Enantioselective Reaction of Diethylzinc with Arenecarbaldehydes in the Presence of Ephedrine Derivatives

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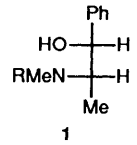
The reaction of diethylzinc with a range of arenecarbaldehydes has been catalysed by *N*-alkyl ephedrines to give 1-arylpropan-1-ols with good to excellent optical yields. The enantioselectivity of the reaction was substantially improved by the use of a 4 molar excess of the organozinc reagent.

There has been considerable interest in the enantioselective reactions of dialkylzinc compounds with aldehydes in the presence of chiral amino alcohols[1–5] and the reaction may be accomplished with good yield and stereoselectivity. We now report the full details of the reactions with arenecarbaldehydes in the presence of *N*-substituted ephedrines, with variations in the substrate, the substitution in the ephedrine catalyst, and the relative concentrations of the reaction components. Preliminary accounts of some of this work have been published.[6,7]

Results and Discussion

In order to have available racemic samples of the alcohols to be prepared in the reactions of diethylzinc with arenecarbaldehydes, standard Grignard syntheses were undertaken (Table 1). The availability of these samples was essential in assessing the methods for determination of the optical purity of the optically enriched materials (*vide infra*). (1R,2S)-Ephedrine derivatives, **1**, were prepared according to adaptations of the published synthesis of *N*-ethylephedrine.[14]



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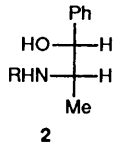
a; R = H
b; R = Me
c; R = Et
d; R = Pr
e; R = Pr^i
f; R = $CH_2CH_2CH_2OH$



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a; R = H
b; R = Pr^i

The results of the alkylation of benzaldehyde by diethylzinc, in the presence of various catalysts are summarised in Table 2 and several points are worthy of note. First, both the hydroxy and the amino group of the catalyst are essential to obtain a good optical yield, the use of the related chiral amines and alcohols as catalysts giving very poor results. Second, the optical yield increases with the size of the alkyl substituent at nitrogen. In the light of Noyori's results[1] using DAIB as catalyst, it is perhaps surprising that these reactions were so successful; using a 1:1 molar ratio of Et_2Zn:PhCHO in his system gave no alkylation, but an extrmely slow reduction to benzyl alcohol. Benzyl alcohol was not detected in any of these reactions.

Reactions of benzaldehyde with other organometallics in the presence of ephedrine were also studied (Table 3), with uniformly unsuccessful results. Since there are a wide variety of reports in the literature of reactions at different temperatures a brief study of the temperature dependence of the reaction was undertaken (Table 4); fortuitously, the reaction at room temperature seems to be close to optimal.

The reactions of other arenecarbaldehydes were also studied, with the hope of seeing correlations between the electronic nature of the substituent on the aromatic ring and either chemical or optical yield (Table 5). Reasonable chemical and optical yields were obtained for a range of aldehydes bearing either electron withdrawing or electron donating groups, but

Table 1 Reactions of arenecarbaldehydes, RC_6H_4CHO, with ethylmagnesium bromide

R	Chemical yield[a] (%)	B.p. [t/°C (p/mmHg)] Found	Lit.	Ref.
4-Me	90	30–32 (0.1)	118–125 (18)	8
3-Me	95	40–41 (0.02)	113–118 (15)	8
4-Br	89	35–36 (0.1)	138–139 (11)	9
4-Cl	90	40–42 (0.01)	128–132 (17)	8
3-Cl	86	34–36 (0.2)	129–132 (17)	8
4-CF_3	93	45–46 (0.01)	107–108 (13)	10
3-CF_3	90	29–30[b]	85–88 (5)	11
4-MeO	98.5	45–46 (0.01)	137–140 (11.5)	12
2-MeO	98	30–31 (0.01)	88–90 (0.6)	13

[a] Isolated yields, *ca.* 150 mmol scale. [b] M.p.

Table 2 Reactions of benzaldehyde with Et_2Zn in the presence of ephedrines and related catalysts

Catalyst[a]	Chemical yield[b] (%)	$[\alpha]_D$/[c]	Ee (%)
Ephedrine[e] **1a**	60	+28.17	66 *R*
N-Methylephedrine **1b**	66	+27.10	64 *R*
N-Ethylephedrine **1c**	63	+32.80	77 *R*
N-Propylephedrine **1d**	70	+31.04	73 *R*
N-Isopropylephedrine **1e**	70	+33.78	79.6 *R*
N-(3-Hydroxypropyl)ephedrine **1f**	89	+30.1	71 *R*
(*S*)-1-Phenylethylamine	55	−0.51	1.2 *S*
(*S*)-1-Phenylethanol	58	−1.42	3.3 *S*
(*S*)-*N*,*N*-Dimethyl-1-phenylethylamine	50	+1.98	4.7 *R*

[a] 5 Mol% catalyst. [b] Measured by GLC (OV17, 200 °C). [c] 20 °C, *c* 0.5–1, C_6H_6. [d] Average of 2 values within 2%, confirmed by ^{31}P NMR spectroscopy on the mixture formed by reaction of the crude alcohol with PCl_3 according to the method of Wynberg.[15] $[\alpha]_D$ for (*R*)-PhCH(OH)Et is given by Pickard to be (+)40.05° (C_6H_6),[16] but was redetermined on an optically pure sample (Aldrich) to be (+)42.46° (C_6H_6). The latter value was used in all calculations and was found to be in good agreement with the value from ^{31}P NMR spectroscopy. [e] (1*R*,2*S*)-(−)-Ephedrine [α-(1-methylaminoethyl)benzyl alcohol]; all the ephedrine derived catalysts have the same configuration.

Table 3 Reaction of benzaldehyde with other organometallics in the presence of ephedrine

Reagent	Chemical yield[a] (%)	$[\alpha]_D$/°[b]	Ee (%)
EtZnCl[c]	50	0	0
EtZnCl	56	0	0
EtZnCl[d]	59	0	0
EtLi	40	+0.94	2.2 *R*
EtMgBr	81	−0.28	0.7 *S*

[a] By GLC (OV17, 200 °C). [b] *c* 0.5–1.0, benzene. [c] No ephedrine added. [d] *N*-Methylephedrine added.

Table 4 Temperature dependence of the reaction of Et_2Zn with benzaldehyde in the presence of ephedrine[a]

Temp. (°C)	Time (h)	Yield[b] (%)	$[\alpha]_D$/°[c]	Ee[d]
−20	48	70	+11.86	27.9 *R*
0	48	70	+19.87	46.8 *R*
20	48	60	+28.17	66.3 *R*
69	8	55	+3.07	7.2 *R*

[a] 1.2 mol Et_2Zn per mol aldehyde. [b] By GLC (OV17, 200 °C). [c] Benzene, *c* = 0.5–1.0. [d] Based on $[\alpha]_D^{20}$ 42.46 °.

Table 5 Reaction of arenecarbaldehydes, RC_6H_4CHO, with Et_2Zn[a] in the presence of (1R,2S)-*N*-isopropylephedrine

Substituent	Chemical yield[b] (%)	$[\alpha]_D$/°[c]	Temp. (°C)	Ee (%)
4-Me	73	+28.9	21	73.7[d] *R*
3-Me	80	+32.29	24	72[e] *R*
4-Br	79	+13.33	20	76[e] *R*
4-Cl	76	+20.21	20	83.5[f] *R*
3-Cl	73	+24.53	21	85[g] *R*
4-CF_3	39.3	+11.55	25	53[h] *R*
3-CF_3	61	+17.9	25	56[e] *R*
4-MeO[i]	99	+21.7	27	63[j] *R*
2-MeO[i]	100	+35.37	25	66.9[k] *R*

[a] 1.2 mol Et_2Zn per mol ArCHO. [b] Determined by GLC (OV17, 200 °C). [c] *c* = 0.5–1.0, C_6H_6. [d] Rotation for pure (*S*)-1-(4-methylphenyl)propan-1-ol $[\alpha]_D$ −39.2° (*c* 5, C_6H_6), based on a rotation of −20.4° for a sample of optical purity 52% *S*.[17] [e] Based on ^{19}F NMR method.[18] [f] Rotation for pure (*R*)-1-(4-chlorophenyl)propan-1-ol +24.18 based on a rotation of +20.1° for a sample of optical purity 83% *R*[2]. [g] Optical yield by ^{31}P NMR method.[15] [h] Rotation for pure (*S*)-1-(4-trifluoromethylphenyl)propan-1-ol −21.8° based on a rotation of − 4.8° for a sample of optical purity 22% *S*.[17] [i] 2 mol Et_2Zn per mol ArCHO; very low yields were obtained with 1 mol. [j] Rotation for pure (*R*)-1-(4-methoxyphenyl)propan-1-ol +33.52° based on a rotation of + 18.1° for a sample of 54% *R* optical purity.[2] [k] Rotation for pure (*S*)-1-(2-methoxyphenyl)propan-1-ol −53.6° (*c* 3, toluene, 27 °C), based on a rotation of −50.63° for material of 94% *S* optical purity.[19]

Table 6 Dependence of the reaction between Et_2Zn and benzaldehyde in the presence of *N*-isopropylephedrine on stoichiometry

Et_2Zn:PhCHO	Yield[a] (%)	$[\alpha]_D$/°[b]	Ee(%)[c]
1.1	70	+33.8	79.6 *R*
2.0	98	+34.0	80.0 *R*
2.5	98.3	+37.4	88.0 *R*
3.0	98.3	+37.8	89.0 *R*
4.0	99.8	+40.2	94.6 *R*
4.5	99.7	+39.8	93.7 *R*

[a] Yield by GLC (OV-17, 80 °C). [b] *c* 0.5–1.0, C_6H_6. [c] Based on $[\alpha]_D^{20}$ 42.6° (*c* 5, C_6H_6), confirmed by ^{31}P NMR spectroscopy.

Table 7 Dependence of the reaction of Et_2Zn with benzaldehyde in the presence of *N*-(3-hydroxypropyl)ephedrine on stoichiometry

Et_2Zn:PhCHO	Yield[a] (%)	$[\alpha]_D$/°[b]	Ee (%)
1.0	89	+30.1	71 *R*
3.0	91.4	+30.5	72 *R*
4.0	93.5	+30.7	73 *R*

[a] Yield by GLC (OV-17, 80 °C). [b] *c* 0.5–1.0, C_6H_6. [c] Based on $[\alpha]_D^{20}$ 42.6 (*c* 5, C_6H_6), confirmed by ^{31}P NMR spectroscopy.

there were no obvious correlations with σ. Arenecarbaldehydes bearing ester groups gave a complex mixture of products, as did those with nitrile substituents. Tarry mixtures were obtained from nitrobenzaldehydes. Although the Grignard reactions of furan-2-carbaldehyde and pyridine-4-carbaldehyde were successful, the reactions of these substrates with diethylzinc gave complex mixtures from which no characterisable material could be isolated.

Given the diversity of reaction conditions for this process which had been reported in the literature, a study was undertaken of the dependence of the enantiomer excess on the reaction stoichiometry (Tables 6 and 7). Examination of the data for *N*-isopropylephedrine clearly shows that a good chemical yield for the reaction is generally obtained for any Et_2Zn:PhCHO ratio of 2.0 or above, but that the best optical yields were obtained only at molar ratios of 4.0 and above. The results for the *N*-(3-hydroxypropyl)ephedrine catalysed reactions showed much less variation in either chemical or optical yield with concentration. Results for norephedrine derivatives **2** (Table 8) were predictably less good, in line with our original supposition that optical yields were enhanced by the presence of large groups substituted at nitrogen.

Measurement of the optical purity of the product alcohols involved several different techniques. For 1-phenylpropan-1-ol, the rotation of the pure *R* enantiomer was given by Pickard[16] as +40.05°,* but a remeasurement on an authentic pure sample gave a value of +42.46°. This was the value used for the polarimetric measurements. The polarimetric measurements were checked by the use of the ^{31}P NMR spectroscopic method described by Wynberg and his co-workers;[15] the values for optical purity were within 3% of those obtained polarimetrically. The method was checked to exclude the possibility of enantiomer recognition by carrying out an experiment using racemic material (Table 9). In all cases the values quoted are an average of at least two determinations which agreed within 2%. The optical purity of 1-(3-chlorophenyl)propan-1-ol was similarly determined.

The ^{31}P NMR spectroscopic method failed to give satisfactory results for 1-(3-methylphenyl)propan-1-ol, 1-(4-bromophenyl)propan-1-ol or 1-(3-trifluoromethylphenyl)propan-1-ol. For these samples the determination of optical purity was made by ^{19}F NMR spectroscopy after reaction with 1-methoxy-1-phenyl-1-trifluoromethylacetyl chloride, after the method of Mosher and co-workers.[18] Again a racemic sample was analysed in each case to ensure that there was no significant enantiomer recognition by the added acyl halide (Table 10). Uncertainties by this method were estimated at ±5%.

The generally accepted mechanism for this reaction is due to Noyori (Scheme 1).[1] He proposes that the key reacting intermediate is **5**, which is formed by an equilibrium with **3** or **4**. The position of this equilibrium, and hence the concentration of

* Throughout, units for $[\alpha]_D$ are recorded in ° for consistency with literature values. Current IUPAC practice is to record $[\alpha]_D$ values in units of 10^{-1} deg cm^2 g^{-1}. Numerically the values are identical.

Table 8 Reaction of Et_2Zn with benzaldehyde in the presence of norephedrine derivatives

Catalyst	Et_2Zn:PhCHO	Yield[a] (%)	$[\alpha]_D$/°	Ee (%)
(1*R*,2*S*)-Norephedrine **2a**	3.0	99	+23.7	55.8 *R*
(1*R*,2*S*)-*N*-Isopropylnorephedrine **2b**	2.0	98	+30.5	72 *R*
	3.0	99	+32.5	75.4 *R*

[a] By GLC (OV-17, 80 °C). [b] Based on $[\alpha]_D^{20}$ 42.46° (*c* 5, C_6H_6).

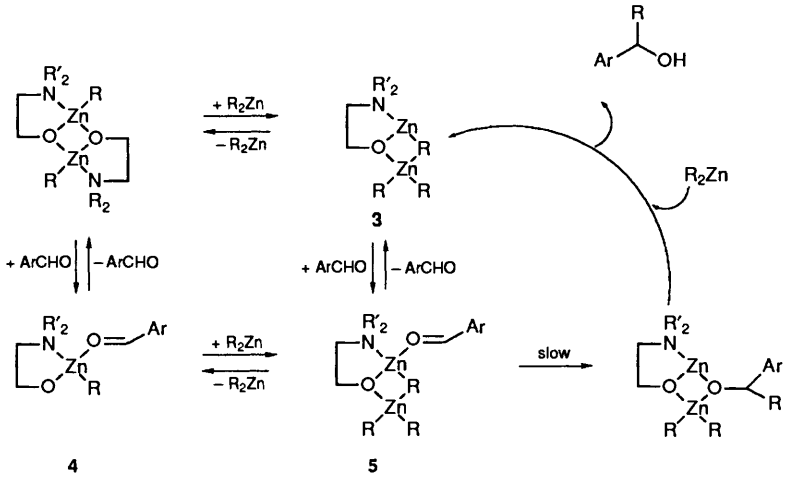
Table 9 Determination of optical purity by ^{31}P NMR spectroscopy

Alcohol	Catalyst	Ee from polarimetry	Ee by ^{31}P NMR spectroscopy
PhCH(OH)Et	*a*	0	0
	N-Ethylephedrine **1c**	77	76
	N-Propylephedrine **1d**	73	70
	N-Isopropylephedrine **1e**	80	80
3-$ClC_6H_4CH(OH)Et$	*a*	0	0
	N-Isopropylephedrine **1e**	*b*	85

[a] Racemic sample from Grignard reaction. [b] Optical rotation for the pure enantiomer is unknown.

Table 10 Determination of optical purity by ^{19}F NMR spectroscopy

Alcohol	Ratio of enantiomers in racemic sample	Ee by ^{19}F NMR spectroscopy (%)
1-(4-Methylphenyl)propan-1-ol	48:52	74 *R*
1-(3-Methylphenyl)propan-1-ol	50:50	72 *R*
1-(3-Trifluoromethylphenyl)propan-1-ol	48:52	56 *R*
1-(4-Bromophenyl)propan-1-ol	50:50	76 *R*



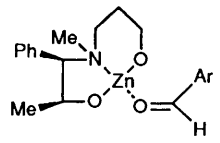
Scheme 1

the reactive species will be affected by the concentration of diethylzinc present, accounting for the observed dependence of the chemical yield on stoichiometry. If we assume that other alkylation reactions, occurring through different intermediates, are less optically efficient, this would account for the dependence of the optical yield on the Et_2Zn:ArCHO ratio. It is reasonable to suppose that the equilibrium constants in this system are dependent on the nature of the chiral amino alcohol ligand, and hence the concentration dependence may be substantial, as noted here, or less obvious, as observed elsewhere. It may be worthy of some note that in our system, unlike others reported in the literature, the nitrogen atom is not symmetrically substituted. Thus, in the zinc complexes, the nitrogen is an additional chiral centre. It is not at present clear whether the coordination is stereoselective, and further experiments to clarify this point are in progress. The reactions in the presence of *N*-3-hydroxypropylephedrine are a special case; no significant dependence of either the chemical or the optical yield on the zinc:aldehyde ratio was noted. This may be due to the formation of the three-coordinate intermediate, **6**, which is then attacked by external or weakly associated diethylzinc.

We should note that under our conditions (25 °C, 48 h) there is a significant uncatalysed reaction (65% yield). At the lower temperature used by Noyori (0 °C), no uncatalysed alkylation was observed, but merely a slow reduction to benzyl alcohol.

Experimental

All reactions involving diethylzinc or Grignard reagents were



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carried out in flame dried apparatus, purged with dry nitrogen. Light was excluded from reactions involving diethylzinc. Solvents were dried and distilled by standard methods. Analyses by gas-liquid chromatography were carried out on an AI-93 instrument. ^1H and ^{31}P NMR spectra were recorded on a Bruker WM360 spectrometer. ^{19}F NMR spectra were recorded on a Bruker WP80 FT NMR spectrometer, and were calibrated with respect to internal $CFCl_3$. Optical rotations were recorded using a Perkin-Elmer 241 Polarimeter.

Preparation of N-*Ethylephedrine* **1c**.—This compound was prepared in 49% yield by the method of Uedo.[14]

Preparation of N-*Propylephedrine* **1d**.—Ephedrine (3.0 g, 18 mmol) was heated with 1-bromopropane (2.78 g, 230 mmol) in a sealed ampoule for 3 h at 130 °C. The reaction mixture was cooled, diluted with water (10 ml), acidified with 10% HCl (100 ml) and washed with ether (2 × 100 ml). The aqueous phase was brought to pH 12 with aqueous 15% sodium hydroxide (150 ml), and the liberated amine was extracted with ether (3 × 250 ml). The combined layers were dried (KOH) and evaporated under reduced pressure to give an oily residue. Column chromatography (SiO_2, 60–120 mesh, Et_2O) of this, followed by trap-to-bucket distillation yielded *N*-propylephedrine (2.385 g, 64%), m.p. 42–43 °C (b.p.[14] 130–135 °C, 7 mmHg); ν_{max}(liquid film)/cm^{-1} 3600, 3010, 1605 and 750; δ($CDCl_3$) 0.84–0.67 (m, 6 H, $CHCH_3$ and $NCH_2CH_2CH_3$), 1.53–1.2 (m, 2 H, $NCH_2CH_2CH_3$), 2.15 (s, 3 H, NCH_3), 2.36–2.25 (m, 2 H, $NCH_2CH_2CH_3$), 2.77–2.43 (m, 1 H, $CHCH_3$), 4.7 (d, *J* 4, 1 H, CHOH) and 7.3 (s, 5 H, C_6H_5); *m/z* 207 (M^+); $[\alpha]_D^{28}$ −6.76° (EtOH).

Preparation of N-*Isopropylephedrine* **1e**.—Ephedrine (5 g, 30 mmol) was heated with 2-bromopropane (4.6 g, 37 mmol) in a sealed ampoule for 3 h at 130 °C. The procedure for work-up and purification was as before to give *N*-isopropylephedrine as a pale yellow oil (3.78 g, 61%), b.p. 130–133° C/7 mmHg; ν_{max}(liquid film)/cm^{-1} 3600, 3010, 1601, 1500, 950 and 760; δ($CDCl_3$) 0.75 (d, 3 H, *J* 6.8, $CHCH_3$), 0.99 (d, *J* 6.6, $NCHCH_3$), 0.95 (d, 3 H, *J* 6.6, $NCHCH_3$), 2.09 (s, 3 H, NCH_3), 2.9 [2 H, m, $CHCH_3$ and $NCH(CH_3)_2$], 4.71 (d, 1 H, *J* 4.1, CHOH) and 7.2 (s, 5 H, C_6H_5); *m/z* 207 (M^+); $[\alpha]_D^{22}$ −3.18° (EtOH).

Preparation of N-(3-*Hydroxypropyl*)*ephedrine* **1f**.—A mixture of ephedrine (5 g, 30 mmol) and 3-bromopropanol (5 g, 36 mmol) was heated in an ampoule at 150 °C for 72 h. After work-up, the excess of 3-bromopropanol was distilled off to give *N*-(3-hydroxypropyl)ephedrine as an involatile viscous yellow oil (5.3 g, 79%); *m/z* 224.1641 ($[M + 1]^+$, $C_{13}H_2NO_2$ requires 224.1650) and 222.1494 ($[M-1]^+$, $C_{13}H_{20}NO_2$ requires 222.1494); ν_{max}(liquid film)/cm^{-1} 3600–3400, 3000, 2600–2500, 1400 and 730; δ_H(CD_3OD) 1.02 (d, 3 H, *J* 4, $CHCH_3$), 1.67 (2 H, m, $NCH_2CH_2CH_2OH$), 2.43 (s, 3 H, NCH_3), 2.80 (m, 2 H, NCH_2), 2.90 (m, 1 H, $CHCH_3$), 3.52 (t, 2 H, *J* 6, CH_2OH), 4.92 (d, 1 H, *J* 4, PhCHOH) and 7.21 (m, 5 H, C_6H_5); δ_C(CD_3OD) δ 8.52 ($CHCH_3$), 29.97 ($CH_2CH_2CH_2OH$), 38.23 (NCH_3), 53.76 (NCH_2), 61.88 (CH_2OH), 65.95 ($CHCH_3$), 74.65 (CHOH), 127.24, 128.21, 129.15 (CH aromatic) and 144.71 (C quaternary, aromatic); $[\alpha]_D^{20}$ −10.1° (*c* 4 × 10^{-3}, EtOH).

Preparation of N-*Isopropylnorephedrine* **2b**.—A mixture of norephedrine (3 g, 20 mmol) and 2-bromopropane (4.9 g, 40 mmol) was heated in a sealed ampoule for 10 h at 130 °C. After work-up and purification of the product by column chromatography, crystallisation from light petroleum (60–80) gave the title compound as white needles (2.5 g, 60%), m.p. 104–105 °C (Found: C, 74.6; H, 9.8; N, 7.20. $C_{12}H_{19}NO$ requires C, 74.6; H, 9.85; N, 7.25%); ν_{max}(Nujol)/cm^{-1} 3500, 3010, 1600, 1200, 900 and 700; δ_H($CDCl_3$) 0.78 (d, 3 H, *J* 6, $CHCH_3$), 1.03 (d, 3 H, *J* 6, $NCHCH_3$), 1.05 (d, 3 H, *J* 6, $NCHCH_3$), 2.89 (m, 2 H, $CHCH_3$ and NHCH), 4.65 (d, 1 H, *J* 4, PhCHOH) and 7.2 (m, 5 H, C_6H_5); δ_C($CDCl_3$) 14.1 ($CHCH_3$), 22.45 ($NCHCH_3$), 22.55 ($NCHCH_3$), 44.63 [$NCH(CH_3)_2$], 54.25 ($CHCH_3$), 72.77 (CHOH), 125.17, 125.93, 126.99 (CH aromatic) and 140.81 (C quaternary aromatic); *m/z* (EI) 193 (M^+, 2%), 86 ($[Me_2CHNHCHMe]^+$, 100%) and 77 (Ph^+, 40%); $[\alpha]_D^{20}$ −6.00° (*c* 2 × 10^{-3}, EtOH).

Preparation of (−)-N,N-*Dimethyl*-1-*phenylethylamine*.[20]—To acetic acid (90%; 25.6 g, 0.5 mol) in a flask cooled by running water was added 1-phenylethylamine (12.1 g, 0.1 mol) to give a clear solution. Formaldehyde (37%; 22.5 ml, 0.3 mol) was added to this and the mixture was then placed in an oil bath at 90–100 °C. A vigorous evolution of gas began after 2–3 min, and the flask was removed from heat until it subsided. The mixture was then heated under reflux for 8 h. The solution was cooled and HCl (4 mol dm^{-3}; 50 ml) was added. The solution was evaporated to dryness and the residue was dissolved in aqueous NaOH (18 mol dm^{-3}; 35 ml); the organic layer was then separated and the aqueous layer extracted with benzene. The combined organic layers were dried and evaporated under reduced pressure to give the crude title compound. Distillation of this afforded a pure colourless oil (11.18 g, 75%); b.p. 73–76 °C at 16 mmHg (lit.,[20] b.p. 194–195 °C); $[\alpha]_D^{22}$ −65.94° (C_6H_6).

Preparation of 1-*Phenylpropan*-1-*ol by the Reaction of Diethylzinc with Benzaldehyde in the Presence of* N-*Isopropylephedrine*.—Diethylzinc (15% w/v in toluene; 20 ml, 22 mmol) was added to benzaldehyde (2 ml, 20 mmol) and *N*-isopropylephedrine (0.4 g, 2 mmol) under nitrogen. The reaction mixture was stirred in the dark at room temperature for 48 h after which it was cooled to 0 °C in an ice bath; HCl (1.5 mol dm^{-3}; 100 ml) was then added dropwise to it until the effervescence ceased. The organic layer was separated and the aqueous layer extracted with ether (3 × 100 ml). The combined organic layers were dried (Na_2SO_4), and evaporated under reduced pressure to give crude 1-phenylpropan-1-ol (70% by GC, OV 17, 200 °C). Pure 1-phenylpropan-1-ol was obtained by column chromatography (SiO_2, 60–120, CH_2Cl_2), followed by trap-to-bucket distillation.

This procedure was followed for all the catalysts discussed, and for the range of arenecarbaldehydes.

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