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Catalytic Asymmetric Aziridination with Borate Catalysts Derived from VANOL and VAPOL Ligands: Scope and Mechanistic Studies

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Abstract: An extended study of the scope and mechanism of the catalytic asymmetric aziridination of imines with ethyl diazoacetate mediated by catalysts prepared from the VANOL and VAPOL ligands and triphenylborate is described. Nonlinear studies with scalemic VANOL and VAPOL reveal an essentially linear relationship between the optical purity of the ligand and the product suggesting that the catalyst incorporates a single molecule of the ligand. Two species are present in the catalyst prepared from $B(OPh)_3$ and either VANOL or VAPOL as revealed by ^1H NMR studies. Mass spectral analysis of the catalyst mixture suggests that one of the species involves one ligand molecule and one boron atom (B1) and the other involves one ligand and two boron atoms (B2). The latter can be formulated as either a linear or cyclic pyroborate and the ^{11}B NMR spectrum is most consistent with the linear pyroborate structure. Several new protocols for catalyst preparation are developed which allow for the generation of mixtures of the B1 and B2 catalysts in ratios that range from 10:1 to 1:20. Studies with catalysts enriched in the B1 and B2 species reveal that the B2 catalyst is the active catalyst in the VAPOL catalyzed asymmetric aziridination reaction giving significantly higher asymmetric inductions and rates than the B1 catalyst. The difference is not as pronounced in the VANOL series. A series of 12 different imines were surveyed with the optimal catalyst preparation procedure with the finding that the asymmetric inductions are in the low to mid 90s for aromatic imines and in the mid 80s to low 90s for aliphatic imines for both VANOL and VAPOL catalysts. Nonetheless, the crystallinity of the *N*-benzhydryl aziridines is such that nearly all of the 12 aziridine products screened can be brought to $>99\%$ *ee* with a single recrystallization.

Keywords: asymmetric catalysis · asymmetric synthesis · aziridines · chiral ligands

Introduction

The formation of aziridines from the Lewis acid mediated reaction of imines with diazo compounds has been known for quite some time dating to the early observations involving boron trifluoride etherate and zinc iodide.[1–3] The mechanism of these reactions (Scheme 1) is distinctively different from those involving copper or rhodium catalysts where a metal carbene or metal carbenoid is involved.[4] The scope of the Lewis acid mediated reactions was not appreciated until the reports by Brookhart and Templeton in 1996[5] and Jorgensen in 1997.[6] The reaction of ethyl diazoacetate with imines mediated by a Lewis acid is normally selective for the formation of the *cis*-substituted aziridine **3**. The process is thought to involve coordination of the Lewis acid to the imine and then carbon–carbon bond formation resulting from the attack of the diazo carbon in **1** on the activated imine **6**. From steric considerations, the approach of **1** and **6** may be expected to most favorably generate the zwitterion **7**, which after bond rotation to give **8** and then backside displacement of nitrogen would give the *cis*-isomer of **3**. The reaction is also known to give varying amounts of the isomeric enamines **4** and **5** which are likely the result of nitrogen loss concomitant with a 1,2-carbon or 1,2-hydrogen shift in the zwitterionic intermediate **8**, respectively. Consistent with this view are the increased amounts of enamine products observed in more polar solvents in which the zwitterion **8** may be expected to have a longer lifetime. Interestingly, Brookhart and Templeton reported that aziridine **3** could only be observed with substoichiometric amounts of Lewis acids.[5] In the presence of one equivalent of $BF_3{\cdot}Et_2O$, no aziridine is observed even though complete conversion is

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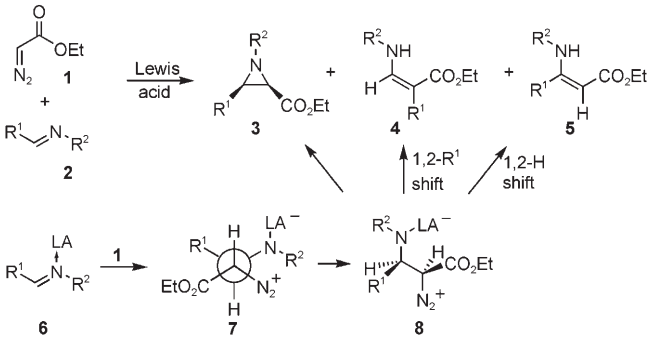
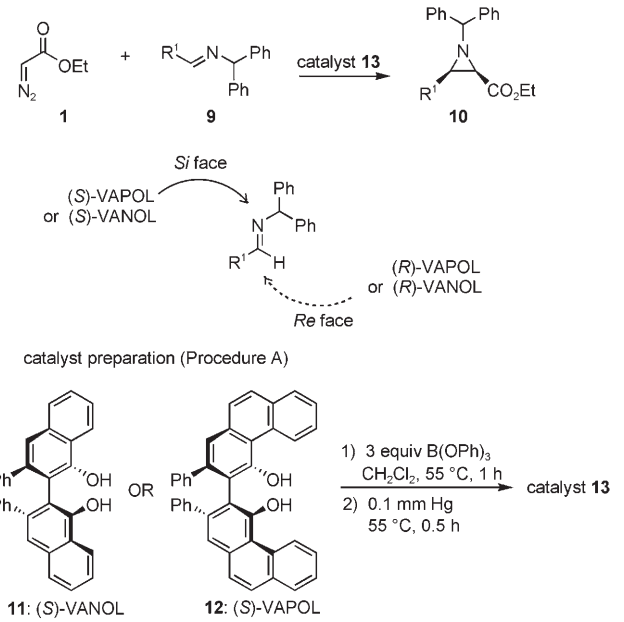
presumably achieved. Apparently, a stoichiometric complex of the aziridine **3** with $BF_3{\cdot}Et_2O$ is not stable relative to ring opening processes.



Scheme 1. Mechanism of the Lewis acid mediated aziridination reaction.

Taking the lead from the pioneering studies of Brookhart and Templeton[5] and of Jorgensen,[6] we developed a catalytic asymmetric version of this reaction[7,8] with chiral boron derived Lewis acids of the vaulted biaryl ligands[7g] VANOL and VAPOL in 1999[7a] from $BH_3{\cdot}THF$ and the following year with similar catalysts prepared from triphenylborate.[7b] The latter catalysts were quite general giving high asymmetric inductions and high *cis*-selectivities for the aziridines **10** from benzhydryl imines **9** prepared from both aliphatic and aromatic aldehydes. One of the more remarkable observations is that the VANOL and VAPOL ligands give very closely related profiles of asymmetric induction over the entire scope of substrates that were examined. We have never seen this before for any other reaction that we have studied with these ligands[9] and it is certainly not understood at this point. In all cases that have been determined, catalysts derived from the *R* enantiomers of VANOL and VAPOL give *Re*-face addition to the benzhydryl imines and those from the *S* enantiomers give *Si*-face addition. The procedure for generation of the catalyst is shown in Scheme 2 (Procedure A) and involves heating either ligand with three equivalents of $B(OPh)_3$ in methylene chloride at 55 °C for 1 h and then removing the volatiles under vacuum (0.1 mm Hg) at 55 °C for 30 min providing the catalyst as a white to pale-yellow semi-solid. Part of the purpose of the present work is to shed light on possible structures for this catalyst and another is to optimize and examine the scope of the catalytic asymmetric aziridination (AZ) reaction.

In the course of pursuing various applications of this catalytic asymmetric aziridination reactions over the last several years, we began to find that some of the reactions we had published in 2000[7b] were not reproducible. For example, the reaction of the benzhydryl imine of benzaldehyde **9b** was originally reported to give 95 % *ee* but more recently we have found that this reaction gives 89 % *ee*. We first noticed this difference somewhere near the end of 2002. Prior to 2003 at least six members of our research group had repeated this reaction and measured an asymmetric induction



Scheme 2. Lewis acid catalyzed asymmetric aziridination using VANOL and VAPOL as chiral ligands.

for this reaction of 95 ± 2 % *ee*. When this discrepancy was first discovered it was assumed that the purity of one of the reagents had either been compromised or an impurity was making an appearance in one of the reagents. Possible sources of this change in asymmetric induction could include: 1) the purity of the imine, 2) the purity of the commercially available triphenylborate, 3) the purity of the commercially available ethyl diazoacetate, 4) the optical purity or chemical purity of the ligand, and 5) experimental techniques including the introduction or exclusion of water. All of these variables were thoroughly investigated over a period of several months to no avail. This included the independent synthesis of triphenylborate and ethyl diazoacetate by at least two different published procedures. We were left to conclude that whatever the source of this difference, with rigorously purified reagents, the reaction of imine **9b** with ethyl diazoacetate gives the aziridine **10b** in 89 ± 2 % *ee*. A reevaluation of a few other imines are shown in Table 1 and as can be seen, the asymmetric inductions are 0–8 % *ee* lower with aryl imines and 8–16 % lower with alkyl imines. Thus, the purpose of the present investigation is to optimize this catalytic asymmetric aziridination reaction. This will include efforts to identify the structure of the active catalyst and the optimization of catalyst formation as well as evaluation of the reactions conditions. Finally, the new optimized protocol will be employed in a study of a thorough reevaluation of the scope of this catalytic asymmetric aziridination which will include 12 different imines.

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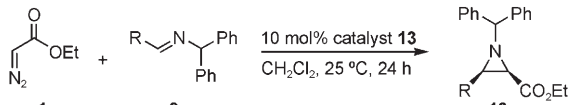
Table 1. Reinvestigation of aziridinations with catalyst prepared by Procedure A in Scheme 2.[a]



1 9 10

Entry	Series	R	Ligand	Yield **10** [%][b] (ref. [7b])	*ee* **10** [%][c] (ref. [7b])	Yield **10** [%][b] (this work)	*ee* **10** [%][c] (this work)
1	**a**	1-naphthyl	(*S*)-VAPOL	87	92[d]	87	93
2	**b**	Ph	(*S*)-VAPOL	77[e]	95	83	89
3			(*S*)-VANOL	85	96	81	88
4	**c**	*o*-MeC_6H_4	(*S*)-VAPOL	69	94	68	88
5			(*S*)-VANOL	65	91	69	83
6	**f**	*p*-BrC_6H_4	(*S*)-VAPOL	91[f]	98	85[f]	90
7			(*S*)-VANOL	85	98	86	90
8	**k**	cyclohexyl	(*S*)-VAPOL	74	94	74	78
9	**l**	*tert*-butyl	(*S*)-VAPOL	78	91	83	83
10			(*S*)-VANOL	77[g]	97	93[g]	83

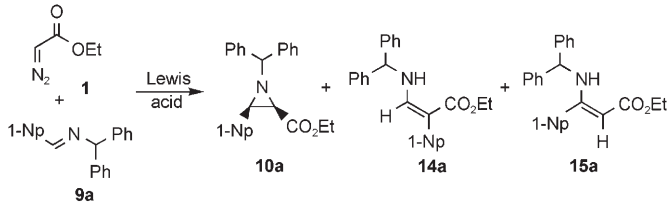
[a] Unless otherwise specified, all reactions were run in CH_2Cl_2 containing 0.5 M imine at 25 °C for 24 h with 1.1 equiv of ethyl diazoacetate and 10 mol % of the catalyst which was prepared by Procedure A in Scheme 2. The reactions with (*R*)-VANOL give *ent*-**10**. [b] Isolated yield after purification by chromatography on silica gel. [c] Determined by HPLC on a Chiralcel OD-H column. [d] The retention time for the minor enantiomer was mis-assigned in the original report. [e] Reaction with 2.5 mol % catalyst. [f] Solvent is toluene/CH_2Cl_2 1:1. [g] Reactions conditions: toluene, 0 °C for 4 h and then 25 °C for 20 h.

Results and Discussion

Background reaction and Lewis acid evaluation: Triphenylborate is not a particularly strong Lewis acid and would not be expected to promote the reaction of ethyl diazoacetate and benzhydryl imines as readily as other stronger Lewis acids.[10] This expectation was borne out by the data in Table 2 for the reaction of the 1-naphthyl imine **9a** with ethyl diazoacetate. Nonetheless, triphenylborate will promote the reaction to some extent but not as well as BF_3•etherate or $Yb(OTf)_3$.[11] Catalysis with $B(OPh)_3$ leads to 20 % conversion with 10 mol % catalyst in 24 h at room temperature in methylene chloride. Interestingly, the best catalyst for this reaction was that generated from either VANOL or VAPOL and triphenylborate. They were so efficient in fact, that it was found that the best method for the preparation of the racemates to be used as standards in the measurement of asymmetric inductions of the various aziridines examined in the present work was to employ catalysts prepared from racemic VAPOL. The VANOL and VAPOL catalysts gave lower amounts of the enamine side-products **14** and **15** as well as higher yields of the aziridine product **10** and higher *cis*/*trans* selectivities for the aziridine **10**.

Catalyst loading and reaction scale-up: The standard catalyst loading that was employed in our original report was 10 mol %.[7b] In an effort to define the turnover efficiency of this catalyst, a catalyst loading study was carried out with the reaction of imine **9b** and ethyl diazoacetate with the VAPOL catalyst **13** generated as shown in Scheme 2. This study was carried out in both methylene chloride and carbon tetrachloride as solvent and the results are presented in Table 3. The reaction of **9b** in carbon tetrachloride under the standard catalyst loading of 10 mol % was found to give higher asymmetric induction than the reaction in methylene chloride; 93 % *ee* for the former and 89 % *ee* for the latter (Table 3, entries 1 vs 5). All of the reactions in Table 3 were carried out with 0.1 mmol of VAPOL and as the catalyst loading was decreased the amount of substrate was increased. As a result of the increased scale of the reactions at low loading, the product from all of the reactions in Table 3 carried out at less than 10 mol % catalyst was first isolated by recrystallization. In order to monitor the effect of catalyst loading on the total reaction yield and on the total asymmetric induction, in each reaction after two crops of the product were taken, the remaining product was isolated from the mother liquor by column chromatography on silica gel. The total yield for the

Table 2. Lewis acid mediated aziridination of benzhydryl imine **9a**.[a]



9a 10a 14a 15a

Entry	Lewis acid	Conv. [%][b]	Yield **10a** [%][c]	*cis*/*trans* **10a**[b]	*ee* **10a** [%][d]	Ratio **10a**/**14a**/**15a**[b]
1	BF_3•OEt_2	100	43	25:1	–	1.0:0.35:0.02
2	$Yb(OTf)_3$	85	39	25:1	–	1.0:0.30:0.05
3	$Yb(OTf)_3$	70[e]	37	10:1	–	1.0:–[f]:0.04
4	$B(OPh)_3$	20	15	30:1	–	1.0:0.17:0.21
5	*rac*-VAPOL catalyst **13**	100	88	33:1	–	1.0:0.03:0.01
6	(*S*)-VAPOL catalyst **13**	100	87	>30:1	92	1.0:0.03:0.06
7	(*S*)-VANOL catalyst **13**	100	85	>30:1	88	1.0:0.01:0.05

[a] Unless otherwise specified, all reactions were carried out at 0.5 M in **9a** in CH_2Cl_2 at 25 °C for 24 h with 10 mol % catalyst and 1.1–1.2 equiv of ethyl diazoacetate. The VAPOL and VANOL catalysts were prepared as indicated in Scheme 2. [b] Determined by ^1H NMR on the crude reaction mixture. [c] Isolated yield after chromatography on silica gel. [d] Determined by HPLC on a Chiralcel OD-H column. [e] Reaction in hexane. [f] Not determined due to absorptions for **14a** being obscured by those from unidentified compounds.

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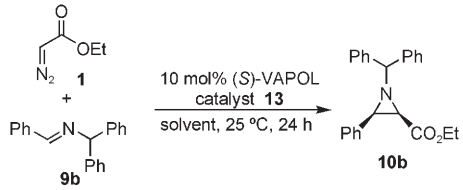
reaction does not significantly change as the catalyst loading is reduced and the total induction only drops slightly. The reaction does not fail to go to completion until the catalyst loading is reduced to 0.25 mol% in methylene chloride (44% completion, entry 4) and 0.125 mol% in carbon tetrachloride (68% completion, entry 9). Thus, the reaction of **9b** with the VAPOL catalyst **13** will turnover 176 times in methylene chloride and 544 times in carbon tetrachloride. Although the asymmetric induction of the reaction drops to 86% *ee* in carbon tetrachloride at 0.25 mol% catalyst, the reaction goes to completion and the product can be obtained in 64% yield and 98% *ee* with a single recrystallization. In this reaction 54 mg of VAPOL was used to give 8.78 g of **10b** of 98% *ee*.

Given the finding of the increased asymmetric induction in carbon tetrachloride, a screen of solvents for the asymmetric aziridination reaction was carried out on the benzhydryl imine **9b** and ethyl diazoacetate (Table 4). Given its Lewis basic nature, it was not a surprise that the reaction in acetonitrile was sluggish and only went to 77% completion in 24 h with 10 mol% of the VAPOL derived catalyst **13**. What was surprising is that the reaction in THF did go to completion and gave essentially the same yield and asymmetric induction as methylene chloride. Toluene and benzene both gave slightly better inductions than methylene chloride and gave about the same yield. A variety of other halogenated solvents were also examined but none gave a higher asymmetric induction than carbon tetrachloride (93% *ee*). The differences in the asymmetric inductions between methylene chloride, toluene and carbon tetrachloride are small but reproducible; each reaction was carried out a minimum of 4–6 times with an induction of 89±2, 91±2, and 93±2% *ee*, respectively.

Table 4. Effect of solvent on the aziridination of imine **9b**.[a]

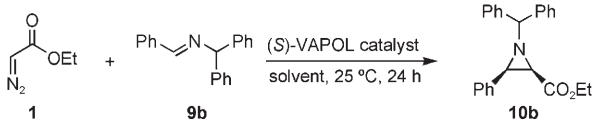


Entry	Solvent	Yield **10b** [%][b]	*ee* **10b** [%][c]
1	CH_3CN	60[d]	26
2	CH_2Cl_2	83	89
3	$CF_3C_6H_5$	82	90
4	$CHCl_3$	81	90
5	THF	79	90
6	$CH_3C_6H_5$	83	91
7	CS_2	73	91
8	C_6H_6	83	92
9	CCl_4	84	93

[a] Unless otherwise specified, all reactions were carried out at 0.5 M in imine at 25°C with 1.1–1.2 equiv of ethyl diazoacetate and 10 mol% catalyst which was prepared by Procedure A in Scheme 2, and all reactions went to completion. [b] Isolated yield after chromatography on silica gel. [c] Determined by HPLC on a Chiralcel OD-H column. [d] 77% conversion.

The rate of the reaction of imine **9b** and ethyl diazoacetate was examined in the solvents methylene chloride, carbon tetrachloride and toluene. This was done by lowering the catalyst loading to 2 mol% and then stopping the reaction after various time intervals. The results in Table 5 reveal that the reaction is slowest in methylene chloride and fastest in carbon tetrachloride with toluene close behind. Thus, the solvent of choice is clearly toluene when the factors of rates, asymmetric induction, expense and environmental concerns are taken into consideration.

Table 3. Catalyst loading study with imine **9b** with the VAPOL catalyst.[a]



Entry	**9b** [mmol]	Solvent	Loading [mol%]	1st Crop		2nd Crop		*ee* mother liquor [%][c]	Overall	
				yield [%][b]	*ee* [%][c]	yield [%][b]	*ee* [%][c]		yield [%][d]	*ee* [%][c,e]
1	1	CH_2Cl_2	10	nd	nd	nd	nd	nd	83	89
2	10	CH_2Cl_2	1	62	98	16	60	59	83	89
3	20	CH_2Cl_2	0.5	53	98	22	59	66	79	86
4[f]	40	CH_2Cl_2	0.25	–	–	–	–	–	–	–
5	1	CCl_4	10	nd	nd	nd	nd	nd	84	93
6	10	CCl_4	1	59	99	24	77	62	86	91
7	20	CCl_4	0.5	58	98	25	65	65	88	86
8	40	CCl_4	0.25	64	98	19	50	66	88	86
9[g]	80	CCl_4	0.125	–	–	–	–	–	–	–

[a] Unless otherwise specified, all reactions were carried out at 0.5 M in **9b** with 1.1 equiv of ethyl diazoacetate at 25°C for 24 h and reached 100% conversion. nd = not determined. The catalyst was prepared by Procedure A in Scheme 2. [b] Yield from **9b**. recrystallization of the crude product was performed with a mixture of CH_2Cl_2 and hexanes and after two crops were taken, the mother liquor was purified by silica gel chromatography to give the remainder of **10b**. [c] Determined by HPLC on a Chiralcel OD-H column. [d] Determined by the weight of the combined **10b** from the first and second crops and from the mother liquor. [e] Determined after the first and second crops were combined with the **10b** recovered from the mother liquor. [f] Reaction went to 44% conversion. [g] Reaction performed with 1.0 M in imine and went to 68% conversion.

Catalyst structure and nonlinear effects: It has been well established that catalysts prepared from triphenylborate and the BINOL ligand can have two equivalents of BINOL per boron.[12] Given the increased size of the VANOL and VAPOL ligands compared with BINOL it might be anticipated that the formation of catalysts composed of two equivalents of VANOL or VAPOL per boron would not be favorable. However, an examination of CPK models reveals that this could be possible. A popular method for probing the stoichiometric composition of a catalyst is to test for a nonlinear relationship between the optical purity of the ligand and that of the product. This method and its short-

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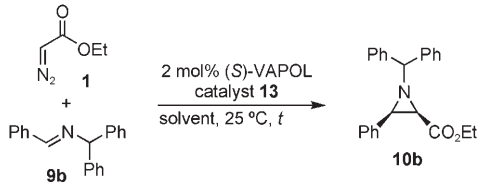
Table 5. Relative rate study in toluene, CH_2Cl_2 and CCl_4.[a]



Entry	Solvent	t [min]	Conversion [%][b]
1	CH_2Cl_2	15	38
2	toluene	15	40
3	CCl_4	15	56
4	CH_2Cl_2	30	50
5	toluene	30	55
6	CCl_4	30	66
7	CH_2Cl_2	60	59
8	toluene	60	75
9	CCl_4	60	79
10	CH_2Cl_2	200	90
11	toluene	200	99
12	CCl_4	200	95
13	CH_2Cl_2	20[c]	84
14	toluene	20[c]	98
15	CCl_4	20[c]	98

[a] Unless otherwise specified, all reactions were carried out at 0.5 M in imine at 25 °C with 1.1 equiv of ethyl diazoacetate and 2 mol% catalyst which was prepared by Procedure A in Scheme 2 with the exception that the catalyst was prepared in toluene at 80 °C. [b] Determined by ^{1}H NMR on the crude reaction mixture by the relative integration of **10b** and **9b**. [c] Reaction with 10 mol% catalyst.

comings were first clearly defined by Kagan.[13] This technique was applied to the reaction of the imine **9b** with ethyl diazoacetate in carbon tetrachloride at 25 °C with 10 mol% catalyst. The catalyst was prepared by a variation of Procedure A (Scheme 2) which involves heating three equivalents of triphenylborate with either the VANOL or VAPOL ligand in carbon tetrachloride at 80 °C for 1 h and then removing the volatiles under high vacuum at 80 °C for 30 min. As shown by the plot in Figure 1, the relationship between the optical purity of each ligand and the product is essentially linear. Although, an observed linearity does not disprove the association of the boron with two or more ligands, nonetheless, the results of these experiments suggest that it is likely that only one molecule of the ligand is involved in the active catalyst.

Spectroscopic analysis of the catalyst prepared by the original Procedure A shown in Scheme 2 revealed the presence of two species. The bay region proton in the VAPOL ligand (H^b in **12**, Scheme 3) is a convenient spectroscopic handle for probing the number of catalyst species that are generated because this proton ($\delta = 9.77$ ppm) is significantly deshielded relative to the rest of the aromatic protons. The catalyst prepared from VAPOL and $B(OPh)_3$ by Procedure A gives two species in a ratio that ranged from 3:1 to 5:1 (over 5 runs) with the bay proton doublet for the minor species at $\delta = 9.51$ ppm and a doublet for the major species at $\delta = 9.22$ ppm (see Figure 2 for spectrum of catalyst generated by Procedure E). The high resolution mass spectrum of the catalyst mixture gives two ions with the molecular formulas $C_{46}H_{29}BO_3$ and $C_{52}H_{34}B_2O_5$. Catalyst structures consistent with these formulas are the borate **18a** for the former and either of the pyroborates **16a** or **17a** for the latter. The assignment of the pyroborate as the major catalyst species was made possible by a catalyst mixture prepared from *p*-tolylborate. The major species in this mixture was determined by integration of the methyl signals in the ^{1}H NMR to have two *p*-methylphenol units per VAPOL ligand and the minor species only had one *p*-methylphenol per VAPOL. The high resolution mass spectrum of the mixture of the two species generated from *p*-tolylborate had ions for the molecular formulas $C_{47}H_{31}BO_3$ and $C_{54}H_{38}B_2O_5$ consistent with the structures **18b** and **16b**/**17b**, respectively.

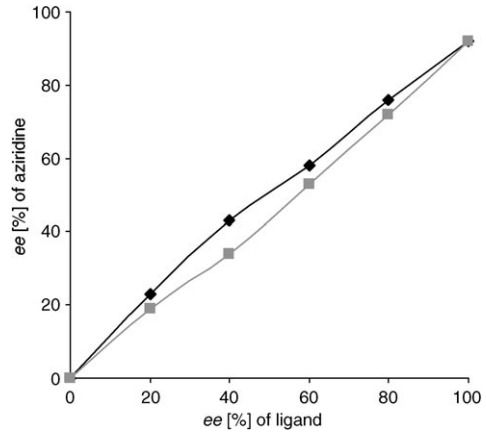
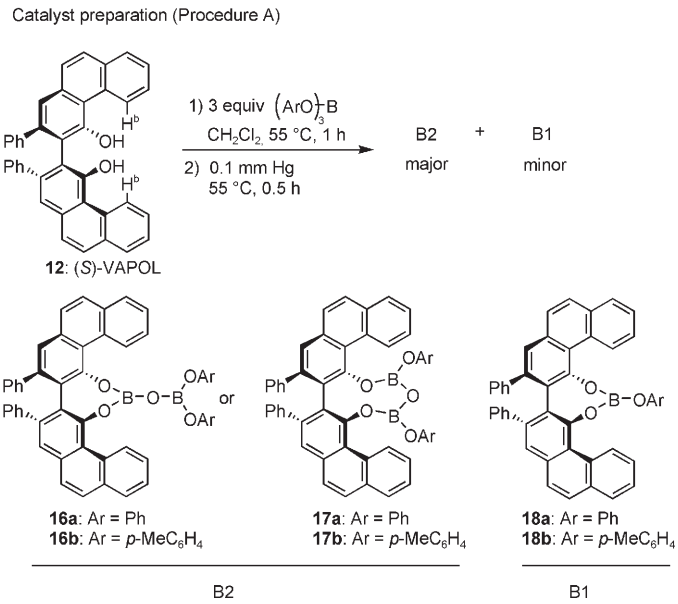


Figure 1. Plot of optical purity of ligand versus product in the reaction of imine **9b**; ◆: VAPOL as ligand, ■: VANOL as ligand.

The next question to be addressed is what is the active catalyst in the asymmetric catalytic aziridination reaction,



Scheme 3. The B1 and B2 catalysts generated from VAPOL and triaryl borates.

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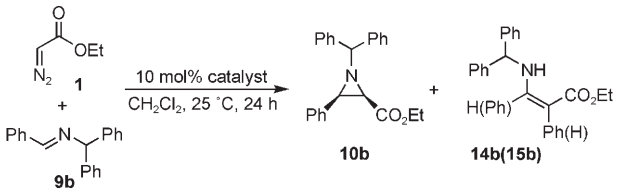
the borate **18** (B1 catalyst), the pyroborate **16**/**17** (B2 catalyst) or both? In the preparation of the catalyst by Procedure A we had seen variation in the ratio of B2 to B1 from 3:1 to 5:1 but these different ratios gave the same asymmetric induction in the aziridination reaction. Thus procedures were sought that could selectively produce either the B1 or B2 catalyst or at least produce substantially enriched samples of each. The data in Table 6 summarize the asymmetric aziridination of imine **9b** with catalysts prepared from the VANOL and VAPOL ligands with five different procedures which give B2/B1 ratios ranging from 1:10 to 20:1. At a B2/B1 ratio of 1:10 the aziridine **10b** is obtained in 50% *ee* (entry 1) whereas, with a B2:B1 ratio of 20:1, **10b** is formed in 91% *ee* (entry 6). These results clearly reveal that the pyroborate species B2 is responsible for the high asymmetric induction observed in the aziridination reaction and that the B1 species is not the active catalyst as might have been anticipated. Interestingly, the differences in induction between the B2 and B1 forms of VANOL are not large (Table 6, entry 7 vs 8 and 9). Furthermore, the ratio of VANOL derived B2 to B1 catalyst could not be driven past 2:1 even with conditions (Procedure F) that gave a 20:1 selectivity for the VAPOL ligand. The B2 and B1 forms of VANOL were also tentatively assigned by ^{1}H NMR and high resolution mass spectrum.

The formation of a pyroborate from VAPOL and B(OPh)$_3$ was certainly unexpected especially since its formation requires an equivalent of H_2O. The original procedure for the preparation of the aziridination catalyst (Procedure A, Scheme 2) involves moisture-free conditions and is performed in oven and flame-dried Schlenk flasks and employs freshly distilled and dried solvents. Thus, it was considered most likely that the H_2O comes from the commercially available B(OPh)$_3$. In fact, B(OPh)$_3$ is prone to hydrolysis and most samples of commercially available B(OPh)$_3$ are partially hydrolyzed and contain free phenol. The purity of B(OPh)$_3$ obtained from a variety of suppliers was never higher than 85%. Thus, perhaps it would be possible to increase the proportion of the B2 catalyst if H_2O were added during catalyst preparation. The results of such an investigation are summarized in Table 7. First, it can be seen that without H_2O, catalyst formation can be driven to a 10.6:1 ratio in favor of B2 by increasing the amount of B(OPh)$_3$ to 5 equiv (entries 1–3). As expected, the addition of H_2O leads to an increase in the B2/B1 ratio (entries 4 and 5 vs entry 2) but the addition of too much water (1.5 equiv) leads to substantial amounts of unreacted VAPOL (entry 6). With the addition of a given quantity of H_2O, the conversion of VAPOL is higher when the catalyst is prepared at 80°C rather than at 55°C (entries 4 and 5 vs 7 and 8). After much experimentation, the optimal conditions for effecting high conversion and high selectivity for the B2 catalyst includes the use of 4 equiv of B(OPh)$_3$ and 1 equiv of H_2O and catalyst preparation at 80°C (entry 11). This is Procedure F and as can be seen from entry 6 in Table 6 the catalyst prepared with this procedure gives the highest induction observed for aziridine **10b** in CH_2Cl_2.

Procedure F gives a 19.6:1 mixture of B2 to B1 catalysts and gives the highest induction (91% *ee*) of any of the other procedures compared in Table 6, however, since this procedure calls for the use of 4 equiv of B(OPh)$_3$ it is not clear whether a 19.6:1 mixture of B2 to B1 in the absence of any extra B(OPh)$_3$ might actually give higher than 91% *ee*. To probe for the effects of excess B(OPh)$_3$, a series of aziridinations were performed with the imine **9f** in which the catalyst was prepared with various amounts of excess B(OPh)$_3$ up to 30 equiv and the results are summarized in Table 8. The control reaction reveals that 3 mol% B(OPh)$_3$ will catalyze this reaction in toluene to the tune of 26% conversion in 24 h at room temperature (entry 8). However, the reaction with a catalyst prepared from B(OPh)$_3$ and VAPOL does not show any drop off in asymmetric induction until a 10-fold excess of B(OPh)$_3$ is used in the catalyst preparation (the error in the % *ee* measurements is ±2%).

Table 6. Effect of B2:B1 ratio on the induction in the aziridination of imine **9b**.[a]



Entry	Ligand	Cat prep[b]	B2/B1[c]	Yield **10b** [%][d]	*ee* **10b** [%][e]	*cis*/*trans* **10b**[f]	Yield **14**/**15**[f]
1	(*S*)-VAPOL	B	1:10	47	50	nd	nd
2	(*S*)-VAPOL	D	1:4	66	72	16:1	21
3	(*S*)-VAPOL	A	4.5:1	83	89	>30:1	3
4	(*S*)-VAPOL	C	8:1	80	89	nd	nd
5	(*S*)-VAPOL	E	11:1	75	91	>50:1	4
6	(*S*)-VAPOL	F	20:1	67	91	≥33:1	2
7	(*S*)-VANOL	B	1:8	81	84	nd	nd
8	(*R*)-VANOL	A[g]	1.7:1	81	88	50:1	13
9	(*S*)-VANOL	C	1.8:1	82	93	nd	nd
10	(*R*)-VANOL	F[g]	2.1:1	77	91	100:1	5

[a] Unless otherwise specified, all reactions were carried out at 0.5 M in **9b** with 1.1–1.2 equiv of ethyl diazoacetate at 25°C for 24 h. nd = not determined. [b] Procedure A is shown in Scheme 2. Procedure B involves catalyst preparation from 1 equiv of $BH_3{\cdot}Me_2S$ and 1 equiv of phenol in toluene at 100°C. Procedure C involves catalyst preparation from 2 equiv $BH_3{\cdot}Me_2S$, 3 equiv of phenol and 1 equiv of H_2O in toluene at 100°C. Procedure D involves syringe pump addition of 1.5 equiv B(OPh)$_3$ to a solution of VAPOL in toluene at 100°C. Procedure E involves syringe pump addition of VAPOL to a solution of 5 equiv B(OPh)$_3$ in toluene at 80°C. Procedure F: See entry 11 in Table 7. [c] Determined by ^{1}H NMR. [d] Isolated yield after chromatography on silica gel. [e] Determined by HPLC on a Chiralcel OD-H column. [f] Determined by ^{1}H NMR on the crude reaction mixture. [g] 5 mol% catalyst is used. The product is *ent*-**10b**.

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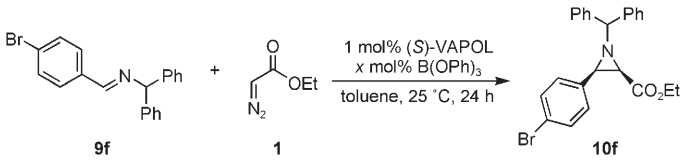
Table 7. Optimization of the preparation of the catalyst.[a]

Entry	T [°C]	$B(OPh)_3$ [equiv]	H_2O [equiv]	B2/B1/VAPOL[b]
1	55	2	0	4.5:1:1.2
2	55	3	0	7.5:1:3.0
3	55	5	0	10.6:1:0.1
4	55	3	0.5	13.8:1:7.5
5	55	3	1.0	12.4:1:3.8
6	55	3	1.5	9.9:1:19.1
7	80	3	0.5	13.9:1:0.8
8	80	3	1.0	12.5:1:0.4
9	80	4	0	13.2:1:0.0
10	80	4	0.5	13.4:1:0.0
11	80	4	1.0	19.6:1:<0.1
12[c]	80	4	1.0	11.8:1:0.03
13[d]	80	4	1.0	11.8:1:0.02
14[e]	80	4	1.0	12.8:1:0.0
15	80	5	1.0	14.6:1:0.06

[a] The catalyst is prepared by heating the VAPOL ligand with the indicated amount of $B(OPh)_3$ and H_2O in CH_2Cl_2 at 55°C (or in toluene at 80°C) for 1 h and then exposure to high vacuum (0.1 mm Hg) for 0.5 h at 55°C (or 80°C). Unless otherwise specified, a newly opened bottle of $B(OPh)_3$ was used. [b] Determined by ^{1}H NMR. [c] A one year old bottle of $B(OPh)_3$ was used which had been stored in a desiccator. [d] A three year old bottle of $B(OPh)_3$ was used which had been stored in a desiccator. [e] A three year old bottle of $B(OPh)_3$ was used that had been stored on the bench.

Table 8. Effect of excess triphenylborate on the asymmetric induction.[a]



Entry	$B(OPh)_3$ [mol%]	Conv. [%][b]	Yield **10f** [%][c]	*ee* **10f** [%][d]
1	1.5	26	25	83
2	2	98	82	85
3	2.5	97	82	88
4	3	100	85	88
5	5	100	85	89
6	10	100	85	87
7	30	100	84	83
8[e]	3	26	–	–

[a] The catalyst is prepared by heating (*S*)-VAPOL (1 mol%) with the requisite number of equivalents of $B(OPh)_3$ in toluene at 80°C for 1 h, and then removal of the volatiles under vacuum (0.1 mm Hg) at 80°C for 30 min. Unless otherwise specified, all reactions were carried out at 0.5 M of imine in toluene at 25°C with 1.1 equiv of ethyl diazoacetate for 24 h. [b] Determined by ^{1}H NMR on the crude reaction mixture and the relative integration of **10f** and **9f**. [c] Isolated yield after chromatography on silica gel. [d] Determined by HPLC on a Chiralcel OD-H column. [e] VAPOL was not used. The catalyst consisted only of 3 mol% $B(OPh)_3$.

Thus, it is concluded that Procedure F represents the optimal procedure both in terms of B2/B1 ratio and in terms of induction in the aziridination reaction.

In an effort to further support the structures of the B1 species **18a** and the B2 species **16a** or **17a** and in an effort to distinguish between the latter, the ^{11}B NMR spectrum of the catalyst was taken and this is shown in Figure 2. Entry a is the ^{1}H NMR spectrum of the catalyst prepared by Procedure F and entry b is the corresponding ^{11}B NMR spectrum. The ^{1}H NMR spectrum reveals the presence of some unreacted VAPOL ($\delta = 9.77$) and the presence of the species B1 ($\delta = 9.51$) and the B2 species ($\delta = 9.22$). In principle it should be possible to distinguish between the linear pyroborate **16a** and the cyclic pyroborate **17a** on the basis of the ^{11}B NMR since **16a** should have two different boron signals whereas, **17a** is symmetrical and should give a single boron signal. However, the boron spectrum from the catalyst prepared by Procedure F (entry b in Figure 2) is expected to be complicated by the fact that Procedure F utilizes excess $B(OPh)_3$ and by the fact that $B(OPh)_3$ would not be expected

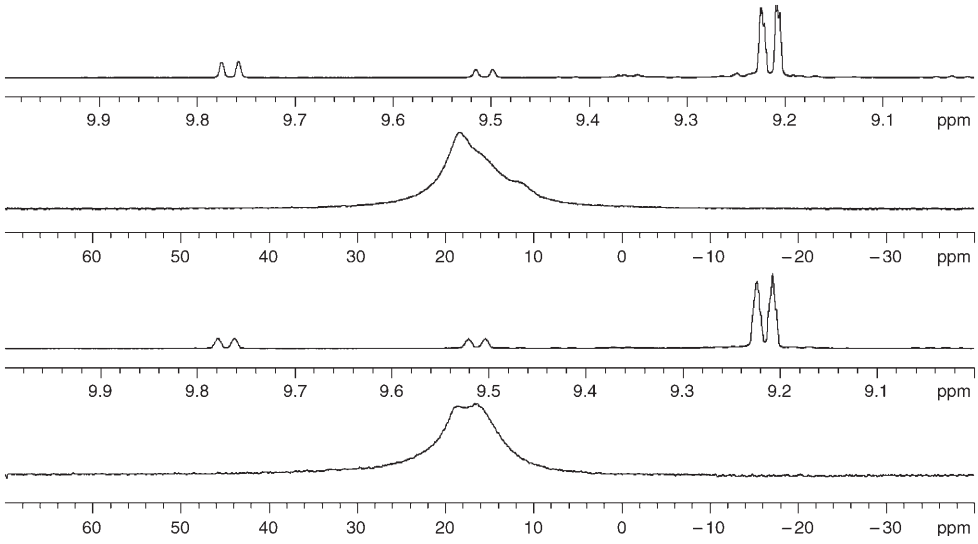


Figure 2. a) ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of VAPOL catalyst prepared from 4 equiv $B(OPh)_3$ and 1 equiv H_2O in toluene at 80°C (Procedure F). b) ^{11}B NMR spectrum corresponding to ^{1}H NMR spectrum a. c) ^{1}H NMR spectrum of VAPOL catalyst prepared from 2 equiv $BH_3{\cdot}Me_2S$, 3 equiv PhOH and 1 equiv H_2O in toluene at 80°C (Procedure C). d) ^{11}B NMR spectrum corresponding to ^{1}H NMR spectrum c.

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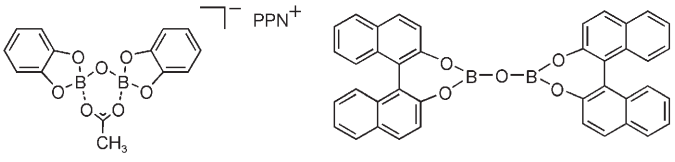
to be removed under high vacuum. Therefore, a different procedure for the generation of the catalyst was employed (Procedure C, Table 6) which utilizes a combination of $BH_3{\cdot}Me_2S$ and phenol where any unreacted boron can be removed after the catalyst is prepared. The ^1H NMR of the catalyst prepared from this method is shown in entry c in Figure 2 and is essentially the same as that for Procedure F (entry a, Figure 2). However, the ^{11}B NMR spectrum (entry d, Figure 2) is quite different and shows two partially resolved peaks that appear to be of roughly equal intensity. On this basis we tentatively assigned the major species present in the mixture as the linear pyroborate **16a**.

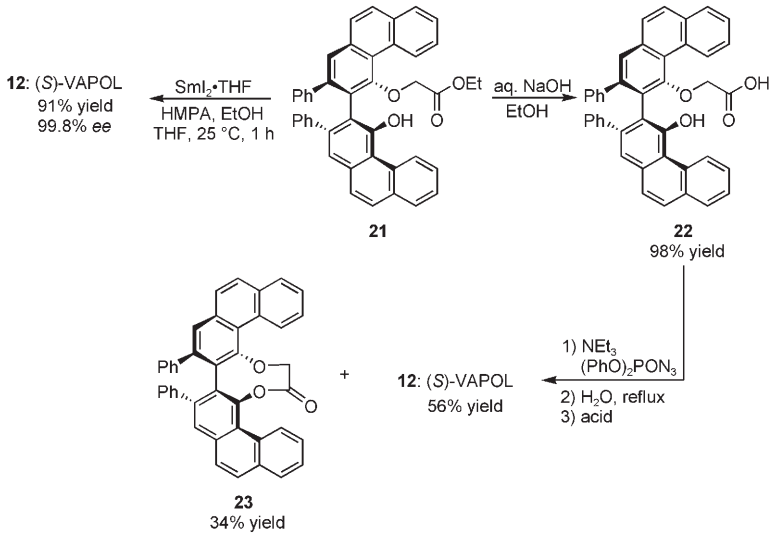
At this point it is not known whether the pyroborate catalyst **16** can function as a mono- or bidentate Lewis acid. Many examples of pyroborates are known, however, only one example is known in which both of the borons form Lewis acid–Lewis base complexes (Scheme 4). The bis-catechol pyroborate **19** has been characterized as its complex with acetate ion by X-ray analysis in the solid state.[14] An attempt to prepare a related acetate complex with a pyroborate derived from a chiral diol failed.[14] The only pyroborate that we are aware of that contains a chiral diol is compound **20** which had been reported from the reaction of BINOL with boric acid.[15] The pyroborate **20** was used in the resolution of BINOL but its properties as a chiral Lewis acid catalyst have not been explored.



19 20

Scheme 4. Known examples of pyroborates.

The VAPOL can be recovered from the reaction in high optical purity, however, usually part or all of the VAPOL is recovered as the ethyl diazoacetate (EDA) adduct **21**.[7f] The ratio of VAPOL **12** to the VAPOL-EDA adduct **21** that is recovered at the end of the reaction depends on the amount of excess EDA that is used in the reaction. For example, with 1.1 equivalents of EDA, the reaction performed with the catalyst prepared by Procedure F (Table 7, entry 11, 5 mol% catalyst) gave, after purification by silica gel chromatography, a 46% recovery of (*S*)-VAPOL with >99% *ee* along with a 49% yield of the EDA adduct **21**. The same reaction with 1.2 equivalents of EDA gives only the EDA adduct **21** in 98% yield. The EDA adduct **21** can be recycled to optically pure (*S*)-VAPOL via a Curtius rearrangement[16] or by samarium diiodide reduction (Scheme 5).[17] After hydrolysis of **21**, carboxylic acid **22** is treated with diphenylphosphoryl azide (DPPA) and triethylamine and the resulting acyl azide is rearranged to an isocyanate. Trapping the isocyanate with H_2O gives a carbamate that decarboxylates to give a hemiaminal that hydrolyzes to (*S*)-VAPOL. However, some of the acyl azide is trapped intramolecularly by the phenol to give lactone **23**. The overall result is a mixture of free (*S*)-VAPOL (56%) and lactone **23** (34%). Although lactone **23** can be recycled to ethyl ester **21**, a more efficient method for the liberation of VAPOL is the direct reduction of **21** with samarium diiodide[17] which gives (*S*)-VAPOL in 91% yield and 99.8% *ee*.



Scheme 5. Recovery of VAPOL ligand.

The data outlined in Table 6 reveals that, at least for the reaction of imine **9b** with ethyl diazoacetate, the optimal catalyst is that prepared by heating the VAPOL or VANOL ligand with 4 equiv of $B(OPh)_3$ and 1 equiv of H_2O at 80°C (Procedure F). Although the present study finds that toluene is the solvent of choice for this reaction, the scope was explored in CH_2Cl_2 as well as toluene since CH_2Cl_2 is the solvent in which these aziridination reactions were originally examined.[7b,c] The scope of the catalytic asymmetric aziridination reaction with catalysts generated from both the VANOL and VAPOL ligands with Procedure F was examined in CH_2Cl_2 with 12 different imines and the results are shown in Table 9. The general finding in CH_2Cl_2 is that imines from aromatic aldehydes typically give higher asymmetric inductions than those from aliphatic aldehydes. In addition the catalyst from VANOL generally gives higher asymmetric induction than that from VAPOL. Averaged

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Table 9. Aziridination of imine **9** in methylene chloride with both VANOL and VAPOL catalysts from Procedure F.[a]

Entry	Series	R	Ligand	Yield **10** [%][b]	*ee* **10** [%][c]	*cis*/*trans*[d]	Yield **14**+**15** [%][d]
1	**a**	1-naphthyl	(*S*)-VAPOL	76	89	26:1	5
2			(*R*)-VANOL	73	93	21:1	8
3	**b**	Ph	(*S*)-VAPOL	67	91	≥33:1	2
4			(*R*)-VANOL	77	91	100:1	5
5	**c**	*o*-MeC_6H_4	(*S*)-VAPOL	56	85	10:1	10
6			(*R*)-VANOL	57	88	11:1	14
7	**d**	*p*-MeC_6H_4	(*S*)-VAPOL	80	88	≥50:1	8
8			(*R*)-VANOL	82	93	>100:1	2
9	**e**	*o*-BrC_6H_4[e]	(*S*)-VAPOL	40	75	2.0:1	13
10			(*R*)-VANOL	41	85	2.2:1	13
11	**f**	*p*-BrC_6H_4	(*S*)-VAPOL	71	84	20:1	2
12			(*R*)-VANOL	81	92	34:1	12
13	**g**	*p*-$NO_2C_6H_4$	(*S*)-VAPOL	61[f]	61	13:1	11
14			(*R*)-VANOL	76[g]	86	34:1	5
15	**h**	*p*-$MeOC_6H_4$	(*S*)-VAPOL	42[h]	77	5:1	2
16			(*R*)-VANOL	51[i]	88	6:1	5
17	**i**	3,4-$(OAc)_2C_6H_3$	(*S*)-VAPOL	83	86	>100:1	7
18			(*R*)-VANOL	88	91	>100:1	10
19	**j**	*n*-propyl	(*S*)-VAPOL	24	73	8:1	15
20			(*R*)-VANOL	55	81	14:1	17
21	**k**	cyclohexyl	(*S*)-VAPOL	76	76	≥50:1	<1
22			(*R*)-VANOL	80	83	≥50:1	4
23	**l**	*tert*-butyl	(*S*)-VAPOL	66[j]	73	≥16:1	5
24			(*R*)-VANOL	85	84	>100:1	6

[a] Unless otherwise specified, all reactions were carried out at 0.5 M in imine in methylene chloride with 1.2 equiv of ethyl diazoacetate and 5 mol% catalyst at 25 °C for 24 h and went to 100% conversion. The catalyst was prepared from either (*S*)-VAPOL or (*R*)-VANOL and 4 equiv of $B(OPh)_3$ and 1 equiv of H_2O in toluene at 80 °C for 1 h and then all volatiles were removed at 80 °C under high vacuum (0.1 mm Hg) for 0.5 h. The reaction with (*R*)-VANOL gives the enantiomer of **10** as drawn in Scheme 2. [b] Isolated yield after chromatography on silica gel. [c] Determined by HPLC with either a Chiralcel OD-H column or Chiralcel OD column. [d] Determined by ^1H NMR on the crude reaction mixture. [e] Reaction time is 48 h. [f] 81% conversion. [g] 97% conversion. [h] 70% conversion. [i] 81% conversion. [j] 87% conversion.

over all 12 substrates, VANOL gives 8% *ee* higher induction than VAPOL which is significantly higher than the ±2% error for these measurements. In addition, the VANOL catalyst gives an 8% higher yield than the VAPOL catalyst when the yield differences are averaged over all 12 substrates. This figure is curious since the VANOL catalyst gives on average a 3% higher yield of the side-products **14** and **15** than the VAPOL catalyst. Since the reactions in Tables 9–11 go to completion (except where indicated), there must obviously be other side-products formed that do not elute from silica gel under conditions in which the aziridines are mobile. There is not a significant difference between VANOL and VAPOL on the *cis*/*trans* selectivity.

A survey of the catalytic asymmetric aziridination reaction with VANOL and VAPOL catalysts prepared by Procedure F with the same 12 substrates in toluene is summarized in Table 10. A common feature of toluene and CH_2Cl_2 is the difference between imines from aliphatic versus aromatic aldehydes. In both solvents, the inductions are generally in the 90s for aromatic substrates and in the 80s for aliphatic substrates. There are, however, some significant differences between the two solvents. The first is that asymmetric inductions for the VAPOL catalyst are higher in toluene than in CH_2Cl_2. Averaged over the 12 substrates, the VAPOL catalyst gives 7% *ee* higher inductions in toluene. This is in contrast to the VANOL catalyst which only gives on average a 0.4% *ee* increase in toluene versus CH_2Cl_2. Interestingly, since as discussed above it was found that the VANOL catalyst gave on average 8% *ee* higher inductions than VAPOL in CH_2Cl_2, the increases for VAPOL in toluene cancels out the advantage that VANOL had in CH_2Cl_2 such that in toluene, the differences in asymmetric induction between VANOL and VAPOL is only 1.2% *ee* averaged over the 12 substrates in favor of VANOL and this is less than the error for these measurements (±2% *ee*). Although the VANOL catalyst has nearly equal asymmetric inductions on average in toluene and CH_2Cl_2, a significant difference is seen in the yields for the VANOL catalyst with an average of 4% higher yields in toluene versus CH_2Cl_2. Furthermore, the VANOL catalyst gives on average 6% higher yields than the VAPOL catalyst in toluene. Similar amounts of the side products **14** and **15** are observed with both the VAPOL and VANOL catalyst in toluene. As in CH_2Cl_2, there does not seem to be a difference between VANOL and VAPOL on the *cis*/*trans* ratios in toluene.

The optimization of the asymmetric induction for a few of the substrates was undertaken by examining their aziridination reactions in toluene at 0 °C and the results are presented in Table 11 along with the data at room temperature for comparison. The substrate that had the greatest response to lowering the temperature from ambient to 0 °C was the *p*-nitrophenyl imine **9g**. The asymmetric induction increased from 79 to 95% *ee* with the VAPOL catalyst, but interestingly, only a small increase was noted for the VANOL catalyst. The imines from cyclohexane carboxaldehyde and pivaladehyde gave small increases in asymmetric induction for the VAPOL catalyst but not for the VANOL catalyst. Finally, for the imine of *n*-butyraldehyde, small increases in induction were seen for both the VAPOL and VANOL catalysts and significant increases in the yield were also seen.

As revealed by the data in Tables 10–11, excellent asymmetric inductions can be generally achieved for the aziridinations of benzhydryl imines in toluene with catalysts generated from both the VAPOL and VANOL ligands. The asymmetric inductions are generally in the low to mid 90s for aromatic imines and from the mid 80s to the low 90s for ali-

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Table 10. Aziridination of imine **9** in toluene with both VANOL and VAPOL catalysts from Procedure F.[a]

Entry	Series	R	Ligand	Yield **10** [%][b]	*ee* **10** [%][c]	*cis*/*trans*[d]	Yield **14**+**15** [%][d]
1	**a**	1-naphthyl	(*S*)-VAPOL	76	93	34:1	<1
2			(*R*)-VANOL	80	93	51:1	2
3	**b**	Ph	(*S*)-VAPOL	82	94	≥50:1	<1
4			(*R*)-VANOL	87	93	100:1	2
5	**c**	*o*-MeC_6H_4	(*S*)-VAPOL	63	91	10:1	14
6			(*R*)-VANOL	67	90	12:1	11
7	**d**	*p*-MeC_6H_4	(*S*)-VAPOL	80	92	≥50:1	<1
8			(*R*)-VANOL	79[e]	94	≥50:1	2
9	**e**	*o*-BrC_6H_4[f]	(*S*)-VAPOL	37	82	1.6:1	10
10			(*R*)-VANOL	43	82	1.9:1	24
11	**f**	*p*-BrC_6H_4	(*S*)-VAPOL	78[e]	90	20:1	<1
12			(*R*)-VANOL	86	94	≥20:1	14
13	**g**	*p*-$NO_2C_6H_4$	(*S*)-VAPOL	79[g]	79	15:1	<1
14			(*R*)-VANOL	86	89	100:1	<1
15	**h**	*p*-$MeOC_6H_4$	(*S*)-VAPOL	51[e,h]	86	6:1	23
16			(*R*)-VANOL	61	87	34:1	<1
17	**i**	3,4-$(OAc)_2C_6H_3$	(*S*)-VAPOL	87	89	100:1	6
18			(*R*)-VANOL	84	93	≥100:1	<1
19	**j**	*n*-propyl	(*S*)-VAPOL	40	81	14:1	7
20			(*R*)-VANOL	54	77	14:1	19
21	**k**	cyclohexyl	(*S*)-VAPOL	73	81	≥50:1	<1
22			(*R*)-VANOL	79	82	≥50:1	6
23	**l**	*tert*-butyl	(*S*)-VAPOL	72[i]	87	100:1	<1
24			(*R*)-VANOL	89	85	≥100:1	4

[a] Unless otherwise specified, all reactions were carried out at 0.5 M in imine in toluene with 1.2 equiv of ethyl diazoacetate and 5 mol% catalyst at 25°C for 24 h and went to 100% conversion. The catalyst was prepared from either (*S*)-VAPOL or (*R*)-VANOL and 4 equiv of $B(OPh)_3$ and 1 equiv of H_2O in toluene at 80°C for 1 h and then all volatiles were removed at 80°C under high vacuum (0.1 mm Hg) for 0.5 h. The reaction with (*R*)-VANOL gives the enantiomer of **10** as drawn in Scheme 2. [b] Isolated yield after chromatography on silica gel. [c] Determined by HPLC with either a Chiralcel OD-H column or Chiralcel OD column. [d] Determined by ^1H NMR on the crude reaction mixture. [e] Solvent is 4:1 toluene:CH_2Cl_2. [f] Reaction time is 48 h. [g] 95% conversion. [h] 73% conversion. [i] 93% conversion.

Table 11. Effect of temperature on the aziridination of imine **9** in toluene with catalysts prepared by Procedure F.[a]

Entry	Series	R	Ligand	*T* [°C]	Yield **10** [%][b]	*ee* **10** [%][c]	*cis*/*trans*[d]	Yield **14**+**15** [%][d]
1	**g**	*p*-$NO_2C_6H_4$	(*S*)-VAPOL	25	79[e]	79	15:1	<1
2			(*R*)-VANOL	25	86	89	100:1	<1
3			(*S*)-VAPOL	0	90	95	33:1	<1
4			(*R*)-VANOL	0	93	93	100:1	<1
5	**j**	*n*-propyl	(*S*)-VAPOL	25	40	81	14:1	7
6			(*R*)-VANOL	25	54	77	14:1	19
7			(*S*)-VAPOL	0	54[f]	86	25:1	13
8			(*R*)-VANOL	0	60[f]	83	33:1	4
9	**k**	cyclohexyl	(*S*)-VAPOL	25	73	81	≥50:1	<1
10			(*R*)-VANOL	25	79	82	≥50:1	6
11			(*S*)-VAPOL	0	70	85	33:1	13
12			(*R*)-VANOL	0	81	82	100:1	5
13	**l**	*tert*-butyl	(*S*)-VAPOL	25	72[g]	87	100:1	<1
14			(*R*)-VANOL	25	89	85	≥100:1	4
15			(*S*)-VAPOL	0	75[f]	93	34:1	3
16			(*R*)-VANOL	0	58[f]	83	100:1	<2

[a] Unless otherwise specified, all reactions were carried out at 0.5 M in imine in toluene with 1.2 equiv of ethyl diazoacetate and 5 mol% catalyst at 25°C for 24 h and went to 100% conversion. The catalyst was prepared from either (*S*)-VAPOL or (*R*)-VANOL and 4 equiv of $B(OPh)_3$ and 1 equiv of H_2O in toluene at 80°C for 1 h and then all volatiles were removed at 80°C under high vacuum (0.1 mm Hg) for 0.5 h. The reaction with (*R*)-VANOL gives the enantiomer of **10** as drawn in Scheme 2. [b] Isolated yield after chromatography on silica gel. [c] Determined by HPLC with either a Chiralcel OD-H column or Chiralcel OD column. [d] Determined by ^1H NMR on the crude reaction mixture. [e] 95% conversion. [f] 10 mol% catalyst; reaction time is 48 h. [g] 93% conversion.

phatic imines. All 12 of the benzhydryl aziridines examined in Tables 9–11 are solids and can be very readily recrystallized. The optical purity of all 12 of the aziridines **10a**–**10l** could be significantly enhanced by a single recrystallization from either hexanes or from an ethyl acetate/hexanes mixture and the data is shown in Table 12. Remarkably, the optical purity of all but two of the aziridines could be increased to ≥99% *ee* with a single recrystallization and with good recovery. The two exceptions were the optical purities of *o*-bromophenyl substituted aziridine **10e** which could be enhanced from 85 to 98.6% *ee* and the *n*-propyl aziridine **10j** which could be enhanced from 86 to 96.6% *ee* with one recrystallization.

Conclusion

In conclusion, the catalytic asymmetric aziridination (AZ) reaction of *N*-benzhydryl imines with ethyl diazoacetate is a broadly applicable method for the asymmetric preparation of aziridines. The scope of the reaction includes electron rich and electron poor aromatic benzhydryl imines and primary, secondary and tertiary aliphatic benzhydryl imines. A set of 12 different imines were screened with catalysts prepared from $B(OPh)_3$ and either the VANOL or VAPOL ligand. The VANOL and VAPOL catalysts gave essentially the same profile of asymmetric inductions across the entire screen with % *ee* values ranging from the mid 80s to the mid 90s for all substrates. The utility is further enhanced by the fact that the optical purity of nearly all of the 12 aziridine products could taken to greater than 99% *ee* with a single recrystallization.

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Table 12. Enhancement of the optical purity of aziridines **10** by recrystallization.[a]

Entry	Series	R	*ee* **10** [%] before recryst	*ee* **10** [%] 1st Crop	Yield **10** [%][b] 1st Crop
1	**a**	1-naphthyl	89	99.9	55
2	**b**	Ph	94	99.4	62
3	**c**	*o*-MeC_6H_4	91	99.3	74
4	**d**	*p*-MeC_6H_4	94	99.2	80
5	**e**	*o*-BrC_6H_4	85	98.6	65
6	**f**	*p*-BrC_6H_4	94	99.4	76
7	**g**	*p*-$NO_2C_6H_4$	94.5	99.7	74
8	**h**	*p*-$MeOC_6H_4$	87	99.9	81
9	**i**	3,4-$(OAc)_2C_6H_3$	92.5	99.0	67
10	**j**	*n*-propyl	86	96.6	40
11	**k**	cyclohexyl	83	99.1	80
12	**l**	*tert*-butyl	87	99.7	76

[a] Recrystallization from boiling hexanes or hexanes/ethyl acetate. [b] Yield based on scalemic aziridine. The *cis*/*trans* ratio was $\geq$50:1 in each case.

The catalyst generated from $B(OPh)_3$ and both the VANOL and VAPOL ligands contains two species and ^{1}H NMR and mass spectral evidence suggests that the major species contains one molecule of the ligand and two boron atoms (B2 catalyst) and the minor species contains one molecule of the ligand and one boron atom (B1 catalyst). A series of new protocols for catalyst generation were developed which allows for the selective generation of the B2 and B1 catalysts in ratios that range from 20:1 to 1:10. With the aid of these enriched samples of each catalyst, it is revealed that the B2 catalyst is the active catalyst in the AZ reaction of the VAPOL series as the B2 catalyst gives much higher asymmetric induction and higher rates than the B1 catalyst. In the VANOL series the difference in the two catalysts is greatly reduced. The structure of the B2 catalyst is tentatively assigned as a pyroborate in which the VAPOL ligand forms a borate ester with one of the boron atoms and the other boron remains as an acyclic borate ester with two phenol groups. Pyroborate esters of chiral diols are not common and at this point it is not clear whether an unsymmetrical chiral pyroborate will function as a monodentate or bidentate Lewis acid or both.

Experimental Section

General: All experiments were performed under an argon atmosphere. Flasks were flame-dried and cooled under argon before use. Dichloromethane and carbon tetrachloride were distilled from calcium hydride under nitrogen. Toluene, diethyl ether and THF were distilled from sodium under nitrogen. Hexanes and ethyl acetate were ACS grade and used as purchased. Reagents were purified by simple distillation or recrystallization with simple solvents. Ethyl diazoacetate and triphenylborate were used as purchased from Aldrich. VAPOL and VANOL were purified by column chromatography with 3:1 hexanes/dichloromethane. All aldimines were synthesized by a known procedure[18] and purified by recrystallization from hexanes or from a mixture of hexanes/ethyl acetate. Aziridines were purified by column chromatography with hexanes/ethyl acetate and further purified by recrystallization from hexanes/ethyl acetate if needed.

Melting points were determined on a Thomas Hoover capillary melting point apparatus. IR spectra were taken on a Nicolet IR/42 spectrometer. ^{1}H NMR and ^{13}C NMR were recorded on a Varian 300 MHz or VXR-500 MHz instrument in $CDCl_3$ unless otherwise noted. $CDCl_3$ was used as the internal standard for both ^{1}H NMR (δ = 7.24) and ^{13}C NMR (δ = 77.0). Low-resolution mass spectra and elemental analysis were performed in the Department of Chemistry at Michigan State University. Analytical thin-layer chromatography (TLC) was performed on Silicycle silica gel plates with F-254 indicator. Visualization was by short wave (254 nm) and long wave (365 nm) ultraviolet light, or by staining with phosphomolybdic acid in ethanol or with potassium permanganate. Column chromatography was performed with silica gel 60 (230–450 mesh).

HPLC analyses were carried out using a Varian Prostar 210 Solvent Delivery Module with a Prostar 330 PDA Detector and a Prostar Workstation. Chiral HPLC data for the aziridines were obtained using a Chiralcel OD-H column, others were obtained using a Chiralcel OD column. Optical rotations were obtained on a Perkin–Elmer 341 polarimeter at a wavelength of 589 nm (sodium D line) using a 1.0 decimeter cell with a total volume of 1.0 mL. Specific rotations are reported in degrees per decimeter at 20 °C and the concentrations are given in gram per 100 mL in CH_2Cl_2 unless otherwise noted.

General procedure for the preparation of the aldimines 9: All liquid aldehydes were distilled before use and all the solid aldehydes were used as purchased from Aldrich. All imines **9** could be purified by recrystallization except imine **9j** which was a liquid at room temperature and was used in the aziridination reaction without further purification. The reaction time for the formation of imine **9h** was 24 h.

***N*-Benzylidene-1,1-diphenylmethanamine (9b)**: $MgSO_4$ (4 g, 33.3 mmol) and dried CH_2Cl_2 (40 mL) were added to a flame-dried 100 mL round-bottom flask filled with argon. This was followed by the addition of diphenylmethanamine (3.46 g, 18.9 mmol). After stirring for 5 min, benzaldehyde (2 g, 18.9 mmol) was added. The reaction mixture was stirred for 15 h at room temperature. Thereafter, the reaction mixture was filtered through Celite; the Celite bed was washed with CH_2Cl_2 (15 mL × 3). The filtrate was then concentrated by rotary evaporation and placed under high vacuum (0.1 mm Hg) for 5 min to give crude imine **9b** as an off-white solid. Recrystallization (ethyl acetate/hexanes 1:9) afforded **9b** (3.9 g, 14.5 mmol, 77 %) as a white solid. M.p. 99–101 °C (lit.[19] 98–100 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.46 (s, 1H), 7.20–7.90 (m, 15H), 5.64 ppm (s, 1H); ^{13}C NMR ($CDCl_3$, 75 Hz): δ = 160.48, 143.64, 136.07, 130.47, 128.24, 128.19, 128.15, 127.40, 126.69, 77.62 ppm.

***N*-(1-Naphthylidene)-1,1-diphenylmethanamine (9a)**:[7b] Recrystallization (ethyl acetate/hexanes 1:5) afforded **9a** in 85 % isolated yield as a white solid. M.p. 105 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.06 (d, J = 7 Hz, 1H), 9.00 (s, 1H), 7.84–7.91 (m, 3H), 7.18–7.55 (m, 12H), 5.62 ppm (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 160.91, 144.02, 131.24, 129.83, 128.57, 128.48, 127.66, 127.22, 126.97, 126.02, 125.15, 124.71, 79.33 ppm.

***N*-(2-Methylbenzylidene)-1,1-diphenylmethanamine (9c)**:[7a] Recrystallization (ethyl acetate/hexanes 1:5) afforded **9c** in 92 % isolated yield as white crystals. M.p. 99–100 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.67 (s, 1H), 7.93 (d, J = 7 Hz, 2H), 7.10–7.40 (m, 12H), 5.52 (s, 1H), 2.48 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.65, 144.09, 137.87, 134.18, 130.81, 130.22, 128.39, 127.60, 126.88, 126.03, 78.74, 19.64 ppm.

***N*-(4-Methylbenzylidene)-1,1-diphenylmethanamine (9d)**:[20] Recrystallization (ethyl acetate/hexanes 1:5) afforded **9d** in 79 % isolated yield as white crystals. M.p. 73–74 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.45 (s, 1H), 7.80 (d, J = 8 Hz, 2H), 7.26–7.48 (m, 12H), 5.64 (s, 1H), 2.44 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 160.67, 143.98, 141.01, 133.88, 129.21, 128.41, 128.38, 127.66, 126.89, 76.57, 21.50 ppm; IR (thin film): $\tilde{\nu}$ = 3026s, 2853s, 1639vs, 1599s, 1452s, 1383s, 1030s, 700s cm^{-1}; MS: m/z (%): 285 (14) $[M]^+$, 168 (16), 167 (100), 152 (27), 76 (9); elemental analysis calcd (%) for $C_{21}H_{19}N$: C 88.38, H 6.71, N 4.91; found: C 88.23, H 6.88, N 4.82.

***N*-(2-Bromobenzylidene)-1,1-diphenylmethanamine (9e)**:[21] Recrystallization (ethyl acetate/hexanes 1:5) afforded **9e** in 81 % isolated yield as a white solid. M.p. 113–114 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.86 (s, 1H), 8.27 (dd, J = 8, 2 Hz, 1H), 7.27–7.61 (m, 13H), 5.71 ppm (s, 1H);

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^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.80, 143.58, 132.96, 131.89, 129.23, 128.47, 127.61, 127.53, 127.06, 78.06 ppm; IR (thin film): $\tilde{\nu}$ = 3061m, 3026m, 1631s, 1493s, 1028s, 756s cm^{-1}; MS: *m*/*z* (%): 351 (4, ^{81}Br) $[M]^+$, 349 (5, ^{79}Br) $[M]^+$, 165 (100), 152 (53), 151 (84), 88 (52); elemental analysis calcd (%) for $C_{20}H_{16}BrN$: C 68.58, H 4.60, N 4.00; found: C 68.39, H 4.73, N 3.93.

***N*-(4-Bromobenzylidene)-1,1-diphenylmethanamine (9f)**:[22] Recrystallization (ethyl acetate/hexanes 1:5) afforded **9f** in 70% isolated yield as a white solid. M.p. 96–97°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.28 (s, 1H), 7.64 (d, *J* = 7 Hz, 2H), 7.47 (d, *J* = 7 Hz, 2H), 7.15–7.35 (m, 10H), 5.23 ppm (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.51, 143.62, 131.75, 129.84, 128.46, 127.60, 127.05, 77.85 ppm.

***N*-(4-Nitrobenzylidene)-1,1-diphenylmethanamine (9g)**:[22] Recrystallization (ethyl acetate/hexanes 1:1) afforded **9g** in 80% isolated yield as an off-white solid. M.p. 132–134°C (lit.[18] 134–135°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.52 (s, 1H), 8.31 (d, *J* = 8 Hz, 2H), 8.08 (d, *J* = 8 Hz, 2H), 7.30–7.40 (m, 10H), 5.76 ppm (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.51, 143.14, 129.10, 128.57, 127.55, 127.28, 123.80, 78.09 ppm.

***N*-(4-Methoxybenzylidene)-1,1-diphenylmethanamine (9h)**: Recrystallization (ethyl acetate/hexanes 1:5) afforded **9h** in 85% isolated yield as white crystals. M.p. 108–109°C (lit.[18] 108–109°C); H NMR ($CDCl_3$, 300 MHz): δ = 8.34 (s, 1H), 7.78 (d, *J* = 8.8 Hz, 2H), 7.28–7.40 (m, 10H), 6.91 (d, *J* = 8.8 Hz, 2H), 5.55 (s, 1H), 3.82 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 160.01, 144.11, 129.99, 128.37, 127.67, 126.85, 113.88, 77.77, 55.32 ppm; IR (thin film): $\tilde{\nu}$ = 2849m, 1632s, 1493m, 1028m, 756s cm^{-1}; MS: *m*/*z* (%): 301 (16) $[M]^+$, 168 (10), 167 (100), 164 (41), 152 (22), 76 (11); elemental analysis calcd (%) for $C_{21}H_{19}NO$: C 83.69, H 6.35, N 4.65; found: C 83.60, H 6.35, N 4.52.

4-((Benzhydrylimino)methyl)-1,2-phenylene diacetate (9i):[7b] Recrystallization (ethyl acetate/hexanes 1:5) afforded **9i** in 66% isolated yield as white crystals. M.p. 138–139°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.37 (s, 1H), 7.77 (d, *J* = 2 Hz, 1H), 7.68 (dd, *J* = 8, 2 Hz, 1H), 7.38 (d, *J* = 8 Hz, 4H), 7.33 (t, *J* = 8 MHz, 4H), 5.62 (s, 1H), 7.24 (m, 3H), 2.30 (s, 3H), 2.29 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 168.22, 168.02, 158.85, 144.07, 143.59, 142.44, 135.16, 128.50, 127.68, 127.11, 126.99, 123.60, 122.88, 77.62, 20.70, 20.64 ppm; IR (thin film): $\tilde{\nu}$ = 1775s, 1640s cm^{-1}; MS: *m*/*z* (%): 387 (10) $[M]^+$, 167 (100); elemental analysis calcd (%) for $C_{24}H_{21}NO_4$: C 74.46, H 5.47, N 3.62; found: C 74.17, H 5.66, N 3.58.

***N*-Butylidene-1,1-diphenylmethanamine (9j)**:[7a] Crude product obtained as a light yellow oil in 74% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.84 (t, *J* = 5 Hz, 1H), 7.1–7.4 (m, 10H), 5.35 (s, 1H), 2.33 (dt, *J* = 7.5, 5 Hz, 2H), 1.60 (q, *J* = 7.5 Hz, 2H), 0.95 ppm (t, *J* = 7.5 Hz, 3H).

***N*-(Cyclohexylmethylene)-1,1-diphenylmethanamine (9k)**:[19] Recrystallization (ethyl acetate/hexanes 1:5) afforded **9k** in 74% isolated yield as an off-white solid. M.p. 49–51°C (lit.[2] 48–49°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.59 (d, *J* = 5.5 Hz, 1H), 7.00–7.60 (m, 10H), 5.21 (s, 1H), 2.20 (brs, 1H), 1.10–1.90 ppm (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.51, 144.41, 128.73, 127.97, 127.20, 78.35, 43.91, 30.13, 26.41, 25.82 ppm.

***N*-(2,2-Dimethylpropylidene)-1,1-diphenylmethanamine (9l)**:[7b] Recrystallization (ethyl acetate/hexanes 1:9) afforded **9l** in 35% isolated yield as white crystals. M.p. 51–51.5°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.85 (s, 1H), 7.49 (d, *J* = 7 Hz, 4H), 7.44 (t, *J* = 7 Hz, 4H), 7.34 (t, *J* = 7 Hz, 2H), 5.50 (s, 1H), 1.27 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75 Hz): δ = 171.48, 144.23, 128.25, 127.44, 126.68, 77.36, 36.38, 26.94 ppm; IR (thin film): $\tilde{\nu}$ = 1666s cm^{-1}; MS: *m*/*z* (%): 251 (<1) $[M]^+$, 167 (100); elemental analysis calcd (%) for $C_{18}H_{21}N$: C 86.08, H 8.43, N 5.58; found: C 85.82, H 8.58, N 5.53.

General procedure for the catalytic asymmetric aziridination with aldimines: Catalyst preparation Procedure F

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-phenylaziridine-2-carboxylate (10b):[7a] The catalyst was prepared by the following method (Procedure F). A magnetic stir bar was added to a 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and then the flask was flame-dried and cooled under argon. To the flask was added (*R*)-VANOL (21.9 mg, 0.05 mmol) and triphenylborate (58 mg, 0.2 mmol). Under an argon flow, dry toluene (2 mL) was added to dissolve the two reagents and this was followed by the addition of water (0.9 μL, 0.05 mmol). The Teflon valve was closed and the flask was heated at 80°C for 1 h. The threaded Teflon valve was opened to gradually apply high vacuum (0.1 mm Hg) and to remove the solvent. The vacuum is maintained for a period of 30 min at a temperature of 80°C. The flask was then filled with argon and the catalyst mixture was allowed to cool to room temperature.

To the flask containing the catalyst was first added aldimine **9b** (271 mg, 1 mmol) and then dry toluene (2 mL). Upon addition of the imine and solvent the reaction mixture turned a yellow color. Ethyl diazoacetate (124 μL, 1.2 mmol) was added via syringe and the Teflon valve was closed and the reaction mixture was stirred at room temperature for 24 h. Immediately upon addition of ethyl diazoacetate the reaction mixture became an intense yellow and the formation of bubbles from the release of nitrogen was noted. The mixture was then diluted with hexanes (15 mL) and transferred to a 100 mL round-bottom flask. The reaction flask was rinsed twice with dichloromethane (5 mL) and the rinse was added to the round-bottom flask. Rotary evaporation of the solvent followed by exposure to high vacuum (0.1 mm Hg) for 5 min gave the crude aziridine as an off-white solid. The conversion was determined from the ^{1}H NMR spectrum of the crude reaction mixture by integration of the aziridine ring methine protons relative to either the imine methine proton or the proton on the imine carbon. The *cis*/*trans* ratio was determined on the crude reaction mixture to be ≥100:1 by ^{1}H NMR integration of the ring methine protons for each aziridine. The *cis* (*J* = 7–8 Hz) and *trans* (*J* = 2–3 Hz) coupling constants were used to differentiate the two isomers. The yields of the acyclic enamine products (**14b**, **15b**) were determined from the ^{1}H NMR spectrum of the crude reaction mixture by integration of the N-H proton of the enamine relative to the aziridine ring methine protons with the aid of the isolated yield of the *cis*-aziridine: <1% yield of **14b** and 2% yield of **15b**. Purification of the crude aziridine by chromatography (35 mm × 400 mm column) on silica gel with an eluent mixture of ethyl acetate/hexanes 1:9 gave the pure aziridine **10b** in 87% isolated yield (310.2 mg, 0.87 mmol). The optical purity of **10b** was determined to be 93% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 90:10, 222 nm, flow rate 0.7 mL min^{-1}). Retention times: t_R = 4.44 min (major enantiomer) and t_R = 8.18 min (minor enantiomer). Spectral data for (2*S*,3*S*)-**10b**: R_f = 0.3 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.69 (d, *J* = 7 Hz, 2H), 7.57 (d, *J* = 7 Hz, 2H), 7.49 (d, *J* = 7 Hz, 2H), 7.41 (t, *J* = 7 Hz, 2H), 7.33 (m, 5H), 7.25 (m, 2H), 4.08 (s, 1H), 4.00 (m, 2H), 3.30 (d, *J* = 7 Hz, 1H), 2.76 (d, *J* = 7 Hz, 1H), 1.03 ppm (t, *J* = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 Hz): δ = 167.65, 142.48, 142.35, 135.00, 128.43, 127.74, 127.71, 127.49, 127.35, 127.27, 127.17, 77.64, 60.48, 47.98, 46.34, 13.88 ppm; IR (thin film): $\tilde{\nu}$ = 3030m, 2981m, 1737s, 1600s, 1200s, 1097s cm^{-1}; MS: *m*/*z* (%): 357 (<1) $[M]^+$, 190 (100), 167 (60), 117 (34); elemental analysis calcd (%) for $C_{24}H_{23}NO_2$: C 80.84, H 6.48, N 3.92; found: C 80.92, H 6.70, N 3.88; $[\alpha]_D^{23}$ = −41.0 (*c* = 1.0, CH_2Cl_2) on 99.4% *ee* material (HPLC); white solid: m.p. 128–129°C on 99.4% *ee* material.

Each aldimine **9a–l** was subjected to the catalytic asymmetric aziridination reaction with the procedure described above (catalyst preparation Procedure F) in four different variations: with catalysts derived from (*R*)-VANOL and (*S*)-VAPOL ligands and with the solvents toluene and CH_2Cl_2. The results for all these reactions can be found in Tables 9 and 10. Aldimines **9g**, **9j**, **9k** and **9l** were also subjected to the catalytic asymmetric aziridination reaction at a reaction temperature of 0°C and these results are presented in Table 11.

Optical purity enhancement by recrystallization: The chemically pure aziridine (2*S*,3*S*)-**10b** (261 mg, 0.73 mmol, 94% *ee*) obtained from column chromatography was placed in a 100 mL round-bottom flask. An air condenser with an argon balloon was attached to the round-bottom flask. A small amount of a 1:9 mixture of EtOAc/hexane (3–5 mL) was added via syringe and the solvents brought to boil with a heat gun as the flask was swirled. Additional solvent mixture was added and mixture was returned to a boil. This process was continued until a clear solution was obtained (10–30 mL). The flask was then kept in an insulated place untouched for 10–15 h, upon which aziridine **10b** crystallized out. The first crop was collected (162 mg, 0.45 mmol, 62% recovery) and determined

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to be 99.4% *ee* by HPLC (see conditions above). A summary of the recrystallization of aziridines **10a**–**10l** is presented in Table 12.

Variation of Procedure F: The above procedure for the preparation of the aziridine **10b** was also repeated with a slight modification of the procedure in which the catalyst solution was transferred to a solution of the imine and identical results were obtained.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-(naphthalen-1-yl)aziridine-2-carboxylate (10a):[7b] Imine **9a** (321 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. Purification by column chromatography on silica gel (ethyl acetate/hexanes 1:9) gave the pure aziridine (2*S*,3*S*)-**10a** in 80% isolated yield (325 mg, 0.80 mmol); *cis*/*trans* 51:1. Enamine side products: <1% yield of **14a** and 2% yield of **15a**. The optical purity of **10a** was determined to be 93% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 99:1, 222 nm, flow rate 0.7 mL min^{-1}). Retention times: t_R = 32.89 min (major enantiomer) and t_R = 25.62 min (minor enantiomer). A single recrystallization (ethyl acetate/hexanes 1:15) of 89% *ee* material gave **10a** with 55% recovery and 99.9% *ee*. R_f = 0.25 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.12 (d, J = 7 Hz, 1H), 7.81 (d, J = 7 Hz, 1H), 7.70 (m, 4H), 7.58 (d, J = 7 Hz, 2H), 7.48 (m, 2H), 7.38 (m, 3H), 7.30 (m, 3H), 7.22 (m, 1H), 4.10 (s, 1H), 3.77 (d, J = 7 Hz, 1H), 3.75 (m, 2H), 2.94 (d, J = 7 Hz, 1H), 0.65 ppm (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 167.75, 142.45, 142.22, 133.01, 131.38, 130.48, 128.54, 128.48, 127.85, 127.58, 127.14, 127.10, 126.51, 125.82, 125.40, 125.29, 122.93, 77.91, 60.35, 46.36, 45.98, 13.55 ppm; IR (thin film): $\tilde{\nu}$ = 3030w, 2980w, 1737s, 1598m, 1191s cm^{-1}; MS: *m*/*z* (%): 407 (5) $[M]^+$, 240 (59), 167 (100), 139 (9); elemental analysis calcd (%) for $C_{28}H_{25}NO_2$: C 82.59, H 6.19, N 3.44; found: C 81.86, H 6.37, N 3.26; $[\alpha]_D^{23}$ = +16.0 (c = 1.0, CH_2Cl_2) on 99.9% *ee* material; white solid: m.p. 128–129°C on 99.9% *ee* material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-o-tolylaziridine-2-carboxylate (10c):[7a] Imine **9c** (285 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. Purification by column chromatography on silica gel (ethyl acetate/hexanes 1:9) gave pure aziridine **10c** in 67% isolated yield (250 mg, 0.67 mmol); *cis*/*trans* 12:1. Enamine side products: 2% yield of **14c** and 9% yield of **15c**. The optical purity of **10c** was determined to be 90% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 99:1, 222 nm, flow rate 1 mL min^{-1}). Retention times: t_R = 6.02 min (major enantiomer) and t_R = 7.47 min (minor enantiomer). A single recrystallization (ethyl acetate/hexanes 1:19) of 91% *ee* material gave **10c** with 74% recovery and 99.3% *ee*. R_f = 0.33 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.75 (d, J = 7 Hz, 2H), 7.68 (d, J = 7 Hz, 1H), 7.65 (d, J = 7 Hz, 2H), 7.45 (t, J = 7 Hz, 2H), 7.38 (m, 3H), 7.28 (m, 1H), 7.22 (m, 2H), 7.15 (d, J = 7 Hz, 1H), 4.07 (s, 1H), 4.00 (q, J = 7 Hz, 2H), 3.34 (d, J = 7 Hz, 1H), 2.86 (d, J = 7 Hz, 1H), 2.43 (s, 3H), 1.00 ppm (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 Hz): δ = 167.80, 142.48, 142.33, 135.90, 133.05, 129.01, 128.41, 128.39, 127.63, 127.43, 127.06, 127.04, 125.26, 77.76, 60.33, 46.81, 45.53, 18.70, 13.73 ppm; IR (thin film): $\tilde{\nu}$ = 3054m, 2982m, 1740s, 1600m, 1184s cm^{-1}; MS: *m*/*z* (%): 371 (<1) $[M]^+$, 204 (100), 167 (43), 131 (41); elemental analysis calcd (%) for $C_{25}H_{25}NO_2$: C 80.83, H 6.78, N 3.37; found: C 80.84, H 6.94, N 3.64; $[\alpha]_D^{23}$ = −42.6 (c = 1.0, CH_2Cl_2) on 99.3% *ee* material; white solid: m.p. 164–165°C on 99.3% *ee* material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-p-tolylaziridine-2-carboxylate (10d): Imine **9d** (285 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. The only difference in the procedure was that a 4:1 toluene/CH_2Cl_2 (2 mL) solvent system was used for the reaction. Purification by column chromatography on silica gel (ethyl acetate/hexanes 1:9) gave the pure aziridine **10d** in 79% isolated yield (293 mg, 0.79 mmol); *cis*/*trans* ≥50:1. Enamine side products: <1% yield of **14d** and 2% yield of **15d**. The optical purity of **10d** was determined to be 94% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 90:10, 222 nm, flow rate 0.7 mL min^{-1}). t_R = 4.29 min (major enantiomer) and t_R = 7.60 min (minor enantiomer). A single recrystallization (ethyl acetate/hexanes 1:19) of 94% *ee* material gave **10d** with 80% recovery and 99.2% *ee* (HPLC). R_f = 0.30 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.60 (d, J = 7.3 Hz, 2H), 7.48 (d, J = 7.2 Hz, 2H), 7.13–7.36 (m, 8H), 7.05 (d, J = 8 Hz, 2H), 3.95 (q, J = 7.2 Hz, 2H), 3.93 (s, 1H), 3.17 (d, J = 6 Hz, 1H), 2.64 (d, J = 6.9 Hz, 1H), 2.28 (s, 3H), 1.00 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 Hz): δ = 167.75, 142.51, 142.41, 136.84, 131.94, 128.41, 127.63, 127.47, 127.31, 127.19, 127.13, 76.57, 60.47, 47.98, 46.29, 21.09, 13.94 ppm; IR (thin film): $\tilde{\nu}$ = 3030m, 2980m, 1739s, 1454m, 1197s, 1178s, 1066 m cm^{-1}; MS: *m*/*z* (%): 371 (<1) $[M]^+$, 204 (83), 203 (58), 167 (40), 164 (46), 131 (58), 130 (100), 129 (58), 77 (26); elemental analysis calcd (%) for $C_{25}H_{25}NO_2$: C 80.83, H 6.78, N 3.77; found: C 80.67, H 6.50, N 3.66; $[\alpha]_D^{23}$ = −27.8 (c = 1.0, CH_2Cl_2) on 99.2% *ee* material; white solid: m.p. 164–165°C on 99.2% *ee* material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-(2-bromophenyl)aziridine-2-carboxylate (10e): Imine **9e** (349 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand, the only difference being the reaction time which was 48 h for this reaction. Purification by column chromatography (ethyl acetate/hexanes 1:9) gave the pure aziridine **10e** in 43% isolated yield (188 mg, 0.43 mmol); *cis*/*trans* ≥100:1. Enamine side products: 11% yield of **14e** and 13% yield of **15e**. The optical purity of **10e** was determined to be 82% *ee* by HPLC analysis (Chiralcel OD-H column, 98:2 hexanes/2-propanol, 222 nm, flow rate 0.7 mL min^{-1}). Retention times: t_R = 6.06 min (major enantiomer) and t_R = 7.91 min (minor enantiomer). A single recrystallization (1:19 ethyl acetate) of 85% *ee* material gave **10e** with 65% recovery and 98.6% *ee*. R_f = 0.33 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.64 (d, J = 7.8 Hz, 3H), 7.56 (d, J = 7.1 Hz, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.22–7.44 (m, 7H), 7.12 (t, J = 7.6 Hz, 1H), 3.98 (s, 1H), 3.92 (q, J = 7.2 Hz, 2H), 3.32 (d, J = 6.8 Hz, 1H), 2.77 (d, J = 7.0 Hz, 1H), 0.94 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 167.54, 142.34, 142.11, 134.40, 131.54, 130.78, 128.77, 128.54, 128.49, 127.65, 127.57, 127.18, 126.98, 126.71, 123.22, 76.57, 60.58, 48.77, 45.86, 13.85 ppm; IR (thin film): $\tilde{\nu}$ = 1738s, 1199s, 1028m, 74m cm^{-1}; MS: *m*/*z* (%):437 (<1, ^{81}Br) $[M]^+$, 435 (<1, ^{79}Br) $[M]^+$, 270 (22), 268 (31), 167 (100), 165 (50); elemental analysis calcd (%) for $C_{24}H_{22}BrNO_2$: C 66.06, H 5.08, N 3.21; found: C 66.01, H 4.98, N 3.06; $[\alpha]_D^{23}$ = −26.0 (c = 1.0, CH_2Cl_2) on 98.6% *ee* material (HPLC); white solid: m.p. 147–148°C on 98.6% *ee* material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-(4-bromophenyl)aziridine-2-carboxylate (10f):[7a] Imine **9f** (349 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. Purification by column chromatography on silica gel (ethyl acetate/hexanes 1:9) gave pure aziridine **10f** in 86% isolated yield (373 mg, 0.86 mmol); *cis*/*trans* ≥20:1. Enamine side products: 5% yield of **14f** and 9% yield of **15f**. The optical purity of **10f** was determined to be 94% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 98:2, 222 nm, flow rate 1 mL min^{-1}). Retention times: t_R = 5.37 min (major enantiomer) and t_R = 13.48 min (minor enantiomer). A single recrystallization (ethyl acetate/hexanes 1:19) of 94% *ee* material gave **10f** with 76% recovery and 99.4% *ee*. R_f = 0.33 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.65 (d, J = 7 Hz, 2H), 7.50 (d, J = 7 Hz, 2H), 7,29–7.45 (m, 9H), 7.23 (t, J = 7 Hz, 1H), 4.01 (s, 1H), 4.00 (q, J = 7 Hz, 2H), 3.19 (d, J = 7 Hz, 1H), 2.74 (d, J = 7 Hz, 1H), 1.07 ppm (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 167.37, 142.29, 142.12, 134.06, 130.86, 129.52, 128.49, 127.46, 127.40, 127.25, 127.11, 121.31, 77.55, 60.67, 47.31, 46.44, 13.96 ppm; IR (thin film): $\tilde{\nu}$ = 1734s, 1201s, 1067 m cm^{-1}; MS: *m*/*z* (%): 437 (<1, ^{81}Br) $[M]^+$, 435 (<1, ^{79}Br) $[M]^+$, 270 (42, ^{81}Br), 268 (43, ^{79}Br), 167 (100, ^{81}Br), 165 (19, ^{79}Br); elemental analysis calcd (%) for $C_{24}H_{22}BrNO_2$: C 66.06, H 5.27, N 3.09; found: C 66.06, H 5.08, N 3.21; $[\alpha]_D^{23}$ = −12.5 (c = 1.0, CH_2Cl_2) on 99.4% *ee* material; white solid: m.p. 155–157°C on 99.4% *ee* material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-(4-nitrophenyl)aziridine-2-carboxylate (10g):[7a] Imine **9g** (316 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. The only difference was that the reaction was carried out at 0°C. Purification by column chromatography on silica gel (ethyl acetate/hexanes 1:5) gave pure aziridine **10g** (371 mg, 0.92 mmol, 93%); *cis*/*trans*:100:1. Enamine side products: <1% yield of **14g** and <1% yield of **15g**. The optical purity of **10g** was determined to be 93% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 90:10, 222 nm, flow rate 0.7 mL min^{-1}). Retention times: t_R = 8.70 min (major enantiomer) and t_R = 11.37 min (minor enantiomer). A single recrystallization (ethyl ace-

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tate/hexanes 1:15) of 94.5% *ee* material gave **10g** with 74% recovery and 99.7% *ee*. R_f=0.3 (ethyl acetate/hexanes 1:5); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=8.15 (d, J=8 Hz, 2H), 7.63 (m, 4H), 7.55 (d, J=8 Hz, 2H), 7.38 (t, J=7 Hz, 2H), 7.29 (m, 3H), 7.23 (t, J=7 Hz, 1H), 4.04 (s, 1H), 3.98 (q, J=7 Hz, 2H), 3.30 (d, J=7 Hz, 1H), 2.84 (d, J=7 Hz, 1H), 1.06 ppm (t, J=7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=166.92, 142.49, 142.03, 141.09, 128.74, 128.60, 128.57, 127.64, 127.40, 127.34, 127.02, 123.00, 60.89, 47.02, 46.88, 29.64, 13.96 ppm; IR (thin film): $\tilde{\nu}$ = 2980w, 1742s, 1605s, 1520s, 1346s, 1340s, 1202s cm^{-1}; MS: m/z (%): 402 (< 1) $[M]^+$, 167 (100), 165 (12), 152 (8), 89 (3); elemental analysis calcd (%) for $C_{24}H_{22}N_2O_4$: C 71,63, H 5.51, N 6.96; found: C 71.58, H 5.71, N 6.82; $[\alpha]_D^{23}$=+11.2 (c 1.0, CH_2Cl_2) on 99.7% *ee* material. White solid: m.p. 139–140°C on 99.7% ee material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-(4-methoxyphenyl)aziridine-2-carboxylate (10h): Imine **9h** (301 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. The silica gel for column chromatography was pre-conditioned by preparing a slurry in a 1:9 mixture of Et_3N/CH_2Cl_2 which was loaded into a column, the solvent was drained and then the silica gel was dried by flushing with nitrogen for 1 h. The silica gel column was then saturated with a 1:9 mixture of ethyl acetate/hexane, the crude aziridine was loaded onto the column and then elution with the same solvent mixture gave the pure aziridine **10h** in 61% isolated yield (236 mg, 0.61 mmol); *cis*/*trans* 34:1. Enamine side products: <1% yield of **14h** and <1% yield of **15h**. The optical purity of **10h** was determined to be 87% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 95:5, 222 nm, flow rate 0.7 mL min^{-1}). Retention times: t_R=6.35 min (major enantiomer) and t_R=15.00 min (minor enantiomer). A single recrystallization (ethyl acetate/hexanes 1:25) of 87% *ee* material gave **10h** with 81% recovery and 99.9% *ee*. R_f=0.2 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.63 (d, J=7.3 Hz, 2H), 7.51 (d, J=7.3 Hz, 2H), 7.15–7.39 (m, 8H), 6.82 (d, J=8.8 Hz, 2H), 3.97 (q, J=7.2 Hz, 2H), 3.96 (s, 1H), 3.74 (s, 3H), 3.19 (d, J=6.7 Hz, 1H), 2.66 (d, J=6.8 Hz, 1H), 1.03 ppm (t, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=167.80, 158.84, 142.53, 142.38, 128.82, 128.40, 127.46, 127.31, 127.15, 127.05, 113.16, 76.57, 60.45, 55.06, 47.67, 46.26, 13.94 ppm; IR (thin film): $\tilde{\nu}$ = 3030w, 2934w, 1738s, 1614m, 1516s, 1250s, 1033s cm^{-1}; MS: m/z (%): 388 (0.9) $[M+1]^+$, 315 (10), 222 (12), 221 (100), 167 (21), 166 (20), 147 (25), 146 (19), 91 (19); elemental analysis calcd (%) for $C_{25}H_{25}NO_3$: C 77.49, H 6.50, N 3.61; found: C 77.67, H 6.63, N 3.58; $[\alpha]_D^{23}$=−27.6 (c = 1.0, CH_2Cl_2) on 99.9% *ee* material; white solid: m.p. 136–137°C on 99.9% *ee* material.

4-((2*S*,3*S*)-1-Benzhydryl-3-(ethoxycarbonyl)aziridin-2-yl)-1,2-phenylene diacetate (10i):[7b] Imine **10i** (387 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. Purification by column chromatography on silica gel (ethyl acetate/hexanes 1:2) gave pure aziridine **10i** in 84% isolated yield (214 mg, 0.45 mmol); *cis*/*trans* ≥100:1. Enamine side products: <1% yield of **14i** and <1% yield of **15i**. The optical purity of **10i** was determined to be 93% *ee* by HPLC analysis (Chiralcel OD column, hexanes/2-propanol 85:15, 222 nm, flow rate 0.7 mL min^{-1}). Retention times: t_R=28.62 min (major enantiomer) and t_R=25.38 min (minor enantiomer). A single recrystallization (ethyl acetate/hexanes 1:5) of 92.5% *ee* material gave **10i** with 67% recovery and 99% *ee*. R_f=0.28 (ethyl acetate/hexanes 1:2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.81 (d, J=7 Hz, 2H), 7.45 (d, J=7 Hz, 2H), 7.28 (m, 7H), 7.19 (m, 1H), 7.07 (d, J=9 Hz, 1H), 3.95 (m, 2H), 3.95 (s, 1H), 3.18 (d, J=7 Hz, 1H), 2.68 (d, J=7 Hz, 1H), 2.25 (s, 3H), 2.24 (s, 3H), 0.99 ppm (t, J=7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ= 168.24, 168.07, 167.45, 142.21, 141.57, 141.35, 133.97, 128.65, 128.55, 127.61, 127.45, 127.30, 127.18, 126.05, 122.78, 122.75, 77.49, 60.89, 47.03, 46.57, 20.64, 13.84 ppm; IR (thin film): $\tilde{\nu}$ = 3030w, 2980w, 1770w, 1731s, 1600 m cm^{-1}; MS: m/z (%): 474 (21) $[M+1]^+$, 306 (12), 195 (10), 167 (100); elemental analysis calcd (%) for $C_{28}H_{27}NO_6$: C 71.02, H 5.75, N 2.96; found: C 71.23, H 5.88, N 2.94; $[\alpha]_D^{23}$=−19.7 (c = 1.0, CH_2Cl_2) on 99% *ee* material; white solid: m.p. 141–143°C on 99% *ee* material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-propylaziridine-2-carboxylate (10j):[7a] Imine **9j** (237 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. The only differences were that the reaction was carried out at 0°C, 10 mol% catalyst loading was used and the reaction time was 48 h. Purification by column chromatography (ethyl acetate/hexanes 1:19) gave pure aziridine **10j** in 60% isolated yield (194 mg, 0.60 mmol); *cis*/*trans* 33:1. Enamine side products: <1% yield of **14j** and 4% yield of **15j**. The optical purity of **10j** was determined to be 83% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 99:1, 222 nm, flow rate 1 mL min^{-1}). Retention times: t_R=3.51 min (major enantiomer) and t_R=7.44 min (minor enantiomer). A single recrystallization (hexanes) of 86% *ee* material gave **10j** with 40% recovery and 96.6% *ee*. R_f=0.33 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.49 (d, J=7 Hz, 2H), 7.39 (d, J=7 Hz, 2H), 7.27 (m, 2H), 7.33 (m, 4H), 4.17 (m, 2H), 3.66 (s, 1H), 2.28 (d, J= 7 Hz, 1H), 2.05 (q, J=7 Hz, 1H), 1.52 (m, 1H), 1.45 (m, 1H), 1.25 (t, J= 7 Hz, 3H), 1.10 (m, 1H), 1.05 (m, 1H), 0.74 ppm (t, J=7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=169.46, 142.77, 142.42, 128.29, 128.27, 127.82, 127.30, 127.10, 126.94, 77.88, 60.62, 46.62, 43.32, 29.85, 20.26, 14.21, 13.57 ppm; IR (thin film): $\tilde{\nu}$ = 3040m, 2959m, 1732s, 1194s cm^{-1}; MS: m/z (%): 323 (2) $[M]^+$, 167 (100), 156 (91), 152 (15), 128 (23), 82 (17); elemental analysis calcd (%) for $C_{21}H_{25}NO_2$: C 77.98, H 7.79, N 4.33; found: C 78.06, H 7.94, N 4.21; $[\alpha]_D^{23}$=−112.2 (c = 1.0, CH_2Cl_2) on 96.6% *ee* material; ehite solid: m.p. 93–95°C on 96.6% *ee* material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-cyclohexylaziridine-2-carboxylate (10k):[7a] Imine **9k** (277 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. The only difference was that the reaction was carried out at 0°C. Purification by column chromatography on silica gel (ethyl acetate/hexanes 1:15) gave pure aziridine **10k** in 81% isolated yield (295 mg, 0.81 mmol); *cis*/*trans* 100:1. Enamine side products: 5% yield of **14k** and <1% yield of **15k**. The optical purity of **10k** was determined to be 82% *ee* by HPLC analysis (Chiralcel OD-H column, hexanes/2-propanol 99:1, 222 nm, flow 1 mL min^{-1}). Retention times: t_R = 3.45 min (major enantiomer) and t_R = 6.99 min (minor enantiomer). A single recrystallization (ethyl acetate/hexanes 1:19) of 83% *ee* material gave **10k** with 80% recovery and 99.1% *ee*. R_f=0.2 (ethyl acetate/hexanes 1:15); ^{1}H NMR ($CDCl_3$, 500 MHz): δ= 7.45 (d, J=7 Hz, 2H), 7.37 (m, 2H), 7.31 (m, 4H), 7.24 (m, 2H), 4.25 (m, 2H), 3.63 (s, 1H), 2.29 (d, J=7 Hz, 1H), 1.83 (dd, J=7, 3 Hz, 1H), 1.28 (t, J=7 Hz, 3H), 0.95–1.66 (m, 10H), 0.52 ppm (dq, J=10, 3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ=169.63, 142.72, 142.33, 128.35, 128.30, 128.26, 127.49, 127.06, 126.82, 126.80, 78.18, 60.67, 52.12, 43.39, 36.27, 30.71, 30.11, 25.53, 25.34, 14.27 ppm; IR (thin film): $\tilde{\nu}$ = 2927 m, 2917 m, 2850 m, 1731s, 1190s, 1180s; MS: m/z (%): 363 (1) $[M]^+$, 196 (100), 167 (64), 102 (18), 95 (29); elemental analysis calcd (%) for $C_{24}H_{29}NO_2$: C 79.44, H 8.07, N 3.64; found: C 79.30, H 8.04, N 3.85; $[\alpha]_D^{23}$=−145.2 (c 1.0, CH_2Cl_2) on 99.1% *ee* material; white solid: m.p. 165–166°C on 99.1% *ee* material.

(2*S*,3*S*)-Ethyl 1-benzhydryl-3-*tert*-butylaziridine-2-carboxylate (10l):[7b] Imine **9l** (251 mg, 1 mmol) was reacted according to the general Procedure F described above with (*R*)-VANOL as ligand. Purification by column chromatography on silica gel (1:9 ethyl acetate:hexanes) gave pure aziridine **10l** in 89% isolated yield (300 mg, 0.89 mmol); *cis*/*trans* ≥100:1. Enamine side products: 4% yield of **14l** and <1% yield of **15l**. The optical purity of **10l** was determined to be 85% *ee* by HPLC analysis (Chiralcel OD-H, hexanes/2-propanol 99:1, 222 nm, flow rate 1 mL min^{-1}). Retention times: t_R=3.60 min (major enantiomer) and t_R= 9.76 min (minor enantiomer). A single recrystallization (ethyl acetate/hexanes 1:19) of 87% *ee* material gave **10l** with 76% recovery and 99.7% *ee*. R_f=0.33 (ethyl acetate/hexanes 1:9); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.67 (d, J=7 Hz, 2H), 7.40 (d, J=7 Hz, 2H), 7.28 (m, 4H), 7.20 (m, 2H), 4.24 (m, 1H), 4.09 (m, 1H), 3.59 (s, 1H), 2.16 (d, J= 7 Hz, 1H), 1.76 (d, J=7 Hz, 1H), 1.29 (t, J=7 Hz, 3H), 0.70 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=169.72, 143.43, 142.07, 128.26, 128.19, 128.17, 127.36, 127.24, 126.83, 79.19, 60.58, 56.07, 43.37, 31.59, 27.39, 14.09 ppm; MS: m/z (%): 338 (14) $[M+1]^+$, 195 (15), 167 (100); elemental analysis calcd (%) for $C_{22}H_{27}NO_2$: C 78.30, H 8.06, N 4.15; found: C 78.27, H 8.27, N 4.13; $[\alpha]_D^{23}$=−149.4 (c 1.0, CH_2Cl_2) on 99.7% *ee* material; white solid: m.p. 150–152°C on 99.7% *ee* material.

General procedure for the preparation of racemic aziridines, illustrated for the reaction of imine 9a catalyzed by triphenylborate

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***rac-cis*-Ethyl 1-benzhydryl-3-(naphthalen-1-yl)aziridine-2-carboxylate (10a)**: A 25 mL round-bottom flask, flame-dried and cooled under argon, was fitted with a rubber septum and an argon balloon. To the flask was added triphenyl borate (29 mg, 0.1 mmol) and imine **9a** (321 mg, 1 mmol). Next was added dry CH_2Cl_2 (2 mL) followed by the addition of ethyl diazoacetate (119 μL, 1.15 mmol) via syringe. The reaction mixture was allowed to stir for 24 h and then was diluted with hexanes (15 mL). Rotary evaporation of the solvent followed by applying high vacuum (0.1 mm Hg) for 5 min afforded crude aziridine **10a** as an off-white solid. The *cis*/*trans* ratio, conversion and enamine side-product amounts were calculated from the crude ^{1}H NMR spectrum as described in the general Procedure F above. Purification of this crude aziridine by column chromatography (35 mm × 400 mm column) on silica gel with ethyl acetate/hexanes 1:9 gave pure aziridine **10a** in 15% isolated yield (61 mg, 0.15 mmol) as a white solid. M.p. 152–154 °C; *cis*/*trans* 30:1. Enamine side products: 1.7% yield of **14a** and 2.1% yield of **15a**. Conversion: 20%. Spectral data for **10a** matches that given above. Other Lewis acids have been examined for the preparation of racemic samples of aziridines **9a**–**9l** utilizing this procedure and the results are presented in Table 2.

Large-scale catalytic asymmetric aziridinations with low catalyst loading, a general procedure illustrated for entry 8 in Table 3: The catalyst was prepared by the following method (Procedure A). A magnetic stir bar was added to a 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and then the flask was flame-dried and cooled under argon. To the flask was added (*S*)-VAPOL (54 mg, 0.1 mmol) and triphenylborate (87 mg, 0.3 mmol). Under an argon flow, dry CCl_4 (2 mL) was added to dissolve the two reagents. The Teflon valve was closed and the flask was heated at 55 °C for 1 h. The threaded Teflon valve was opened to gradually apply high vacuum (0.1 mm Hg) to remove the solvent. The vacuum is maintained for a period of 30 min at a temperature of 55 °C. The flask was then filled with argon and the catalyst mixture was allowed to cool to room temperature.

A 250 mL round-bottom flask was flame-dried, cooled under argon was charged with imine **9b** (10.854 g, 40 mmol) and CCl_4 (76 mL). The catalyst prepared above was dissolved in CCl_4 (2 × 2 mL) and added to the reaction flask via syringe. Stirring for 5 min gave a light yellow solution. To this solution was added ethyl diazoacetate **1** (4.6 mL, 46 mmol) via syringe. Vigorous bubbling was observed after the addition. The solution was stirred at room temperature for 24 h, and then quenched by the addition of hexane (80 mL). The mixture was stirred open to air for 15 min, and then filtered through Celite to remove insoluble solids. The solids were washed with CH_2Cl_2 and then the combined filtrate and washings were evaporated to dryness and the excess EDA was removed under high vacuum (0.1 mm Hg) to afford an off-white solid. The crude product was recrystallized from a boiling mixture of hexane and CH_2Cl_2 98:2 (360 mL). Collection of the first crop afforded aziridine **10b** (9.127 g, 64%) with 98.2% *ee*. The mother liquor was evaporated to dryness and the residue was recrystallized from a mixture of hexane and CH_2Cl_2 98:2 (65 mL) to give additional aziridine **10b** (2.694 g, 19%) with 50% *ee*. The remaining mother liquor was stripped of solvent and the residue purified by chromatography on silica gel (EtOAc/hexane 1:19 to 1:15) to give 0.728 g aziridine **10b** with 66% *ee*. The combined yield for aziridine **10b** was 12.55 g (35.2 mmol, 88% yield) and the overall *ee* was determined to be 86% *ee* by chiral HPLC analysis on the combined product. HPLC conditions and spectral data for **10b** are as given above under Procedure F.

Nonlinear studies on the catalysts generated from VANOL and VAPOL (Table 13): The reaction of imine **9b** and ethyl diazoacetate **1** was carried out utilizing a catalyst derived from either the VANOL or VAPOL ligand with the catalyst preparation Procedure A described above for the large scale preparation of aziridine **10b**. The reactions were carried out in carbon tetrachloride at room temperature for 24 h. The scalemic ligands of 20, 40, 60 and 80% *ee* were prepared by mixing the proper amounts of racemic and the *R* enantiomer of each ligand. The reaction were worked up and analyzed according to the procedure described above for the preparation of aziridine **10b** prepared from a catalyst prepared by general Procedure F. The results are presented in Table 13 and plotted in Figure 1.

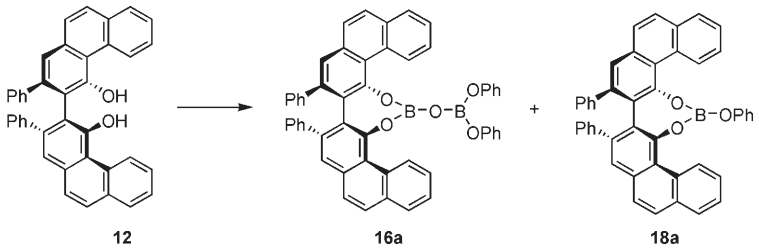
Table 13. Study on nonlinear effects with VAPOL/VANOL-borate catalyst.[a]

Entry	Ligand	*ee* ligand [%]	Yield **10b** [%][b]	*ee* **10b** [%][c]
1	(*R*)-VAPOL	20	84	23
2	(*R*)-VANOL	20	86	19
3	(*R*)-VAPOL	40	84	43
4	(*R*)-VANOL	40	83	34
5	(*R*)-VAPOL	60	82	58
6	(*R*)-VANOL	60	87	53
7	(*R*)-VAPOL	80	85	76
8	(*R*)-VANOL	80	83	72
9	(*R*)-VAPOL	>99.5	78	92
10	(*R*)-VANOL	>99.5	88	92

[a] Reactions were performed with the ligand generated from the proper mixture of racemic and enantiomerically pure ligand. The catalysts were prepared from the ligand with 3 equiv of $B(OPh)_3$ at 80 °C according to Procedure A. [b] Isolated yield after chromatography on silica gel. [c] Determined by HPLC on a Chiralcel OD-H column.

Characterization of borate and pyroborate species present in the VAPOL/$B(OPh)_3$ catalyst (Scheme 6)

Catalyst preparation Procedure A: A 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and which was flame-dried and cooled under argon to room temperature was equipped with a stir bar and charged with (*S*)-VAPOL (54 mg, 0.1 mmol), $B(OPh)_3$ (87 mg, 0.3 mmol, purchased from Aldrich, ≈80% purity) and dry CCl_4 (2 mL). The Teflon valve was closed to seal the flask under argon and the mixture was stirred at 80 °C for 1 h and then a vacuum (0.1 mm Hg) was carefully applied by partially opening the Teflon valve to remove the solvent and volatile materials and the resulting residue was heated at 80 °C under high vacuum for 30 min. The catalyst was dissolved in an appropriate deuterated solvent and examined by ^{1}H NMR which indicated that the ratio of the two catalyst species (**16a**/**18a**) prepared by Procedure A ranges from 3–5:1. The bay protons for these two species were chosen as diagnostic peaks. In [D_6]benzene at 300 MHz the bay protons appear at $\delta = 9.80$ (d, $J = 8.4$ Hz) for **18a** and at $\delta = 9.59$ (d, $J = 8.7$ Hz) for **16a** (Figure 3). In $CDCl_3$ at 300 MHz the bay protons appear at $\delta = 9.59$ (d, $J = 8.4$ Hz) for **18a** and at $\delta = 9.29$ (multiplet) for **16a** (Figure 4). In $CDCl_3$ at 500 MHz the bay protons appear at $\delta = 9.51$ (d, $J = 8.4$ Hz) for **18a** and at $\delta = 9.22$ (d, $J = 8.0$ Hz) for **16a** (see Figure 2 in text). Mass spectrum of catalyst mixture: low resolution in FAB, NPOE matrix, relative intensity of **18a** is 4.6% and relative intensity of **16a** is 12%. High resolution mass spectrum of **18a**: *m*/*z*: calcd for $C_{46}H_{29}BO_3$: 640.2210, found: 640.2214. High resolution mass spectrum of **16a**: *m*/*z*: calcd for $C_{52}H_{34}B_2O_5$: 760.2592, found: 760.2596. The use of this catalyst (10 mol%) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 gives a 83% yield of aziridine **10b** with 89% *ee* and a



Scheme 6. Characterization of borate and pyroborate species present in the VAPOL–$B(OPh)_3$ catalyst.

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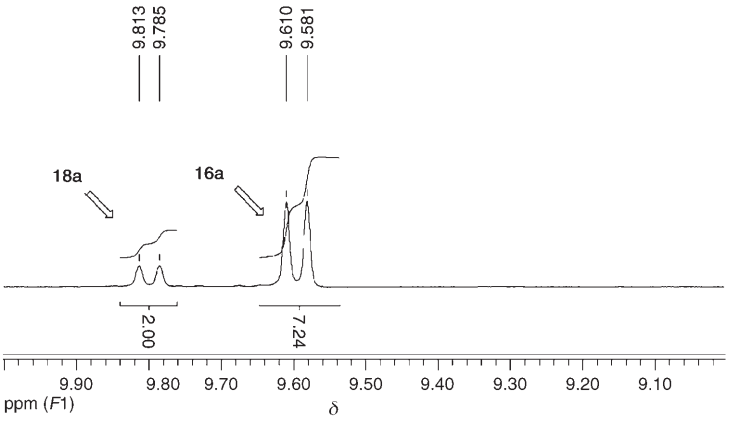

Figure 3. ^{1}H NMR spectrum (C_6D_6, 300 MHz) of the VAPOL catalyst prepared by Procedure A.

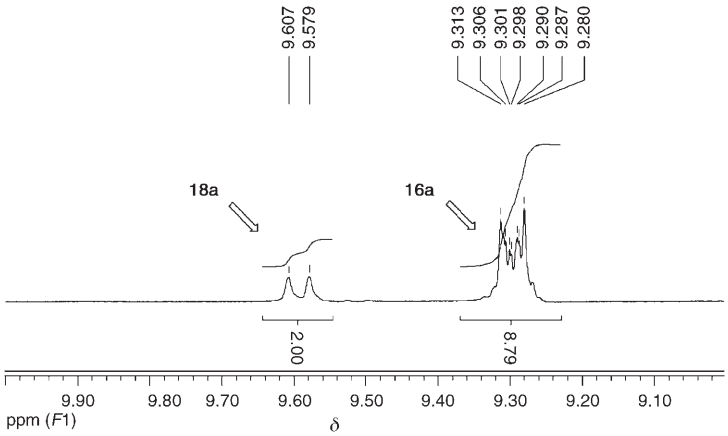

Figure 4. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of the VAPOL catalyst prepared by Procedure A.

>30:1 *cis*/*trans* ratio. A 3% yield of **14b** and **15b** is observed as determined by the crude ^{1}H NMR spectrum.

Catalyst preparation Procedure B: A 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and which was flame-dried and cooled under argon to room temperature was equipped with a stir bar and charged with (*S*)-VAPOL (54 mg, 0.1 mmol), phenol (9.4 mg, 0.1 mmol), toluene (2 mL) and BH_3Me_2S (50 μL, 2.0 M in toluene, 0.1 mmol). The Teflon valve was closed and the sealed flask was heated to 80 °C for 1 h. The threaded Teflon valve was slightly opened under high vacuum such that the volatiles were gradually removed. Once all volatiles were removed, the Teflon valve was opened all the way and the contents of the flask were exposed to high vacuum (0.1 mm Hg) at 80 °C for 0.5 h. After cooling, the flask with the catalyst was moved into a glove box. The catalyst was dissolved into approximately 0.75 mL $CDCl_3$ and analyzed by NMR. The catalyst prepared by this method typically afforded a ratio of VAPOL/**18a**/**16a** 1.0:9.9:1.0 as determined by ^{1}H NMR. ^{1}H NMR ($CDCl_3$, 500 MHz): VAPOL $\delta = 9.77$ (d, $J = 8.5$ Hz), **18a** $\delta = 9.51$ (d, $J = 8.5$ Hz), **16** $\delta = 9.22$ ($J = 8.0$ Hz). The ^{11}B NMR was taken in a Norell quartz NMR tube and shows a broad peak at 19.83 ppm relative to BF_3•Et_2O in $CDCl_3$. The use of this catalyst (10 mol%) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 (in text) gives a 47% yield of aziridine **10b** with 50% *ee*.

Catalyst preparation Procedure C: A 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and which was flame-dried and cooled under argon to room temperature was equipped with a stir bar and charged with (*S*)-VAPOL (54 mg, 0.1 mmol), phenol (28 mg, 0.3 mmol), toluene (2 mL) and BH_3Me_2S (100 μL, 2.0 M in toluene, 0.2 mmol). To this solution was added 1.8 μL H_2O (0.1 mmol). The Teflon valve was closed to seal the flask and the mixture was then heated to 80 °C for 1 h. The volatiles were removed by carefully opening the Teflon valve and applying a high vacuum. When dry, the flask was heated at 80 °C for 0.5 h under high vacuum (0.1 mm Hg). After cooling, the flask with the catalyst was moved into a glove box and the catalyst was dissolved into approximately 0.75 mL $CDCl_3$ and analyzed by NMR. The catalyst prepared by this method typically gave a ratio of VAPOL/**18a**/**16a** 0.1:1.0:8.2 as determined by ^{1}H NMR. The spectrum shown in Figure 2 has a small amount of unreacted VAPOL. The ^{11}B NMR was taken in $CDCl_3$ in a quartz NMR tube and as indicated in Figure 2 shows two broad peaks at 18.25 and 16.20 ppm (baseline separation not achieved) relative to BF_3•Et_2O. The use of this catalyst (10 mol%) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 gives a 80% yield of aziridine **10b** with 89% *ee*.

Catalyst preparation Procedure D: To a flame-dried Schlenk flask cooled under argon was added (*S*)-VAPOL (54 mg, 0.1 mmol) and dry toluene (9 mL). The flask was stirred at 100 °C under argon protection. A solution of triphenyl borate (0.15 mmol, 1.5 mL of 1 M solution in toluene) was added via syringe pump to the VAPOL solution over 30 min. After the addition, the solution was stirred for 40 min, then a vacuum (0.1 mm Hg) was applied to remove the solvent and volatile materials and the residue was heated at 100 °C under high vacuum for 30 min. The prepared catalyst was dissolved in $CDCl_3$ and examined by ^{1}H NMR which indicated that the conversion of VAPOL was > 95% and the ratio of the two catalyst species (**18a**/**16a**) is 4.3:1. The use of this catalyst (10 mol%) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 gives a 66% yield of aziridine **10b** with 72% *ee* and a 16:1 *cis*/*trans* ratio. A 21% yield of **14b** and **15b** is observed as determined by the crude ^{1}H NMR spectrum.

Catalyst preparation Procedure E: To a flame-dried Schlenk flask cooled under argon was added triphenylborate (145 mg, 0.5 mmol) and dry toluene (9 mL). The flask was stirred at 80 °C under argon protection. A solution of VAPOL (54 mg, 0.1 mmol) in toluene (1 mL) was added via syringe pump to the solution of triphenylborate over 30 min. After the addition, the solution was stirred for 40 min, then a vacuum (0.1 mm Hg) was applied to remove the solvent and volatile materials and the residue was heated at 80 °C under high vacuum for 30 min. The prepared catalyst was dissolved in $CDCl_3$ and examined by ^{1}H NMR which indicated that the conversion of VAPOL was 100% and the ratio of the two catalyst species (**18a**/**16a**) is 1:11. The use of this catalyst (10 mol%) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 gives a 75% yield of aziridine **10b** with 91% *ee* and a >50:1 *cis*/*trans* ratio. A 4% yield of **14b** and **15b** is observed as determined by the crude ^{1}H NMR spectrum.

Catalyst preparation Procedure F: To a 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and which was oven-dried and cooled under argon to room temperature, was added (*S*)-VAPOL (54 mg, 0.1 mmol) and triphenyl borate (116 mg, 0.4 mmol). The mixture was dissolved in dry toluene (2 mL), followed by the addition of H_2O (1.8 μL, 0.1 mmol). All operations were done under the protection of argon. The flask was sealed under argon by closing the Teflon valve and the solution was stirred at 80 °C for 1 h and then a vacuum (0.1 mm Hg) was applied carefully. Upon removal of solvent, the vacuum was maintained for 30 min while the flask was heated at 80 °C. The flask was then filled with argon and allowed to cool down to room temperature. To this prepared catalyst was added freshly neutralized dry $CDCl_3$ (1 mL, the $CDCl_3$ was passed through a short pipette column packed with activated basic Al_2O_3 prior to each NMR experiment. The basic Al_2O_3 was activated at 100 °C under vacuum for 16 h, then cooled to room temperature and stored under N_2). The NMR tube was flame-dried and cooled to room temperature under the protection of argon; the catalyst solution was then transferred to the NMR tube via syringe.The ratio of **16a**/**18a** by ^{1}H NMR is 19.6:1 with no detectable amount of VAPOL remaining. The use of this catalyst (10 mol%) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 gives a 67% yield of aziridine **10b** with 91% *ee* and ≥33:1 *cis*/*trans*. A 2% yield of **14b** and **15b** is observed as determined by the crude ^{1}H NMR spectrum.

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Characterization of borate and pyroborate species present in the VAPOL–B(*p*-tolyl)$_3$ catalyst

***Preparation of* p-*tris-tolylborate*:** A 250 mL round-bottom flask fitted with a Dean-Stark trap was charged with boric acid (3.09 g, 50 mmol), *p*-cresol (18.9 g, 175 mmol) and 50 mL toluene. The solution was refluxed under argon for 48 h, and the water produced in the reaction was removed until complete conversion was indicated by the cessation of water generation. The solvent was removed in vacuo and the crude product was distilled under high vacuum. The product boiled at 181 °C (0.1 mm Hg), and the viscous oil that was collected solidified upon standing. The product was isolated as white solid (13.54 g, 41 mmol, 82 %). The ^{1}H NMR of the product indicated that the isolated *p*-tris-tolylborate[23] was greater than 95 % chemical purity.

Catalyst preparation Procedure A: A 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and which was flame-dried and cooled under argon to room temperature was equipped with a stir bar and charged with (*S*)-VAPOL (54 mg, 0.1 mmol), *p*-tris-tolylborate (133 mg, 0.4 mmol) and dry CH_2Cl_2 (2 mL). The Teflon valve was closed to seal the flask under argon and the mixture was stirred at 55 °C for 1 h. A vacuum (0.1 mm Hg) was gradually applied by slightly opening the Teflon valve under a high vacuum to remove the solvent and volatile materials. The residue was heated at 55 °C under a high vacuum for 30 min. The catalyst was dissolved in $CDCl_3$ and examined by ^{1}H NMR which indicated that the ratio of the two catalyst species (**16b**/**18b**) is 1.3:1 by integration of the bay protons and 1.2:1 by integration of the *p*-tolyl protons. VAPOL was completely consumed as indicated by the absence of a doublet at $\delta = 9.77$ ppm. ^{1}H NMR ($CDCl_3$, 300 MHz) for **18b**: $\delta = 9.63$ (d, $J = 8.4$ Hz), 2.50 (s), the relative integration is 1:1.8, respectively. ^{1}H NMR ($CDCl_3$, 300 MHz) for **16b**: $\delta = 9.35$ (multiplet), 2.24 (s), the relative integration is 1:3.5, respectively. Mass spectrum of catalyst mixture: low resolution in FAB, NPOE matrix, relative intensity of **18b** is 11 % and the relative intensity of **16b** is 14 %. High resolution mass spectrum of **18b**: *m*/*z*: calcd for $C_{47}H_{31}BO_3$: 654.2366, found: 654.2376. High resolution mass spectrum of **16b**: *m*/*z*: calcd for $C_{54}H_{38}B_2O_5$: 788.2905, found: 788.2918.

Catalyst preparation Procedure F: A 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and which was flame-dried and cooled under argon to room temperature was equipped with a stir bar and charged with (*S*)-VAPOL (54 mg, 0.1 mmol), *p*-tris-tolylborate (133 mg, 0.4 mmol), 1.8 μL of water (0.1 mmol) and dry toluene (2 mL). The Teflon valve was closed to seal the flask under argon and the mixture was stirred at 80 °C for 1 h. A vacuum (0.1 mm Hg) was gradually applied by slightly opening the Teflon valve to remove the solvent and volatile materials and the residue was heated at 80 °C under high vacuum for 30 min. The catalyst was dissolved in $CDCl_3$ and examined by ^{1}H NMR which indicated that the ratio of the two catalyst species (**16b**/**18b**) is 8.4:1 by integration of the bay protons and 8.2:1 by integration of the *p*-tolyl protons. VAPOL was completely consumed as indicated by the absence of a doublet at $\delta =$ 9.77 ppm. ^{1}H NMR ($CDCl_3$, 300 MHz) for **18b**: $\delta = 9.63$ (d, $J = 8.4$ Hz), 2.50 (s), the relative integration is 1:1.8, respectively. ^{1}H NMR ($CDCl_3$, 300 MHz) for **16b**: $\delta = 9.35$ (multiplet), 2.24 (s), the relative integration is 1:3.4, respectively.

Characterization of borate and pyroborate species present in the VANOL–B(OPh)$_3$ catalyst (Scheme 7)

Catalyst preparation Procedure A: A 25 mL pear-shaped flask that had its 14/20 joint replaced by a high vacuum threaded T-shaped Teflon valve and which was flame-dried and cooled under argon to room temperature was equipped with a stir bar and charged with (*S*)-VANOL (44 mg, 0.1 mmol), $B(OPh)_3$ (87 mg, 0.3 mmol, purchased from Aldrich, ≈80 % purity) and dry CCl_4 (2 mL). The Teflon valve was closed to seal the flask under argon and the mixture was stirred at 80 °C for 1 h. A vacuum (0.1 mm Hg) was gradually applied by slightly opening the Teflon valve to remove the volatile materials and the residue was heated at 80 °C under high vacuum for 30 min. The catalyst was dissolved in $CDCl_3$ and examined by ^{1}H NMR which indicated that the ratio of the two catalyst species (**25**/**24**) is 2.8:1 by integration of the multiplet at $\delta = 8.16$ and the doublet at $\delta = 8.07$, respectively. The ratio of the two catalyst species (**25**/**24**) is 3.0:1 by integration of the multiplet at $\delta = 7.88$ and the doublet at $\delta = 7.79$, respectively. The spectrum of the aromatic region is shown in Figure 5. In a different run the catalyst was obtained with a ratio of **25**/**24** 1.7:1. The use of this catalyst (5 mol %) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 gives an 81 % yield of aziridine **10b** with 88 % *ee* and ≥50:1 *cis*/*trans*. A 13 % yield of **14b** and **15b** is observed as determined by the crude ^{1}H NMR spectrum.

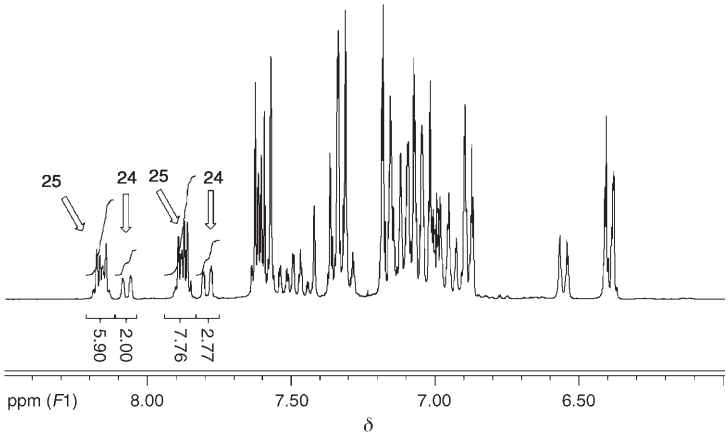
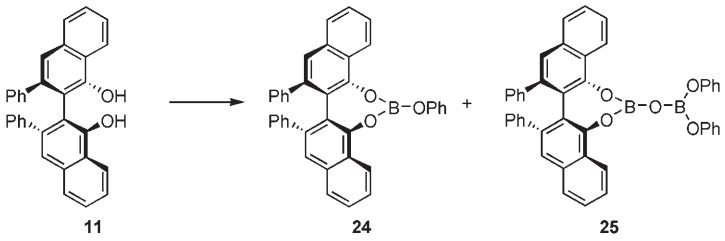


Figure 5. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of the VANOL catalyst prepared by Procedure A.



Scheme 7. Characterization of borate and pyroborate species present in the VANOL–B(OPh)$_3$ catalyst.

***Catalyst preparation Procedure B*:** The protocol described for the preparation of the VAPOL borate complex **18a** and VAPOL pyroborate complex **16a** with the catalyst preparation Procedure B was followed exactly except that (*S*)-VANOL (44 mg, 0.1 mmol) was added in place of VAPOL. The catalyst made by this method typically afforded a ratio of VANOL/**24**/**25** 0.2:8.0:1.0 as determined by ^{1}H NMR. The aromatic hydrogen on the naphthalene ring *peri* to the oxygen was chosen as the diagnostic peak: VANOL $\delta = 8.43$ (m), **24** $\delta = 8.07$ (d, $J = 8.0$ Hz), **25** $\delta =$ 8.16 (m). The use of this catalyst (10 mol %) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 gives a 81 % yield of aziridine **10b** with 84 % *ee*.

Catalyst preparation Procedure C: The protocol described for the preparation of the VAPOL borate complex **18a** and VAPOL pyroborate complex **16a** with the catalyst preparation Procedure C was followed except (*S*)-VANOL (44 mg, 0.1 mmol) was added in place of VAPOL. The catalyst made by this method typically afforded a ratio of VANOL/**24**/**25** <0.1:1.0:1.8. Mass spectrum (EI$^+$, direct probe) *m*/*z* (%): 660 (13), 540 (100); HRMS: *m*/*z*: calcd for $C_{38}H_{25}BO_3$: 540.1897, found: 540.1896. HRMS: *m*/*z*: calcd for $C_{44}H_{30}B_2O_5$: 660.2279, found: 660.2289. The use of this catalyst (10 mol %) in the aziridination of imine **9b** in CH_2Cl_2 as shown in Table 6 gives a 82 % yield of aziridine **10b** with 93 % *ee*.

Catalyst preparation Procedure D: A 25 mL flame-dried Schlenk flask was cooled under argon to room temperature, equipped with a stir bar

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and charged with (*S*)-VANOL (44 mg, 0.1 mmol) and dry toluene (9 mL). The flask was stirred at 100 °C under argon protection. A solution of triphenyl borate (0.15 mmol, 1.5 mL of 1 M solution in toluene) was added via syringe pump to the VANOL solution over 30 min. After the addition, the solution was stirred for 40 min and then a vacuum (0.1 mm Hg) was gradually applied to remove the solvent and volatile materials and then the residue was heated at 100 °C under high vacuum for 30 min. The prepared catalyst was dissolved in $CDCl_3$ and examined by ^{1}H NMR which indicated that the conversion of VANOL was 100% ($\delta = 8.43$, doublet) and the ratio of the two catalyst species (**25**/**24**) is 1:4.8 by integration of the multiplet at $\delta = 8.14$ and the doublet at $\delta = 8.04$, respectively. The ratio of the two catalyst species (**25**:**24**) is 1:5.0 by integration of the multiplet at $\delta = 7.86$ and the doublet at $\delta = 7.77$, respectively. The spectrum of the aromatic region is shown in Figure 6.

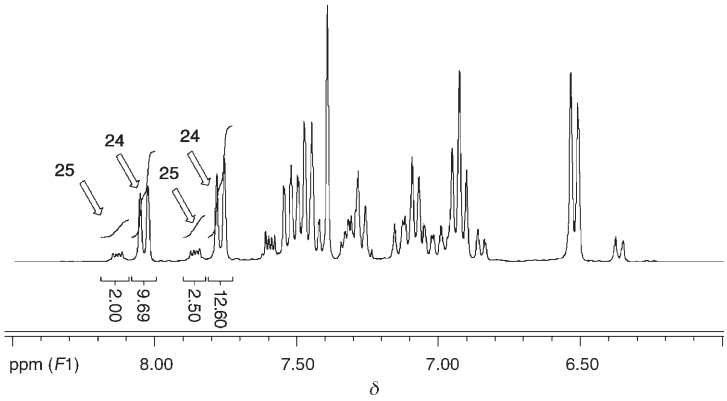

Figure 6. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of the VANOL catalyst prepared by Procedure D.

General procedure for the recovery and recycling of VAPOL from the catalytic asymmetric aziridination reaction

Recovery of VAPOL–EDA adduct 21: The aziridination reaction of the imine **9b** (542 mg, 2 mmol) with ethyl diazoacetate **1** (250 μL, 2.4 mmol) was carried out in toluene, for 24 h at room temperature and with 5 mol% of the (*S*)-VAPOL–borate catalyst generated according to the general Procedure F described above. Thus for the preparation of the catalyst, (*S*)-VAPOL (54 mg, 0.1 mmol), $B(OPh)_3$ (116 mg, 0.4 mmol), H_2O (1.8 μL, 0.1 mmol) and toluene (2 mL) were heated at 80 °C for 1 h, then a vacuum (0.1 mm Hg) was applied carefully. Upon removal of solvent, the vacuum was kept for 30 min with continual heating at 80 °C. After the aziridination reaction, the crude reaction mixture obtained was subjected to separation by column chromatography with a mixture EtOAc/hexanes 1:9, which afforded pure aziridine **10b** in 73% yield (522 mg, 1.46 mmol) as well as the VAPOL-EDA adduct **21** in 98% yield (61 mg, 0.098 mmol). No VAPOL was detected under these reactions conditions. The R_f values for VAPOL, the aziridine **10b** and the VAPOL–EDA adduct **21** with a mixture of EtOAc/hexanes 1:9 are 0.34, 0.30 and 0.25, respectively. The characterization data for **21** was identical to that previously reported by our group.[7f] The amount of the EDA **21** that is formed is variable and depends on the amount of excess ethyl diazoacetate that is used. For example, if 1.1 equivalents of ethyl diazoacetate is used then the adduct **21** is isolated in 49% yield along with a 46% recovery of unreacted VAPOL that is >99% *ee*.

Samarium diiodide[17] reduction of EDA adduct 21: A 25 mL round-bottom flask was flame dried and cooled under argon and charged with samarium metal (128 mg, 0.85 mmol) and dry THF (5.2 mL). The flask was then fitted with a rubber septum and an argon balloon. Freshly distilled diiodomethane (63 μL, 0.784 mmol) was then added via syringe. The reaction mixture was stirred for 2 h at room temperature to give a dark blue slurry. To another 25 mL round-bottom flask which had been flame dried and cooled under argon was added the VAPOL–EDA adduct **21** (61 mg, 0.098 mmol) and dry THF (1 mL). After fitting the flask with a rubber septum and an argon balloon, ethanol (reagent grade, 17 μL, 0.294 mmol) and hexamethylphosphoramide (HMPA, 153 μL, 0.882 mmol) were added via syringe. The SmI_2/THF solution (0.392 mmol, 2.6 mL) was then transferred via syringe to the solution of **21**. The reaction mixture was stirred at room temperature for 1 h, during which time the reaction went to completion (TLC, ethyl acetate/hexanes 1:9). To the reaction flask was then added saturated $NaHCO_3$ solution (20 mL) and the mixture extracted with ethyl acetate (4×20 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$ and the solvent removed by rotary evaporation to afford the crude VAPOL ligand **12**. The ligand was then purified by column chromatography on silica gel with a mixture of ethyl acetate/hexanes 1:19, which afforded the pure (*S*)-VAPOL product **12** (48 mg, 0.089 mmol, 91%). The optical purity of the recovered VAPOL was determined to be 99.8% *ee* by chiral HPLC analysis (Regis Pirkle Covalent D-Phenylglycine column, hexanes/2-propanol 75:25, 260 nm, flow rate 2 mL min^{-1}). Retention times: (*S*)-VAPOL = 18.54 min, (*R*)-VAPOL = 12.50 min.

Liberation of the VAPOL ligand via Curtius rearrangement[16]

Hydrolysis of the EDA adduct to acid 22: A 100 mL round-bottom flask was flame dried and cooled under argon and then the VAPOL–EDA adduct **21** (232 mg, 0.372 mmol) was introduced into the flask. The adduct was dissolved in ethanol (20 mL) and then 20% (w/v) aqueous solution of NaOH (20 mL) was added. This resulted in an instant color change from colorless to intense yellowish green. The reaction mixture was stirred at room temperature for 1 h. Thereafter, 1 N HCl (140 mL) was added to adjust the pH of the mixture to pH 1, upon which the product carboxylic acid **22** precipitated from the reaction mixture. The product was isolated by vacuum filtration and then dissolved in ethyl acetate. The filtrate was extracted once with ethyl acetate (30 mL) and the organic layers combined, washed with brine (2×30 mL), dried over $MgSO_4$ and then the solvent was removed via rotary evaporation to afford crude carboxylic acid product **22** as a yellow solid (217.2 mg, 0.36 mmol, 98%). ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 9.71$ (d, $J = 8.7$ Hz, 1H), 9.31 (d, $J = 8.1$ Hz, 1H), 7.92 (d, $J = 7.7$ Hz, 1H), 7.82 (d, $J = 8.7$ Hz, 1H), 7.71–7.64 (m, 3H), 7.47–7.64 (m, 7H), 7.43 (s, 1H), 7.04–7.13 (m, 2H), 6.95–7.04 (m, 4H), 6.78–6.86 (m, 4H), 6.51 (br s, 1H), 4.39 (d, $J = 15.7$ Hz, 1H), 4.29 ppm (d, $J = 15.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 171.64$, 154.63, 152.07, 142.32, 140.41, 139.76, 139.19, 135.15, 134.55, 133.10, 132.84, 130.40, 129.61, 129.23, 129.07, 129.02, 128.90, 128.86, 128.77, 128.53, 128.19, 128.08, 127.73, 127.71, 127.62, 127.30, 127.12, 127.05, 126.99, 126.84, 126.73, 126.63, 126.09, 126.03, 123.13, 123.01, 120.74, 119.92, 118.70, 115.25, 67.72 ppm (one sp^2 carbon not located).

Curtius rearrangement[16] of acid 22: A 25 mL round-bottom flask was flame dried and cooled under argon and then charged with crude carboxylic acid **22** (41.2 mg, 0.069 mmol). The solid was then dissolved by the addition of toluene (3 mL) and DMF (1 mL). This was followed by the addition of triethyl amine (11 μL, 0.079 mmol) and diphenylphosphoryl azide (DPPA, 15.7 μL, 0.072 mmol). The flask was then fitted with a water condenser and an argon balloon and the reaction mixture was refluxed for 3 h. After cooling down to room temperature, water (3 mL) was added via syringe and the reaction mixture was refluxed again for 2 h. After cooling to room temperature, 2 N HCl (5 mL) and ethyl acetate (10 mL) were added and the layers separated. The aqueous layer was extracted with ethyl acetate (2×10 mL), the organic layers combined, washed twice with brine, dried over $MgSO_4$ and the solvent evaporated by rotary evaporation to afford the crude reaction product. This crude product was then subjected to column chromatography on silica gel with ethyl acetate/hexanes 1:9 to afford (*S*)-VAPOL **12** (20.8 mg, 0.039 mmol, 56%, >99% *ee*) and lactone **23** (13.6 mg, 0.024 mmol, 34%). Spectral data for **23**: ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 9.29$–9.34 (m, 2H), 7.95–8.0 (m, 2H), 7.79–7.85 (m, 2H), 7.64–7.76 (m, 7H), 7.60 (s, 1H), 7.04–7.10 (m, 2H), 6.89–6.98 (m, 4H), 6.67 (d, $J = 7.1$ Hz, 2H), 6.54 (d, $J = 7.1$ Hz, 2H), 5.25 (d, $J = 13.5$ Hz, 1H), 4.92 ppm (d, $J = 13.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 166.31$, 154.25, 147.74, 140.45, 140.06, 139.24, 139.14, 135.03, 134.20, 133.47, 133.21, 129.21, 129.18, 129.12, 128.99, 128.94, 128.93, 128.84, 128.67, 128.37, 128.28, 127.83, 127.55, 127.49, 127.40, 127.25, 127.10, 127.01, 126.93, 126.82, 126.74, 122.01, 121.14, 71.29 ppm (four sp^2 carbons not located); IR (thin film): $\tilde{\nu}$ = 3055w,

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2920w, 1761 m, 1641 m cm^{-1}; MS: *m*/*z* (%): 578 (32) $[M]^+$, 295 (17), 294 (100), 221 (25).

Ethanolysis of lactone 23: A 25 mL round-bottom flask was flame dried and cooled under argon and then the crude reaction mixture (**12**+**23**) from the Curtius rearrangement reaction (77.8 mg, 0.0975 mmol (scale determined from the amount of the original starting material: the carboxylic acid **22**)) was added which was dissolved in EtOH (4 mL) and THF (1.2 mL) to obtain a clear yellow solution. To this mixture was added K_2CO_3 (134.7 mg, 0.975 mmol) and the reaction mixture stirred for 6 h to obtain a brownish green slurry at which point the TLC indicated complete disappearance of the lactone **23**. To this solution was then added 2 N HCl (5 mL) and diethyl ether (10 mL) and the layers separated. The aqueous layer was extracted with diethyl ether (2×10 mL), the organic layers combined and washed twice with brine, dried over $MgSO_4$ and the solvent removed by rotary evaporation to give the crude reaction mixture. This was then subjected to purification by column chromatography on silica gel with ethyl acetate/hexanes 1:19 to afford (*S*)-VAPOL **12** (26.1 mg, 0.042 mmol, 38%, >99% *ee*) and the VAPOL-EDA adduct **21** (26.7 mg, 0.05 mmol, 32%).

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