Enantioselective Reduction of Prochiral Ketones by Catecholborane Catalysed by Chiral Group 13 Complexes

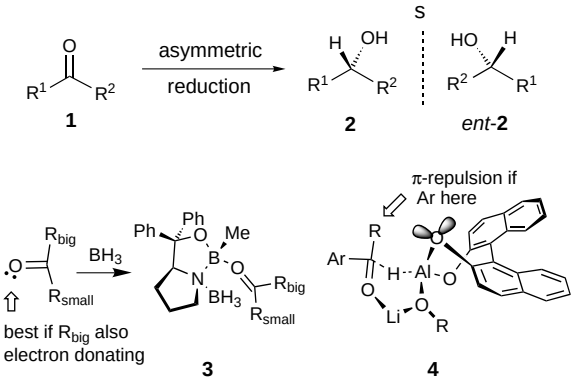
Alexander J. Blake,[a] Anthony Cunningham,[a] Alan Ford,[b] Simon J. Teat,[c] and Simon Woodward*[a]

Abstract: $LiGaH_4$, in combination with the *S*,*O*-chelate 2-hydroxy-2′-mercapto-1,1′-binaphthyl ($MTBH_2$), forms an active catalyst for the asymmetric reduction of prochiral ketones, with catecholborane as the hydride source. Enantioface differentiation is on the basis of the steric requirements of the ketone substituents. Aryl/*n*-alkyl ketones are reduced in 90–93 % *ee* and RC(O)Me (e.g. R = *i*Pr, *cyclo*C_6H_{11}, *t*Bu) in 60–72 % *ee*. Other borane sources and alternative catalyst structures based on indium do not form enantioselective catalysts.

Keywords: asymmetric catalysis · gallium · indium · S ligands

Introduction

Enantioselective reduction of prochiral ketones $R^1C(O)R^2$ (**1**, Scheme 1) is an important transformation in asymmetric synthesis as the resultant chiral *sec*-alcohols $R^1CH(OH)R^2$ (**2**)



Scheme 1. Asymmetric reduction of prochiral ketones and the "loaded" states of the CBS and BINAL reagents.

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are present in numerous targets of synthetic interest. One effective method for carrying out this reaction is use of the ruthenium transfer hydrogenation catalysts introduced by Noyori and typified by the structure (*R*,*R*)-[RuCl(η^6-Ar)($H_2NCH(Ph)CH(Ph)NSO_2Ar$)] (Ar = aryl).[1] Superlative enantioselectivities, turnover numbers and rates are attained providing R^1 in **1** is an aryl or a closely related unsaturated (Un) group. However, substrates outside this range, for example, dialkyl or α,β-unsaturated enones are often much less suitable. Synthetically useful *ee* values for such substrates, and many others, can sometimes be attained by using oxazaborolidine catalysed borane reductions (CBS reduction).[2] In this case, the enantioselectivity results from the propensity of the CBS catalyst to bind the ketone by the most electron rich and sterically accessible lone pair (as in the "loaded" catalyst structure **3**, Scheme 1). The primary borate product is hydrolysed on workup to afford **2**. However, for CBS reduction relatively high catalyst loadings are required (5–20 mol %). This, taken together with the relatively narrow substrate range for ruthenium transfer hydrogenation, indicates that there is still a need to identify new efficient catalysts in ketone reduction, especially for "problematic" substrates.

In 1979, Noyori noted that a 1,1′-(bi-2-naphthol) modified $LiAlH_4$ reagent (BINAL-H) could reduce aryl/alkyl ketones in ≈100 % *ee*.[3] This remarkable selectivity was proposed to be attained by the electronically controlled transition state **4**. We determined to attempt the design of a *catalytic* version of Noyori's BINAL-H reagent, as electronic control is rarely used as an enantioselection mechanism in asymmetric catalysis. This paper describes our full investigation of this area, elements of which have been communicated.[4]

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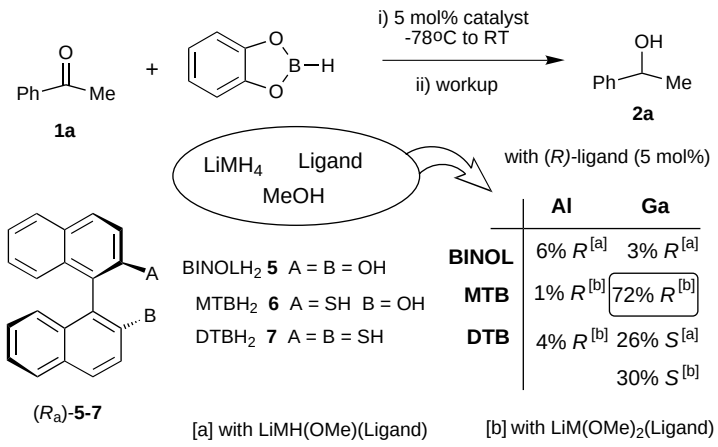
Results and Discussion

HSAB matching studies: When one designs a catalytic version of the BINAL-H reagent, two significant problems have to be overcome. Firstly, the reactivity of the catalyst system must be improved relative to BINAL-H [typically 300 mol% BINAL-H is required to reduce PhC(O)Me (**1a**) at $-100\,^{\circ}C$].[3] Secondly, only release of the product *sec*-alkoxide (produced from **4**) should occur and not the bound chiral auxiliary [the dialkoxide of 1,1′-(bi-2-naphthol)]. If this is not realised, the enantioselectivity of the catalyst system will soon be compromised by chiral ligand loss. To attempt to solve these problems we applied Pearson's "Hard/Soft Acid/Base" (HSAB) principle.[5] As the product *sec*-alkoxide contains a "hard" oxygen donor we reasoned that use of "hard" catecholborane would rapidly remove the product alkoxide from the catalytic centre, whilst a suitable metal hydride is regenerated. To avoid chiral ligand dissociation at the metal centre, we proposed to use analogues of 1,1′-(bi-2-naphthol) that contain "soft" thiolate donors in conjunction with a "softer" gallium Lewis acid. That is, the reagent and catalyst requirements are matched into two HSAB pairs ("hard/hard" for the substrate/reagent and "soft/soft" for the catalytic metal/chiral ligand). To test this proposal a series of trial reactions was carried out using $LiMH_4$ (M = Al, Ga) and the ligands $BINOLH_2$ **5**, $MTBH_2$ **6** and $DTBH_2$ **7** (Scheme 2). Mixtures of $LiMH_4$ and **5**–**7** were



Scheme 2. HSAB matching experiments in the reduction of acetophenone **1a**.

stirred at room temperature and in the presence of 1–2 equivalents of methanol and then cooled to $-78\,^{\circ}C$. Once twenty equivalents of acetophenone (**1a**, R^1 = Ph, R^2 = Me) and catecholborane had been added (at $-78\,^{\circ}C$), the mixture was allowed to come to room temperature overnight. Typically 70–80% yields of alcohol **2a** were isolated in all cases. The table in Scheme 2 shows the enantiomeric purity of the **2a** produced as a function of catalyst type. It is helpful to know at this point that the Noyori transition state **4** predicts that the (R_a) binaphthyl ligand leads to the (*R*) *sec*-alcohol product and that in the original formulations methanol was added in the BINAL-H preparation to improve the enantioselectivity.[3] The initial screen matrix soon revealed the apparent usefulness of the HSAB matching approach as high chemical yields, with significant enantioselectivity (72%), were realised for the gallium-MTB complex. Additionally, the moderate and reversed enantioselectivity shown by the gallium-DTB species provided the insight that although the "soft–soft" interaction of the catalytic metal/ligand is important, matching of all the Lewis acid base pairs must be accommodated. That is, binding of the hard lithium cation in the bimetallic catalyst must also be achieved. For example, the poor selectivity of the $LiGaH_{2-n}(OMe)_n$(DTB) species (n = 1, 2) suggests that the BINAL transition state **4** may involve additional Li···BINOL contacts at the binaphthyl alkoxides as has been suggested before for enantioselective aldehyde alkylation by $MgEt_2$ in the presence of Li_2(BINOL).[3e]

If the catalysis was conducted at a fixed temperature of $-40\,^{\circ}C$, using $LiGa(OMe)_2$(MTB), both the chemical yield and *ee* fell to 32 and 64%, respectively. Below this temperature only low yields of essentially racemic **2a** were produced. However, in reactions catalysed by $LiGaH_2$(MTB) [prepared from $LiGaH_4$ and just $MTBH_2$ **6**], with warming from $-78\,^{\circ}C$ to room temperature, a quantitative yield of **2a** with 82% *ee* was realised. These reactions suggest that the presence of lithium alkoxide sources can promote a competing achiral catalytic cycle. Control reactions of catecholborane and **1a** in the presence of 10 mol% LiOMe led to 45% yield of (±)-**2a** (-78 to $22\,^{\circ}C$, 16 h), while a similar reaction using $LiBHEt_3$ gave a 60% yield of (±)-**2a**. The simplest explanation of these findings is that alkoxide sources promote the formation of borohydride species $[C_6H_4O_2BH(OR)]^-$ and that these reduce **1a** with negligible enantioselectivity and give a racemic borate product and regenerate the alkoxide. DiMare[6] and Arase[7] have noted similar findings. At temperatures below $-20\,^{\circ}C$, the rate of the selective gallium catalysed reaction becomes slow and the achiral alkoxide manifold significantly erodes the overall enantioselectivity of the product **2a**.

To maximise the enantioselectivity, the reaction temperature was fixed at $-25\,^{\circ}C$ and use of thiolate rather than methoxide spectator ligands investigated. Addition of 2-$HSC_{10}H_7$ to $LiGaH_2$(MTB) lowered the selectivity to 72% *ee*, while $HSCH_2CH_2OH$ was worse (20% *ee*). Fortunately, addition of a second equivalent of $MTBH_2$ led to a rather selective catalyst, $LiGa(MTB)_2$, which showed high activity. This formulation proves rather robust to the reaction conditions and additional stirring of the reaction mixture is not required (runs could be conducted in any cryostat or even a domestic freezer). The activity and selectivity of this catalyst system (2 to 2.5 mol%) with a range of substrates were then investigated (Table 1).

In general, substrates with a phenyl/*n*-alkyl motif are reduced in good chemical yield and *ee* (ketones **a**–**c**, **f**–**g**). The reaction is slightly affected by the presence of (±)-I substituents on the 4-position. However, the presence of more sterically demanding alkyl substituents is detrimental both to the reaction rate and the enantioselectivity (ketones **d**–**e**, **h**–**i**). Similarly, the enantioselectivities realised are dependent on the size of the aryl substituent in the ketone; both smaller (ketone **j**) and larger (ketones **k**–**l**) aryl substituents lead to lower enantioselectivities. As the enantioselectivity criterion for these substrates appeared to be steric rather than electronic, as in the BINAL transition state **4**, further ketones

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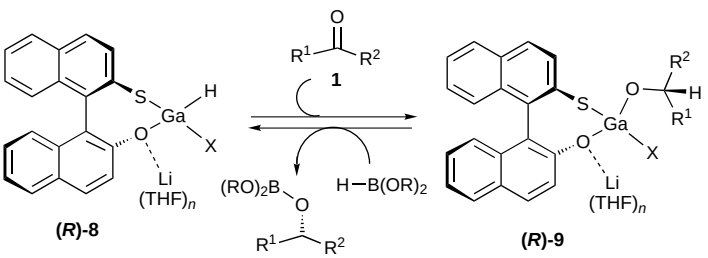
Table 1. Enantioselective reduction of ketones **1** by (R_a,R_a)-LiGa(MTB)$_2$ (2 or 2.5 mol% unless otherwise stated) and catecholborane (1.1 equivalents).

Ketone	R^1	R^2	Temp [°C]	Time [h]	Yield [%][a]	*ee* [%][b]
a	Ph	Me	−25	18	90	90
b	Ph	Et	−25	18	96	93
c	Ph	*n*Bu	−25	18	80	92
d	Ph	*i*Pr	−15[c]	60	65	24
e	Ph	*i*Bu	−15[c]	60	65	92
f	4-BrPh	Me	−25	18	80	87
g	4-MePh	Me	−25	18	95	87
h	Ph	CH_2Br	−25	18	60	70
i	Ph	CH_2Ph	−20	19	88	68
j	2-furyl	nC_6H_{13}	−25	18	76	81
k	1-$C_{10}H_7$	Me	−20	20	82	59
l	2-$C_{10}H_7$	Me	−20	20	83	73
m	Ph	C≡CH	−15[c]	60	50	0
n	PhCH=CH	Me	−25	18	70	75
o	C≡CEt	Me	−25	18	60	63
p	C≡CH	nC_5H_{11}	−25	18	88	22[d]
q	$CH=CH_2$	nC_5H_{11}	−25	18	50	12[d]
r	*i*Pr	Me	−20	18	81	69
s	*i*Bu	Me	−20	18	93	46
t	*c*C_6H_{11}	Me	−20	18	72	72
u	*t*Bu	Me	−20	18	76	79

[a] Determined by ^{1}H NMR, GC or by isolation. [b] Determined by GC, HPLC or MTPA ester formation. [c] 4 mol% **10**. [d] Absolute stereochemistry not determined.

were selected to shed light on the mechanism. Consistent with electronic control PhC(O)CCH (**m**) gave a low yield of racemic product, while significant selectivities were realised with benzylidene acetone (**n**) and 3-hexyn-2-one (**o**). However, the former result may be indicative of poor Li^+ binding in the transition state due to the poor electron density in the ketonic lone pairs of **m**. The negligible enantioselectivities shown in the reduction of ynone (**p**) and enone (**q**) are not indicative of an electronically controlled transition state. Few asymmetric studies of the reduction of **q** have been reported but stoichiometric BINAL reduces ynone **p** in 84% *ee*;[3] this suggests that the gallium and aluminium systems may operate by different mechanisms. Studies with dialkyl ketones also support steric discrimination in the transition state of the gallium catalysed process. The *ee* values for the reduction of ketones **r**–**u** correlate well with the steric demands of the larger group.

Mechanistic studies: One working model for the gallium/MTB catalysed ketone reductions is shown in Scheme 3 (where X is the spectator ligand, normally a second MTB ligand). Under this proposal, an initial gallium hydride (**8**) reacts with the ketone **1** to provide a gallium alkoxide (**9**). Interaction of **9** with catecholborane [represented in Scheme 3 as H-B(OR)$_2$] leads to selective decomplexation of the alkoxide, while the MTB ligand remains anchored to the gallium centre by virtue of a strong thiolate bond. To investigate this hypothesis, stoichiometric reaction studies of $LiGaH_4$, $MTBH_2$ (**6**) and catecholborane were carried out.



Scheme 3. Working model for the gallium catalysed reduction (X = MTB ligand).

When treated with two equivalents of $MTBH_2$ (**6**) at room temperature, 20 mM solutions of $LiGaH_4$ in Et_2O/THF mixtures spontaneously lose four equivalents of hydrogen. The nature of the clear solution formed can be investigated by ^{1}H NMR spectroscopy. The undeuterated solvents cause intense peaks in the spectrum at approximately $\delta = 1.1$ (Et_2O), 1.7 (THF), 3.3 (Et_2O) and 3.6 (THF). However, the MTB aryl C–H region is clear and reproducibly indicates the presence of two different types of MTB ligand in a 3:1 ratio consistent with the formulation [Ga_2(MTB)$_3$][Li_2(MTB)]. An identical spectrum is obtained from mixtures of $GaCl_3$ etherate, $MTBH_2$ (**6**) and BuLi after filtration of the precipitated LiCl. In the signal derived from the three equivalent MTB ligands, one of the H3(3′) binaphthyl protons suffers a large downfield shift relative to the free ligand $MTBH_2$ (**6**). These electronic effects are also apparent in the ^{13}C NMR spectrum of [Ga_2(MTB)$_3$][Li_2(MTB)], in which one of the signals appears at appreciably higher frequency (^{13}C NMR: $\delta = 158.4$) than the rest (^{13}C NMR: $\delta = 120.0$–139.3). Full assignment of the carbon spectrum was not possible because of problems in obtaining adequate signal/noise in the ^{1}H:^{13}C COSY spectrum. However, complete connectivity for all the MTB ^{1}H environments could be established by ^{1}H:^{1}H COSY studies. Mass spectrometry is an ideal technique to probe the constitution of such species: two natural gallium isotopes ($^{69/71}$Ga) exist approximately in a 60:40 ratio. When these solutions, assayed by ^{1}H NMR spectroscopy as containing only [Ga_2(MTB)$_3$][Li_2(MTB)], are subjected to negative ion electrospray mass spectrometry, a major peak at m/z 669 with a Ga_1 isotope pattern can be identified. This peak corresponds to the formulation [LiGa(MTB)$_2$]. A small (≈1% of the base peak) signal is observed at m/z 1347 and its isotope pattern indicates it is [Ga_2(MTB)$_3$][Li(MTB)].

When the reaction mixture from the addition of two equivalents of $MTBH_2$ (**6**) to $LiGaH_4$ is layered with pentane, colourless crystals form. This procedure reproducibly gives not the solution species [Ga_2(MTB)$_3$][Li_2(MTB)] but [Li(THF)$_3$Ga(MTB)$_2$] (**10**), whose x-ray structure is shown in Figure 1. This compound is isostructural with [Li(THF)$_3$Al(BINOL)$_2$], which has been characterised by Shibasaki from reactions of $AlCl_3$ and $BINOLH_2$ (**5**) in the presence of BuLi.[8] If one changes from an Al-BINOL to a Ga-MTB complex, the average M–Y (Y = O, S) distances increase from 1.75 Å in [Li(THF)$_3$Al(BINOL)$_2$] to 1.89 (Y = O) and 2.24 (Y = S) Å in [Li(THF)$_3$Ga(MTB)$_2$] (**10**).

On redissolution in THF, the solid-state structure of [Li(THF)$_3$Ga(MTB)$_2$] (**10**) is not retained. Proton spectra of these solutions indicate regeneration of [Ga_2(MTB)$_3$]-[Li_2(MTB)]. However, this situation is complicated by the apparent decomposition of some **10** by minor protonolysis

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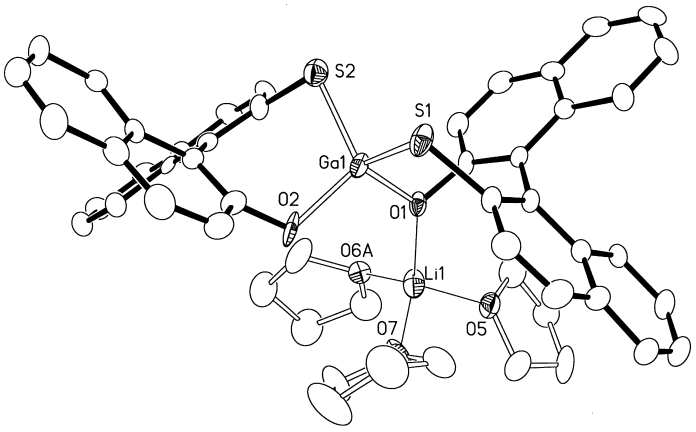


Figure 1. Molecular structure of $[Li(THF)_3Ga(MTB)_2]$ (**10**) shown with 30% probability ellipsoids. Hydrogens have been omitted for clarity and only one component of the disorder is shown. Selected bond lengths and angles [Å, °]: Ga(1)–O(1) 1.880(5), Ga(1)–O(2) 1.898(7), Ga(1)–S(1) 2.238(2), Ga(1)–S(2) 2.243(2), Li(1)–O(1) 1.900(14), O(1)–Ga(1)–S(1) 104.75(15), O(2)–Ga(1)–S(2) 108.52(19), O(1)–Ga(1)–O(2) 102.7(2), S(1)–Ga(1)–S(2) 106.08(9).

reactions. It is clear that in solution there exists only a minor energy difference between $[Li(THF)_3Ga(MTB)_2]$ (**10**) and a dimer of constitution $[Ga_2(MTB)_3][Li_2(MTB)]$ but at present unknown structure.

To try and access the structural type of the dimer, $[InCl_3(THF)_3]$ was treated with two equivalents of MTB dianions (generated from $MTBH_2$ **6** and BuLi) in THF. It was hoped that because of longer In–Y (Y = O, S) bonds, any potential steric clashes in the dimer would be minimised and this structure favoured. However, after removal of the precipitated LiCl and layering with pentane, colourless blocks of $[Li_2(THF)_5InCl(MTB)_2]$ (**11**) are obtained in moderate yield. The molecular structure of $[Li_2(THF)_5InCl(MTB)_2]$ (**11**), together with selected bond lengths and angles, is shown in Figure 2. Clearly the chemistry for the indium analogue

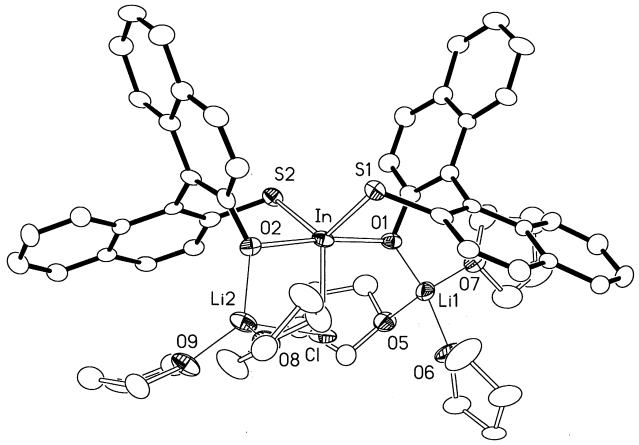


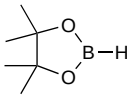
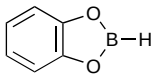
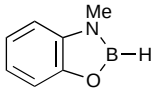
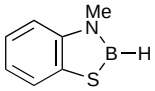
Figure 2. Molecular structure of $[Li_2(THF)_5InCl(MTB)_2]$ (**11**) shown with 30% probability ellipsoids. Hydrogens have been omitted for clarity. Selected bond lengths and angles [Å, °]: In–Cl 2.452(3), In–O1 2.206(7), In–O2 2.196(7), In–S1 2.480(2), In–S2 2.471(3), Li–O1 1.92(2), Li2–O2 1.91(2), O1–In–S1 91.11(17), O2–In–S2 91.09(17), O1–In–O2 173.9(3), S1–In–S2 124.37(10), Cl–In–O1 91.64 (18), Cl–In–O2 82.29(19), Cl–In–S1 115.63(11), Cl–In–S2 119.85(10).

is quite different and not all of the chlorides are liberated. The solution structure of **11** could not be unequivocally determined because of its relatively low solubility, fluxionality and its pronounced tendency to undergo MTB ligand solvolysis. For example, positive ion FAB mass spectra of **11** show $[Li_2InCl(MTB)_2]^+$ as the highest mass ion. Additional peaks assigned to $In_4Cl_4O_4$ and its daughter ions are observed in some samples of aged **11**. The proton NMR spectra of **11** at ambient temperature indicate that the MTB ligands are equivalent in solution. Use of freshly prepared mixtures of $Li_2(MTB)$ and $InCl_3(THF)_3$ leads to the clean reduction of cyclohexylmethylketone **1t** in 70% yield but negligible enantioselectivity at a 2 mol% catalyst loading.

Addition of a slight excess of catecholborane to a 20 mM solution of $[Ga_2(MTB)_3][Li_2(MTB)]$ in THF (prepared from $LiGaH_4$ and $MTBH_2$ **6**) leads to the clean formation of a new species. Only very broad and uninformative NMR resonances could be observed at room temperature. On cooling the sample to −50 °C, these sharpen significantly. In addition to unreacted catecholborane, the spectra suggest that two non-equivalent MTB ligands are present together with a bound catechol fragment. However, no gallium or boron hydride signal could be detected. Layering of these ^1H NMR samples with pentane led only to the formation of oils. A second catalytic state can be identified spectroscopically by sequentially treating 20 mM solutions of $[Ga_2(MTB)_3][Li_2(MTB)]$ with catecholborane followed by pinacolone **1u** (as a representative ketone). However, the ^1H NMR spectra in the aryl region are complex and fluxional and complete assignment of the spectrum is not possible. The speciation of the catalyst at the enantio-discriminating step was also investigated by searching for a Nonlinear Effect (NLE) in the catalytic asymmetric reaction.[9] No significant NLE was detected. The data (six points for the reduction of **1a**) fit a straight line: $ee_{obs} = 0.93 ee_{lig}$ with $R = 0.999$. The absence of any NLE may be taken as indicative of three possibilities: either the asymmetric transition state contains only one MTB ligand (despite the 2:1 MTB:Ga mixing formulation); or alternatively diastereomeric mixtures of catalyst species that are formed all react at the same rate with **1a**; or the active catalyst is not able to form heterochiral species, as is observed in Kaufmann's $B_2(BINOL)_3$ species.[10] The present data do not allow differentiation between these possibilities. The working model of the gallium catalysed reduction is suggested to involve attack of a gallium hydride **8** on the ketone **1** to yield an alkoxide **9** (Scheme 3). If this mechanism does indeed operate then the enantioselectivities realised should, for a given ketone (**1**), be independent of the borane used in the reaction. This is not the case. Five representative boranes were compared in their efficiency for the reduction of acetophenone **1a** under standard conditions (Table 2).[6, 11–14]

The absence of any enantioselection in reactions using $BH_3 \cdot THF$ and $(iPrO)_2BH$ (runs 1–2) can be attributed to the formation of reactive borohydrides $Li[BHY_2\{(R)\text{-}OCH(Me)(Ph)\}]$ (2 mol%, Y = H, O*i*Pr). Such species could be formed by $Li[(R)\text{-}OCH(Me)(Ph)]$ abstraction from **9** by BHY_2 and would be efficient catalytic activators of the remaining BHY_2, but would be expected to show negligible enantioselectivity. As judged by literature ^{11}B NMR shifts, the

Table 2. Enantioselective reduction of acetophenone **1** by (*R*,*R*)-LiGa(MTB)$_2$ (2 mol%) and various boranes.

Run	Borane	Equiv. used	δ ^{11}B	Yield [%][a]	*ee* [%][b]
1	$BH_3 \cdot THF$	4.5	−0.6[11]	95	< 2
2	$(i\text{PrO})_2BH$	4.5	27.0[6]	81	< 2
3		1.5	28.7[12]	41	< 2
4		1.5	29.9[13]	90	90 (*R*)
5		1.5	28.1[14]	49	5 (*R*)
6		1.5	22.3[14]	9	< 2

[a] Determined by GC. [b] Determined by GC, absolute stereochemistry in parentheses.

Lewis acidities of pinacolborane (run 3), catecholborane (run 4), and the very closely related oxazaborole (run 5) and thiazaborole (run 6) are very similar, as are their structures. These values are not significantly changed for samples run in THF with the exception of 1,2-C_6H_4S(NMe)BH, which resonates at higher frequency (^{11}B NMR: $\delta = 41.0$, $J_{BH} = 158$ Hz), and catecholborane itself, which shows the presence of the free borane and its THF adduct. Only reactions using catecholborane reduced acetophenone **1a** in high yield and *ee*. This specific dependence on catecholborane is not in accord with the proposed working model for the catalytic cycle (Scheme 3). One explanation of these observations is that the role of $[Li(THF)_3Ga(MTB)_2]$ (**10**) is to bind the catecholborane and activate it by Lewis acid/base interactions akin to those in the CBS "loaded" catalyst state **3**. In this case as the hydride is delivered from a coordinated borane, the enantioselectivity for the reduction of **1** is expected to be highly dependent on the nature of the R_2BH species used. In further support of this idea the enantioselective transition state is strongly affected by even minor solvent changes. For example, use of (±)-2-methyl-THF in runs otherwise identical to Table 1 (substrate **1a**, THF solvent, 90% *ee*, *R*-product) leads to the alcohol being isolated in only 43% *ee* (*R*). Further experiments are required to prove this hypothesis and to identify the exact reasons for the specific need for catecholborane in this chemistry.

Experimental Section

General: Infrared spectra were recorded by using a Perkin-Elmer 983 G infrared spectrophotometer and a Perkin-Elmer 882 infrared spectrophotometer. Proton and ^{13}C NMR spectra were recorded on either Jeol (JNM GX270, JNM LA400) or Bruker (DRX500) spectrometers (tetramethylsilane as a standard, *J* values given in Hz). The ^{11}B NMR spectra were acquired on the JNM LA400 or Bruker DRX500 machines. All spectra were recorded at ambient temperature unless otherwise noted. Mass spectra were obtained on Finnigan MAT 1020 or Autospec VG (electron impact ionisation, EI), Finnigan QMS (electrospray ionisation, ESI), VG ZAB or Autospec VG (fast atom bombardment, FAB) machines. Elemental analyses were performed by using a Fisons Instruments EA 1108 CHN elemental analyser. Optical rotations were measured on an Optical Activity AA 10 instrument in units of $10^{-1}\,^{\circ}\,cm^2\,g^{-1}$ (*c* in g/100 cm^3). Light petroleum refers to that fraction with b.p. 40–60 °C.

The ligands **5**–**7**[15–17] and ketones **2j**,[18] **2m**,[19] and **2p**–**q**[20, 21] were obtained by literature procedures. All boranes, except $BH_3 \cdot THF$ and catecholborane, were obtained by known techniques (see Table 3). All other compounds were commercial products (Aldrich).

Procedure for the preparation of $LiGaH_4$: This compound was prepared by a modification of Shriver and Shirk's procedure.[22] A solution of anhydrous $GaCl_3$ (0.57 M in Et_2O) was prepared by slow addition of Et_2O to a chilled (0 °C) suspension of $GaCl_3$ so that generation of HCl was minimised. A sample (10 mL, 5.7 mmol) of this solution was added dropwise to an ice-cooled suspension of LiH (finely powdered under argon, 0.74 g, 92 mmol) in Et_2O (10 mL) and the resulting mixture was stirred overnight and then filtered through an oven-dried medium porosity Schlenk frit. The resulting solution was analysed for active hydrogen by quenching into a 1:1 mix of THF/1 M HCl and measuring the gas evolved. The titre was typically 0.23–0.28 M and the solution could be kept in a suitable storage flask at −20 °C under argon for at least four months without appreciable decomposition.

Representative reduction of ketone 1a (cryostat method): A solution of (*R*)-(−)-MTBH$_2$ (**6**, 15 mg, 0.05 mmol) in THF (5 mL) was treated with $LiGaH_4$ (0.25 M in Et_2O, 0.025 mmol) and the resulting colourless solution, nominally containing $[Li(THF)_3Ga(MTB)_2]$ (**10**), was stirred at room temperature for 25 minutes and then placed in a pre-equilibrated cryostat at −25 °C. Acetophenone **1a** (145 μL, 1.25 mmol) was added and after five minutes a solution of catecholborane (1.0 M in THF, 1.5 mmol) was added dropwise over five mins. The mixture was swirled in the cryostatic bath and allowed to stand overnight at −25 °C. After quenching with dilute HCl, the reaction was diluted with Et_2O. The aqueous phase was extracted with Et_2O. The combined organic phases were washed successively with water, 1 M NaOH (×2), water and then brine, dried over $MgSO_4$ and concentrated to afford, after filtration through SiO_2 (9:1 hexanes/Et_2O), 137 mg (89%) of (*R*)-(+)-1-phenylethan-1-ol (90% *ee* by GC). ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 7.37$–7.21 (m, 5H; ArH), 4.84 (q, $J = 6$ Hz, 1H; CH), 1.19 (br s, 1H; OH), 1.46 (d, $J = 6$ Hz, 3H; Me). Stirring the cooled mixture had no affect on the chemical yield or enantioselectivity realised. Equivalent reactions could be carried out in a domestic freezer. Other ketones were reduced by similar procedures. Chemical yields were determined by isolation, GC or ^{1}H NMR conversion.

Representative reduction of ketone 1a (warm-up method): A stirred solution of **10** (prepared from $LiGaH_4$ and (*R*)-MTBH$_2$ **6**; 0.025 M, ca. 0.025 mmol) was diluted with THF (1 mL) and the solution was cooled to −78 °C. Acetophenone **1a** (58 μL, 0.5 mmol) was added and after five minutes a solution of catecholborane (1.0 M in THF, 0.55 mmol) was added dropwise over 5 mins. The mixture was stirred and allowed to warm slowly overnight, then quenched with dilute HCl and worked up as described above to yield (*R*)-(+)-1-phenylethan-1-ol (58 mg, 95%, 90% *ee* by GC). Other ketones were reduced by similar procedures.

(*R*)-(+)-1-Phenyl-1-propanol (2b): Reduction of propiophenone **1b** (2.5 mol% **10**, −25 °C, 18 h); yield 96% (93% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 7.37$–7.23 (m, 5H; ArH), 4.59 (t, $J = 6.5$ Hz, 1H; CH), 1.89 (br s, 1H; OH), 1.82–1.72 (m, 2H; CH_2), 0.92 (t, $J = 7$ Hz, 3H; Me).

(*R*)-(+)-1-Phenyl-1-pentanol (2c): Prepared by the reduction of valerophenone **1c** (2.5 mol% **10**, −25 °C, 18 h); yield 80% (92% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.45$–7.24 (m, 5H; ArH), 4.68–4.64 (m, 1H; CH), 1.85 (d, $J = 3.2$ Hz, 1H; OH), 1.83–1.70 (m, 2H; CH_2), 1.42–1.26 (m, 4H; CH_2CH_2), 0.88 (t, $J = 7$ Hz, 3H; Me).

(*R*)-(+)-1-Phenyl-2-methyl-1-propanol (2d): Prepared by the reduction isobutyrophenone **1d** (4 mol% **10**, −15 °C, 60 h); yield 65% (24% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 7.37$–7.26 (m, 5H; Ar), 4.37 (dd, $J = 6.5$, 3 Hz, 1H; CHO), 1.96 (octet, $J = 6.5$ Hz, 1H; C*H*Me$_2$), 1.85 (d, $J = 3$ Hz, 1H; OH), 1.00 (d, $J = 6.5$ Hz, 3H; CH*Me*$_2$), 0.80 (d, $J = 6.5$ Hz, 3H; CH*Me*$_2$).

(*R*)-(+)-1-Phenyl-3-methyl-1-butanol (2e): Prepared by the reduction of isovalerophenone **1e** (4 mol% **5**, −15 °C, 60 h); yield 65% (92% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.38$–2.28 (m, 5H; Ar), 4.79–4.71 (m,

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Table 3. Methods used for the determination of the enantiopurity of the alcohols **2**.

Ketone	Product	Conditions for *ee* assay	Elution order and retention time [min]
1a	1-phenylethanol **2a**	GC. Lipodex A: initial temp 75 °C ramp rate 1 °C min^{-1} GC. Cyclodex B: 120 °C isothermal	*S* 16:47 *R* 17:12 *R* 14:52 *S* 15:20
1b	1-phenyl-1-propanol **2b**	GC. Cyclodex B: 120 °C isothermal	*R* 22:38 *S* 23:35
1c	1-phenyl-1-pentanol **2c**	GC. Lipodex A: initial temp 100 °C ramp rate 1 °C min^{-1}	*S* 24:41 *R* 25:07
1d	1-phenyl-2-methyl-1-butanol **2d**	HPLC. Chiralcel OD: 0.5 mL min^{-1} 20:1 hexane:isopropanol	*S* 22:44 *R* 26:00
1e	1-phenyl-3-methyl-1-butanol **2e**	GC. Lipodex A: initial temp 100 °C ramp rate 0.3 °C min^{-1}	*S* 27:35 *R* 28:37
1f	1-(4-bromophenyl)-ethanol **2f**	GC. Cyclodex B: 140 °C isothermal	*R* 37:50 *S* 38:58
1g	1-(4-methylphenyl)-ethanol **2g**	Cyclodex B 120 °C isothermal	*R* 20:30 *S* 21:50
1h	1-phenyl-2-bromo-ethanol **2h** (as epoxide)	GC on epoxide Lipodex A: initial temp 100 °C ramp rate 0.3 °C min^{-1}	*S* 13:52 *R* 14:09
1i	1,2-diphenyl-1-ethanol **2i**	HPLC. Chiralcel OD: 1.0 mL min^{-1} 39:1 hexane:isopropanol	*R* 23:18 *S* 29:54
1j	1-(2-furyl)hexanol **2j**	Lipodex A: initial temp 100 °C ramp rate 0.3 °C min^{-1}	*S* 25:50 *R* 26:19
1k	1-(1-naphthyl)-ethanol **2k**	HPLC. Chiralcel OD: 0.5 mL min^{-1} 9:1 hexane:isopropanol	*R* 24:36 *S* 39:12
1l	1-(2-naphthyl)-ethanol **2l**	HPLC. Chiralcel OD: 0.5 mL min^{-1} 9:1 hexane:isopropanol	*R* 25:06 *S* 26:36
1m	1-phenyl-propyn-1-ol **2m**	Lipodex A: initial temp 100 °C ramp rate 0.3 °C min^{-1}	21:16[a] 21:54[a]
1n	4-phenyl-3-buten-2-ol **2n**	MTPA ester	see text
1o	3-hexyn-2-ol **2o**	Lipodex A: initial temp 50 °C ramp rate 0.3 °C min^{-1}	*R* 13:18 *S* 13:28
1p	1-heptyn-3-ol **2p**	Lipodex A: initial temp 75 °C ramp rate 0.3 °C min^{-1}	15:14[a] 15:30[a]
1q	1-hepten-3-ol **2q**	Lipodex A: initial temp 75 °C ramp rate 0.3 °C min^{-1}	9:51[a] 10:08[a]
1r	3-methyl-butan-2-ol **2r**	GC on acetate γ-Cyclodex[b] 50 °C isothermal	*R* 6:05 *S* 7:12
1s	4-methyl-pentan-2-ol **2s**	GC on acetate γ-Cyclodex[b] 50 °C isothermal	*R* 8:31 *S* 10:20
1t	1-cyclohexylethanol **2t**	GC on acetate γ-Cyclodex[b] initial temp 60 °C ramp rate 5.0 °C min^{-1} to 90 °C	*R* 14:20 *S* 15:26
1u	3,3-dimethyl-butan-2-ol **2u**	GC on acetate γ-Cyclodex[b] 50 °C isothermal	*R* 8:21 *S* 9:12

[a] Absolute configuration order not determined. [b] *Oktakis*-(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin (6-me-2,3-pe-γ-CD).

1H; C*H*OH), 1.81–1.63 (m, 2H; CH_2), 1.58–1.43 (m, 1H; C*H*Me_2), 0.91 (2 × d, J = 6.5 Hz, 6H; CHMe_2).

(*R*)-(+)-1-(4-Bromophenyl)ethanol (2f): Prepared by the reduction of 4-bromoacetophenone **1f** (2.5 mol% **10**, −25 °C, 18 h); yield 80% (87% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.49–7.44 (m, 2H; Ar), 7.27–7.21 (m, 2H; Ar), 4.89–4.82 (m, 1H; CH), 1.90 (br d, $J \approx 3$ Hz, 1H; OH), 1.47 (d, J = 6.2 Hz, 3H; Me).

(*R*)-(+)-1-(4-Methylphenyl)ethanol (1g): Prepared by the reduction of 4-methylacetophenone **1g** (2.5 mol% **10**, −25 °C, 18 h); yield 95% (87% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.29–7.23 (m, 2H; Ar), 7.18–7.82 (m, 2H; Ar), 4.85 (q, J = 6.5 Hz, 1H; CH), 2.34 (s, 3H; ArMe), 1.47 (d, J = 6.5 Hz, 3H; Me).

(*S*)-(−)-Styrene epoxide (from 2h): Prepared by reduction of 2-bromoacetophenone **1h** (2.5 mol% **10**, −25 °C, 16 h). The (*S*)-**2h** produced was cyclised directly during the workup to yield (*S*)-styrene epoxide (60%, 70% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.21 (m, 5H; Ar), 3.83 (dd, J = 4, 2 Hz, 1H; CH), 3.10 (dd, J = 5.5, 4 Hz, 3H; CH_2), 2.76 (dd, J = 5.5, 2.5 Hz, 1H; CH_2).

(*R*)-(−)-2-Phenyl-1-phenylethanol (2i): Prepared by the reduction of deoxybenzoin **1i** (2 mol% **10**, −20 °C, 19 h); yield 88% (68% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.35 (m, 10H; Ar), 4.90 (m, 1H; CH), 3.04 (dd, J = 14, 5 Hz, 1H; CH_2), 2.99 (dd, J = 14, 8 Hz, 1H; CH_2), 1.93 (d, J = 3 Hz, 1H; OH).

(*R*)-(+)-1-(2-Furyl)hexanol (2j): Prepared by the reduction of 2-hexanoylfuran **1j** (2.5 mol% **10**, −25 °C, 18 h); yield 76% (81% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.36 (m, 1H; H-5), 6.43–6.31 (m, 1H; H-4), 6.24–6.22 (m, 1H; H-3), 4.68 (t, J = 8 Hz, 1H; CH), 1.9–1.8 (m, 2H; CH_2) 1.45–1.3 (m, 6H; $(CH_2)_3$), 0.83 (t, J = 12 Hz, 3H; Me).

(*R*)-(+)-1-Naphthylethanol (2k): Prepared by reduction of 1-acetonaphthone **1k** (2 mol% **10**, −20 °C, 20 h); yield 82% (59% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08–8.05 (m, 1H; Ar), 7.86–7.83 (m, 1H; Ar), 7.74 (d, J = 8 Hz, 1H; Ar), 7.63 (d, J = 7 Hz, 1H; Ar), 7.51–7.42 (m, 3H; Ar), 5.60 (q, J = 6 Hz, 1H; CH), 2.18 (br s, 1H; OH), 1.62 (d, J = 6 Hz, 3H; Me).

(*R*)-(+)-2-Naphthylethanol (2l): Prepared by reduction of 2-acetonaphthone **1l** (2 mol% **10**, −20 °C, 20 h); yield 83% (73% *ee*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.80 (m, 4H; Ar), 7.51–7.43 (m, 3H; Ar), 5.06 (q, J = 6.5 Hz, 1H; CH), 1.94 (br s, 1H; OH), 1.58 (d, J = 6.5 Hz, 3H; Me).

1-Phenyl-prop-2-yn-1-ol (2m): Prepared by the reduction of 1-phenylpropynone **1m** (4 mol% **10**, −15 °C, 60 h); yield 50% (<2% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.57–7.35 (m 5H; Ar), 5.47 (s, 1H; CHO), 2.68 (s, 1H; alkyne CH), 2.29 (br s, 1H; OH).

(*R*)-(+)-4-Phenyl-3-buten-2-ol (2n): Prepared by the reduction of benzylidenacetone **1n** (2.5 mol% **5**, −25 °C, 18 h); yield 82% (75% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.39–7.36 (m, 2H; Ar), 7.33–7.29 (m, 2H; Ar), 7.25–7.21 (m, 1H; Ar), 6.56 (d, J = 16 Hz, 1H; PhCH=), 6.26 (dd, J = 16, 6.4 Hz, 1H; =CH), 4.52–4.45 (m, 1H; CH), 1.64 (br s, OH), 1.37 (d, J = 6.4 Hz, 1H; Me).

(*R*)-(+)-3-Hexyn-2-ol (2o): Prepared by the reduction of 3-hexyn-2-one **1o** (2.5 mol% **5**, −25 °C, 18 h); yield 52% (63% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 4.47–4.55 (m, 1H; CH), 2.27–2.18 (m, 2H; CH_3CH_2), 1.42 (d, J = 7 Hz, 3H; Me), 1.13 (t, J = 8 Hz, 3H; *Me*CH_2).

Oct-1-yn-3-ol (2p): Prepared by the reduction of oct-1-yne-3-one **1p** (2.5 mol% **10**, −25 °C, 16 h); yield 88% (22% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 4.29 (dt, J = 7, 2 Hz, 1H; CHO), 2.39 (d, J = 2 Hz, 1H; alkyne CH), 1.89 (br s, 1H; OH), 1.69–1.18 (m, 8H; $(CH_2)_4$), 0.83 (t, J = 7 Hz, 3H; Me). Absolute stereochemistry not determined.

Oct-1-en-3-ol (2q): Prepared by the reduction of oct-1-en-3-one **1q** (2.5 mol% **10**, −25 °C, 16 h); yield 50% (12% *ee*). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.80 (m, 1H; CH=), 5.21 (dt, J = 17, 1.5 Hz, 1H; =CH_2), 5.10 (dt, J = 10, 1.5 Hz, 1H; =CH_2), 4.10 (m, 1H; CHO), 1.66–1.20 (m, 9H; $(CH_2)_4$ and OH), 0.89 (t, J = 7 Hz, 3H; Me). Absolute stereochemistry not determined.

(*R*)-(−)-3-Methyl-2-butanol (2r): Prepared by the reduction of methylisopropylketone **1r** (2 mol% **10**, −20 °C, 18 h); yield 81% (69% *ee*). Determination of *ee* by GC analysis on acetate. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.56 (quintet, J = 6 Hz, 1H; CHO), 1.68 (br s, 1H; OH), 1.61 (m, 1H; C*H*Me_2) 1.15 (d, J = 6 Hz, 3H; Me), 0.92 (d, J = 7 Hz, 3H; CHMe_2), 0.91 (d, J = 7 Hz, 3H; CHMe_2).

(*R*)-(−)-4-Methyl-2-pentan-2-ol (2s): Prepared by the reduction of methylisobutylketone **1s** (2 mol% **10**, −20 °C, 18 h); yield 93% (46% *ee*). Determination of *ee* by GC analysis on acetate. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.88 (m, 1H; CHO), 1.75 (m, 1H; C*H*Me_2), 1.55 (br s, 1H; OH), 1.41 (ddd, J = 13.5, 8, 6 Hz, 1H; CH_2), 1.23 (ddd, J = 13.5, 8, 6 Hz, 1H; CH_2), 1.19 (d, J = 6 Hz, 3H; Me), 0.92 (d, J = 7 Hz, 3H; CHMe_2), 0.91 (d, J = 7 Hz, 3H; CHMe_2).

(*R*)-(−)-1-Cyclohexylethanol (2t): Prepared by the reduction of methylcyclohexylketone **1t** (2 mol% **10**, −20 °C, 18 h); yield 72% (72% *ee*). Determination of *ee* by GC analysis on acetate. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.54 (quintet, J = 6 Hz, 1H; CHO), 1.86–1.65 (m, 5H; *c*C_6H_{11}), 1.39 (br s, 1H; OH), 1.15 (d, J = 6 Hz, 3H; Me), 1.29–0.86 (m, 6H; *c*C_6H_{11}).

(*R*)-(−)-3,3-Dimethyl-butan-2-ol (2u): Prepared by the reduction of pinacolone **1u** (2 mol% **10**, −20 °C, 18 h); yield 76% (79% *ee*). Determination of *ee* by GC analysis on acetate. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.48 (q, J = 6 Hz, 1H; CHO), 1.26 (br s, 1H; OH), 1.13 (d, J = 6 Hz, 3H; Me), 0.90 (s, 9H; *t*Bu).

Chromatographic conditions for separation of the enantiomers: All compounds, with the exception of **2i–h**, **2k–l**, **2n** and **2r–2u**, were baseline separated by using GC with Lipodex-A (25 m, Machery-Nagel) or Cyclodex-B (J&W Scientific). The analyses were run on a Varian 3380 machine with a head pressure of approximately 12 psi (150 °C injector port temp. 250 °C detector temp). Details of the temperature programming and enantiomer elution order are given in Table 3. The configuration of the product alcohols was confirmed by comparison with authentic samples where possible. For **2d**, **2i** and **2k–l**, the *ee* measurement was carried out by HPLC by using a Hewlett Packard Series 1100 machine under conditions described in Table 3. The enantioselectivity of **2h** was determined by derivatisation to styrene epoxide and subsequent analysis on Lipodex-A. For **2n**, the assay was carried out by formation of the (trifluoromethyl)-phenylacetic acid (MTPA) esters. For **2r–2u**, the *ee* values were determined by GC analysis of the derived acetates (see below) on a 25 m *oktakis*-(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin (6-me-2,3-pe-γ-CD; γ-Cyclodex) column by using the general procedure given above and the conditions in Table 3.

Preparation of MTPA ester of 4-phenyl-3-buten-2-ol (2n): A mixture of 4-phenyl-3-buten-2-ol (74 mg, 0.5 mmol), dicyclohexylcarbodiimide (113 mg, 0.55 mmol), (*S*)-(−)-α-methoxy-α-trifluoromethylphenylacetic acid (129 mg, 0.55 mmol) and dimethylaminopyridine (7 mg, 0.05 mmol) in CH_2Cl_2 (about 5 mL) was stirred at room temperature for 24 h and then filtered. The solution was concentrated, taken up in 1:1 light petroleum/Et_2O and then filtered through SiO_2. After removal of the solvents, the residue was examined directly by ^{1}H NMR spectroscopy.

Preparation of acetates of aliphatic alcohols (2r–2u): Pyridine (2.5 mL) and acetic anhydride (0.15 mL, 1.6 mmol) were added to the crude alcohol **2** and the mixture was stirred (16 h). The reaction was quenched with 2 M hydrochloric acid and extracted with diethyl ether. The organic phase was washed successively with 2 M HCl, 2 M NaOH, water and brine. The solution was dried ($MgSO_4$) and analysed directly by GC (Table 3).

Investigation of potential nonlinear effects: Portions of scalemic MTB were made up as follows: 20% *ee* from 3 mg (−) and 12 mg (±), 33% *ee* from 5 mg (−) and 10 mg (±), 50% *ee* from 7.5 mg (−) and 7.5 mg (±) and 66% *ee* from 10 mg (−) and 5 mg (±). These were each dissolved in THF (5 mL) and treated with $LiGaH_4$ (0.25 M in Et_2O, 0.025 mmol) and the solution was stirred at room temperature for 25 minutes and then placed in a pre-equilibrated cryostat at −25 °C. Acetophenone **1a** (116 μL, 1 mmol) was added and after five minutes a solution of catecholborane (1.0 M in THF, 1.1 mmol) was added dropwise over five minutes. The mixture was allowed to stand for 18 h at −25 °C, then quenched with dilute HCl and worked up as described above to afford the product, which was examined by GC. The results of this study showed (ee_{SM}, $ee_{PROD.}$): (20%, 20%), (33%, 33%), (50%, 47%), (66%, 63%) and (100%, 92%).

Catalysis of the reduction of 1a with catecholborane by LiOMe: A solution of MeOH (8 μL, 0.2 mmol) in THF (2.5 mL) was treated with *n*-BuLi (2.5 M in hexanes, 0.08 mL, 0.2 mmol) and the resulting solution cooled to −78 °C. Acetophenone (240 mg, 232 μL, 2.0 mmol) was added followed by catecholborane (1.0 M in THF, 2.2 mmol). The mixture was allowed to warm to room temperature overnight, quenched with 2 M HCl and pentadecane (100 μL) was added. The organic phase was washed with 1 M NaOH, after which GC analysis revealed 42% yield of alcohol.

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Spectral studies of $LiGaH_4$/$MTBH_2$ (6)/catecholborane/(1u) mixtures: Solution ^{1}H NMR spectra were recorded by using a sample prepared from (*S*)-(+)MTB (30 mg, 0.1 mmol) and $LiGaH_4$ (0.25 M in Et_2O, 0.05 mmol) in THF (2.5 mL). Proton NMR spectra were recorded at 400 MHz relative to external [D_6]acetone. The ^{1}D and ^{2}D spectra indicate the presence of two different MTB ligands present in the ratio 3:1. ^{1}H NMR (400 MHz, [D_6]acetone): $\delta = 7.44$ (d, $J = 8.7$ Hz, 1H; H-3 major), 7.33 (d, $J = 8.7$ Hz, 1H; H-4′ major), 7.32–7.19 (m, 4 1/3H; H-4, 5, 5′ major, H-4, 4′, 5, 5′ minor), 6.95 (d, $J = 9.3$ Hz, 1/3H; ArH minor), 6.81 (d, $J = 8.9$ Hz, 1H; H-3′ major), 6.73–6.71 (m, 1H; ArH major), 6.71–6.65 (m, 1/3H; ArH minor), 6.63–6.57 (m, 1 1/3H; ArH major, ArH minor), 6.53–6.43 (m, 4H; 3 ArH major, 3 ArH minor), 6.38 (d, $J = 9.3$ Hz, 1/3H; ArH minor), 6.25 (d, $J = 8.7$ Hz, 1/3H; ArH minor), 6.22 (d, $J = 9.3$ Hz, 1H; ArH major); ^{13}C NMR (125.7 MHz, THF): $\delta = 158.4$, 139.3, 139.0, 135.4, 134.3, 134.0, 131.5, 127.9, 127.5, 127.1 (2C), 126.9 (2C), 126.1, 125.6, 125.2, 124.5, 124.0 (2C), 123.6, 122.6, 120.0. Signals from the quaternary carbons of the minor MTB ligand could not be detected because of insufficient intensity. Electrospray MS data were collected on a Finnigan LCQ instrument in the negative ionisation mode which gave: *m*/*z* 1347 [$Ga_2(MTB)_3$][$Li(MTB)_2$] (dimer M – Li, 1%), 669 [$LiGa(MTB)_2$] (100).

When [$Ga_2(MTB)_3$][$Li_2(MTB)$] was treated with catecholborane, only broad resonances were observed in the ^{1}H NMR spectrum of the reaction mixture at room temperature. On cooling, the signals sharpened: ^{1}H NMR (500 MHz, THF, −50 °C, aryl region only): $\delta = 8.55$ (d, $J = 8$ Hz, H-4 or 5), 8.17–8.12 (m, 1H; Ar), 8.09 (d, $J = 8$ Hz, 1H; H-4 or 5), 8.05–7.98 (m, 2H; Ar), 7.91 (d, $J = 8$ Hz, 1H; H-4 or 5), 7.56–7.53 (m, 2H; Ar), 7.48–7.42 (m, 2H; Ar), 7.39–7.27 (m, 6H; Ar), 7.24–7.19 (m, 2H; Ar), 7.15–7.12 (m, 1H; Ar), 7.09–7.02 (m, 2H; Ar), 7.02–6.88 (m, 7H; Ar). On addition of pinacolone at room temperature followed by cooling to −50 °C, a new species appeared: ^{1}H NMR (500 MHz, THF, −50 °C, aryl region only): $\delta =$ 8.24–8.15 (m, 1H; Ar), 8.14–8.06 (m, 1H; Ar), 8.05–8.01 (m, 2H; Ar), 8.01–7.94 (m, 3H; Ar), 7.92–7.86 (m, 1H; Ar), 7.52–7.48 (m, 2H; Ar), 7.45–7.40 (m, 3H; Ar), 7.38–7.26 (m, 8H; Ar), 7.22–7.14 (m, 4H; Ar), 7.05–7.00 (m, 1H; Ar), 6.98–6.89 (m, 2H; Ar).

Preparation of (R_a,R_a)-[Li_2(THF)$_5$-InCl(MTB)$_2$] (11): A solution of $MTBH_2$ **7** (302 mg, 1.00 mmol) in THF (1.0 mL) was deprotonated with BuLi (0.8 mL of 2.5 M solution in hexane, 2.00 mmol). A solution of [$InCl_3(THF)_3$][23] (4.4 mL of 0.11 M solution in THF, 0.50 mmol) was added at 0 °C. The mixture was allowed to come to room temperature while stirring (16 h) and the suspension formed filtered under argon to remove LiCl. The solution was layered with pentane to afford colourless blocks. ^{1}H NMR (500 MHz, THF, aryl region only): $\delta =$ 7.76 (d, $J = 8.5$ Hz, 1H; Ar), 7.71 (d, $J = 8.5$ Hz, Ar), 7.56 (apparent t, $J =$ 8 Hz, 2H; Ar), 7.47 (d, $J = 8.5$ Hz, 1H; Ar), 7.26 (apparent s, 1H; Ar), 7.13 (apparent t, $J = 8$ Hz, 1H; Ar), 7.03 (d, $J = 8$ Hz, 1H; H-8), 6.94 (apparent t, 2H; Ar), 6.86 (apparent t, 1H; Ar), 6.79 (d, $J = 8$ Hz, 1H; H-8); MS (FAB): *m*/*z*: 764 [Li_2InCl-$(MTB)_2]^+$.

X-ray structure determination of (R_a, R_a)-[Li(THF)$_3$Ga(MTB)$_2$] (10) and (R_a,R_a)-[Li_2(THF)$_5$InCl(MTB)$_2$] (11): Crystals of **10**–**11** were grown by layering solutions in THF (ca. 1 mL containing 0.01 mmol of complex) with dry pentane (ca. 3 mL) under argon. Small, moisture-sensitive, colourless crystals formed over several days. Representative crystals of (R_a,R_a)-**10** and (R_a,R_a)-**11** were mounted using oil. Compound **10** was collected on Station 9.8[24] at the Daresbury Synchrotron Radiation Source by using a Bruker SMART CCD area detector diffractometer and silicon monochromated radiation ($\lambda =$ 0.6890 Å). Compound **11** was collected on a SMART area detector diffractometer by using graphite monochromated Mo_K radiation ($\lambda =$ 0.71073 Å). The SAINT[25] software was used to integrate the data sets and apply the Lorentz and polarisation corrections. Crystal data and details of the data collection and refinement are given in Table 4. An absorption and incident beam decay correction were performed by using SADABS for **10**.[26] No absorption or decay correction was made for **11**.

The structures were solved by direct methods by using SHELXS-97 for **10**[27] and SIR92 for **11**.[28] The structures were refined on F^2 by using full-matrix least squares (SHELXL-97).[29] For **10**, the disorder in two of the THF ligands was modelled with the aid of 1,2 and 1,3 distance restraints. For **11**, all five THF ligands were restrained to have local C_2 symmetry and to have similar geometry. For both compounds, all ordered non-hydrogen atoms were refined with anisotropic displacement parameters. Also, H atoms were placed geometrically and refined by riding models with $U_{iso}(H) = 1.2U_{eq}(C)$.

The absolute configurations of **10** and **11** were confirmed from the value of the Flack parameter (x)[30] at the end of the refinement, for **10** $x = 0.06(2)$ and for **11** $x = 0.00(4)$. Neutral atom scattering factors and anomalous dispersion corrections were taken from the *International Tables for Crystallography*.[31]

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications nos. CCDC-141 195 [compound (R_a,R_a)-**10**] and CCDC-141 196 [compound (R_a,R_a)-**11**]. Copies of the data can be obtained free of charge on application to CCDC, 12

Table 4. Crystallographic data for (R_a,R_a)-**10** and (R_a,R_a)-**11**.

Crystal data	(R_a,R_a)-**10**	(R_a,R_a)-**11**
formula	$C_{52}H_{48}GaLiO_5S_2$	$C_{60}H_{64}ClInLi_2O_7S_2$
M_w	893.68	1125.4
crystal system	hexagonal	monoclinic
space group	$P6_5$	$P2_1$
a [Å]	10.1729(12)	11.437(4)
b [Å]	10.1729(12)	17.656(7)
c [Å]	73.623(8)	14.280(5)
α [°]	90	90
β [°]	90	106.518(7)
γ [°]	120	90
V [Å^3]	6598.3(13)	2765(2)
Z	6	2
ρ_{calcd} [g cm^{-3}]	1.349	1.352
absorption coefficient [mm^{-1}]	0.769	0.603
$F(000)$	2796	1168
crystal size [mm]	0.20 × 0.18 × 0.04	0.25 × 0.12 × 0.05
data collection		
T [K]	150(2)	150(2)
$\theta_{min} - \theta_{max}$	2.24–25.00	1.86–26.00
scan type	ω	ω
h, k, l ranges	−12 to 9, −12 to 12, −90 to 69	−15 to 13, −24 to 18, −18 to 18
total reflections collected	24614	17820
independent reflections	7227 ($R_{int} = 0.060$)	8211 ($R_{int} = 0.107$)
reflections with $I > 2\sigma(I)$	6579	3959
absorption	$T_{min} = 0.86$	$T_{max} =$ none
correction	0.96	
refinement		
data/restraints/parameters	7224/269/543	8211/453/658
final R indices	$R1 = 0.0799$, $wR2 =$	$R1 = 0.0646$, $wR2 =$
$[I > 2\sigma(I)]$	0.175	0.123
final R indices	$R1 = 0.0912$, $wR2 =$	$R1 = 0.143$, $wR2 =$
(all data)	0.179	0.144
goodness-of-fit on F^2	1.166	0.837
absolute structure parameter	0.06(2)	0.00(4)
final $(\Delta/\sigma)_{max}$	0.001	0.001
largest diff. peak and hole	0.88/−0.76 e Å^{-3}	0.98/−1.07 e Å^{-3}

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