (CO). δ_H 0.90 (3H, t, *J* = 7.4 Hz, *Me*CH_2), 1.57–1.86 (2H, m, CH_2), 2.48 (1H, s, OH), 3.76 (6H, s, 2×Me), 4.47 (1H, t, *J* = 6.6 Hz, CHO), 6.34 (1H, t, *J* = 2.3 Hz, 1×ArH), 6.48 (2H, d, *J* = 2.3 Hz, 2×ArH). δ_C 10.1 (*Me*CH_2), 31.7 (CH_2), 55.2 (2C, 2×MeO), 75.9 (CHO), 99.2, 103.9 (2C), 147.3, 160.7 (2C) (ArC). EI-MS: *m/z* (%) 197 (6) [M^++1], 196 (48) [M^+], 168 (15), 167 (71), 139 (100), 124 (25), 77 (10).

3-Nonanol (2h).[26] Yellow oil; R_f 0.60 (hexane/ethyl acetate 1:1). IR (film): $\tilde{\nu}$ 3344 (OH), 1121 cm^{-1} (CO). δ_H 0.89 (3H, t, *J* = 6.8 Hz, 1×Me), 0.94 (3H, t, *J* = 7.4 Hz, 1×Me), 1.16–1.69 (12H, m, 6×CH_2), 3.40–3.60 (1H, m, CH). δ_C 9.9, 14.1 (2×Me), 22.6, 25.6, 29.4, 30.1, 31.8, 36.9 (6×CH_2), 73.3 (CO). EI-MS: *m/z* (%) 144 (<1) [M^+], 115 (39), 97 (91), 69 (18), 59 (100), 58 (10), 57 (13), 55 (69).

1-Phenyl-3-pentanol (2i).[27] Yellow oil; R_f 0.53 (hexane/ethyl acetate 1/:1). IR (film): $\tilde{\nu}$ 3394 (OH), 3093, 3066, 3033, 1602, 1498 (HC=C), 1121 cm^{-1} (CO); δ_H 0.94 (3H, t, *J* = 7.4 Hz, Me), 1.38–1.62 (2H, m, 1×CH_2CO), 1.63–1.88 (3H, m, 1×CH_2CO and OH), 2.55–2.88 (2H, m, C*H*$_2$Ph), 3.42–3.62 (1H, m, CHO), 7.05–7.40 (5H, m, ArH). δ_C 9.9 (Me), 30.4, 32.2, 38.7

(3×CH_2), 72.7 (CO), 125.9, 128.45 (2C), 128.5 (2C), 142.3 (ArC); EI-MS: *m/z* (%) 164 (5) [M^+], 146 (51), 117 (79), 105 (11), 104 (34), 92 (35), 91 (100), 78 (14), 65 (11).

1-Cyclohexyl-1-propanol (2j).[26] Colorless oil; R_f 0.28 (hexane/ethyl acetate 4:1). IR (film): $\tilde{\nu}$ 3366 (OH), 1121 cm^{-1} (CO); δ_H 0.95 (3H, t, *J* = 7.5 Hz, Me), 1.00–1.90 (14H, m, 6×CH_2, CHCO and OH), 3.16–3.37 (1H, m, CHO). δ_C 10.2 (Me), 26.2, 26.4, 26.5, 26.8, 27.7, 29.3 (6×CH_2), 43.1 (CH), 77.6 (CO). EI-MS: *m/z* (%) 142 (<1) [M^+], 113 (48), 95 (100), 82 (17), 67 (23), 59 (59), 58 (21), 55 (22).

Nickel-catalysed enantioselective addition of diethylzinc to benzaldehyde 1a in the presence of aziridino alcohols 3. General procedure. Ligand **3** (0.2 mmol) was weighed into a Schlenk tube and any moisture was azeotropically removed by dissolving the ligand in benzene (1 mL) and evaporating the solvent at reduced pressure; the process was repeated four times. $Ni(acac)_2$ (26 mg, 0.1 mmol) was then added under an argon atmosphere inside the flask. Anhydrous toluene (1 mL) was added and the resulting suspension was stirred for 15 min under argon at room temperature. Benzaldehyde (**1a**; 0.2 mL, 2.0 mmol) was added, the reaction flask was cooled to the temperature indicated in Table 2, and diethylzinc (4.0 mL of a 1.1 M solution in toluene, 4.4 mmol) was added dropwise during *ca.* 5 min. After stirring for the time indicated in Table 2, the reaction was hydrolyzed with aqueous saturated NH_4Cl solution (5 mL). The mixture was acidified with 2M HCl until a clear solution was obtained, which was then extracted with ethyl acetate (3 × 20 mL). The organic layers were combined, successively washed with a saturated solution of $NaHCO_3$ (5 mL), water (5 mL) and brine (5 mL), and dried (Na_2SO_4). After evaporation of the solvents the resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate), affording the addition product **2ab** (for yields and ee's see Table 2). The enantiomeric excess was determined by HPLC analysis using a chiral column (ChiralCel OD-H), a 254 nm UV detector, 5% isopropyl alcohol in hexane as mobile phase and a flow rate of 0.5 mL/min. The retention times were 16.4 (*R*) and 17.8 min (*S*). The absolute configuration of the major enantiomer was determined by comparing the optical rotation with the data given in the literature.[28]

Acknowledgements

This work was financially supported by the DGI of the Spanish Ministerio de Educación y Ciencia (project no. CTQ2004-01261) and the Generalitat Valenciana (project no. GRUPOS03/135). R. A. thanks the Spanish Ministerio de Educación y Ciencia for a fellowship.

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