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Multicomponent Catalytic Asymmetric Synthesis of *trans*-Aziridines

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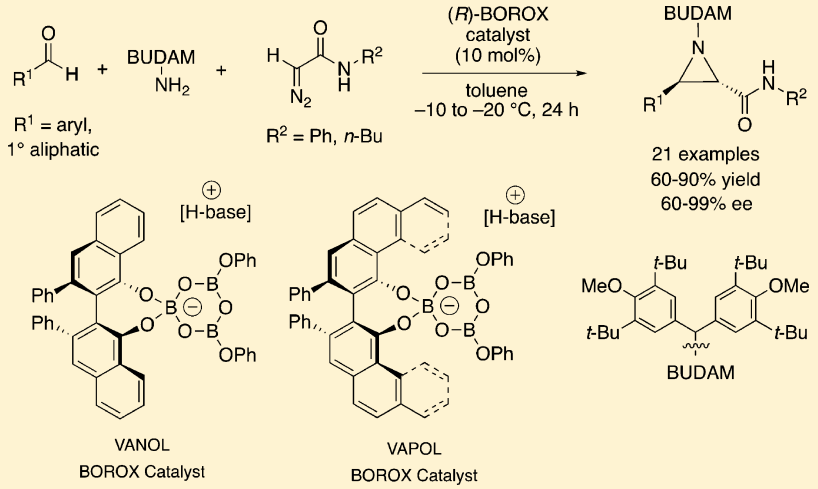
Supporting Information



ABSTRACT: A multicomponent *trans*-aziridination of aldehydes, amines, and diazo compounds with BOROX catalysts is developed. The optimal protocol is slightly different for aryl aldehydes than for aliphatic aldehydes. The key to the success with aryl aldehydes was allowing the catalyst, aldehyde, and amine to react for 20 min before addition of the diazo compound. A variety of 11 different electron-poor and electron-rich aryl aldehydes were screened to give *trans*-aziridines in 73−90% yield with 82−99% ee and *trans*/*cis* selectivities of 19:1 to >99:1. The optimal protocol for the *trans*-aziridination of aliphatic aldehydes did not require prereaction of the catalyst, aldehyde, and amine, and instead, the diazo compound could be added directly. The scope of the reaction is limited to unbranched aliphatic aldehydes and was tolerant of a number of functional groups including ethers, esters, epoxides, carbamates, and phthalimides. A total of 10 aliphatic aldehydes were examined and found to give *trans*-aziridines in 60−88% yield with 60−98% ee and *trans*/*cis* selectivities of 6:1 to >99:1. Alkenyl aldehydes did not react, but an alkynyl aldehyde gave a 71% yield and 95% ee of an aziridine that was found to be the *cis*- and not the *trans*-diastereomer. The aryl and aliphatic aldehydes both gave the *trans*-aziridines with the same absolute configuration with the same catalyst; however, in those cases where *cis*-aziridines were formed, the configuration was opposite for those formed from aryl versus aliphatic aldehydes.

1. INTRODUCTION

We have recently reported the development of the first catalytic asymmetric multicomponent synthesis of aziridines from an amine, an aldehyde, and a diazo acetate (Scheme 1).[1] This reaction gives *cis*-aziridines with high enantioselectivity with BOROX catalysts that can be generated from either the VANOL or VAPOL ligand by allowing the amine **1** to react with the ligand and triphenylborate at room temperature for 1 h. Once the catalyst is generated, the aldehyde and ethyl diazoacetate are rapidly added (in either order) to initiate the reaction, which gives the aziridine **4** with high diastereoselectivity for the *cis*-isomer (>50:1) and with excellent yields and enantioselectivity. The reaction can be extended to a variety of aryl and aliphatic aldehydes with the same high levels of *cis*-selection and enantioselection.

Whereas diazoacetate esters give *cis*-aziridines in their reactions with imines catalyzed by Brønsted or Lewis acids,[2,3] 2° diazo acetamides are known to react with imines to give *trans*-aziridines (Scheme 2).[4,5] We have carried out computational analysis of reactions of both a diazo acetate and a diazo acetamide with an imine and found that the origin of this diastereochemical switch is the result of an H-bonding interaction of the hydrogen on the amide nitrogen with the anionic core of the BOROX catalyst.[6] For *cis*-aziridination, the protonated imine **5a** and the ethyl diazoacetate **3** are both H-bonded to the chiral boroxinate anionic core in the transition state for carbon−carbon bond formation as indicated in Scheme 2. The iminium is hydrogen bonded to O-1 (1.94 Å), and the ethyl diazoacetate is H-bonded to O-2 via the hydrogen on the diazo carbon (1.99 Å). For *trans*-aziridination, the position of the two substrates is switched. It is now the diazo acetamide that is H-bonded to O-1 by the N−H moiety on the amide (1.94 Å), and in addition, the diazo acetamide is H-bonded to O-2 by the hydrogen on the diazo

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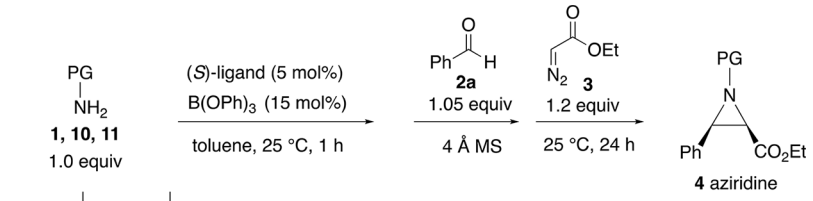
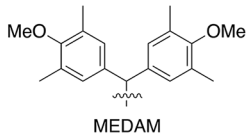
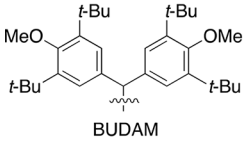
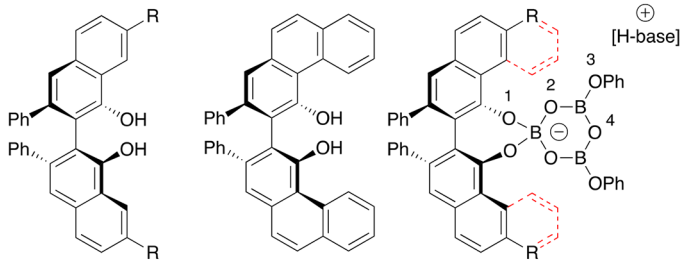
Scheme 1. Multi-component *cis*-Aziridination of Benzaldehyde



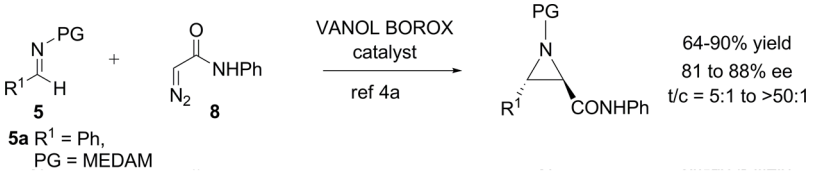


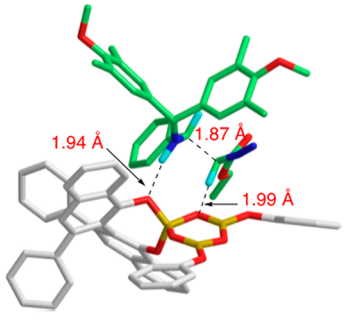
amine	PG	ligand	% yield	% ee	dr	ref	4
11	Ph_2CH	VAPOL	77	92	>50:1	1b	**4a**
11	Ph_2CH	VANOL	72	91	>50:1	1b	**4a**
1	MEDAM	VAPOL	98	98	>50:1	1a, 1b	**4b**
1	MEDAM	VANOL	95	95	>50:1	1b	**4b**
10	BUDAM	VAPOL	85	99	6:1	this work	**4c**
10	BUDAM	VANOL	91	97	8:1	this work	**4c**



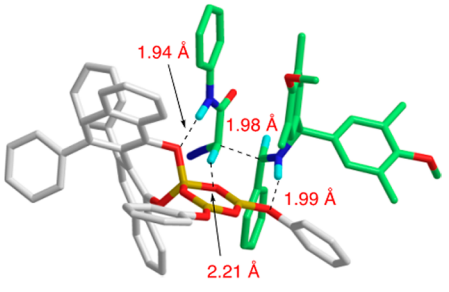


Scheme 2. *trans*-Aziridination of Imines with Diazo Acetamides and Initial Attempts Towards a Multicomponent Protocol

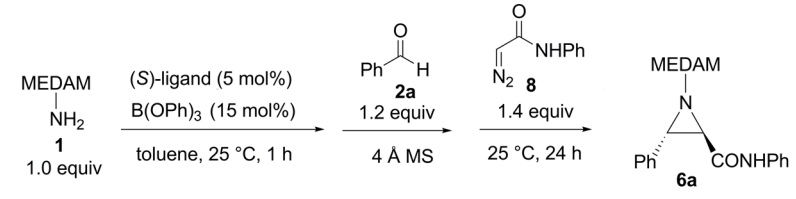




imine **5a** with ethyl diazoacetate **3**



imine **5a** with diazoacetamide **8**



ligand	% yield	% ee	trans:cis
VAPOL	67	73	2:1
VANOL	63	14	2:1

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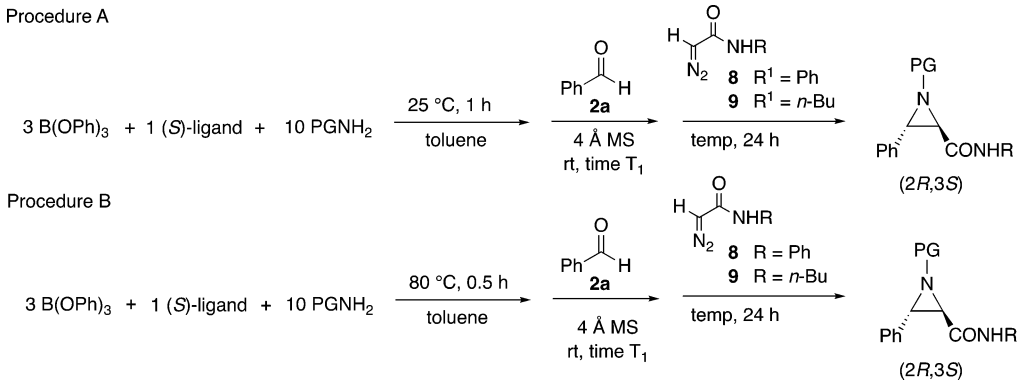
Table 1. Optimization of the Multicomponent *trans*-Aziridination of Benzaldehyde[a]



entry	proc	PG	ligand	R	temp (°C)	time T_1 (min)	aziridine	aziridine (% yield)[b]	aziridine (% ee)[c]	*trans*/*cis*[d]	% imine[e]
1	A	MEDAM	(*S*)-VANOL	Ph	23	0	**6a**	63	14	2:1	18
2	A	MEDAM	(*R*)-VAPOL	Ph	23	0	*ent*-**6a**	67	73	2:1	22
3	A	BUDAM	(*S*)-VANOL	Ph	23	0	**12a**	63	70	8:1	3
4	A	BUDAM	(*R*)-VAPOL	Ph	23	0	*ent*-**12a**	43	32	2:1	12
5	B	BUDAM	(*S*)-VANOL	Ph	23	0	**12a**	38	67	7:1	15
6[f]	A	BUDAM	(*S*)-VANOL	Ph	23	20	**12a**	50	73	7:1	5
7[g]	B	BUDAM	(*S*)-VANOL	Ph	23	20	**12a**	38	71	8:1	5
8	B	BUDAM	(*S*)-VANOL	*n*-Bu	23	0	**13a**	29	72	6:1	23
9	B	BUDAM	(*S*)-VANOL	Ph	−20	0	**12a**	(14)		13:1	59
10	**B**	**BUDAM**	**(S)-VANOL**	**Ph**	**−20**	**20**	**12a**	**90**	**92**	**18:1**	nd
11	B	BUDAM	(*R*)-^{t}Bu$_2$VANOL	Ph	−20	20	*ent*-**12a**	36	40	2:1	23
12	A	BUDAM	(*S*)-VANOL	Ph	−20	20	**12a**	80	95	19:1	nd
13	B	BUDAM	(*S*)-VANOL	*n*-Bu	−20	20	**13a**	43	86	8:1	21
14	B	MEDAM	(*R*)-VAPOL	Ph	−20	20	*ent*-**6a**	57	87	2:1	32
15[h]	B	MEDAM	(*R*)-VANOL	Ph	−20	20	*ent*-**6a**	63	87	4:1	nd
16[i]	B	MEDAM	(*R*)-^{t}Bu$_2$VANOL	Ph	−20	20	*ent*-**6a**	9	55	1:8	nd
17[j]	B	MEDAM	(*R*)-VANOL	*n*-Bu	−20	20	*ent*-**7a**	36	76	1:1.4	nd
18[k]	B	MEDAM	(*R*)-^{t}Bu$_2$VANOL	*n*-Bu	−20	20	*ent*-**7a**	8	89	1:9	nd
19	B	Ph$_2$CH	(*S*)-VANOL	Ph	−20	20	**14a**	62	69	4:1	20
20	B	Ph$_2$CH	(*R*)-VAPOL	Ph	−20	20	*ent*-**14a**	49	75	4:1	11

[a]Unless otherwise specified, all reactions were on a 0.2 mmol scale at 0.2 M amine in toluene with 10 mol % catalyst prepared by either procedure A or B with 1.2 equiv of aldehyde **2a** and 1.4 equiv of diazo compound. [b]Isolated yield of purified *trans*-aziridine. [c]Determined by HPLC. [d]Determined from the ^{1}H NMR spectrum of the crude reaction mixture. [e]Determined from the ^{1}H NMR spectrum of the crude reaction mixture with the aid of an internal standard. nd = not determined. [f]A 24% yield of an amino amide was isolated which resulted from opening of the aziridine at the benzylic carbon and was found to be 93% ee. [g]An 18% yield of an amino amide was isolated which resulted from opening of the aziridine at the benzylic carbon and was found to be 93%. [h]The *cis*-aziridine was isolated in 17% yield and 73% ee (Scheme 5). [i]The *cis*-aziridine was isolated in 75% yield and 95% ee (Scheme 5). [j]A 50% yield of *cis*-aziridine was isolated with 86% ee (Scheme 5). [k]A 73% yield of *cis*-aziridine was isolated with 91% ee (Scheme 5).

carbon (2.21 Å). The protonated imine is located remote from the ligand and is H-bonded to O-3 of a phenoxide ligand of the boroxinate core (1.99 Å). It is this reversal in the ordering of the substrates H-bonding to the boroxinate core that causes a flip in the face selectivity of bond formation to the imine carbon.

Given the differences in the mechanisms of the *cis*- and *trans*-aziridinations,[2b,6] it was not clear if the optimal procedure for the multicomponent *cis*-aziridination shown in Scheme 1 would be the optimal procedure for the multicomponent *trans*-aziridination. Indeed, it was not as can be seen from the data in Scheme 2. The yields were lower for both the VANOL and VAPOL boroxinate catalysts, and the *trans*/*cis* selectivities were not very high, but most distressing, the asymmetric inductions fell dramatically for the VANOL catalyst (95% ee to 14% ee). The drop-off for the VAPOL catalyst was not as drastic (98% ee to 73% ee) but, nonetheless, rendered this a less than desirable reaction.

2. RESULTS AND DISCUSSION

The first effort to optimize the multicomponent *trans*-aziridination reaction for aryl aldehydes was directed at exploring the use of the BUDAM protecting group on the nitrogen as it was found to be comparable or slightly better than the MEDAM group in *cis*-aziridination of imines (Scheme 1).[7] In the reaction of BUDAM amine **10**, a very unusual and interesting ligand effect was found between the VANOL and VAPOL ligands. With the MEDAM amine, the VAPOL catalyst was superior to the VANOL catalyst (Table 1, entries 1 vs 2), whereas with the BUDAM amine the situation was reversed with the VANOL catalyst being superior (entries 3 vs 4). Dropping the temperature from ambient to −20 °C resulted in a significant slowing of the reaction with only a 14% yield (by NMR) of the aziridines **12a** (entries 5 vs 9). However, if the catalyst was allowed to interact with the amine and the aldehyde with a curing time of 20 min prior to the addition of the diazo compound, the aziridine could be isolated in 90% yield with 92% ee at −20 °C

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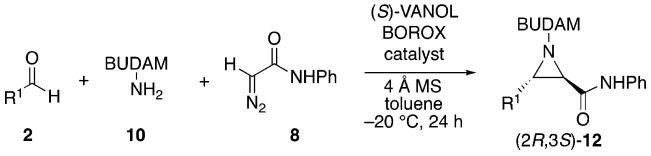
(entry 10). In the diazo substrate, an *N*-phenyl substituent was found to be superior to an *N*-butyl substituent (entries 10 vs 13). Procedure A gave a lower yield under the optimal conditions, although the asymmetric induction was a bit higher (entries 10 vs 12). The pairing of the MEDAM amine with the VAPOL catalyst was not as efficient as the pairing of the BUDAM amine and the VANOL catalyst under the optimal conditions (entries 10 vs 14). Finally, benzhydrylamine was not very effective when paired with either the VANOL or VAPOL catalyst (entries 19 and 20). The 7,7′-di-*tert*-butyl VANOL ligand **5b** was significantly less effective than the VANOL ligand **5a** (entries 10 vs 11). This was unexpected since this ligand was superior to VANOL in the *cis*-aziridination reactions.[1c] In fact, it was interesting to observe that the *cis*-aziridine was the major diastereomer when 7,7′-di-*tert*-butyl VANOL ligand **5b** and the MEDAM group were employed (entries 16 and 18).

The scope of the multicomponent aziridination of aryl aldehydes is summarized by the data in Table 2. A variety of

Table 2. Scope of the Multicomponent *trans*-Aziridination with Aryl Aldehydes[a]



2 **10** **8** (2*R*,3*S*)-**12**

entry	series	R^1	*trans*/*cis*[b]	% yield **12**[c]	% ee**12**[d]
1	a	C_6H_5	18:1	90	92
2[f]	b	2-naphthyl	62:1	82	92
3	c	1-naphthyl	>99:1	88	87
4	d	4-$AcOC_6H_4$	25:1	82	>99
5	e	4-$MeOC_6H_4$	1.3:1	9[e]	nd
6[f]	f	4-MeC_6H_4	19:1	73	85
7	g	2-MeC_6H_4	>99:1	85	93
8	h	4-BrC_6H_4	23:1	82	96
9	i	3-BrC_6H_4	27:1	89	95
10	j	2-BrC_6H_4	19:1	86	93
11	k	4-CF3C6H4	31:1	78	96
12	l	4-$NO_2C_6H_4$	29:1	16[g]	nd
13	m	4-$CO_2MeC_6H_4$	42:1	89	>99
14	n	4-CNC_6H_4	13:1	8[h]	nd

[a]Unless otherwise specified, all reactions were performed on a 0.2 mmol scale at 0.2 M amine in toluene with 1.2 equiv aldehyde and 1.4 equiv diazo compound with 10 mol % catalyst with procedure B under the conditions of entry 10 of Table 1. [b]Determined from the ^{1}H NMR spectrum of the crude reaction mixture. [c]Isolated yield of purified *trans*-aziridine. [d]Determined by HPLC. nd = not determined. [e]A 76% yield of imine was observed by NMR. [f]Precatalyst is subjected to high vacuum for 30 min. [g]A 52% yield of the imine from **2l** and **10** was observed in the ^{1}H NMR spectrum of the crude reaction mixture. [h]A 66% yield of the imine from **2n** and **10** was observed in the ^{1}H NMR spectrum of the crude reaction mixture.

electron-rich and electron-poor aromatic aldehydes were found to be effective in giving high selectivity for *trans*- over *cis*-aziridines in high yields and excellent asymmetric inductions employing the optimal conditions given in entry 10 of Table 1. The reaction of 4-methoxybenzaldehyde **2e** is very slow, and only a 9% yield of aziridines **12e** could be detected along with a 76% yield of the imine from **2e** and **10** by ^{1}H NMR (Table 2, entry 5). However, the acetoxy group in aldehyde **2d** could serve as a surrogate for the methoxy group in aldehyde **2e** since aldehyde **2d** gave the *trans*-aziridine **12d** in 82% yield and >99% ee with a 25:1 selectivity for the *trans*-isomer (entry 4). Both the *p*-nitro- and *p*-cyanobenzaldehydes **2l** and **2n** were very slowly converted to *trans*-aziridines (Table 2, entries 12 and 14). This is in contrast to the *p*-(trifluoromethyl)- and *p*-(carbomethoxy)benzaldehydes **2k** and **2m**, which also have electron-withdrawing groups in the *para*-position but, nonetheless, gave the aziridines **12k** and **12m** in high yields with excellent inductions (entries 11 and 13). At this point, the failure of *p*-nitro- and *p*-cyanobenzaldehydes to significantly react under the optimum conditions is not understood. There is also the interesting observation that while an *o*-bromo substitutent on benzaldehyde gives a lower induction than the *p*-bromo isomer (93% ee vs 96% ee, entries 10 vs 8), the reverse is true for the corresponding methyl derivatives. *o*-Methylbenzaldehyde gives higher inductions that the *para*-isomer (93% ee vs 85% ee, entries 7 vs 6).

The optimal conditions for the *trans*-aziridinations of aryl aldehydes did not directly translate to the *trans*-aziridinations of aliphatic aldehydes. The optimization studies were carried out on hexadecanal **15a**, and the results are presented in Table 3. The optimal temperature for this reaction was −10 °C, and applying the optimized conditions obtained for benzaldehyde (entry 10 of Table 1) led to aziridine **19a** in 78% yield and 88% ee (Table 3, entry 9). Note that, as was the case with benzaldehyde, not allowing the catalyst and amine and aldehyde to react for 20 min prior to adding the diazo acetamide was deleterious to the yield and induction for the *trans*-aziridines **19a** (Table 3, entries 8 vs 9). However, the drop in yield and induction with benzaldehyde was far greater than that for hexadecanal if the catalyst and amine and aldehyde were not allowed to react before the diazo acetamide was added (Table 1, entries 9 vs 10). The final key to the optimization was the finding that *N*-butyl diazo acetamide **9** was superior to the *N*-phenyl analogue (entries 6 vs 8). The reaction with *N*-butyl diazo acetamide **9** was surprisingly found to be essentially unaffected by whether or not the formation of the imine was allowed to occur before the addition of the diazo compound (entries 6 vs 7). It was also found that, with the aliphatic aldehyde **15a**, both the VAPOL and tBu_2VANOL ligands gave excellent results when paired with the BUDAM amine but not quite as good as the VANOL ligand (entries 6, 10, and 11). This was quite surprising given the large difference in the VANOL and tBu_2VANOL catalysts with benzaldehyde (Table 1, entries 10 and 11). All three ligands were slightly less satisfactory when paired with the MEDAM amine **1** (entries 3−5). The reactions with benzhydryl amine **11** were much slower and gave low yields even though they went to ∼90% completion for both the VANOL and tBu_2VANOL ligands (entries 1 and 2). We have recently shown that the multicomponent *cis*- and *trans*-aziridination of hexadecenal **15a** can be used in the syntheses of all four stereoisomers of sphinganine.[8]

The substrate scope of the multicomponent *trans*-aziridination with aliphatic aldehydes is shown in Table 4. Unless otherwise specified, the results were obtained under the optimized conditions indicated in entry 6 of Table 3 for aldehyde **15a**. The reactions in Table 4 were run on a 0.2 mmol scale with 10 mol % catalyst, and in all cases, the yield is of the isolated and purified *trans*-isomer. The aziridination of aldehyde **15a** was also run on a 15-fold larger scale and gave the aziridine **18a** in 88% yield with a 28:1 *trans*/*cis* selectivity and the same asymmetric induction as on a 0.2 mmol scale (Table 4, entry 1). The biggest take-away from the data in Table 4 is that the aziridination of unbranched aldehydes is best performed by the multicomponent method, but for branched aldehydes the best method involves

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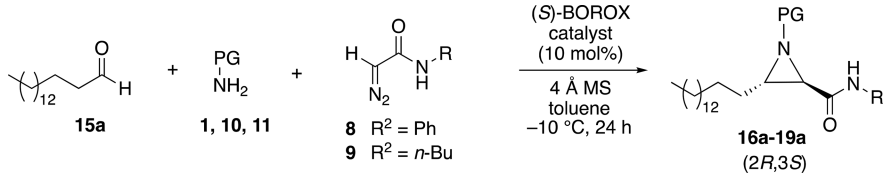
Table 3. Optimization of the Multicomponent Aziridination with the Aliphatic Aldehyde 15a[a]



entry	amine	PG	ligand	R	aziridine	*trans*/*cis*[b]	% yield trans aziridine[c]	% ee trans aziridine[d]
1	**11**	Ph_2CH	(*S*)-VANOL	*n*-Bu	**16a**	14:1	33 (30)[e]	77
2	**11**	Ph_2CH	(*R*)-tBu_2VANOL	*n*-Bu	*ent*-**16a**	14:1	45 (36)[f]	33
3	**1**	MEDAM	(*R*)-VANOL	*n*-Bu	*ent*-**17a**	6:1	66	86
4	**1**	MEDAM	(*S*)-VAPOL	*n*-Bu	**17a**	15:1	79	86
5	**1**	MEDAM	(*R*)-tBu_2VANOL	*n*-Bu	*ent*-**17a**	0.9:1	40[g]	92[h]
6	**10**	**BUDAM**	**(*S*)-VANOL**	***n*-Bu**	**18a**	**24:1**	**85**	**96**
7[i]	**10**	BUDAM	(*S*)-VANOL	*n*-Bu	**18a**	21:1	88	96
8	**10**	BUDAM	(*S*)-VANOL	Ph	**19a**	6:1	70	68
9[i]	**10**	BUDAM	(*S*)-VANOL	Ph	**19a**	12:1	78	88
10	**10**	BUDAM	(*S*)-VAPOL	*n*-Bu	**18a**	14:1	91	91
11	**10**	BUDAM	(*R*)-tBu_2VANOL	*n*-Bu	*ent*-**18a**	17:1	71	90

[a]Unless otherwise specified, all reactions were performed with 0.2 M amine in toluene with 0.2 mmol of amine, 1.1 equiv of **15a**, and 1.2 equiv of diazo compound with 10 mol % catalyst, which was prepared by procedure B in Table 1 with T^1 = 0 min. [b]Determined by ^{1}H NMR analysis of the crude reaction mixture. [c]Isolated yield of purified *trans*-aziridine. Yields in parentheses are ^{1}H NMR yields with internal standards. [d]Determined on purified *trans*-aziridine by HPLC. [e]Reaction went to 87% conversion. [f]Reaction went to 92% conversion. [g]Isolated yield of *cis*-aziridine is 45%. [h]The *cis*-aziridine was 93% ee. [i]The catalyst was stirred with the aldehyde and imine for 20 min before the diazo compound was added.

the prior preparation of the imine as previously reported.[4a] This is best illustrated in the reaction of α,α-branched aldehyde pivaloyl aldehyde **15l** (entry 12). Under the optimal conditions where the aldehyde, amine and the diazo compound are added at the same time, aziridination product **18l** is not observed. However, if the catalyst is allowed to interact with the amine and aldehyde **15l** for 20 h before the addition of the diazo compound, then aziridine **18l** can be isolated in 61% yield and 76% ee. However, this still does not match the results from the reaction of the preformed imine where aziridine **23** can be isolated in 89% yield and 90% ee (Scheme 3).[4a] The situation with the α-branched cyclohexane carboxaldehyde **15k** is similar. The reaction does proceed without a delay time for imine formation but only gives a 45% yield of **18k** with 28% ee. The use of a 20 min delay time does improve the yield to 61%, but the asymmetric induction falls to 8% ee. As was the case for α,α-dibranched aldehydes, the synthesis of aziridines from α-branched aldehydes is best realized via the preformed imine (Scheme 3).[4a] The reaction also does not proceed with the enal **15m**, but the ynal **15n** gives a high yield of the aziridine **19n** with excellent asymmetric induction (entry 14). The ynal **15n** gives the *cis*- instead of the *trans*-aziridine product, and the same switch in diastereoselectivity was also observed for the preformed imine.[5] A rationale for this switch was proposed to arise from the preferential reaction of the *Z*-imine for alkynyl aldehydes and the *E*-imines for other aldehydes.[5]

The multicomponent *trans*-aziridination of unbranched aliphatic aldehydes is fairly tolerant of a number of functional groups including silyl ethers, esters, epoxides, Boc-protected amines, and phthalimides. The cyano function, on the other hand, seems to negatively impact the reactions as aldehyde **15d** can be converted to aziridines **18d** with low asymmetric induction. The *trans*/*cis* selectivities are generally quite high as indicated by the data in Table 4, and for a few substrates (**15c** and **15d**), the *trans*/*cis* selectivity could not be determined due to overlap of key peaks in the ^{1}H NMR spectrum of the crude reaction mixtures. There does not seem to be an ideal ligand for these reactions since, in the 10 cases where they are directly compared, VANOL **5a** gives the highest asymmetric induction for five and *t*-Bu_2VANOL **5b** gives the highest asymmetric induction for five. Finally, the aziridination of epoxide **15b** was carried out on racemic material, but there does not seem to be a matched or mismatched interaction between the substrate and the catalyst since, after the *trans*- and *cis*-aziridines were separated, the *trans*-aziridine **18b** was a 49:49:1:1 mixture of isomers.

3. ABSOLUTE STEREOCHEMISTRY

The determination of the absolute configuration of the aryl-substituted *trans*-aziridine **6a** (Table 1, from benzaldehyde) with a MEDAM substituent on the nitrogen had been previously reported, and the aziridines from the other aryl aldehydes shown in Table 2 were assumed to be homochiral.[4a] The absolute stereochemistry of the aliphatic substituted *trans*-aziridine *ent*-**18a** (Table 3, entry 11, from hexadecanal) with a BUDAM substituent generated from the (*R*)-tBu_2VANOL BOROX catalyst was confirmed by its conversion to L-*erythro*-sphinganine,[8] and the rest of the *trans*-aziridines in Table 4 were assumed to be homochiral. In a control, it was verified, as expected, that the absolute configuration of the aziridine was the same whether the nitrogen protecting group was MEDAM or BUDAM. The protecting groups in the aziridines *ent*-**18a** and *ent*-**17a** were both removed with triflic acid to give the same enantiomer of the N–H aziridines **28a** (Scheme 4). Thus, the *trans*-isomers of aziridines from both aliphatic and aromatic aldehydes have the same absolute configuration. However, the same was not found to be true for the *cis*-isomers (usually minor) from aliphatic and aromatic aldehydes.

We had previously isolated the minor *cis*-isomer of the *trans*-aziridination of the imine **24** from benzaldehyde with the diazo acetamide **8** with a VANOL BOROX catalyst and found that the *cis*-isomer **25a** produced by the (*S*)-VANOL catalyst had the 2*R*,3*R* configuration (Scheme 4).[4a] The same was found to be the case in the present work on multicomponent *trans*-aziridinations

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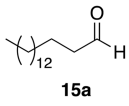
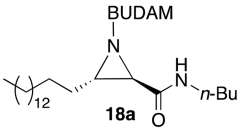
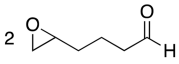
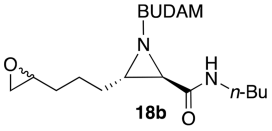
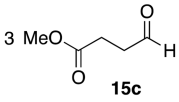
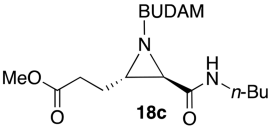
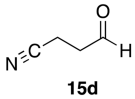
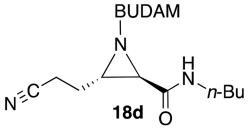
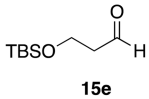
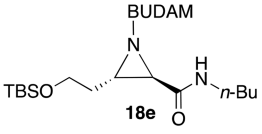
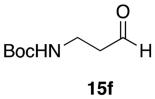
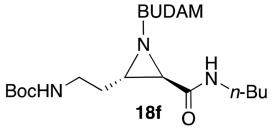
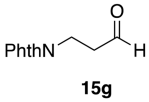
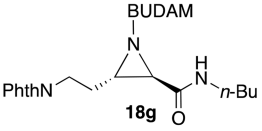
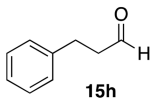
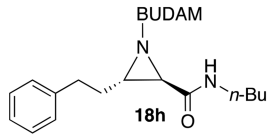
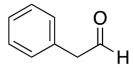
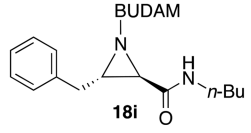
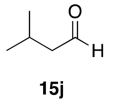
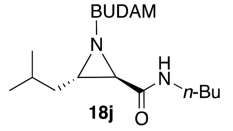
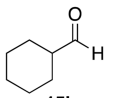
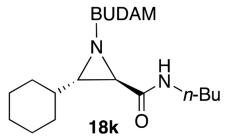
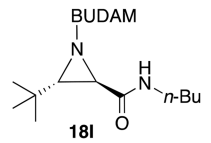
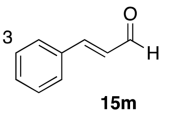
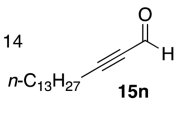
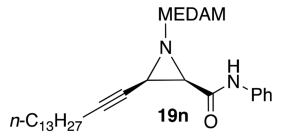
Table 4. Asymmetric Catalytic Multicomponent frans-Aziridinaton of Aliphatic Aldehydes[a]

entry	aldehyde	ligand	aziridine yield [b]	% ee [c]	trans/cis [d]
1	 **15a**	 **18a**			
		(*S*)-VANOL	88 [e]	96	28 : 1
		(*R*)-*t*-Bu$_2$VANOL	71	–90	17 : 1
2	 (±)-**15b**	 **18b**			
		(*S*)-VANOL	90	96	8 : 1 [f]
		(*R*)-*t*-Bu$_2$VANOL	62	–98	17 : 1 [g]
3	 **15c**	 **18c**			
		(*S*)-VANOL	78	86	nd
		(*R*)-*t*-Bu$_2$VANOL	59	–93	nd
4	 **15d**	 **18d**			
		(*S*)-VANOL	88	40	nd
		(*R*)-*t*-Bu$_2$VANOL	51	–60	nd
		(*R*)-VAPOL	61	–47	nd
5	 **15e**	 **18e**			
		(*S*)-VANOL	60	96	>99 : 1
		(*R*)-*t*-Bu$_2$VANOL	56	–98	>99 : 1
6	 **15f**	 **18f**			
		(*S*)-VANOL	67	85	25 : 1
		(*R*)-*t*-Bu$_2$VANOL	68	–88	10 : 1
7	 **15g**	 **18g**			
		(*S*)-VANOL	71	91	6 : 1
		(*R*)-*t*-Bu$_2$VANOL	64	–60	6 : 1
8	 **15h**	 **18h**			
		(*S*)-VANOL	87	98	45 : 1
		(*R*)-*t*-Bu$_2$VANOL	77	–73	nd
9	 **15i**	 **18i**			
		(*S*)-VANOL	71	88	19 : 1
		(*R*)-*t*-Bu$_2$VANOL	86	–96	27 : 1
10	 **15j**	 **18j**			
		(*S*)-VANOL	88	95	12 : 1
		(*R*)-*t*-Bu$_2$VANOL	70	–75	19 : 1
11	 **15k**	 **18k**			
		(*S*)-VANOL	45	28	12 : 1
		(R)-VAPOL	56	–57	—
		(*S*)-VANOL [h]	61	8	—
		(*S*)-VANOL [h,i]	32	34	—
12	 **15l**	 **18l**			
		(*S*)-VANOL	no reaction		
		(*S*)-VANOL [j]	7	42	nd
		(*S*)-VANOL [k]	61	76	nd
13	 **15m**				
		(*S*)-VANOL	no reaction		
14	 **15n**	 **19n**			
	0 °C	(*R*)-VANOL	92	91	cis only
	–20 °C	(*R*)-VANOL	71	95	cis only

[a]Unless otherwise specified, all reactions were run with 1.2 equiv of **9** and 1.1 equiv of **15** in the presence of 4 Å MS with 10 mol % catalyst under the conditions in entry 6 of Table 3. [b]Isolated yield of purified *trans*-aziridine. [c]Determined by HPLC on isolated aziridine. The use of an (*R*)-ligand gives the enantiomer of the aziridine shown. [d]Determined by ^{1}H NMR analysis of the crude reaction mixture. nd means not determined. [e]Reaction run on 3 mmol scale. [f]The isolated *trans*-isomer is a 49:49:1:1 mixture of isomers. [g]The isolated *trans*-isomer is a 49.5:49.5:0.5:0.5 mixture of isomers. [h]The diazo compound **9** was added 20 min after the aldehyde as indicated in Table 1. [i]The MEDAM amine **1** was used. [j]The diazo compound **9** was added 30 min after the aldehyde as indicated in Table 1. [k]The diazo compound **9** was added 20 h after the aldehyde as indicated in Table 1.

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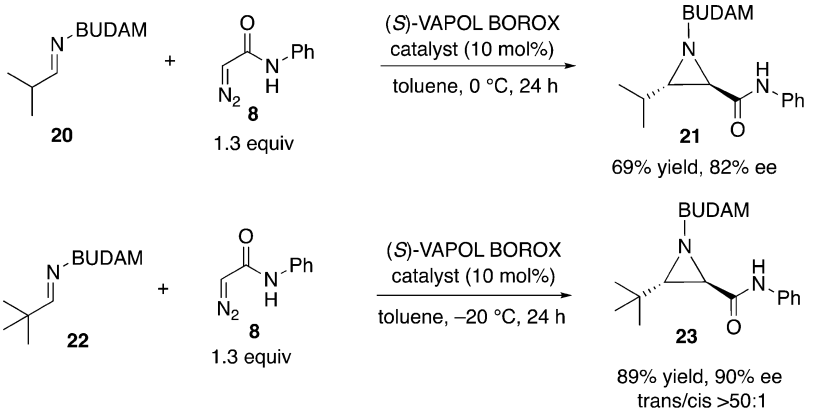
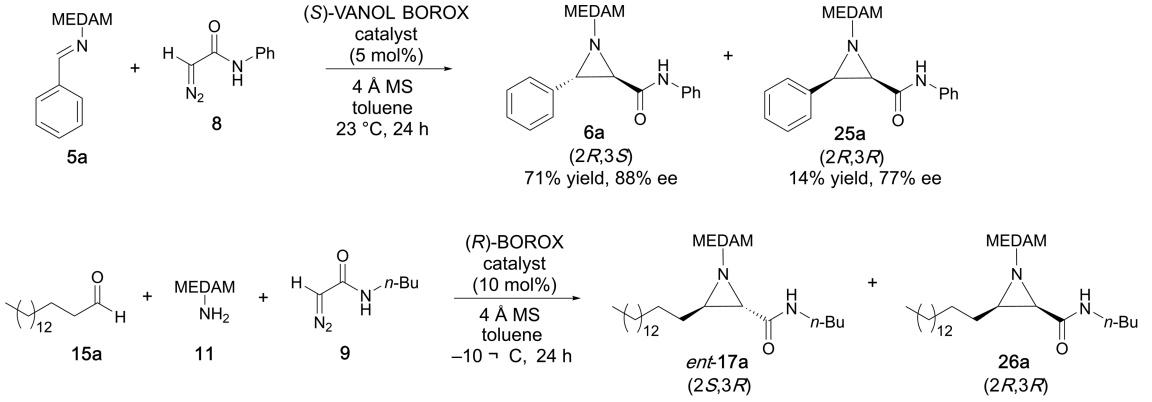
Scheme 3. Absolute Stereochemistry of Preformed Imines with Branched Aliphatic Aldehydes

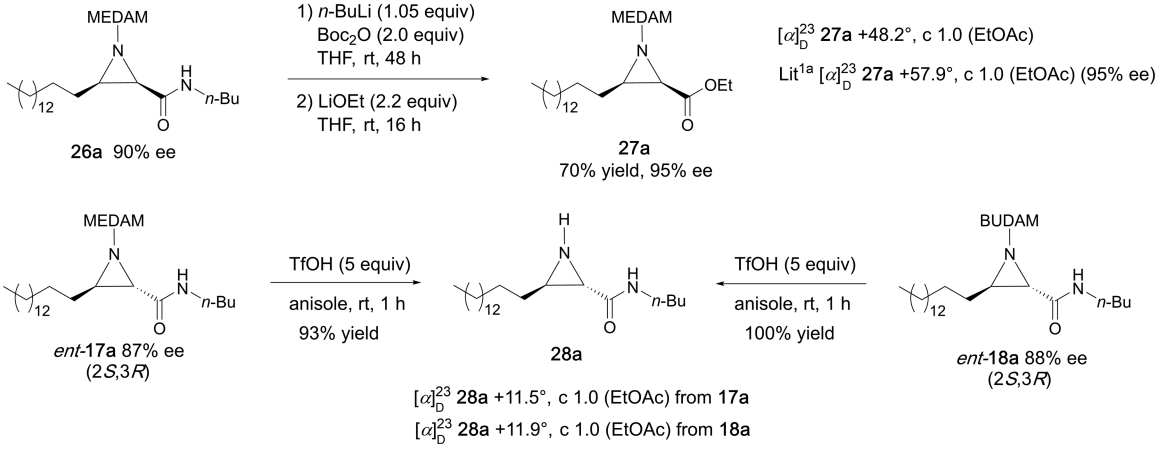


Scheme 4. Absolute Stereochemistry of *trans*- and *cis*-Aziridines from Aliphatic Aldehyde 15a



entry	ligand	% yield *ent*-**17a** [a]	% ee *ent*-**17a** [b]	$[\alpha]_D^{23}$ *ent*-**17a** [c]	% yield **26a** [a]	% ee **26a** [b]	$[\alpha]^{23}$ **26a** [c]	trans:cis
1	(*R*)-VANOL	66	86	+16.1° c 1.0	11	87	+13.9° c 1.0	6:1
2	(*R*)-tBu$_2$VANOL	40	92	+17.0° c 1.0	45	93	+15.1° c 1.0	0.9:1

Reactions were performed with 0.2 M amine in toluene with 0.6 mmol of amine (0.2 mmol for entry 2) and 1.1 equiv of **15a** and 1.2 equiv of diazo compound with 10 mol% catalyst which was prepared by Procedure B in Table 1 with T^1 = 0 min; nd = not determined.
[a] Isolated yield. [b] Determined by HPLC. [c] Optical rotations in CH_2Cl_2.



where the 2*S*,3*S* configuration of **25a** was produced with an (*R*)-BOROX catalyst (Scheme 5). This is opposite to the configuration of the minor *cis*-isomer isolated from the BOROX-catalyzed reaction of aldehyde **15a** found in the present work. The absolute stereochemistry of the *cis*-isomer **26a** produced with the BOROX catalyst generated from (*R*)-7,7′-di-*tert*-butylVANOL ligand **5b** was shown to have the (2*R*,3*R*)-configuration by converting the amide **26a** to the known ester

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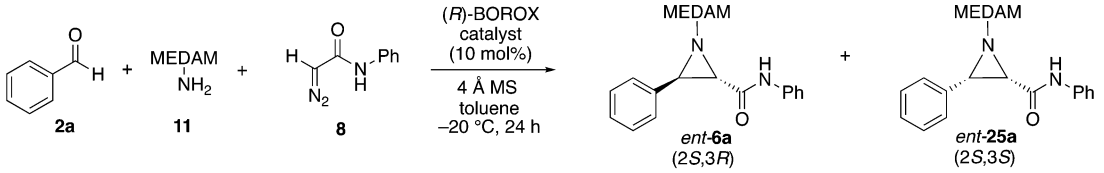
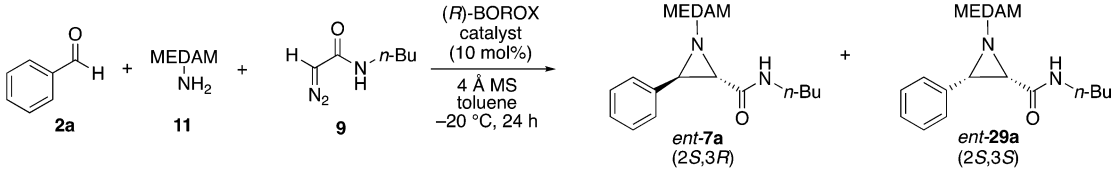
Scheme 5. Absolute Stereochemistry of *trans*- and *cis*-Azididines from Benzaldehyde 2a



entry	ligand	% yield *ent*-**6a** [a]	% ee *ent*-**6a** [b]	$[\alpha]_D^{23}$ *ent*-**6a** [c]	% yield *ent*-**25a** [a]	% ee *ent*-**25a** [b]	$[\alpha]_D^{23}$ *ent*-**25a** [c]
1	(*R*)-VANOL	63	87	–4.6° c 1.0	17	73	–13.6° c 1.0
2	(*R*)-tBu$_2$VANOL	9	55	–3.1° c 1.0	75	95	–26.2° c 1.0

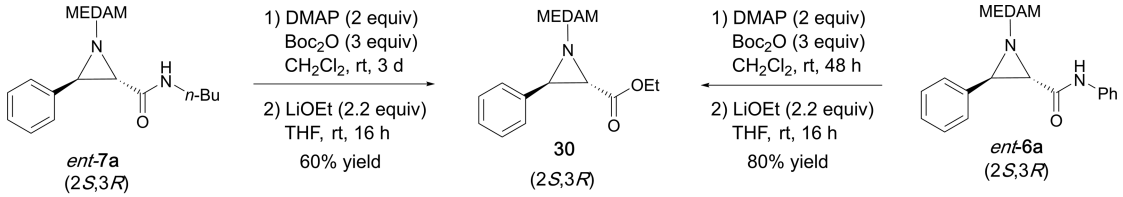
Both reactions were performed with 0.2 M amine in toluene with 0.2 mmol of amine and 1.1 equiv of **2a** and 1.2 equiv of diazo compound with 10 mol% catalyst which was prepared by Procedure B in Table 1 with T^1 = 20 min. [a] Isolated yield. [b] Determined by HPLC. [c] Optical rotations in EtOAc.



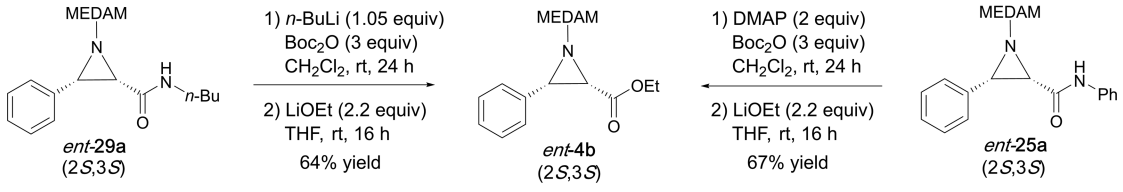
entry	ligand	% yield *ent*-**7a** [a]	% ee *ent*-**7a** [b]	$[\alpha]_D^{23}$ *ent*-**7a** [c]	% yield *ent*-**29a** [a]	% ee *ent*-**29a** [b]	$[\alpha]_D^{23}$ *ent*-**29a** [c]
3	(*R*)-VANOL	36	76	+20.0° c 1.0	50	86	–6.6° c 1.0
4	(*R*)-tBu$_2$VANOL	8	89	+22.9° c 1.0	73	91	–7.5° c 1.0

Both reactions were performed with 0.2 M amine in toluene with 0.2 mmol of amine and 1.1 equiv of **2a** and 1.2 equiv of diazo compound with 10 mol% catalyst which was prepared by Procedure B in Table 1 with T^1 = 20 min. [a] Isolated yield. [b] Determined by HPLC. [c] Optical rotations in EtOAc.

Scheme 6. Chemical Correlation of the Stereochemistry of the *trans*- and *cis*-Aziridines from Benzaldehyde 2a and Diazoacetamides 8 and 9



$[\alpha]_D^{23}$ **30** +3.1°, c 1.0 (EtOAc) from *ent*-**13a**
$[\alpha]_D^{23}$ **30** +5.6°, c 1.0 (EtOAc) from *ent*-**4a**
Lit[4a] $[\alpha]^{23}$ **30** –4.4¬ , c 1.0 (EtOAc) (90% ee) from (*S*)-VANOL



$[\alpha]_D^{23}$ **31** –26.2¬ , c 1.0 (EtOAc) from *ent*-**25a** (95% ee)
$[\alpha]_D^{23}$ **31** –24.1¬ , c 1.0 (EtOAc) from *ent*-**29a** (91% ee)
Lit[2a] $[\alpha]_D^{23}$ **31** +41.3°, c 1.0 (EtOAc) (99% ee) from (*S*)-VANOL

27a.[1a] It was thought that the difference may be due to that between and aryl and aliphatic substrates; however, it could also be due to the difference between the VANOL and *t*-Bu$_2$VANOL ligand since large swings in the relative stereochemistry (*trans*/*cis* ratios) were seen between these two ligands (Table 1, entries 15−18, Table 3, entries 3 and 5). Thus, we decided to examine the absolute stereochemistry of *cis*- and *trans*-aziridines produced from catalysts generated from both VANOL and *t*-Bu$_2$VANOL

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(Scheme 4). As can been seen from the data in Scheme 4, the absolute stereochemistry of both the *trans*- and *cis*-aziridines *ent*-**17a** and **26a** are the same with catalysts generated from both ligands.

Large changes in the ratios of *trans*- and *cis*-aziridines were also observed between VANOL and tBu_2VANOL ligands with benzaldehyde, and thus, it was then deemed prudent to check the absolute configuration of the *trans*- and *cis*-diastereomers from each catalyst, and this was done with both the diazo acetamides **8** and **9** (Scheme 5). The absolute configuration of *ent*-**6a** from the *N*-phenyl diazo acetamide **8** was established as (2*S*,3*R*) on the basis of previous studies on aziridine **6a**.[4a] In the present study, it is shown that the absolute configuration of *trans*-aziridine **6a** is independent of whether the catalyst is prepared from VANOL **5a** or *t*-Bu_2VANOL **5b** (Scheme 5). The same is true for the formation of *cis*-aziridine **25a** from the *N*-phenyl diazo acetamide **8**. It was also found that there is no difference between the ligands on the absolute configuration of both *trans*- and *cis*-aziridines **13a** and **29a** from the reaction of *N*-butyl diazoacetamide **9**.

Finally, it was shown that the nature of the *N*-substituent on the diazo acetamide (phenyl vs *n*-butyl) is not responsible for any change in the stereochemistry from the multicomponent *trans*-aziridination of benzaldehyde for either the major or minor diastereomers (trans or cis). This was done by chemical correlation with the conversion of *N*-butyl aziridine amide *ent*-**7a** and *N*-phenyl aziridine amide *ent*-**6a** to known aziridinyl ester **30**,[4a] hence establishing the homochiral nature of *ent*-**7a** and *ent*-**6a** as well as the absolute configuration of both (Scheme 6). A similar chemical correlation allowed for the assignment of the relative and absolute stereochemistry of *N*-phenyl *cis*-aziridine amide *ent*-**25a** and *N*-butyl *cis*-aziridine amide *ent*-**29a** via known aziridinyl ester **31**.[2a] The overall finding of these chemical assignments is that the stereochemical outcome of the multicomponent *trans*-aziridination is that the *same absolute configuration* is observed for the major *trans*-diastereomers of the aziridines from both aliphatic and aromatic aldehydes, but the *opposite absolute configuration* is observed for the minor *cis*-diastereomers of the aziridines from aliphatic and aromatic aldehydes.

4. CONCLUSIONS

The goal of the present work was to develop a multicomponent *trans*-aziridination of aldehydes, amines, and α-diazo carbonyl compounds. We had previously developed a multicomponent *cis*-aziridination of aldehydes, amines, and α-diazo carbonyl compounds with a BOROX catalyst; however, application of the optimal conditions for the *cis*-aziridination to the *trans*-aziridination for aryl aldehydes resulted in poor asymmetric inductions and very low *trans*/*cis* selectivities. After considerable effort, it was found that the key to the optimization was to allow the aryl aldehyde, the amine, and the catalyst to interact for 20 min before exposure to the diazo compound. Final tweaking of the conditions lead to the use of the bis(3,5-di-*tert*-butyl-4-methoxyphenyl)methylamine (BUDAM amine), the VANOL BOROX catalyst, and *N*-phenyl diazoacetamide. The scope of the multicomponent *trans*-azirdination of aryl aldehydes was determined to be quite broad, giving high asymmetric induction, yields, and *trans*-selectivities for a variety of electron-rich and electron-poor aryl aldehydes.

The optimization of the multicomponent *trans*-aziridination of aliphatic aldehydes did not follow directly from the optimized protocol for aryl aldehydes. In this case, it was found that *N*-butyl diazoacetamide gave the optimal results with BUDAM amine. Furthermore, it was found that it was not necessary to react the aldehyde, catalyst, and amine for 20 min prior to addition of the diazo compound. The scope of the reaction is limited to unbranched aliphatic aldehydes as α-branched and α,α-dibranched aldehydes give low yields and inductions. Thus, for branched aliphatic aldehydes the aziridination is best performed on preformed imines since they give high yields, asymmetric inductions, and *trans*/*cis* selectivity. The scope of the multicomponent *trans*-aziridination of unbranched aliphatic aldehydes is quite broad and will tolerate a range of functional groups including ethers, esters, epoxides, carbamates, and phthalimides. Here, both the VANOL and VAPOL BOROX catalysts are effective and the proper choice can be used to optimize a particular aldehyde. Enals are not effective as aldehyde substrates, but ynals are but give *cis*-aziridines in contrast to aryl and aliphatic aldehydes, which give *trans*-aziridines.

With regard to absolute stereochemistry, the major *trans*-aziridines from aryl and aliphatic aldehydes give the same absolute stereochemistry with the same catalyst. However, the minor *cis*-aziridines from aryl aldehydes have the opposite absolute configuration as the minor *cis*-aziridines from aliphatic aldehydes.

5. EXPERIMENTAL SECTION

5.1. General Information. All experiments were performed under an argon atmosphere. Flasks were flame-dried and cooled under argon before use. All solvents used were dried appropriately. Toluene, dichloromethane, and acetonitrile were dried from calcium hydride under nitrogen. THF was dried from sodium with benzophenone as the indicator under nitrogen. The ligands VAPOL, VANOL, and 7,7′-di-*tert*-butylVANOL were prepared according to the published procedure.[1c] Phenol was sublimed and stored under argon in a dry desiccator; each batch was used for a maximum of 20 days. The commercially available aldehydes were purchased from Aldrich or other commercial sources and purified appropriately before use. Solid aldehydes were sublimed, and liquid aldehydes were distilled. The aldehydes were stored under argon; each batch was used for a maximum of 5 days. Benzhydrylamine was purchased from Aldrich and distilled before use. The tetramethyldianisylmethyl (MEDAM) amine and the tetra-*tert*-butyldianisylmethyl (BUDAM) amine were prepared according to the procedures previously reported by our group.[7] The *n*-butyl diazoacetamide and phenyl diazoacetamide were also prepared according to the previously reported procedures.[4a] All other reagents were used as newly purchased either from Aldrich or other commercial sources or purified appropriately.

5.2. Multi-Component *cis*-Aziridination. *Ethyl (2R,3R)-1-(Bis-(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-phenylaziridine-2-carboxylate (2R,3R)-**4c**: (Scheme 1, Entries 5 and 6).* To a 10 mL flame-dried homemade Schlenk flask, prepared from a 10 mL pear-shaped flask that had its 14/20 glass joint replaced with a high vacuum threaded Teflon valve, equipped with a stir bar and filled with argon were added (S)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), $B(OPh)_3$ (17.4 mg, 0.060 mmol, 0.30 equiv), and BUDAM amine **10** (94 mg, 0.20 mmol). Under an argon flow through the side arm of the Schlenk flask, dry toluene (1.0 mL) was added. The flask was sealed by closing the Teflon valve and then placed in an oil bath (80 °C) for 0.5 h. The flask was then allowed to cool to room temperature and opened to argon through the side arm of the Schlenk flask. To the flask containing the catalyst was added 4 Å molecular sieves (60 mg, freshly flame-dried), benzaldehyde **2a** (21 μL, 0.21 mmol), and ethyl diazoacetate **3** (29 μL, 0.24 mmoL, 1.2 equiv). The resulting mixture was stirred for 24 h at room temperature. The reaction was diluted by addition of hexane (3 mL) before the reaction mixture was filtered through a silica gel plug to a 100 mL round-bottom flask. The reaction flask was rinsed with EtOAc (10 mL × 3), and the rinse was filtered through the same silica gel plug. The resulting solution was then concentrated in vacuo followed by

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exposure to high vacuum (0.05 mmHg) for 1 h to afford the crude aziridine as an off-white solid. Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 15:1 hexanes/Et_2O as eluent, flash column) afforded aziridine (2*R*,3*R*)-**4c** as a white foam (mp 155−156 °C on 97% ee material) in 91% yield (117 mg, 0.182 mmol); cis/trans 8:1. The enantiomeric purity of (2*R*,3*R*)-**4c** was determined to be 97% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 99.5:0.5 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 13.25 min (minor enantiomer, ent-**4c**) and t_R = 29.14 min (major enantiomer, **4c**). The aziridination of **2a** in the presence of (S)-VAPOL BOROX catalyst afforded (2*R*,3*R*)-ent-**4c** in 99% ee and 85% yield (109 mg, 0.170 mmol); cis/trans 6:1. Spectral data for **4c**: R_f = 0.56 (5:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (t, 3H, *J* = 7.2 Hz), 1.35 (s, 18 H), 1.43 (s, 18H), 2.67 (d, 1H, *J* = 6.5 Hz), 3.19 (d, 1H, *J* = 6.5 Hz), 3.62 (s, 3H), 3.69 (s, 3H), 3.85 (s, 1H), 3.87−4.00 (m, 2H), 7.21 (t, 1H, *J* = 7.5 Hz), 7.27 (t, 2H, *J* = 7.5 Hz), 7.35 (s, 2H), 7.45 (s, 2H), 7.51 (d, 2H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 32.2, 32.3, 35.9, 35.9, 46.5, 48.9, 60.7, 64.1, 64.2, 125.5, 125.6, 127.4, 127.7, 128.3, 135.5, 136.8, 137.0, 143.1, 143.2, 158.4, 158.4, 168.4 (1 sp^2 C not located). These spectral data match those previously reported for this compound.[7]

5.3. Multicomponent *trans*-Aziridination of Aromatic Aldehydes. *General Procedure A.* To a 10 mL flame-dried homemade Schlenk flask, prepared from a 10 mL pear-shaped flask that had its 14/20 glass joint replaced with a high vacuum threaded Teflon valve, equipped with a stir bar and filled with argon was added ligand **5a**, **5b**, or **5c** (0.020 mmol), $B(OPh)_3$ (17 mg, 0.060 mmol), and amine **1**, **10**, or **11** (0.200 mmol). Under an argon flow through the side arm of the Schlenk flask, dry toluene (1.0 mL) was added. The flask was sealed by closing the Teflon valve, and the mixture was stirred at room temperature for 1 h. To the flask containing the catalyst was added 4 Å molecular sieves (60 mg, freshly flame-dried) and aldehyde (0.24 mmol, 1.2 equiv). The reaction mixture was allowed to stir at room temperature for 20 min so that the corresponding imine was formed completely. This solution was then allowed to cool to −20 °C, and diazoacetamide **8** or **9** (0.28 mmol, 1.4 equiv) was added rapidly. The resulting mixture was stirred for 24 h at −20 °C. The reaction was diluted by addition of precooled hexane (3 mL) at −20 °C before the reaction mixture was filtered through a silica gel plug into a 100 mL round-bottom flask. The reaction flask was rinsed with EtOAc (10 mL × 3), and the rinse was filtered through the same silica gel plug. The resulting solution was then concentrated in vacuo followed by exposure to high vacuum (0.05 mmHg) for 1 h to afford the crude aziridine as a yellow viscous oil. The *trans*/*cis* ratio was determined by ^{1}H NMR analysis of the crude reaction mixture. Purification of the crude aziridine by silica gel chromatography (20 mm × 150 mm column, gravity column) afforded the *trans*-aziridine as a white solid.

general procedure B. To a 10 mL flame-dried homemade Schlenk flask, prepared from a 10 mL pear-shaped flask that had its 14/20 glass joint replaced with a high vacuum threaded Teflon valve, equipped with a stir bar and filled with argon was added ligand **5a**, **5b**, or **5c** (0.020 mmol), $B(OPh)_3$ (17 mg, 0.060 mmol) and amine **1**, **10**, or **11** (0.200 mmol). Under an argon flow through the side arm of the Schlenk flask, dry toluene (1.0 mL) was added. The flask was sealed by closing the Teflon valve and then placed in an oil bath (80 °C) for 0.5 h. The flask was then allowed to cool to room temperature and opened to argon through the side arm of the Schlenk flask. The aziridination was completed according to the general procedure A. The *trans*/*cis* ratio was determined by ^{1}H NMR analysis of the crude reaction mixture. Purification of the crude aziridine by silica gel chromatography (20 mm × 150 mm column, gravity column) afforded the *trans*-aziridine as a white solid.

*(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N,3-diphenylaziridine-2-carboxamide (2R,3S)-**12a** (Table 1, Entry 10).* Benzaldehyde **2a** (24 μL, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide **8** (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12a** as a white foam (mp 88−90 °C on 92% ee material) in 90% yield (124 mg, 0.180 mmol); *trans*/*cis* 18:1. The enantiomeric purity of (2*R*,3*S*)-**12a** was determined to be 92% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 13.56 min (minor enantiomer, *ent*-**12a**) and t_R = 21.43 min (major enantiomer, **12a**). The aziridination of aldehyde **2a** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**12a** in 40% ee and 36% yield (49.6 mg, 0.072 mmol); *trans*/*cis* 2:1 (Table 1, entry 11). The aziridination of aldehyde **2a** according to general procedure A in the presence of (*S*)-VANOL BOROX catalyst afforded (2*R*,3*S*)-**12a** in 95% ee and 80% yield (110 mg, 0.160 mmol); *trans*/*cis* 19:1 (Table 1, entry 12). Spectral data for (2*R*,3*S*)-**12a**: R_f = 0.44 (5:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.22 (d, 36H, *J* = 5.5 Hz), 2.99 (d, 1H, *J* = 2.5 Hz), 3.38 (d, 1H, *J* = 2.5 Hz), 3.41 (s, 3H), 3.53 (s, 3H), 5.23 (s, 1H), 7.02 (t, 1H, *J* = 7.2 Hz), 7.20 (s, 2H), 7.22−7.26 (m, 3H), 7.31 (s, 2H), 7.32−7.37 (m, 4H), 7.50 (d, 2H, *J* = 8.5 Hz), 10.30 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 31.8, 31.8, 35.2, 35.3, 46.3, 46.6, 63.7, 63.9, 65.4, 119.0, 123.4, 125.2, 125.7, 126.1, 127.3, 128.3, 128.6, 137.8, 138.73, 139.0, 142.1, 142.3, 157.3, 157.4, 165.1 (1 sp^2 C not located); These spectral data match those previously reported for this compound.[4a] $[\alpha]_D^{20}$ +12.7 (*c* 1.0, EtOAc) on 95% ee material (HPLC), lit.[4a] $[\alpha]_D^{20}$ +11.2 (*c* 1.0, EtOAc) on 91% ee (2*R*,3*S*)-isomer.

*(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-phenylaziridine-2-carboxamide (2R,3S)-**13a** (Table 1, Entry 13).* Benzaldehyde **2a** (24 μL, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (40 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 6:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**13a** as a white solid (mp 212−215 °C on 86% ee material) in 43% yield (58 mg, 0.086 mmol); *trans*/*cis* 8:1. The enantiomeric purity of (2*R*,3*S*)-**13a** was determined to be 86% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 10.22 min (minor enantiomer, *ent*-**13a**) and t_R = 27.49 min (major enantiomer, **13a**). Spectral data for (2*R*,3*S*)-**13a**: R_f = 0.38 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (t, 3H, *J* = 7.2 Hz), 1.32 (s, 18H), 1.38 (s, 18H), 1.40−1.41 (m, 33m), 1.50−1.53 (m, 33m), 2.96 (d, 1H, *J* = 3.0 Hz), 3.20 (dt, 1H, *J* = 8.5, 1.8 Hz), 3.32 (dt, 1H, *J* = 8.7, 1.8 Hz), 3.43 (d, 1H, *J* = 3.0 Hz), 3.59 (s, 1H), 3.64 (s, 3H), 3.66 (s, 3H), 3.80 (s, 1H), 6.87 (d, 2H, *J* = 7.5 Hz), 7.07 (d, 2H, *J* = 7.5 Hz), 7.19 (s, 2H), 7.22 (d, 2H, *J* = 8.0 Hz), 7.30−7.32 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 20.1, 31.7, 32.1, 35.6, 35.7, 38.6, 43.0, 49.6, 64.0, 64.2, 67.74 125.3, 125.4, 127.8, 128.1, 130.1, 131.9, 136.8, 136.8, 142.61, 143.3, 158.10 158.4, 170.2 (1 sp^3 C not located); IR (thin film) 3447s, 2960s, 2870s, 1647vs, 1546s, 1455s, 1413vs, 1264s, 1222vs, 1115s, 1014s cm^{-1}; HRMS (ESI-TOF) *m*/*z* 669.4978 [(M + H^+), calcd for $C_{44}H_{65}N_2O_3$ 669.4995]; $[\alpha]_D^{20}$ −13.6 (*c* 1.0, CH_2Cl_2) on 86% ee material (HPLC).

*(2S,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-N,3-diphenylaziridine-2-carboxamide (2S,3R)-ent-**6a** and Its (2S,3S) Isomer ent-**25a** (Table 1, Entry 15; Scheme 5, Entry 1).* Benzaldehyde **2a** (61 μL, 0.60 mmol, 1.2 equiv) was reacted according to general procedure B with MEDAM amine **10** (150 mg, 0.500 mmol), (*R*)-VANOL (22 mg, 0.050 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (112 mg, 0.700 mmol, 1.40 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 6:1 hexanes/EtOAc as eluent, flash column) afforded pure *trans*-aziridine (2*S*,3*R*)-*ent*-**6a** as a white foam (mp 86−88 °C on 87% ee material) in 63% yield (164 mg, 0.315 mmol) and a *trans*/*cis* 3.7:1. The *cis*-isomer *ent*-**25a** was isolated as a white foam in 17% yield (44 mg, 0.085 mmol). The enantiomeric purity of (2*S*,3*R*)-*ent*-**6a** was determined to be 87% ee by HPLC analysis (CHIRALCEL OD-H column, 97:3 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 23.68 min (major enantiomer, *ent*-**6a**) and t_R = 36.64 min (minor enantiomer, **6a**). The enantiomeric purity of (2*S*,3*S*)-*ent*-**25a** was determined to be 73% ee ($[\alpha]_D^{20}$ −13.6 (*c* 1.0, CH_2Cl_2)) HPLC analysis (CHIRALCEL OD-H column, 97:3 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times;

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t_R = 10.56 min (minor enantiomer, **25a**) and t_R = 25.75 min (major enantiomer, *ent*-**25a**). The aziridination of **2a** in the presence of (*R*)-VAPOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**6a** in 87% ee and 57% yield (148 mg, 0.285 mmol); *trans*/*cis* 2:1 (Table 1, entry 14). The aziridination of **2a** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**6a** in 55% ee ($[\alpha]_D^{20}$ −3.1 (*c* 1.0, CH_2Cl_2)) and 9% yield (23 mg, 0.045 mmol); *trans*/*cis* 1:8 (Table 1, entry 16; Scheme 5, entry 2). The *cis*-isomer (2*S*,3*S*)-*ent*-**25a** was isolated as a white foam (mp 67−69 °C on 95% ee material) in 75% yield (195 mg, 0.375 mmol) and 95% ee ($[\alpha]_D^{20}$ −26.2 (*c* 1.0, CH_2Cl_2)). Spectral data for (2*S*,3*R*)-*ent*-**6a**: R_f = 0.57 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.02 (s, 6H), 2.07 (s, 6H), 2.93 (d, 1H, *J* = 2.8 Hz), 3.35 (d, 1H, *J* = 2.8 Hz), 3.49 (s, 3H), 3.55 (s, 3H), 5.06 (s, 1H), 6.99 (s, 2H), 7.05 (s, 2H), 7.05−7.07 (m, 1H), 7.28−7.36 (m, 7H), 7.49 (d, 2H, *J* = 7.5 Hz), 10.30 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 15.7, 15.9, 45.9, 47.5, 59.0, 59.1, 65.4, 119.2, 123.6, 126.1, 127.3, 127.3, 127.9, 128.4, 128.7, 129.7, 129.7, 138.6, 138.7, 138.9, 138.9, 155.1, 155.3, 164.9; these spectral data match those previously reported for this compound;[4a] $[\alpha]_D^{20}$ −4.6 (*c* 1.0, CH_2Cl_2) on 87% ee material (HPLC), lit.[4a] $[\alpha]_D^{20}$ +5.1 (*c* 1.0, CH_2Cl_2) on 96% ee (2*R*,3*S*)-isomer. Spectral data for (2*S*,3*S*)-*ent*-**25a**: R_f = 0.35 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.27 (s, 12H), 2.75 (d, 1H, *J* = 7.2 Hz), 3.30 (d, 1H, *J* = 7.2 Hz), 3.70 (s, 6H), 3.83 (s, 1H), 7.03 (t, 1H, *J* = 7.5 Hz), 7.11−7.16 (m, 6H), 7.18−7.32 (m, 7H), 8.10 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 16.2, 16.3, 47.3, 48.7, 59.6, 59.6, 76.7, 120.3, 124.4, 127.5, 127.5, 127.6, 127.7, 128.3, 128.8, 130.9, 131.1, 134.9, 136.6, 137.2, 137.2, 156.3, 156.3, 166.0; these spectral data match those previously reported for this compound;[3] $[\alpha]_D^{20}$ −13.6 (*c* 1.0, CH_2Cl_2) on 73% ee material (HPLC), lit.[3] $[\alpha]_D^{20}$ +4.0 (*c* 1.0, CH_2Cl_2) on 13% ee (2*R*,3*R*)-isomer.

*(2S,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-N-butyl-3-phenylaziridine-2-carboxamide (2S,3R)-ent-**7a** and Its (2S,3S) Isomer ent-**29a** (Table 1, Entry 17; Scheme 5, Entry 3).* Benzaldehyde **2a** (61 μL, 0.60 mmol, 1.2 equiv) was reacted according to general procedure B with MEDAM amine **10** (150 mg, 0.500 mmol), (*R*)-VANOL (22 mg, 0.050 mmol, 0.10 equiv), and *N*-butyl diazoacetamide (99 mg, 0.70 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 6:1 hexanes/EtOAc as eluent, flash column) afforded pure *trans*-aziridine (2*S*,3*R*)-*ent*-**7a** as a white foam (mp 51−52 °C on 76% ee material) in 36% yield (90 mg, 0.18 mmol), *trans*/*cis* = 0.72:1. The *cis*-isomer *ent*-**29a** was isolated as a white foam in 50% yield (125 mg, 0.25 mmol) and 86% ee. The enantiomeric purity of (2*S*,3*R*)-*ent*-**7a** was determined to be 76% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 85:15 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 16.74 min (major enantiomer, *ent*-**7a**) and t_R = 48.70 min (minor enantiomer, **7a**). The enantiomeric purity of (2*S*,3*S*)-*ent*-**29a** was determined to be 86% ee by HPLC analysis (CHIRALCEL OD-H column, 97:3 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 8.70 min (minor enantiomer, **29a**) and t_R = 16.43 min (major enantiomer, *ent*-**29a**). The aziridination of **2a** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**7a** in 89% ee ($[\alpha]_D^{20}$ +22.9 (*c* 1.0, CH_2Cl_2)) and 8% yield (20 mg, 0.040 mmol). The *cis*-isomer (2*S*,3*S*) *ent*-**29a** was isolated in 73% yield and 91% ee ($[\alpha]_D^{20}$ −7.5 (*c* 1.0, CH_2Cl_2)) (Table 1, entry 18 and Scheme 5, entry 4). Spectral data for (2*S*,3*R*)-*ent*-**7a**: R_f = 0.45 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.78 (t, 3H, *J* = 7.0 Hz), 1.05−1.11 (m, 2H), 1.12−1.19 (m, 2H), 2.05 (s, 6H), 2.17 (s, 7H), 2.71 (s, 1H), 2.79−2.86 (m, 1H), 3.09−3.21 (m, 1H), 3.54 (s, 3H), 3.59 (s, 3H), 5.07 (s, 1H), 7.01 (s, 4H), 7.22−7.37 (m, 5H), 8.24 (t, 1H, *J* = 5.7 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.6, 15.9, 16.0, 19.3, 30.9, 39.0, 45.2, 46.9, 59.1, 59.1, 65.0, 126.0, 127.1, 127.3, 127.7, 128.3, 128.5, 129.5, 129.7, 139.1, 139.3, 155.1, 155.3, 165.9; these spectral data match those previously reported for this compound;[4a] $[\alpha]_D^{20}$ +20.0 (*c* 1.0, CH_2Cl_2) on 76% ee material (HPLC). Spectral data for (2*S*,3*S*)-*ent*-**29a**: R_f = 0.18 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.77 (t, 3H, *J* = 7.2 Hz), 0.99−1.10 (m, 4H), 2.26 (d, 12H, *J* = 2.5 Hz), 2.61 (d, 1H, *J* = 7.2 Hz), 2.88−2.98 (m, 2H), 3.18 (d, 1H, *J* = 7.2 Hz), 3.69 (d, 6H, *J* = 8.0 Hz), 3.73 (s, 1H), 6.32 (t, 1H, *J* = 6.0 Hz), 7.03 (s, 2H), 7.11 (s, 2H), 7.19−7.25 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7, 16.2, 16.3, 20.1, 31.5, 38.2, 46.9, 48.2, 59.6, 59.6, 76.8, 127.4, 127.5, 127.7, 127.8, 128.1, 130.8, 130.8, 135.3, 137.3, 137.5, 156.2, 156.2, 167.5; IR (thin film) 3350vs, 2954vs, 2870s, 1645vs, 1536vs, 1485s, 1222s, 1147s, 1015s cm^{-1}; HRMS (ESI-TOF) *m*/*z* 501.3110 [(M + H$^+$), calcd for $C_{32}H_{41}N_2O_3$ 501.3117]; $[\alpha]_D^{20}$ −6.6 (*c* 1.0, CH_2Cl_2) on 86% ee material (HPLC).

*(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(naphthalen-2-yl)-N-phenylaziridine-2-carboxamide (2R,3S)-**12b** (Table 2, Entry 2).* To a 10 mL flame-dried homemade Schlenk flask, prepared from a 25 mL pear-shaped flask that had its 14/20 glass joint replaced with a high vacuum threaded Teflon valve equipped with a stir bar and filled with argon was added (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), $B(OPh)_3$ (17 mg, 0.059 mmol), and BUDAM amine **10** (94 mg, 0.20 mmol). Under an argon flow through the side arm of the Schlenk flask, dry toluene (0.40 mL) was added. The flask was sealed by closing the Teflon valve and then placed in an oil bath (80 °C) for 0.5 h. The precatalyst was subjected to high vacuum (0.05 mmHg) at 80 °C for 30 min to remove all of the volatile substances. The flask was then allowed to cool to room temperature and opened to argon through the side arm of the Schlenk flask. To the flask containing the catalyst was added dry toluene (1.0 mL) to dissolve all of the materials, followed by the addition of 4 Å molecular sieves (60 mg, freshly flame-dried) and 2-naphthaldehyde **2b** (38 mg, 0.24 mmol, 1.2 equiv). The reaction mixture was allowed to stir at room temperature for 20 min to ensure that the corresponding imine was formed completely. This solution was then cooled to −20 °C, and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv) was rapidly added. The resulting mixture was stirred for 24 h at −20 °C. The reaction mixture was diluted by addition of precooled hexane (3 mL) at −20 °C before the reaction mixture was filtered through a silica gel plug into a 100 mL round-bottom flask. The reaction flask was rinsed with EtOAc (10 mL × 3), and the rinse was filtered through the same silica gel plug. The resulting solution was then concentrated in vacuo followed by exposure to high vacuum (0.05 mmHg) for 1 h to afford the crude aziridine as a yellow viscous oil. The *trans*/*cis* ratio was determined by ^{1}H NMR on the crude reaction mixture. Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12b** as a white foam (mp 65−68 °C on 92% ee material) in 82% yield (121 mg, 0.164 mmol); *trans*/*cis* 62:1. The enantiomeric purity of (2*R*,3*S*)-**12b** was determined to be 92% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 20.65 min (minor enantiomer, *ent*-**12b**) and t_R = 33.34 min (major enantiomer, **12b**). Spectral data for (2*R*,3*S*)-**12b**: R_f = 0.28 (5:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.16 (s, 18H), 1.23 (s, 18H), 3.11 (d, 1H, *J* = 2.5 Hz), 3.40 (s, 3H), 3.48 (s, 3H), 3.57 (d, 1H, *J* = 2.0 Hz), 5.29 (s, 1H), 7.00 (t, 1H, *J* = 7.5 Hz), 7.22 (s, 2H), 7.24 (t, 2H, *J* = 7.2 Hz), 7.35 (s, 2H), 7.43−7.48 (m, 3H), 7.51 (d, 2H, *J* = 7.5 Hz), 7.81 (d, 1H, *J* = 8.0 Hz), 7.86−7.89 (m, 3H), 10.33 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 31.77, 31.80, 35.2, 35.4, 46.7, 47.5, 63.7, 63.9, 65.6, 115.3, 119.0, 123.5, 123.9, 125.3, 125.7, 126.3, 127.4, 128.6, 129.4, 132.5, 132.8, 136.6, 137.83, 138.8, 142.2, 142.3, 157.4, 157.4, 165.2 (3 sp^2 carbons not located); IR (thin film) 3439s, 2963s, 1636vs, 1445s, 1413s, 1384s, 1265vs, 1222s, 1115s cm^{-1}; HRMS (ESI-TOF) *m*/*z* 739.4840 [(M + H$^+$), calcd for $C_{50}H_{63}N_2O_3$ 739.4839]; $[\alpha]_D^{20}$ +13.9 (*c* 1.0, CH_2Cl_2) on 92% ee material (HPLC).

*(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(naphthalen-1-yl)-N-phenylaziridine-2-carboxamide (2R,3S)-**12c** (Table 2, Entry 3).* 1-Naphthaldehyde **2c** (38 mg, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12c** as a white foam (mp 68−71 °C on 87% ee material) in 88% yield (130 mg, 0.176 mmol); *trans*/*cis* > 99:1. The enantiomeric purity of (2*R*,3*S*)-**12c** was determined to be 87% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 16.25 min (minor enantiomer, *ent*-**12c**) and t_R = 49.74 min (major enantiomer, **12c**). Spectral data for (2*R*,3*S*)-**12c**: R_f = 0.23 (5:1

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hexanes/Et_2O); ^1H NMR (500 MHz, DMSO-d_6) δ 1.24 (s, 18H), 1.28 (s, 18H), 3.01 (d, 1H, J = 2.5 Hz), 3.36 (s, 3H), 3.52 (s, 3H), 3.98 (d, 1H, J = 2.5 Hz), 5.20 (s, 1H), 7.01 (t, 1H, J = 7.2 Hz), 7.05−7.11 (m, 1H), 7.24 (t, 2H, J = 7.8 Hz), 7.28−7.39 (m, 2H), 7.32 (s, 2H), 7.43−7.56 (m, 2H), 7.52 (s, 2H), 7.65 (d, 2H, J = 6.5 Hz), 7.83 (d, 1H, J = 8.0 Hz), 7.87−7.96 (m, 1H), 10.20 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.8, 31.9, 35.2, 35.4, 44.7, 46.5, 63.7, 63.9, 67.1, 115.3, 119.0, 122.7, 123.3, 123.5, 124.56 125.5, 125.9, 126.5, 127.6, 128.6, 129.4, 131.1, 133.0, 134.4, 137.7, 138.1, 138.7, 142.2, 142.5, 157.4, 157.6, 165.1; IR (thin film) 3327s, 2960vs, 2869s, 1675vs, 1529vs, 1445vs, 1413s, 1222vs, 1115s, 1013s cm^{-1}; HRMS (ESI-TOF) m/z 739.4836 [$(M + H^+)$, calcd for $C_{50}H_{63}N_2O_3$ 739.4839]; $[\alpha]_D^{20}$ +19.6 (c 1.0, CH_2Cl_2) on 87% ee material (HPLC).

4-((2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(phenylcarbamoyl)aziridin-2-yl)phenyl Acetate ***12d*** *(Table 2, Entry 4).* 4-Formylphenyl acetate **2d** (34 μL, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12d** as a white foam (mp 106−108 °C on >99% ee material) in 82% yield (123 mg, 0.164 mmol); *trans*/*cis* 25:1. The enantiomeric purity of (2*R*,3*S*)-**12d** was determined to be 99.6% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 34.72 min (minor enantiomer, *ent*-**12d**) and t_R = 38.27 min (major enantiomer, **12d**). Spectral data for (2*R*,3*S*)-**12d**: R_f = 0.30 (5:1 hexanes/EtOAc); ^1H NMR (500 MHz, DMSO-d_6) δ 1.21 (s, 36H), 2.24 (s, 3H), 2.98 (s, 1H), 5.23 (s, 1H), 3.40 (s, 3H), 3.52 (s, 3H), 7.00 (t, 1H, J = 7.5 Hz), 7.08 (d, 2H, J = 8.0 Hz), 7.18 (s, 2H), 7.24 (t, 2H, J = 7.5 Hz), 7.29 (s, 2H), 7.37 (d, 2H, J = 8.0 Hz), 7.49 (d, 2H, J = 8.0 Hz), 10.30 (s, 1H) (one proton not located); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.9, 31.8, 31.8, 35.2, 35.3, 45.8, 47.6, 63.7, 63.9, 65.4, 119.0, 121.8, 123.5, 125.2, 125.7, 127.1, 128.6, 131.1, 136.5, 137.8, 138.8, 142.2 142.3, 149.8, 157.4, 157.4, 165.1, 169.2; IR (thin film) 3331s, 2960s, 1765vs, 1682vs, 1601vs, 1538s, 1447s, 1413s, 1367s, 1262vs, 1194vs, 1115s, 1013s cm^{-1}; HRMS (ESI-TOF) m/z 747.4734 [$(M + H^+)$, calcd for $C_{48}H_{63}N_2O_5$ 747.4737]; $[\alpha]_D^{20}$ +46.6 (c 1.0, CH_2Cl_2) on >99% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(4-methoxyphenyl)-N-phenylaziridine-2-carboxamide ***12e*** *(Table 2, Entry 5).* 4-Anisaldehyde **2e** (29 μL, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). A 76% yield of the imine from **2e** and **10** was observed in the ^1H NMR spectrum of the crude reaction mixture along with a 9% yield of aziridine (2*R*,3*S*)-**12e**; *trans*/*cis* 1.3:1.

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-phenyl-3-(p-tolyl)aziridine-2-carboxamide ***12f*** *(Table 2, Entry 6).* To a 10 mL flame-dried homemade Schlenk flask, prepared from a 25 mL pear-shaped flask that had its 14/20 glass joint replaced with a high vacuum threaded Teflon valve, equipped with a stir bar and filled with argon were added (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), $B(OPh)_3$ (17 mg, 0.059 mmol), and BUDAM amine **10** (94 mg, 0.20 mmol). Under an argon flow through the side arm of the Schlenk flask, dry toluene (0.40 mL) was added. The flask was sealed by closing the Teflon valve and then placed in an oil bath (80 °C) for 0.5 h. The precatalyst was subjected to high vacuum (0.05 mmHg) at 80 °C for 30 min to remove all of the volatile substances. The flask was then allowed to cool to room temperature and opened to argon through the side arm of the Schlenk flask. To the flask containing the catalyst was added dry toluene (1.0 mL) to dissolve all of the materials, followed by the addition of the 4 Å molecular sieves (60 mg, freshly flame dried) and 4-tolualdehyde **2f** (28 μL, 0.24 mmol, 1.2 equiv). The reaction mixture was allowed to stir at room temperature for 20 min so that the corresponding imine was formed completely. This solution was then cooled to −20 °C, and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv) was added rapidly. The resulting mixture was stirred for 24 h at −20 °C. The reaction mixture was diluted by addition of precooled hexane (3 mL) at −20 °C before the reaction mixture was filtered through a silica gel plug into a 100 mL round-bottom flask. The reaction flask was rinsed with EtOAc (10 mL × 3), and the rinse was filtered through the same silica gel plug. The resulting solution was then concentrated in vacuo followed by exposure to high vacuum (0.05 mmHg) for 1 h to afford the crude aziridine as a yellow viscous oil. The *trans*/*cis* ratio was determined by ^1H NMR analysis of the crude reaction mixture. Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12f** as a white foam (mp 82−83 °C on 85% ee material) in 73% yield (103 mg, 0.146 mmol); *trans*/*cis* 19:1. The enantiomeric purity of (2*R*,3*S*)-**12f** was determined to be 85% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 14.46 min (minor enantiomer, *ent*-**12f**) and t_R = 34.63 min (major enantiomer, **12f**). Spectral data for (2*R*,3*S*)-**12f**: R_f = 0.23 (5:1 hexanes/Et_2O); ^1H NMR (500 MHz, $CDCl_3$) δ 1.33 (s, 36H), 2.32 (s, 3H), 3.03 (d, 1H, J = 2.8 Hz), 3.58 (d, 1H, J = 2.8 Hz), 3.62 (d, 6H, J = 7.5 Hz), 3.90 (s, 1H), 6.89 (s, 2H), 6.98 (d, 2H, J = 7.8 Hz), 7.03 (d, 2H, J = 7.8 Hz), 7.10 (t, 1H, J = 7.5 Hz), 7.25 (s, 2H), 7.33 (t, 2H, J = 7.8 Hz), 7.54 (d, 2H, J = 7.5 Hz), 8.76 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 32.0, 35.6, 35.7, 43.3, 49.5, 64.0, 64.2, 67.6, 119.4, 124.1, 125.3, 125.4, 128.3, 128.6, 129.0, 130.0, 136.6, 136.6, 137.4, 136.0, 142.7, 143.4, 143.5, 158.2, 158.5, 168.4; IR (thin film) 3317s, 2961vs, 2869s, 1668vs, 1602vs, 1533vs, 1446vs, 1413s, 1394s, 1361s, 1222vs, 1115s, 1013s cm^{-1}; HRMS (ESI-TOF) m/z 703.4850 [$(M + H^+)$, calcd for $C_{47}H_{63}N_2O_3$ 703.4839]; $[\alpha]_D^{20}$ +11.9 (c 1.0, CH_2Cl_2) on 85% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-phenyl-3-(o-tolyl)aziridine-2-carboxamide ***12g*** *(Table 2, Entry 7).* 2-Tolualdehyde **2g** (28 μL, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12g** as a white foam (mp 72−74 °C on 93% ee material) in 85% yield (120 mg, 0.170 mmol); *trans*/*cis* > 99:1. The enantiomeric purity of (2*R*,3*S*)-**12g** was determined to be 93% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 34.37 min (minor enantiomer, *ent*-**12g**) and t_R = 43.62 min (major enantiomer, **12g**). Spectral data for (2*R*,3*S*)-**12g**: R_f = 0.27 (5:1 hexanes/Et_2O); ^1H NMR (500 MHz, DMSO-d_6) δ 1.22 (s, 18H), 1.28 (s, 18H), 2.14 (s, 3H), 2.90 (d, 1H, J = 2.0 Hz), 3.34 (s, 3H), 3.45 (d, 1H, J = 2.5 Hz), 3.54 (s, 3H), 5.12 (s, 1H), 6.99 (t. 1H, J = 7.5 Hz), 7.06−7.18 (m, 2H), 7.22 (t, 2H, J = 8.0 Hz), 7.26 (s, 2H), 7.29−7.37 (m, 2H), 7.42 (s, 2H), 7.46 (d, 2H, J = 8.0 Hz), 10.19 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 18.4, 31.8, 31.9, 35.2, 35.3, 63.7, 64.0, 66.6, 115.2, 119.0, 123.4, 125.1, 125.4, 125.7, 127.0, 128.5, 129.6, 135.8, 136.8, 137.8, 138.1, 138.8, 142.1, 142.4, 157.3, 157.5, 165.2; IR (thin film) 3323s, 2960vs, 2869s, 1678vs, 1602vs, 1531vs, 1445vs, 1413vs, 1392s, 1361s, 1221vs, 1115s, 1013s cm^{-1}; HRMS (ESI-TOF) m/z 703.4838 [$(M + H^+)$, calcd for $C_{47}H_{63}N_2O_3$ 703.4839]; $[\alpha]_D^{20}$ +3.0 (c 1.0, CH_2Cl_2) on 92% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(4-bromophenyl)-N-phenylaziridine-2-carboxamide ***12h*** *(Table 2, Entry 8).* 4-Bromobenzaldehyde **2h** (44 mg, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12h** as a white foam (mp 74−76 °C on 96% ee material) in 82% yield (126 mg, 0.164 mmol); *trans*/*cis* 23:1. The enantiomeric purity of (2*R*,3*S*)-**12h** was determined to be 96% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 18.83 min (major enantiomer, **12h**) and t_R = 25.16 min (minor enantiomer, *ent*-**12h**). Spectral data for (2*R*,3*S*)-**12h**: R_f =

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0.58 (2:1 hexanes/Et_2O); ^1H NMR (500 MHz, DMSO-d_6) δ 1.21 (s, 36H), 2.98 (d, 1H, J = 2.5 Hz), 3.38 (d, 1H, J = 2.5 Hz), 3.40 (s, 3H), 3.52 (s, 3H), 5.23 (s, 1H), 7.00 (t, 1H, J = 7.2 Hz), 7.17 (s, 2H), 7.23 (t, 2H, J = 7.5 Hz), 7.27 (s, 2H), 7.30 (d, 2H, J = 7.5 Hz), 7.50 (d, 4H, J = 8.0 Hz), 10.32 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 31.8, 31.8, 35.2, 35.3, 45.6, 47.7, 63.7, 63.9, 65.4, 115.2, 119.0, 123.5, 125.2, 125.7, 128.3, 128.6, 131.2, 137.6, 137.7, 138.6, 138.7, 142.2, 142.3, 157.4, 157.4, 164.9; IR (thin film) 3313s, 2960vs, 1663vs, 1602s, 1534s, 1489s, 1445s, 1413s, 1393s, 1361s, 1222vs, 1115s, 1011s cm^{-1}; HRMS (ESI-TOF) m/z 767.3763 [(M + H^+), calcd for $C_{46}H_{60}N_2O_3{}^{79}Br$ 767.3787]; $[\alpha]_D^{20}$ +7.2 (c 1.0, CH_2Cl_2) on 96% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(3-bromophenyl)-N-phenylaziridine-2-carboxamide ***12i*** *(Table 2, Entry 9).* 3-Bromobenzaldehyde **2i** (28 μL, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12i** as a white foam (mp 64−67 °C on 95% ee material) in 89% yield (137 mg, 0.178 mmol); *trans*/*cis* 27:1. The enantiomeric purity of (2*R*,3*S*)-**12i** was determined to be 95% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 14.48 min (major enantiomer, **12i**) and t_R = 19.11 min (minor enantiomer, *ent*-**12i**). Spectral data for (2*R*,3*S*)-**12i**: R_f = 0.58 (2:1 hexanes/Et_2O); ^1H NMR (500 MHz, DMSO-d_6) δ 1.22 (d, 36H, J = 6.5 Hz), 3.00 (d, 1H, J = 2.0 Hz), 3.39 (s, 3H), 3.43 (d, 1H, J = 2.0 Hz), 3.52 (s, 3H), 5.24 (s, 1H), 6.99 (t, 1H, J = 7.5 Hz), 7.19 (s, 2H), 7.20−7.29 (m, 3H), 7.31 (s, 2H), 7.35 (d, 1H, J = 7.5 Hz), 7.42 (d, 1H, J = 7.5 Hz), 7.49 (d, 2H, J = 8.0 Hz), 7.54 (s, 1H), 10.28 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 31.8, 31.8, 35.2, 35.3, 45.3, 47.8, 63.67 63.9, 65.4, 115.2, 119.0, 121.9, 123.5, 125.1, 125.5, 125.6, 128.6, 129.4, 130.01 130.5, 137.6, 137.7, 138.7, 140.0, 142.2, 142.4, 157.4, 164.9; IR (thin film) 3316s, 2960vs, 1664vs, 1600vs, 1534vs, 1445vs, 1412vs, 1360s, 1222vs, 1115s, 1013s cm^{-1}; HRMS (ESI-TOF) m/z 767.3783 [(M + H^+), calcd for $C_{46}H_{60}N_2O_3{}^{79}Br$: 767.3787]; $[\alpha]_D^{20}$ +5.4 (c 1.0, CH_2Cl_2) on 95% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(2-bromophenyl)-N-phenylaziridine-2-carboxamide ***12j*** *(Table 2, Entry 10).* 2-Bromobenzaldehyde **2j** (28 μL, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12j** as a white foam (mp 170−172 °C on 93% ee material) in 86% yield (132 mg, 0.172 mmol); *trans*/*cis* 19:1. The enantiomeric purity of (2*R*,3*S*)-**12j** was determined to be 93% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 13.14 min (minor enantiomer, *ent*-**12j**) and t_R = 31.61 min (major enantiomer, **12j**). Spectral data for (2*R*,3*S*)-**12j**: R_f = 0.35 (5:1 hexanes/Et_2O); ^1H NMR (500 MHz, DMSO-d_6) δ 1.23 (s, 18H), 1.27 (s, 18H), 2.92 (d, 1H, J = 2.5 Hz), 3.36 (s, 3H), 3.53 (s, 3H), 3.64 (d, 1H, J = 2.5 Hz), 5.18 (s, 1H), 7.00 (t, 1H, J = 7.5 Hz), 7.18 (t, 1H, J = 8.0 Hz), 7.22 (t, 2H, J = 8.2 Hz), 7.25 (s, 2H), 7.37 (t, 1H, J = 7.5 Hz), 7.38 (s, 2H), 7.45 (d, 1H, J = 7.5 Hz), 7.47 (d, 2H, J = 7.5 Hz), 7.54 (d, 1H, J = 8.5 Hz), 10.24 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 31.8, 31.8, 35.2, 35.3, 46.6, 46.9, 63.7, 63.9, 66.2, 115.2, 119.0, 122.8, 123.5, 125.3, 125.5, 127.4, 127.7, 128.5, 129.4, 132.2, 137.4, 137.8, 138.7, 142.2, 142.5, 157.4, 157.6, 164.6; IR (thin film) 3324s, 2960vs, 1665vs, 1602vs, 1531vs, 1444vs, 1413vs, 1394s, 1361s, 1262s, 1222s, 1115s, 1014s cm^{-1}; HRMS (ESI-TOF) m/z 767.3777 [(M + H^+), calcd for $C_{46}H_{60}N_2O_3{}^{79}Br$ 767.3787]; $[\alpha]_D^{20}$ +1.7 (c 1.0, CH_2Cl_2) on 93% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-phenyl-3-(4-(trifluoromethyl)phenyl)aziridine-2-carboxamide ***12k*** *(Table 2, Entry 11).* 4-(Trifluoromethyl)benzaldehyde **2k** (33 μL, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12k** as a white foam (mp 82−84 °C on 96% ee material) in 78% yield (118 mg, 0.156 mmol); *trans*/*cis* 31:1. The enantiomeric purity of (2*R*,3*S*)-**12k** was determined to be 96% ee by HPLC analysis (CHIRALCEL OD-H column, 95:5 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 9.11 min (minor enantiomer, *ent*-**12k**) and t_R = 14.56 min (major enantiomer, **12k**). Spectral data for (2*R*,3*S*)-**12k**: R_f = 0.27 (5:1 hexanes/Et_2O); ^1H NMR (500 MHz, DMSO-d_6) δ 1.18 (s, 18H), 1.21 (s, 18H), 3.08 (d, 1H, J = 2.5 Hz), 3.42 (s, 3H), 3.48 (d, 1H, J = 2.5 Hz), 3.51 (s, 3H), 5.24 (s, 1H), 7.02 (t, 1H, J = 7.2 Hz), 7.16 (s, 2H), 7.24 (s, 2H), 7.26 (t, 2H, J = 8.0 Hz), 7.51 (d, 2H, J = 8.0 Hz), 7.58 (d, 2H, J = 8.5 Hz), 7.71 (d, 2H, J = 7.5 Hz), 10.37 (s, 1H); ^{19}F-NMR (470 MHz, $CDCl_3$) δ 62.65; IR. (thin film) 3319s, 2960vs, 2871s, 1665vs, 1602vs, 1536vs, 1446s, 1413s, 1395s, 1361s, 1325vs, 1223vs, 1168s, 1129s, 1116s, 1067s, 1016s cm^{-1}; HRMS (ESI-TOF) m/z 757.4536 [(M + H^+), calcd for $C_{47}H_{60}F_3N_2O_3$ 757.4556]; $[\alpha]_D^{20}$ +8.5 (c 1.0, CH_2Cl_2) on 96% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(4-nitrophenyl)-N-phenylaziridine-2-carboxamide ***12l*** *(Table 2, Entry 12).* 4-Nitrobenzaldehyde **2l** (36 mg, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). A 52% yield of the imine from **2l** and **10** was observed in the ^1H NMR spectrum of the crude reaction mixture along with a 16% yield of aziridine (2*R*,3*S*)-**12l** *trans*/*cis* 29:1.

Methyl 4-((2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)-methyl)-3-(phenylcarbamoyl)aziridin-2-yl)benzoate ***12m*** *(Table 2, Entry 13).* Methyl 4-formylbenzoate **2m** (39 mg, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 5:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**12m** as a white foam (mp 94−95 °C on >99% ee material) in 89% yield (133 mg, 0.178 mmol); *trans*/*cis* 42:1. The enantiomeric purity of (2*R*,3*S*)-**12m** was determined to be 99.5% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 32.11 min (minor enantiomer, ent-**12m**) and t_R = 39.16 min (major enantiomer, **12m**). Spectral data for (2*R*,3*S*)-**12m**: R_f = 0.37 (2:1 hexanes/Et_2O); ^1H NMR (500 MHz, $CDCl_3$/DMSO-d^6 1:1, v/v) δ 1.20 (s, 18H), 1.22 (s, 18H), 3.04 (d, 1H, J = 2.0 Hz), 3.42 (s, 3H), 3.45 (d, 1H, J = 2.5 Hz), 3.52 (s, 3H), 3.82 (s, 3H), 5.23 (s, 1H), 6.97 (t, 1H, J = 7.0 Hz), 7.16 (s, 2H), 7.20 (t, 2H, J = 7.5 Hz), 7.24 (s, 2H), 7.45 (d, 2H, J = 8.0 Hz), 7.51 (d, 2H, J = 8.0 Hz), 7.91 (d, 2H, J = 8.0 Hz), 10.27 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.2, 30.2, 35.6, 35.7, 43.8, 48.9, 52.2, 64.0, 64.3, 68.3, 115.3, 119.5, 120.4, 124.4, 125.1, 125.1, 125.8, 129.0, 129.1, 129.5, 130.0, 142.9, 143.7, 155.9, 158.3, 158.6, 166.5, 167.8; IR (thin film) 3348s, 2960vs, 1725vs, 1688vs, 1602vs, 1543vs, 1445vs, 1413s, 1395s, 1279vs, 1222s, 1115vs, 1016vs cm^{-1}; HRMS (ESI-TOF) m/z 747.4731 [(M + H^+), calcd for $C_{48}H_{63}N_2O_5$ 747.4737]; $[\alpha]_D^{20}$ +49.4 (c 1.0, EtOAc) on >99% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(4-cyanophenyl)-N-phenylaziridine-2-carboxamide ***2n:*** *(Table 2, Entry 14).* 4-Formylbenzonitrile **2n** (26 mg, 0.24 mmol, 1.2 equiv) was reacted according to general procedure B with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.28 mmol, 1.4 equiv). A 66% yield of the imine from **2n** and **10** was observed in the ^1H NMR spectrum of the crude reaction mixture along with an 8% yield of aziridine (2*R*,3*S*)-**12m**; *trans*/*cis* 13:1.

5.4. Multicomponent *trans*-Aziridination of Aliphatic Aldehydes. *General Procedure C for the Multicomponent trans-Aziridination of Aliphatic Aldehydes.* To a 10 mL flame-dried homemade Schlenk flask, prepared from a 10 mL pear-shaped flask that had its 14/20 glass joint replaced with a high vacuum threaded

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Teflon valve equipped with a stir bar and filled with argon were added ligand **5a**, **5b**, or **5c** (0.020 mmol), $B(OPh)_3$ (17 mg, 0.060 mmol) and amine **1**, **10**, or **11** (0.200 mmol). Under an argon flow through the side arm of the Schlenk flask was added dry toluene (1.0 mL). The flask was sealed by closing the Teflon valve and then placed in an oil bath (80 °C) for 0.5 h. The flask was cooled to room temperature and then cooled to −10 °C and opened to argon through the side arm of the Schlenk flask. To the flask containing the catalyst were rapidly added 4 Å molecular sieves (60 mg, freshly flame-dried), an aldehyde (0.22 mmol, 1.1 equiv), and diazoacetamide **8**, **9** (0.24 mmoL, 1.2 equiv). The resulting mixture was stirred for 24 h at −10 °C. The reaction was diluted by addition of precooled hexane (3 mL) at −10 °C before the reaction mixture was filtered through a silica gel plug into a 100 mL round-bottom flask. The reaction flask was rinsed with EtOAc (10 mL × 3), and the rinse was filtered through the same silica gel plug. The resulting solution was then concentrated in vacuo followed by exposure to high vacuum (0.05 mmHg) for 1 h to afford the crude aziridine as a viscous oil. The *trans*/*cis* ratio was determined by ^{1}H NMR analysis of the crude reaction mixture. Purification of the crude aziridine by silica gel chromatography (20 mm × 150 mm column, gravity column) afforded the *trans*-aziridine as a white solid.

General procedure D for the Multicomponent trans-Aziridination of Aliphatic Aldehydes. In general procedure D, the catalyst was stirred with the aldehyde and amine for 20 min at room temperature before the solution was cooled to −10 °C and the diazoacetamide added. The rest of the procedure follows general procedure C.

General Procedure E for the multicomponent trans-aziridination of aliphatic aldehydes. In general procedure E, the catalyst was stirred with the aldehyde and amine for 20 h at room temperature before the solution was cooled to −10 °C and the diazoacetamide was added. The rest of the procedure follows general procedure C.

(2R,3S)-1-(Bis(3,5-ditert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-pentadecylaziridine-2-carboxamide ***18a*** *(Table 3, Entry 6).* Hexadecanal **15a**[1c] (53 mg, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 6:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18a** as an off-white solid (mp 78−80 °C on 96% ee material) in 85% yield (137 mg, 0.170 mmol); *trans*/*cis* 24:1. The enantiomeric purity of (2*R*,3*S*)-**18a** was determined to be 96% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 95:5 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 9.25 min (minor enantiomer, *ent*-**18a**) and t_R = 19.24 min (major enantiomer, **18a**). The aziridination of **15a** according to general procedure D in the presence of (*S*)-VANOL BOROX catalyst afforded (2*R*,3*S*)-**18a** in 96% ee and 88% yield (141 mg, 0.176 mmol); *trans*/*cis* 21:1 (Table 3, entry 7). The aziridination of **15a** in the presence of (*S*)-VAPOL BOROX catalyst afforded (2*R*,3*S*)-**18a** in 91% ee and 91% yield (146 mg, 0.182 mmol); *trans*/*cis* 14:1 (Table 3, entry 10). The aziridination of **15a** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18a** in 90% ee and 71% yield (114 mg, 0.142 mmol); *trans*/*cis* 17:1 (Table 3, entry 11). Spectral data for (2*R*,3*S*)-**18a**: R_f = 0.44 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 6.8 Hz), 0.91 (t, 3H, *J* = 7.2 Hz), 1.13−1.33 (m, 30H), 1.38 (s, 18H), 1.41 (s, 18H), 1.53−1.62 (m, 2H), 2.08 (d, 1H, *J* = 3.0 Hz), 2.18 (td, 1H, *J* = 6.3, 2.8 Hz), 3.10 (m, 1H), 3.21 (m, 1H), 3.65 (d, 6H, *J* = 2.5 Hz), 4.18 (s, 1H), 6.66 (t, 1H, *J* = 5.8 Hz), 7.21 (s, 2H), 7.30 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 14.1, 20.1, 22.7, 26.4, 28.2, 29.4, 29.5, 29.5, 29.5, 29.6, 29.7, 29.7, 31.7, 31.9, 32.1, 32.1, 35.7, 35.7, 38.4, 45.0, 47.3, 64.0, 64.2, 68.5, 125.2, 125.3, 137.3, 137.4, 143.1, 143.2, 158.2, 158.3, 170.8 (three sp^3 carbons not located); IR (thin film) 3312vs, 2958vs, 2926s, 2855s, 1652vs, 1540s, 1456s, 1413s, 1264s, 1223s, 1116s, 1014s cm^{-1}; HRMS (ESI-TOF) *m*/*z* 803.7001 [(M + H$^+$), calcd for $C_{53}H_{91}N_2O_3$: 803.7030]; $[\alpha]_D^{20}$ −10.5 (*c* 1.0, EtOAc) on 96% ee material (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-pentadecyl-N-phenylaziridine-2-carboxamide ***19a*** *(Table 3, Entry 9).* Hexadecanal **15a** (53 mg, 0.22 mmol, 1.1 equiv) was reacted according to general procedure D with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide **8** (39 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**19a** as a semisolid in 78% yield (128 mg, 0.156 mmol); *trans*/*cis* 12:1. The enantiomeric purity of (2*R*,3*S*)-**19a** was determined to be 88% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 98:2 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 20.53 min (minor enantiomer, *ent*-**19a**) and t_R = 35.84 min (major enantiomer, **19a**). (Table 3, entry 8). The aziridination of **15a** according to general procedure C in the presence of (*S*)-VANOL BOROX catalyst afforded (2*R*,3*S*)-**19a** in 68% ee and 70% yield (115 mg, 0.140 mmol); *trans*/*cis* 6:1 (Table 3, entry 8). Spectral data for (2*R*,3*S*)-**19a**: R_f = 0.57 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 7.0 Hz), 1.10−1.31 (m, 28H), 1.34 (s, 18H), 1.43 (18H), 1.62−1.67 (m, 2H), 2.20 (d, 1H, *J* = 3.0 Hz), 2.38−2.41 (m, 1H), 3.62 (s, 3H), 3.68 (s, 3H), 4.27 (s, 1H), 7.07 (t, 1H, *J* = 7.8 Hz), 7.27 (s, 2H), 7.30 (t, 2H, *J* = 8.0 Hz), 7.48 (d, 2H, *J* = 8.0 Hz), 8.57 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 22.7, 26.4, 28.1, 29.4, 29.4, 29.5, 29.5, 29.6, 29.7, 29.7, 31.9, 32.0, 32.1, 35.7, 35.8, 45.3, 47.5, 64.0, 64.2, 68.4, 119.2, 123.9, 125.2, 125.2, 128.9, 137.0, 137.2, 137.6, 143.2, 143.5, 158.3, 158.4, 168.9 (three sp^3 carbons not located); IR (thin film) 3327vs, 2924vs, 2854s, 1679vs, 1602s, 1528s, 1465s, 1412s, 1221s, 1115s, 1014s cm^{-1}; HRMS (ESI-TOF) *m*/*z* 823.6707 [(M + H$^+$), calcd for $C_{55}H_{87}N_2O_3$: 823.6717]; $[\alpha]_D^{20}$ +17.6 (*c* 1.0, EtOAc) on 88% ee material (HPLC).

(2R,3S)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-N-butyl-3-pentadecylaziridine-2-carboxamide ***17a*** *(Table 3, Entry 4).* Hexadecanal **15a** (132 mg, 0.550 mmol, 1.10 equiv) was reacted according to general procedure C with MEDAM amine **1** (150 mg, 0.500 mmol), (*S*)-VAPOL (27 mg, 0.050 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (85 mg, 0.60 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**17a** as an oily liquid in 79% yield (251 mg, 0.395 mmol); *trans*/*cis* 15:1. The enantiomeric purity of (2*R*,3*S*)-**17a** was determined to be 86% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 12.62 min (minor enantiomer, *ent*-**17a**) and t_R = 26.32 min (major enantiomer, **17a**). Spectral data for (2*R*,3*S*)-**17a**: R_f = 0.46 (1:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (t, 3H, *J* = 6.8 Hz), 0.88 (t, 3H, *J* = 7.0 Hz), 1.14−1.27 (m, 30H), 1.34−1.56 (m, 2H), 2.01 (d, 1H, *J* = 3.0 Hz), 2.20 (s, 6H), 2.21−2.24 (m, 1H), 2.25 (s, 6H), 2.94−3.00 (m, 1H), 3.29−3.36 (m, 1H), 3.64 (s, 3H), 3.67 (s, 3H), 4.08 (s, 1H), 6.61 (dd, 1H, *J* = 7.2, 4.8 Hz), 6.92 (s, 2H), 7.95 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 14.1, 16.2, 16.3, 19.9, 22.7, 26.1, 28.1, 29.3, 29.6, 29.5, 29.5, 29.6, 29.6, 29.7, 31.9, 31.9, 38.3, 44.8, 47.3, 59.5, 59.6, 67.6, 126.90 127.6, 130.5, 130.7, 138.6, 155.8, 156.1, 170.5 (three sp^3 carbon and one sp^2 carbons not located); IR (thin film) 2924vs, 2853s, 1646vs, 1538s, 1483s, 1466s, 1221s, 1137s, 1019s cm^{-1}; HRMS (ESI-TOF) *m*/*z* 635.5176 [(M + H$^+$), calcd for $C_{41}H_{67}N_2O_3$ 635.5152]; $[\alpha]_D^{20}$ +19.1 (*c* 1.0, CH_2Cl_2) on (2*S*,3*R*)-*ent*-**17a** of 93% ee (HPLC).

*(2S,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-N-butyl-3-pentadecylaziridine-2-carboxamide ent-***17a** *and (2R,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-N-butyl-3-pentadecylaziridine-2-carboxamide (2R,3R)-***26a** *(Table 3, Entry 5; Scheme 4).* Hexadecanal **15a** (53 mg, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with MEDAM amine **1** (60 mg, 0.200 mmol), (*R*)-^{t}Bu$_2$VANOL (11 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*S*,3*R*)-*ent*-**17a** as an oily liquid in 40% yield (50 mg, 0.079 mmol) and pure *cis*-aziridine (2*R*,3*R*)-**26a** as an oily liquid in 45% yield (58 mg, 0.091 mmol). The enantiomeric purity of (2*S*,3*R*)-*ent*-**17a** was determined to be 92% ee ($[\alpha]_D^{20}$ +17.0 (*c* 1.0, CH_2Cl_2) by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R

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= 12.62 min (major enantiomer, *ent*-**17a**) and t_R = 26.32 min (minor enantiomer, **17a**). The enantiomeric purity of (2*R*,3*R*)-**26a** was determined to be 93% ee by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 14.96 min (major enantiomer, **26a**) and t_R = 21.33 min (minor enantiomer, *ent*-**26a**). The spectra data for **17a** is given above. Spectral data for (2*R*,3*R*)-**26a**: R_f = 0.33 (1:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 7.0 Hz), 0.91 (t, 3H, J = 7.5 Hz), 1.13−1.30 (m, 26H), 1.33−1.41 (m, 6H), 1.90 (q, 1H, J = 6.8 Hz), 2.22 (s, 6H), 2.33−2.25 (m, 1H), 2.27 (s, 6H), 3.12 (hex, 1H, J = 6.5 Hz), 3.33 (hex, 1H, J = 7.0 Hz), 3.43 (s, 1H), 3.68 (d, 6H, J = 6.0 Hz), 6.65 (t, 1H, J = 6.0 Hz), 6.94 (s, 2H), 7.02 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 14.3, 16.4, 20.2, 22.8, 27.3, 28.6, 29.5, 29.5, 29.7, 29.8, 29.8, 32.1, 32.1, 38.6, 45.4, 47.2, 59.7, 59.8, 77.0, 127.5, 127.5, 130.5, 130.7, 137.8, 137.9, 156.0, 156.1, 168.8 (six sp^3 carbons not located); IR (thin film) 2924vs, 2853s, 1646vs, 1538s, 1483s, 1465s, 1221s, 1137s, 1019s cm^{-1}; HRMS (ESI-TOF) m/z 635.5178 [(M + H$^+$), calcd for $C_{41}H_{67}N_2O_3$ 635.5152]; $[\alpha]_D^{20}$ +15.1 (c 1.0, CH_2Cl_2) on 93% ee material (HPLC).

*(2S,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-N-butyl-3-pentadecylaziridine-2-carboxamide ent-**17a** and (2R,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-N-butyl-3-pentadecylaziridine-2-carboxamide (2R,3R)-**26a** (Table 3, entry 3; Scheme 4).* Hexadecanal **15a** (159 mg, 0.660 mmol, 1.10 equiv) was reacted according to general procedure C with MEDAM amine **1** (180 mg, 0.600 mmol), (*R*)-VANOL (26 mg, 0.060 mmol, 0.10 equiv), and *N*-butyl diazoacetamide (102 mg, 0.720 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*S*,3*R*)-*ent*-**17a** as an oily liquid in 66% yield (252 mg, 0.397 mmol) and pure *cis*-aziridine (2*R*,3*R*)-**26a** as an oily liquid in 11% yield (44 mg, 0.069 mmol). The enantiomeric purity of (2*S*,3*R*)-*ent*-**17a** was determined to be 86% ee ($[\alpha]_D^{20}$ +16.1 (c 1.0, CH_2Cl_2)) by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 12.62 min (major enantiomer, *ent*-**17a**) and t_R = 26.32 min (minor enantiomer, **17a**). The enantiomeric purity of (2*R*,3*R*)-**26a** was determined to be 87% ee ($[\alpha]_D^{20}$ +13.9 (c 1.0, CH_2Cl_2) by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 14.96 min (major enantiomer, **26a**) and t_R = 21.33 min (minor enantiomer, *ent*-**26a**).

*4-Oxiranylbutanal **15b**.* 5-Hexen-1-ol (1.20 mL, 10.0 mmol) was dissolved in 60 mL of dry CH_2Cl_2 and cooled to 0 °C. *m*-CPBA (77 wt %, 2.69 g, 12.0 mmol, 1.2 equiv) was added in portions, and the resulting mixture was allowed to stir at 0 °C for 2 h and was then allowed to slowly warm to room temperature. After another 12 h, the mixture was cooled to 0 °C, and 10 mL of satd $Na_2S_2O_3$ was added. The aqueous phase was extracted with CH_2Cl_2, and the combined organic phases were washed with satd $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product (895 mg) consisted of a mixture of a 22% recovery of 5-hexen-1-ol and a 56% yield of 4-oxiranylbutan-1-ol which was used in the next step without further purification.

The above 4-oxiranylbutan-1-ol was oxidized by the method of Vatele.[9] To a 50 mL flame-dried round-bottom flask equipped with a stir bar was added the above mixture containing 4-oxiranylbutan-1-ol (5.25 mmol) in dry CH_2Cl_2 (28 mL). To the resulting solution were added TEMPO (41 mg, 0.26 mmol, 0.050 equiv) and PhIO (1.39 g, 6.30 mmol, 1.20 equiv). The suspension was cooled to 0 °C, and Yb(OTf)$_3$ (65 mg, 0.10 mmol, 0.020 equiv) was added. The reaction mixture was stirred at room temperature for 12 h (until the alcohol was no longer detectable by TLC). The resulting suspension was filtered through a Celite pad and concentrated under reduced pressure. Purification of the crude aldehyde by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/Et_2O as eluent, flash column) afforded the aldehyde **15b** as a colorless liquid in 48% yield (287 mg, 2.52 mmol). Spectral data for **15b**: R_f = 0.31 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42−1.52 (m, 1H), 1.61−1.70 (m, 1H), 1.75−1.83 (m, 2H), 2.46 (dd, 1H, J = 5.0, 2.5 Hz), 2.51 (td, 2H, J = 7.0, 1.2 Hz), 2.74 (dd, 1H, J = 5.0, 4.0 Hz), 2.86−2.93 (m, 1H), 9.77 (t, 1H, J = 1.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.6, 31.7, 43.5, 46.8, 51.8, 202.0.

*(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-(3-oxiranylpropyl)-aziridine-2-carboxamide (2R,3S)-**18b** (Table 4, Entry 2).* Racemic 4-oxiranylbutanal **15b** (25 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 4:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18b** as a white foam in 90% yield (121 mg, 0.179 mmol); *trans*/*cis* 8:1. The ratio of isomers of **18b** was determined to be 49:49:1:1 by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 18.47, 18.98 min (minor diastereomer, (2*S*,3*R*)-**18b**) and t_R = 35.33, 36.71 min (major diastereomer, (2*R*,3*S*)-**18b**). The aziridination of **18b** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18b** in 0.5:0.5:49.5:49.5 dr and 62% yield (85 mg, 0.12 mmol); *trans*/*cis* 17:1. Spectral data for (2*R*,3*S*)-**18b**: R_f = 0.32 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, 3H, J = 7.5 Hz), 1.10−1.48 (m, 8H), 1.35 (s, 18H), 1.38 (s, 18H), 1.59−1.66 (m, 2H), 2.10 (dd, 1H, J = 6.8, 2.8 Hz), 2.13−2.21 (m, 1H), 2.31−2.38 (m, 1H), 2.60−2.67 (m, 1H), 2.73 (d, 1H, J = 2.5 Hz), 3.03−3.13 (m, 1H), 3.15−3.25 (m, 1H), 3.63 (d, 6H, J = 2.0 Hz), 4.15 (s, 1H), 6.62 (t, 1H, J = 5.2 Hz), 7.18 (s, 2H), 7.28 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 20.04 24.6, 26.0, 26.0, 32.0, 32.1, 35.7, 35.7, 38.4, 45.0, 46.7, 46.8, 51.8, 51.9, 64.0, 64.1, 68.6, 125.9, 125.3, 137.1, 137.3, 143.2, 143.3, 158.2, 158.3, 170.5 (one sp^3 carbon not located); HRMS (ESI-TOF) m/z 677.5252 [(M + H$^+$), calcd for $C_{43}H_{69}N_2O_4$ 677.5257];

*Methyl 4-Oxobutyrate **15c**.* To a solution of γ-butyrolactone (0.76 mL, 10 mmol) in MeOH (50 mL) was added triethylamine (8.4 mL, 60 mmol, 6.0 equiv). The reaction mixture was heated at 60 °C and stirred for 20 h. The reaction solution was then cooled, diluted with hexanes (50 mL), and concentrated in vacuo. The residual MeOH was removed azeotropically with hexanes (2 × 20 mL). Purification by silica gel chromatography (20 mm × 200 mm column, 6:1 hexanes/EtOAc as eluent, flash column) afforded methyl 4-hydroxybutyrate as a colorless liquid in 59% yield (696 mg, 5.89 mmol). Spectral data: R_f = 0.60 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.86 (pent, 2H, J = 6.5 Hz), 1.87−1.92 (br, 1H), 2.42 (t, 2H, J = 7.0 Hz), 3.65 (s, 3H), 3.66 (t, 2H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.6, 30.7, 51.9, 62.0, 174.4. These spectral data match those previously reported for this compound.[10]

Methyl 4-hydroxybutyrate was oxidized by the method of Vatele.[9] To a 25 mL flame-dried round-bottom flask equipped with a stir bar was added methyl 4-hydroxybutyrate (390 mg, 3.30 mmol) in dry CH_2Cl_2 (28 mL). To the resulting solution were added TEMPO (26 mg, 0.16 mmol, 0.050 equiv) and PhIO (871 mg, 3.96 mmol, 1.20 equiv). The suspension was cooled to 0 °C, and Yb(OTf)$_3$ (41 mg, 0.066 mmol, 0.020 equiv) was added. The reaction mixture was stirred at 0 °C for 3 h (until the alcohol was no longer detectable by TLC). The resulting suspension was filtered through a Celite pad and concentrated under reduced pressure. Purification of the crude aldehyde by silica gel chromatography (20 mm × 200 mm column, 2:1 hexanes/Et_2O as eluent, flash column) afforded aldehyde **15c** as a colorless liquid in 58% yield (222 mg, 1.91 mmol). Spectral data for **15c**: R_f = 0.52 (1:2 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) 2.60 (t, 2H, J = 6.8 Hz), δ 2.77 (t, 2H, J = 6.8 Hz), 3.66 (s, 3H), 9.78 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.3, 38.5, 51.9, 172.6, 200.0. These spectral data match those previously reported for this compound.[11]

*Methyl 3-((2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)-methyl)-3-(butylcarbamoyl)aziridin-2-yl)propanoate **18c** (Table 4, Entry 3).* Methyl 4-oxobutyrate **15c** (26 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 4:1 hexanes/EtOAc as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18c** as a white foam (mp 160−162 °C on 86% ee material) in 78% yield (106 mg, 0.156 mmol). The enantiomeric purity of (2*R*,3*S*)-**18c** was determined to be 86% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-

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propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 15.72 min (minor enantiomer, *ent*-**18c**) and t_R = 30.32 min (major enantiomer, **18c**). The aziridination of **15c** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18c** in 93% ee and 59% yield (80 mg, 0.12 mmol). Spectral data for (2*R*,3*S*)-**18c**: R_f = 0.28 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, 3H, J = 7.5 Hz), 1.23−1.31 (m, 4H), 1.36 (s, 18H), 1.39 (s, 18H), 1.77−1.84 (m, 1H), 1.86−1.92 (m, 2H), 1.97−2.11 (m, 2H), 2.13 (d, 1H, J = 3.0 Hz), 2.20 (td, 1H, J = 6.2, 2.8 Hz), 3.10 (m, 1H), 3.17 (m, 1H), 3.59 (s, 3H), 3.63 (s, 6H), 4.12 (s, 1H), 6.58 (t, 1H, J = 5.5 Hz), 7.20 (s, 2H), 7.30 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 20.1, 21.8, 31.7, 32.1, 32.1, 32.2, 35.7, 35.7, 38.5, 44.8, 45.6, 51.6, 64.0, 64.2, 68.7, 137.0, 137.1, 143.3, 143.5, 158.4, 170.2, 172.9 (3 sp^2 carbons not located); IR (thin film) cm^{-1}; HRMS (ESI-TOF) m/z 679.5049 [(M + H$^+$), calcd for $C_{42}H_{67}N_2O_5$ 679.5050]; $[\alpha]_D^{20}$ +13.9 (*c* 1.0, EtOAc) on 93% ee (2*S*,3*R*)-*ent*-**18c** (HPLC).

4-Oxobutanenitrile ***15d.*** Following a reported procedure,[12] a mixture of 4,4-dimethoxybutanenitrile (1.29 g, 10.0 mmol), acetone (50 mL), and 6 N HCl (20 mL) was stirred at 0 °C for 8 h. The mixture was then concentrated to approximately 5 mL and was extracted with $CHCl_3$ (4 × 15 mL). The combined organic phase was dried with Na_2SO_4. The solvent was removed by rotary evaporation to give crude aldehyde **15d** as an oil. Purification of the crude aldehyde by silica gel chromatography (20 mm × 200 mm column, 2:1 hexanes/EtOAc as eluent, flash column) afforded aldehyde **15d** as a colorless liquid in 76% yield (635 mg, 7.64 mmol). Spectral data for **15d**: R_f = 0.26 (1:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.60 (t, 2H, J = 7.0 Hz), 2.88 (t, 2H, J = 7.0 Hz), 9.76 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.95, 38.87, 118.48, 197.03. These spectral data match those previously reported for this compound.[11]

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-(2-cyanoethyl)aziridine-2-carboxamide ***18d*** *(Table 4, Entry 4).* 4-Oxobutanenitrile **15d** (20 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/EtOAc as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18d** as a white foam (mp 164−167 °C on 60% ee material) in 88% yield (114 mg, 0.176 mmol). The enantiomeric purity of (2*R*,3*S*)-**18d** was determined to be 40% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 16.97 min (minor enantiomer, *ent*-**18d**) and t_R = 28.53 min (major enantiomer, **18d**). The aziridination of **15d** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18d** in 60% ee and 51% yield (66 mg, 0.10 mmol). The aziridination of **15d** in the presence of (*R*)-VAPOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18d** in 47% ee and 61% yield (79 mg, 0.12 mmol). Spectral data for (2*R*,3*S*)-**18d**: R_f = 0.57 (1:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, 3H, J = 7.0 Hz), 1.09−1.22 (m, 2H), 1.22−1.32 (m, 2H), 1.36 (s, 18H), 1.40 (s, 18H), 1.75−1.87 (m, 2H), 1.87−1.96 (m, 1H), 2.06−2.13 (m, 1H), 2.20 (d, 1H, J = 2.5 Hz), 2.24−2.32 (m, 1H), 3.04−3.24 (m, 2H), 3.64 (d, 6H, J = 8.5 Hz), 4.09 (s, 1H), 6.51 (t, 1H, J = 5.8 Hz), 7.20 (s, 2H), 7.32 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 15.6, 20.0, 22.8, 32.0, 32.1, 32.2, 35.7, 35.8, 38.6, 44.1, 45.0, 64.01 64.36, 69.4, 118.4, 124.8, 125.0, 125.4, 136.7, 143.6, 144.1, 158.6, 169.4 (1 sp^2 C not located); IR (thin film) 3323s, 2962vs, 2872s, 1645vs, 1550s, 1446s, 1413vs, 1394s, 1360s, 1261s, 1221vs, 1114s, 1014s cm^{-1}; HRMS (ESI-TOF) m/z 646.4943 [(M + H$^+$), calcd for $C_{41}H_{64}N_3O_3$: 646.4948]; $[\alpha]_D^{20}$ −43.4 (*c* 1.0, EtOAc) on 40% ee (2*S*,3*R*)-**18d**. (HPLC).

3-(tert-Butyldimethylsilyl)oxypropanal ***15e.*** *n*-BuLi (12.5 mL, 1.6 M in hexanes, 20. mmol) was added dropwise to a solution of freshly distilled 1,3-propanediol (1.44 mL, 20.0 mmol) in THF (40 mL) at 0 °C. A solution of *tert*-butyldimethylsilyl chloride (3.01 g, 20.0 mmol) in THF (2.0 mL) was added after 30 min via cannula. The solution was allowed to warm up to room temperature and stirred for 3 h. The reaction was quenched by water (5 mL) and concentrated in vacuo. The residue was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic phase was washed with brine (10 mL). The organic phase was dried over $MgSO_4$ and concentrated in vacuo to afford a yellow oil. Purification by silica gel chromatography (20 mm × 200 mm column, 6:1 hexanes/EtOAc as eluent, flash column) afforded alcohol 3-(*tert*-butyldimethylsilyl)oxypropan-1-ol as a colorless liquid in 83% yield (3.16 g, 16.6 mmol). Spectral data: R_f = 0.61 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.87 (s, 9H), 1.75 (pent, 2H, J = 5.8 Hz), 2.61−2.64 (br, 1H), 3.78 (q, 2H, J = 5.5 Hz), 3.81 (t, 2H, J = 5.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.52, 25.85, 34.11, 62.46, 62.48, 62.96. These spectral data match those previously reported for this compound.[12]

The above alcohol was oxidized by the method of Vatele.[9] To a 25 mL flame-dried round-bottom flask equipped with a stir bar was added 3-(*tert*-butyldimethylsilyl)oxypropan-1-ol (390 mg, 5.02 mmol) in dry CH_2Cl_2 (20 mL). To the resulting solution was added TEMPO (39 mg, 0.25 mmol, 0.050 equiv) and PhIO (1.38 mg, 6.26 mmol, 1.20 equiv). The suspension was cooled to 0 °C and Yb(OTf)$_3$ (62 mg, 0.10 mmol, 0.020 equiv) was added. The reaction mixture was stirred at 0 °C for 2 h (until the alcohol was no longer detectable by TLC). The resulting suspension was filtered through a Celite pad and concentrated under reduced pressure. Purification of the crude aldehyde by silica gel chromatography (20 mm × 200 mm column, 15:1 hexanes/EtOAc as eluent, flash column) afforded aldehyde **15e** as a colorless liquid in 98% yield (927 mg, 4.92 mmol). Spectral data for **15e**: R_f = 0.34 (10:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.86 (s, 9H), 2.57 (td, 2H, J = 6.0, 2.0 Hz), 3.96 (t, 2H, J = 6.0 Hz), 9.78 (t, 1H, J = 2.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.4, 18.2, 25.8, 46.6, 57.4, 202.1.

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-(2-((tert-butyldimethylsilyl)oxy)ethyl)aziridine-2-carboxamide ***18e*** *(Table 4, Entry 5).* 3-(*tert*-Butyl-dimethylsilyl)propanal **15e** (51 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 4:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18e** as a white foam (mp 61−62 °C on 96% ee material) in 60% yield (90 mg, 0.12 mmol); *trans*/*cis* > 99:1. The enantiomeric purity of (2*R*,3*S*)-**18e** was determined to be 96% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 95:5 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 14.09 min (minor enantiomer, *ent*-**18e**) and t_R = 21.85 min (major enantiomer, **18e**). (Table 4, entry 5). The aziridination of **15e** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18e** in 98% ee and 56% yield (84 mg, 0.11 mmol); *trans*/*cis* > 99:1. Spectral data for (2*R*,3*S*)-**18e**: R_f = 0.34 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.07 (s, 6H), 0.81 (s, 9H), 0.89 (t, 3H, J = 7.2 Hz), 1.35 (s, 18H), 1.39 (s, 18 H), 1.31−1.42 (m, 4H), 1.81 (q, 2H, J = 6.5 Hz), 2.11 (d, 1H, J = 3.0 Hz), 2.34 (td, 1H, J = 6.4, 2.8 Hz), 3.03−3.10 (m, 1H), 3.20−3.27 (m, 1H), 3.40−3.51 (m, 2H), 3.64 (d, 6H, J = 7.0 Hz), 4.14 (s, 1H), 6.65 (t, 1H, J = 6.0 Hz), 7.18 (s, 2H), 7.28 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.5, −5.8, 13.8, 20.0, 25.8, 29.7, 31.7, 32.1, 32.1, 35.7, 35.7, 38.4, 44.1, 44.5, 61.4, 64.0, 64.1, 68.5, 125.1, 125.3, 137.1, 137.2, 143.2, 143.2, 158.2, 158.3, 170.5 (1 sp^3 C not located); IR (thin film) 3396s, 2958s, 1653vs, 1412s, 1361s, 1260s, 1221s, 1114s, 1015s cm^{-1}; HRMS (ESI-TOF) m/z 751.5803 [(M + H$^+$) calcd for $C_{46}H_{79}N_2O_4Si$ 751.5809]; $[\alpha]_D^{20}$ −2.6 (*c* 1.0, EtOAc) on 96% ee material (HPLC).

tert-Butyl (3-Oxopropyl)carbamate ***15f.*** This oxidation employed the method of Vatele.[9] To a 25 mL flame-dried round-bottom flask equipped with a stir bar were added *tert*-butyl (3-hydroxypropyl)-carbamate (0.85 mL, 5.0 mmol) and dry CH_2Cl_2 (20 mL). To the resulting solution were added TEMPO (39 mg, 0.25 mmol, 0.050 equiv) and PhIO (1.32 mg, 6.00 mmol, 1.20 equiv). The suspension was cooled to 0 °C, and Yb(OTf)$_3$ (62 mg, 0.10 mmol, 0.020 equiv) was added. The reaction mixture was stirred at room temperature for 5 h (until the alcohol was no longer detectable by TLC). The resulting suspension was filtered through a Celite pad and concentrated under reduced pressure. Purification of the crude aldehyde by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/EtOAc as eluent, flash column) afforded aldehyde **15f** as a colorless liquid in 92% yield (797 mg, 4.60

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mmol). Spectral data for **15f**: R_f = 0.46 (1:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 9H), 2.69 (t, 2H, J = 5.8 Hz), 3.40 (q, 2H, J = 6.0 Hz), 4.81−5.07 (br, 1H), 9.79 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 33.8, 43.9, 78.9, 155.6, 201.3.

tert-Butyl (2-((2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)-methyl)-3-(butylcarbamoyl)aziridin-2-yl)ethyl)carbamate ***18f*** *(Table 4, Entry 6).* *tert*-Butyl (3-oxopropyl)carbamate **15f** (42 μL, 0.22 mmol, 1.1 equiv) was reacted according to General Procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv) and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/EtOAc as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18f** as a white foam (mp 113−115 °C on 88% ee material) in 67% yield (99 mg, 0.13 mmol); *trans*/*cis* 25:1. The enantiomeric purity of (2*R*,3*S*)-**18f** was determined to be 85% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 95:5 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 19.10 min (minor enantiomer, *ent*-**18f**) and t_R = 24.78 min (major enantiomer, **18f**). The aziridination of **15f** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18f** in 88% ee and 68% yield (100 mg, 0.136 mmol); *trans*/*cis* 10:1. Spectral data for (2*R*,3*S*)-**18f**: R_f = 0.23 (2:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, 3H, J = 7.2 Hz), 1.09−1.20 (m, 4H), 1.35 (s, 18H), 1.37−1.38 (m, 9H), 1.39 (s, 18H), 1.68−1.76 (m, 1H), 1.78−1.88 (m, 1H), 2.13 (d, 1H, J = 3.0 Hz), 2.14−2.21 (m, 1H), 2.86−2.95 (m, 1H), 3.06−3.13 (m, 2H), 3.14−3.23 (m, 1H), 3.60 (s, 1H), 3.63 (d, 6H, J = 2.5 Hz), 4.13 (s, 1H), 6.58 (t, 1H, J = 5.5 Hz), 7.18 (s, 2H), 7.28 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 20.1, 28.4, 28.4, 31.7, 32.1, 32.1, 32.2, 35.7, 35.8, 38.5, 44.78 64.0, 64.2, 68.7, 125.1, 125.3, 126.3, 137.0, 137.1, 143.3, 155.7, 158.3, 158.4, 170.2 (two sp^3 carbons not located); IR (thin film) 3427s, 2961s, 1653vs, 1412s, 1365s, 1261s, 1222s, 1173s, 1115s, 1014s cm^{-1}; HRMS (ESI-TOF) m/z 736.5618 [(M + H$^+$), calcd for $C_{45}H_{74}N_3O_5$ 736.5628]; $[\alpha]_D^{20}$ +15.6 (*c* 1.0, EtOAc) on 88% ee (2*S*,3*R*)-*ent*-**18f** (HPLC).

N-(3-Oxopropyl)phthalimide ***15g.*** This oxidation employed the method of Vatele.[9] To a 25 mL flame-dried round-bottom flask equipped with a stir bar was added 2-(3-hydroxypropyl)isoindoline-1,3-dione (1.03 g, 5.00 mmol) and dry CH_2Cl_2 (20 mL). To the resulting solution was added TEMPO (39 mg, 0.25 mmol, 0.050 equiv) and PhIO (1.32 g, 6.00 mmol, 1.20 equiv). The suspension was cooled to 0 °C and Yb(OTf)$_3$ (62 mg, 0.10 mmol, 0.020 equiv) was added. The reaction mixture was stirred at room temperature for 24 h (until the alcohol was no longer detectable by TLC). The resulting suspension was filtered through a Celite pad and concentrated under reduced pressure. Purification of the crude aldehyde by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/EtOAc as eluent, flash column) afforded aldehyde **15g** as a white solid (mp 136−138 °C) in 49% yield (498 mg, 2.45 mmol). Spectral data for **15g**: R_f = 0.42 (1:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.85 (td, 2H, J = 7.0, 1.2 Hz), 4.01 (t, 2H, J = 7.0 Hz), 7.70 (dd, 2H, J = 5.8, 3.2 Hz), 7.82 (dd, 2H, J = 5.5, 3.5 Hz), 9.79 (t, 1H, J = 1.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.6, 42.3, 123.3, 131.9, 134.1, 168.0, 199.4.

(2R,3S)-1-(bis(3,5-ditert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-(2-phthalylethyl) aziridine-2-carboxamide ***18g****: (Table 4, entry 7).* *N*-(3-Oxopropyl)phthalimide **15g** (45 mg, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 4:1 hexanes/EtOAc as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18g** as a white foam (mp 57−60 °C on 91% ee material) in 71% yield (109 mg, 0.142 mmol); *trans*/*cis* 6:1. The enantiomeric purity of (2*R*,3*S*)-**18g** was determined to be 91% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 85:15 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 26.41 min (minor enantiomer, *ent*-**18g**) and t_R = 37.97 min (major enantiomer, **18g**). The aziridination of **15g** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18g** in 60% ee and 64% yield (98 mg, 0.13 mmol); *trans*/*cis* 6:1. Spectral data for (2*R*,3*S*)-**18g**: R_f = 0.62 (1:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (t, 3H, J = 7.8 Hz), 1.18−1.32 (m, 4H), 1.37 (s, 18H), 1.40 (s, 18H), 2.06 (d, 1H, J = 3.0 Hz), 2.26−2.32 (m, 1H), 3.00−3.11 (m, 1H), 3.13−3.24 (m, 2H), 3.46−3.54 (m, 1H), 3.61 (d, 6H, J = 1.0 Hz), 3.65 (t, 2H, J = 7.5 Hz), 4.17 (s, 1H), 6.55 (t, 1H, J = 5.8 Hz), 7.18 (s, 2H), 7.32 (s, 2H), 7.68 (dd, 2H, J = 5.5, 3.0 Hz), 7.80 (dd, 2H, J = 5.0, 3.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 20.0, 25.9, 32.1, 32.1, 32.2, 35.7, 35.7, 36.9, 38.4, 44.2, 44.6, 64.0, 64.2, 68.6, 123.1, 123.2, 125.1, 125.2, 125.9, 132.0, 133.8, 134.0, 137.0, 143.3, 158.3, 168.2, 169.8; IR (thin film) 3370s, 2957s, 2926s, 2870s, 1773s, 1717vs, 1451s, 1396s, 1372s, 1273vs, 1224vs, 1115s, 1011s cm^{-1}; HRMS (ESI-TOF) m/z 766.5152 [(M + H$^+$), calcd for $C_{48}H_{68}N_3O_5$ 766.5159]; $[\alpha]_D^{20}$ −5.8 (*c* 1.0, EtOAc) on 91% ee (2*R*,3*S*)-**18g** (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-phenethylaziridine-2-carboxamide ***18h****: (Table 4, Entry 8).* Hydrocinnamaldehyde **15h** (29 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 3:1 hexanes/Et$_2$O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18h** as a white foam (mp 114−117 °C on 98% ee material) in 87% yield (121 mg, 0.174 mmol); *trans*/*cis* 45:1. The enantiomeric purity of (2*R*,3*S*)-**18h** was determined to be 98% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 10.04 min (minor enantiomer, *ent*-**18h**) and t_R = 18.39 min (major enantiomer, **18h**). The aziridination of **15h** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18h** in 73% ee and 77% yield (107 mg, 0.154 mmol). Spectral data for (2*R*,3*S*)-**18h**: R_f = 0.20 (2:1 hexanes/Et$_2$O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, 3H, J = 7.5 Hz), 1.23−1.31 (m, 4H), 1.36 (s, 18H), 1.40 (s, 18H), 1.79−1.87 (m, 1H), 1.93−2.00 (m, 1H), 2.13 (d, 1H, J = 3.0 Hz), 2.22 (td, 1H, J = 6.1, 2.7 Hz), 2.30−2.36 (m, 1H), 2.41−2.47 (m, 1H), 3.06−3.12 (m, 1H), 3.16−3.23 (m, 1H), 3.63 (d, 6H, J = 5.5 Hz), 4.19 (s, 1H), 6.62 (t, 1H, J = 5.8 Hz), 6.94 (d, 2H, J = 7.5 Hz), 7.13 (t, 1H, J = 7.2 Hz), 7.19−7.22 (m, 2H), 7.20 (s, 2H), 7.34 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6, 20.1, 28.2, 31.7, 32.1, 32.1, 34.4, 35.7, 35.8, 38.5, 44.9, 46.4, 64.0, 64.2, 68.6, 125.1, 125.3, 126.0, 128.2, 128.3, 129.6, 137.2, 137.3, 141.0, 143.3, 158.3, 158.4, 170.6; IR (thin film) 3441s, 2961s, 1645vs, 1412s, 1221s, 1115s, 1014s cm^{-1}; HRMS (ESI-TOF) m/z 697.5319 [(M + H$^+$), calcd for $C_{46}H_{69}N_2O_3$ 697.5308]; $[\alpha]_D^{20}$ −15.7 (*c* 1.0, EtOAc) on 98% ee material (HPLC).

(2R,3S)-3-Benzyl-1-(bis(3,5-di-tert-butyl-4-methoxyphenyl)-methyl)-N-butylaziridine-2-carboxamide ***18i*** *(Table 4, Entry 9).* Phenylacetaldehyde **15i** (25 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 4:1 hexanes/Et$_2$O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18i** as a white foam (mp 82−84 °C on 96% ee material) in 71% yield (97 mg, 0.14 mmol); *trans*/*cis* 19:1. The enantiomeric purity of (2*R*,3*S*)-**18i** was determined to be 88% ee by HPLC analysis (CHIRALCEL OD-H column, 90:10 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 9.80 min (major enantiomer, **18i**) and t_R = 31.03 min (minor enantiomer, **18i**) (Table 4, entry 9). The aziridination of **15i** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18i** in 96% ee and 86% yield (119 mg, 0.174 mmol); *trans*/*cis* 27:1. Spectral data for (2*R*,3*S*)-**18i**: R_f = 0.30 (2:1 hexanes/Et$_2$O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 7.5 Hz), 1.23−1.30 (m, 2H), 1.37 (s, 36H), 1.34−1.43 (m, 2H), 2.31 (d, 1H, J = 3.0 Hz), 2.45−2.48 (m, 1H), 2.89 (dd, 1H, J = 10.0, 6.0 Hz), 3.00 (dd, 1H, J = 10.0, 6.0 Hz), 3.05−3.12 (m, 1H), 3.14−3.21 (m, 1H), 3.65 (d, 6H, J = 4.5 Hz), 4.29 (s, 1H), 6.61 (t, 1H, J = 5.8 Hz), 6.96 (d, 2H, J = 8.0 Hz), 7.10 (t, 1H, J = 7.2 Hz), 7.15 (t, 2H, J = 7.5 Hz), 7.21 (s, 2H), 7.30 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 20.1, 31.7, 32.1, 35.7, 38.5, 45.2, 47.2, 64.0, 64.2, 68.9, 125.2, 125.3, 126.3, 128.4, 128.4, 137.0, 137.1, 138.7, 143.2, 143.3, 158.3, 158.4, 170.2 (three sp^3 carbons not located); IR (thin film) 3323s, 2960vs, 2871s, 1656vs, 1531s, 1454vs, 1412vs, 1394s, 1361s, 1265s, 1221vs, 1115s, 1013s cm^{-1}; HRMS (ESI-

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TOF) m/z 683.5182 [(M + H^+), calcd for $C_{45}H_{67}N_2O_3$: 683.5152]; $[\alpha]_D^{20}$ +9.7 (c 1.0, EtOAc) on 96% ee (2*S*,3*R*)-*ent*-**18i** (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-isobutylaziridine-2-carboxamide ***18j*** *(Table 4, Entry 10).* Isovaleraldehyde **15j** (24 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 5:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18j** as a white foam (mp 136−139 °C on 95% ee material) in 88% yield (114 mg, 0.176 mmol); *trans*/*cis* 12:1. The enantiomeric purity of (2*R*,3*S*)-**18j** was determined to be 95% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 95:5 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 9.80 min (minor enantiomer, *ent*-**18j**) and t_R = 21.43 min (major enantiomer, **18j**). The aziridination of **15j** in the presence of (*R*)-^{t}Bu$_2$VANOL BOROX catalyst afforded (2*S*,3*R*)-*ent*-**18j** in 75% ee and 70% yield (91 mg, 0.14 mmol); *trans*/*cis* 19:1. Spectral data for (2*R*,3*S*)-**18j**: R_f = 0.42 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.75 (d, 3H, J = 6.5 Hz), 0.86 (d, 3H, J = 6.5 Hz), 0.89 (t, 3H, J = 7.5 Hz), 1.15−1.47 (m, 7H), 1.36 (s, 18H), 1.39 (s, 18H), 2.08 (d, 1H, J = 3.0 Hz), 2.14−2.22 (m, 1H), 3.07−3.13 (m, 1H), 3.16−3.23 (m, 1H), 3.63 (s, 6H), 4.14 (s, 1H), 6.63 (t, 1H, J = 5.8 Hz), 7.20 (s, 2H), 7.28 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 20.1, 21.9, 23.1, 27.3, 31.7, 32.9, 32.1, 35.0, 35.7, 38.4, 45.3, 45.8, 64.0, 64.2, 68.5, 125.2, 125.3, 137.2, 137.4, 143.1, 143.2, 158.2, 158.3, 170.71; IR (thin film) 3318s, 2958vs, 2870s, 1648vs, 1533vs, 1466vs, 1443vs, 1412vs, 1393s, 1361s, 1265s, 1221vs 1115vs, 1014vs cm^{-1}; HRMS (ESI-TOF) m/z 649.5303 [(M + H^+), calcd for $C_{42}H_{69}N_2O_3$ 649.5308]; $[\alpha]_D^{20}$ −14.9 (c 1.0, EtOAc) on 98% ee (2*R*,3*S*)-**18j** (HPLC).

(2R,3S)-1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-N-butyl-3-cyclohexylaziridine-2-carboxamide ***18k*** *(Table 4, Entry 11).* Cyclohexanecarboxaldehyde **15k** (27 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide **9** (34 mg, 0.24 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 5:1 hexanes/Et_2O as eluent, flash column) afforded pure *trans*-aziridine (2*R*,3*S*)-**18k** as a white foam (mp 174−178 °C on 57% ee material) in 45% yield (114 mg, 0.176 mmol); *trans*/*cis* 12:1. The enantiomeric purity of (2*R*,3*S*)-**18k** was determined to be 28% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 95:5 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 10.18 min (minor enantiomer, *ent*-**18k**) and t_R = 20.87 min (major enantiomer, **18k**). The aziridination of **15k** according to General procedure C in the presence of (*R*)-VAPOL BOROX catalyst afforded (2*S*,3*R*)-**18k** in 57% ee and 56% yield. The aziridination of **15k** according to general procedure D in the presence of (*S*)-VANOL BOROX catalyst afforded (2*R*,3*S*)-**18k** in 8% ee and 61% yield. Spectral data for (2*R*,3*S*)-**18k**: R_f = 0.36 (2:1 hexanes/Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.56−0.69 (m, 2H), 0.77−0.93 (m, 2H), 0.90 (t, 3H, J = 7.5 Hz), 0.95−1.18 (m, 5H), 1.19−1.46 (m, 2H), 1.36 (s, 18H), 1.39 (s, 18H), 1.50−1.65 (m, 2H), 1.68−1.75 (m, 1H), 1.76−1.83 (m, 1H), 1.90 (dd, 1H, J = 4.5, 3.0 Hz), 2.03 (d, 1H, J = 3.0 Hz), 3.04−3.13 (m, 1H), 3.15−3.24 (m, 1H), 3.60 (s, 3H), 3.63 (s, 3H), 4.11 (s, 1H), 6.60 (t, 1H, J = 5.8 Hz), 7.25 (s, 2H), 7.33 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 20.1, 25.8, 26.0, 26.0, 29.7, 31.7, 32.1, 32.1, 35.0, 35.7, 38.4, 44.2, 52.9, 64.0, 64.3, 69.5, 125.1, 125.1, 137.4, 137.7, 143.2, 143.2, 158.3, 158.4, 170.8; IR (thin film) 3423s, 2959s, 2926s, 1647vs, 1448s, 1413s, 1360s, 1221vs, 1115s, 1014s cm^{-1}; HRMS (ESI-TOF) m/z 675.5459 [(M + H^+), calcd for $C_{44}H_{71}N_2O_3$: 675.5465]; $[\alpha]_D^{20}$ −2.9 (c 1.0, EtOAc) on 28% ee material (HPLC).

1-(Bis(3,5-di-tert-butyl-4-methoxyphenyl)methyl)-3-(tert-butyl)-N-butylaziridine-2-carboxamide ***18l*** *(Table 4, Entry 12).* Pivaldehyde **15l** (24 μL, 0.22 mmol, 1.1 equiv) was reacted according to general procedure E with BUDAM amine **10** (94 mg, 0.20 mmol), (*S*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-butyl diazoacetamide (34 mg, 0.24 mmol, 1.2 equiv). The ^{1}H NMR spectrum of the crude reaction mixture indicated that a 76% yield of the imine from **15l** and **10** had formed along with a 6% yield of **18l**. The absolute stereochemistry of the product from the (*S*)-VANOL catalyst was assigned as (2*R*,3*S*)-**18h** on the basis of the stereochemistry known for the reaction of the corresponding imine.[4a]

2-Hexadecynal ***15n****.* *n*-BuLi (2.5 *M* in hexanes, 18.8 mL, 30. mmol) was added dropwise to a solution of 1-hexadecyne **41** (6.67 g, 30 mmol) in dry Et_2O (25 mL) at −40 °C under nitrogen. After 30 min, dry DMF (3.5 mL, 45 mmol, 1.5 equiv) was added, the mixture was allowed to warm to room temperature, and stirring was continued for 30 min. The mixture was poured into ice−water and acidified slightly with concentrated HCl. The mixture was then neutralized with saturated aq $NaHCO_3$ until a pH between 6 and 7 was reached. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated. Purification of the crude aldehyde by silica gel chromatography (20 mm × 200 mm column, 2:1 hexanes/CH_2Cl_2 as eluent, flash column) afforded aldehyde **15n** as a colorless liquid in 68% yield (4.82 g, 20.4 mmol). Spectral data for **15n**: R_f = 0.28 (1:1 hexanes/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (t, 3H, J = 7.0 Hz), 1.19−1.31 (m, 18H), 1.33−1.42 (m, 2H), 1.57 (pent, 2H, J = 7.5 Hz), 2.39 (t, 2H, J = 7.2 Hz), 9.16 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 19.1, 22.7, 27.5, 28.8, 29.0, 29.3, 29.4, 29.6, 29.6, 29.7, 31.9, 81.7, 99.5, 177.3 (one sp^3 carbon not located).

(2R,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(pentadec-1-yn-1-yl)-N-phenylaziridine-2-carboxamide ***19n*** *(Table 4, Entry 14).* 2-Hexadecynal **15n** (52 mg, 0.22 mmol, 1.1 equiv) was reacted according to general procedure C with MEDAM amine **1** (60 mg, 0.20 mmol), (*R*)-VANOL (8.8 mg, 0.020 mmol, 0.10 equiv), and *N*-phenyl diazoacetamide (45 mg, 0.24 mmol, 1.4 equiv) except that the temperature was −20 °C. Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 8:1 hexanes/EtOAc as eluent, flash column) afforded pure *cis*-aziridine (2*R*,3*R*)-**19n** as an oily liquid in 71% yield (92 mg, 0.14 mmol). The enantiomeric purity of (2*R*,3*R*)-**19n** was determined to be 95% ee by HPLC analysis (CHIRALCEL AD column, 85:15 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times t_R = 7.98 min (minor enantiomer, *ent*-**19n**) and t_R = 21.54 min (major enantiomer, **19n**). The aziridination of **15n** in the presence of (*R*)-VANOL BOROX catalyst at 0 °C afforded (2*R*,3*R*)-**19n** in 91% ee and 92% yield (120 mg, 0.184 mmol). The absolute configuration of **18n** from the (*R*)-VANOL catalyst was assigned as (2*R*,3*R*) on the basis of earlier observations with alkynyl imines.[5] Spectral data for (2*R*,3*R*)-**19n**: R_f = 0.41 (3:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (t, 3H, J = 7.0 Hz), 1.06−1.33 (m, 20H), 2.05 (t, 3H, J = 6.8 Hz), 2.22 (s, 6H), 2.28 (s, 6H), 2.50 (d, 1H, J = 6.2 Hz), 2.53 (d, 2H, J = 6.2 Hz), 3.66 (s, 4H), 3.70 (s, 3H), 6.95 (s, 2H), 7.07 (s, 2H), 7.08 (t, 1H, J = 7.2 Hz), 7.30 (t, 2H, J = 7.5 Hz), 7.49 (d, 2H, J = 7.5 Hz), 8.38 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 16.3, 16.3, 18.7, 22.7, 28.5, 28.7, 29.1, 29.4, 29.4, 29.7, 29.7, 29.7, 31.9, 35.7, 45.9, 59.6, 59.6, 74.6, 75.4, 84.1, 119.8, 124.2, 127.4, 127.4, 128.9, 130.7, 131.1, 136.7, 136.9, 137.2, 156.1, 156.4, 165.8 (one sp^3 carbon not located); IR (thin film) 3427s, 2924s, 2853s, 1659vs, 1602s, 1529vs, 1444s, 1262s, 1222vs, 1146s, 1096s, 1017s cm^{-1}; HRMS (ESI-TOF) m/z 651.4517 [(M + H^+), calcd for $C_{43}H_{59}N_2O_3$: 651.4526]; $[\alpha]_D^{20}$ −20.4 (c 1.0, EtOAc) on 91% ee material (HPLC).

5.5. Absolute Stereochemistry of *trans*- and *cis*-Aziridines.

*(2R,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-N-butyl-3-pentadecylaziridine-2-carboxamide (2R,3R)-****26a*** *(Scheme 4).* Palmitaldehyde **15a** (132 mg, 0.550 mmol, 1.10 equiv) was reacted according to general procedure C with MEDAM amine **1** (150 mg, 0.500 mmol), (*R*)-^{t}Bu$_2$VANOL (28 mg, 0.050 mmol, 0.10 equiv), and *N*-butyl diazoacetamide (85 mg, 0.60 mmol, 1.2 equiv). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 2:1 hexanes/Et_2O as eluent, flash column) afforded aziridine (2*R*,3*R*)-**26a** as an oily liquid in 44% yield (140 mg, 0.220 mmol) and aziridine (2*S*,3*R*)-*ent*-**17a** as an oily liquid in 79% yield (251 mg, 0.395 mmol). The enantiomeric purity of (2*R*,3*R*)-**26a** was determined to be 90% ee by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 222 nm, flow rate 0.7 mL/min): retention times; t_R = 14.96 min (major enantiomer, **26a**) and t_R = 21.33 min (minor enantiomer, *ent*-**26a**). Spectral data for (2*R*,3*R*)-**26a**: R_f = 0.33 (1:1 hexanes/Et_2O); ^{1}H

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NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 7.0 Hz), 0.91 (t, 3H, J = 7.5 Hz), 1.13−1.30 (m, 26H), 1.33−1.41 (m, 6H), 1.90 (q, 1H, J = 6.8 Hz), 2.23 (s, 6H), 2.25 (d, 1H, J = 7.2 Hz), 2.27 (s,6H), 3.12 (hex, 1H, J = 6.5 Hz), 3.33 (hex, 1H, J = 7.0 Hz), 3.43 (s, 1H), 3.68 (d, 6H, J = 6.0 Hz), 6.65 (t, 1H, J = 6.0 Hz), 6.94 (s, 2H), 7.02 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 14.1, 16.2, 20.0, 22.7, 27.1, 28.5, 29.3, 29.3, 29.5, 29.6, 29.7, 31.9, 38.5, 45.2, 47.0, 59.5, 59.6, 76.8, 127.5, 127.5, 130.5, 130.7, 137.8, 137.9, 156.0, 156.1, 168.8 (six sp^3 carbons not located); IR (thin film) 2924vs, 2853s, 1646vs, 1538s, 1483s, 1465s, 1221s, 1137s, 1019s cm^{-1}; HRMS (ESI-TOF) m/z 635.5178 [(M + H^+) calcd for $C_{41}H_{67}N_2O_3$ 635.5152]; $[\alpha]_D^{20}$ +7.0 (c 1.0, CH_2Cl_2) on 90% ee material (HPLC).

General Procedure F of Preparation of Esters from Secondary Amides. To a flame-dried 10 mL round-bottom flask flushed with nitrogen were added the aziridine-2-carboxamide (0.20 mmol) and THF (1.2 mL). The reaction flask was placed into an ice bath for 5 min before the slow dropwise addition of *n*-butyllithium (0.14 mL, 1.6 M in hexanes, 0.22 mmol, 1.1 equiv). The mixture was stirred at 0 °C for another 10 min to ensure complete deprotonation of the secondary amide. A solution of Boc_2O (131 mg, 0.600 mmol, 3.00 equiv) in THF (0.8 mL) was added to the reaction mixture. The resulting mixture was stirred for 2 days at room temperature under a nitrogen atmosphere. The reaction was quenched by satd aq NH_4Cl (2 mL) and brine (4 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. Purification of the crude product by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded *N*-Boc aziridine-2-carboxylamide, which was used immediately in the next step.

To a flame-dried 10 mL round-bottom flask flushed with nitrogen were added ethanol (58 μL, 1.0 mmol, 5.0 equiv) and THF (1.2 mL). The reaction flask was placed into an ice bath for 5 min before the slow dropwise addition of *n*-butyllithium (0.28 mL, 1.6 M in hexanes, 0.44 mmol, 2.2 equiv). The mixture was stirred at 0 °C for another 10 min to ensure the complete formation of lithium ethoxide. A solution of *N*-Boc aziridinecarboxamide in THF (0.8 mL) was added to the reaction mixture. The resulting mixture was warmed to room temperature and stirred overnight until the *N*-Boc amide was no longer detectable by TLC. The reaction was quenched by sat aq NH_4Cl (2 mL) and brine (4 mL). The aqueous layer was extracted with Et_2O (4 × 10 mL). The combined organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. Purification of the crude ester by silica gel chromatography (20 mm × 200 mm column, 9:1 hexanes/EtOAc as eluent, flash column) afforded the ethyl aziridine-2-carboxylate.

General Procedure G of Preparation of Ester from Secondary Amide. To a flame-dried 10 mL round-bottom flask flushed with nitrogen were added the aziridine-2-carboxamide (0.20 mmol) and dichloromethane (1.0 mL). To the resulting solution were added DMAP (49 mg, 0.40 mmol, 2.0 equiv) and Boc_2O (131 mg, 0.600 mmol, 3.00 equiv). The reaction mixture was stirred for 24 h at room temperature under a nitrogen atmosphere. Thereafter, the reaction mixture was concentrated under reduced pressure to afford a crude dark yellow oil. Purification of the crude product by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded *N*-Boc aziridines-2-carboxylamide, which was used immediately in the next step. Ethyl aziridine-2-caboxylates were prepared from *N*-Boc aziridine-2-carboxylamides according to the second step in General Procedure F.

*Ethyl (2R,3R)-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-pentadecylaziridine-2-carboxylate (2R,3R)-**27a**: (Scheme 4).* The amide (2*R*,3*R*)-**26a** (88 mg, 0.14 mmol, 90% ee) was reacted according to general procedure F with *n*-butyllithium (96 μL, 1.6 *M* in hexanes, 0.15 mmol, 1.1 equiv) and Boc_2O (92 mg, 0.42 mmol, 3.0 equiv). Purification of the crude product by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded the *N*-Boc aziridine-2-carboxylamide as a colorless oil. The Boc-protected aziridine was then reacted with *n*-butyllithium (0.19 mL, 1.6 M in hexanes, 0.31 mmol, 2.2 equiv) and ethanol (41 μL, 0.70 mmol, 5.0 equiv). Purification of the crude ester by silica gel chromatography (20 mm × 200 mm column, 9:1 hexanes/EtOAc as eluent, flash column) afforded aziridine (2*R*,3*R*)-**27a** as a white foam (mp 41−42 °C on 95% ee material) in 70% yield (60 mg, 0.098 mmol) over two steps. The optical purity of (2*R*,3*R*)-**27a** was determined to be 95% ee by HPLC analysis (PIRKLE COVALENT (*R*,*R*) WHELK-O 1 column, 99.5:0.5 hexane/2-propanol at 226 nm, flow rate 0.7 mL/min): retention times; t_R = 24.86 min (major enantiomer, **27a**) and t_R = 42.23 min (minor enantiomer, *ent*-**27a**). Spectral data for (2*R*,3*R*)-**27a**: R_f = 0.55 (5:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 7.0 Hz), 1.14−1.33 (m, 29H), 1.45−1.56 (m, 2H), 1.96 (q, 1H, J = 6.5 Hz), 2.20 (d, 1H, J = 7.0 Hz), 2.24 (s, 12H), 3.40 (s, 1H), 3.68 (d, 6H, J = 8.0 Hz), 4.15−4.23 (m, 2H), 7.01 (s, 2H), 7.10 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 14.3, 16.1, 16.12 22.7, 27.2, 27.9, 29.2, 29.3, 29.5, 29.6, 29.6, 29.7, 31.9, 43.5, 47.0, 59.6, 60.7, 77.3, 127.4, 128.1, 130.4, 130.5, 137.7, 138.4, 155.8, 156.1, 169.7 (five sp^3 carbons not located); $[\alpha]_D^{20}$ +48.2 (c 1.0, EtOAc) on 95% ee material (HPLC), lit.[1c] $[\alpha]_D^{20}$ +59.0 (c 1.0, EtOAc) on 98% ee (2*R*,3*R*)-isomer. These spectral data match those previously reported for this compound.[1c]

*(2S,3R)-N-Butyl-3-pentadecylaziridine-2-carboxamide (2S,3R)-**28a**. From (2S,3R)-ent-**17a** (Scheme 4).* To a flame-dried 10 mL round-bottom flask flushed with nitrogen were added (2*S*,3*R*)-*ent*-**17a** (140 mg, 0.220 mmol) and anisole (2.2 mL). The resulting solution was cooled in an ice-bath for 5 min before the slow addition of trifluoromethanesulfonic acid (97 μL, 1.1 mmol, 5.0 equiv). The reaction mixture was gradually warmed to room temperature and continually stirred for 1 h. The reaction was quenched by pouring the mixture into sat aq Na_2CO_3 (20 mL). The aqueous layer was extracted by EtOAc (4 × 10 mL). The combined organic layer was dried with anhydrous Na_2SO_4 and concentrated by reduced pressure. Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 1:2 hexanes/EtOAc as eluent, flash column) afforded the deprotected aziridine (2*S*,3*R*)-**28a** as a white solid (mp 73−74 °C) in 93% yield (72 mg, 0.20 mmol). Spectral data for (2*S*,3*R*)-**28a**: R_f = 0.24 (1:2 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz), 0.92 (t, 3H, J = 7.2 Hz), 1.25−1.52 (m, 33H), 2.05 (m, 1H), 2.17 (m, 1H), 3.26 (q, 2H, J = 6.7 Hz), 6.06 (br, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7, 14.1, 20.0, 22.7, 27.3, 29.3, 29.4, 29.5, 29.6, 29.6, 29.67 29.7, 31.6, 31.9, 37.3, 39.3, 170.7 (five sp^3 carbons not located); IR (thin film) 3288s, 2915vs, 2847s, 1770s, 1759s, 1640s, 1248vs cm^{-1}; HRMS (ESI-TOF) m/z 353.3501 [(M + H^+), calcd for $C_{22}H_{45}N_2O$ 353.3532]; $[\alpha]_D^{20}$ +11.9 (c 1.0, EtOAc) on 87% ee material.

*From (2S,3R)-ent-**18a**: (Scheme 4).* (2*S*,3*R*)-*ent*-**18a** (161 mg, 0.200 mmol) was reacted according to the procedure above for *ent*-**17a** with trifluoromethanesulfonic acid (88 μL, 1.1 mmol, 5.0 equiv) in anisole (2.0 mL). Purification of the crude aziridine by silica gel chromatography (20 mm × 200 mm column, 1:2 hexanes/EtOAc as eluent, flash column) afforded aziridine (2*S*,3*R*)-**28a** as a white solid in 100% yield (72 mg, 0.20 mmol). This material was identical in all respects with that obtained from the deprotection of *ent*-**17a**.

*Ethyl (2S,3R)-1-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-phenylaziridine-2-carbox-ylate (2S,3R)-**30**. From ent-**6a**.* (2*S*,3*R*)-*ent*-**6a** (130 mg, 0.250 mmol, 87% ee) was reacted according to general procedure G with DMAP (61 mg, 0.50 mmol, 2.0 equiv) and Boc_2O (164 mg, 0.750 mmol, 3.00 equiv). Purification of the crude product by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded an *N*-Boc aziridinecarboxylamide as a colorless oil. The Boc-protected aziridine was then reacted with *n*-butyllithium (0.35 mL, 1.6 *M* in hexanes, 0.55 mmol, 2.2 equiv) and ethanol (73 μL, 1.2 mmol, 5.0 equiv). Purification of the crude ester by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded aziridine (2*S*,3*R*)-**30** as a semisolid in 80% yield (95 mg, 0.20 mmol) over two steps. Spectral data for (2*S*,3*R*)-**30**: R_f = 0.48 (5:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (t, 3H, J = 7.0 Hz), 2.16 (s, 6H), 2.26 (s, 6H), 2.83 (d, 1H, J = 2.5 Hz), 3.41 (d, 1H, J = 2.5 Hz), 3.64 (s, 3H), 3.68 (s, 3H), 3.95−4.08 (m, 2H), 4.91 (s, 1H), 7.03−7.11 (m, 2H), 7.07 (d, 2H, J = 4.0 Hz), 7.23−7.25 (m, 1H), 7.28−7.36 (m, 2H), 7.30 (d, 2H, J = 4.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 16.2, 16.2, 45.1, 48.7, 59.5, 59.5, 60.9, 67.0, 126.5, 127.4, 127.7, 127.9, 128.2, 130.3, 130.4, 138.3, 138.5, 138.7, 155.7, 155.8, 168.7; these spectral data match those previously reported

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for this compound;[4a] $[\alpha]_D^{20}$ +5.6 (*c* 1.0, EtOAc) on 87% ee material, lit.[4a] $[\alpha]_D^{20}$ −4.4 (*c* 1.0, EtOAc) on 90% ee (2*R*,3*S*)-isomer.

*From ent-**7a**.* (2*S*,3*R*)-*ent*-**7a** (90 mg, 0.18 mmol, 76% ee) was reacted according to general procedure G with DMAP (44 mg, 0.36 mmol, 2.0 equiv) and Boc_2O (118 mg, 0.540 mmol, 3.00 equiv) for 3 days. Purification of the crude product by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded *N*-Boc aziridinecarboxylamide as a colorless oil. The Boc-protected aziridine was then reacted with *n*-butyllithium (0.25 mL, 1.6 *M* in hexanes, 0.40 mmol, 2.2 equiv) and ethanol (41 μL, 0.90 mmol, 5.0 equiv). Purification of the crude ester by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded aziridine (2*S*,3*R*)-**30** as a semisolid in 60% yield (51 mg, 0.11 mmol) over two steps. This compound was identical in all respects to that obtained from *ent*-**6a**.

*Ethyl (2S,3S)-1-(**b**is(4-methoxy-3,5-dimethylphenyl)methyl)-3-phenylaziridine-2-carboxylate (2S,3S)-**31**. From ent-**25a**.* (2*S*,3*S*)-*ent*-**25a** (161 mg, 0.310 mmol, 95% ee) was reacted according to general procedure G with DMAP (76 mg, 0.62 mmol, 2.0 equiv) and Boc_2O (203 mg, 0.930 mmol, 3.00 equiv). Purification of the crude product by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded an *N*-Boc aziridinecarboxylamide as a colorless oil. The Boc-protected aziridine was then reacted with *n*-butyllithium (0.43 mL, 1.6 *M* in hexanes, 0.68 mmol, 2.2 equiv) and ethanol (91 μL, 1.6 mmol, 5.0 equiv). Purification of the crude ester by silica gel chromatography (20 mm × 200 mm column, 9:1 hexanes/EtOAc as eluent, flash column) afforded aziridine (2*S*,3*S*)-**31** as a white foam (mp 105−107 °C) in 67% yield (98 mg, 0.21 mmol) over two steps. Spectral data for (2*S*,3*S*)-**31**: R_f = 0.38 (5:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (t, 3H, *J* = 7.0 Hz), 2.20 (s, 6H), 2.26 (s, 6H), 2.58 (d, 1H, *J* = 7.0 Hz), 3.13 (d, 1H, *J* = 7.0 Hz), 3.64 (s, 3H), 3.68 (s, 1H), 3.70 (s, 3H), 3.90−3.97 (m, 2H), 7.11 (s, 2H), 7.20 (s, 2H), 7.23−7.26 (m, 3H), 7.38 (d, 2H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 16.2, 16.2, 46.3, 48.2, 59.5, 59.6, 60.5, 77.0, 127.2, 127.4, 127.7, 127.9, 127.8, 130.6, 130.6, 135.3, 137.8, 138.0, 155.9, 156.1, 168.0; these spectral data match those previously reported for this compound;[1c] $[\alpha]_D^{20}$ −26.2 (*c* 1.0, EtOAc) on 95% ee material, lit.[1c] $[\alpha]_D^{20}$ +41.3 (*c* 1.0, EtOAc) on 99% ee (2*R*,3*R*)-isomer.

*From ent-**29a**.* (2*S*,3*S*)-*ent*-**29a** (190 mg, 0.380 mmol, 91% ee) was reacted according to general procedure F with *n*-butyllithium (0.26 mL, 1.6 M in hexanes, 0.42 mmol, 1.1 equiv) and Boc_2O (249 mg, 1.14 mmol, 3.00 equiv). Purification of the crude product by silica gel chromatography (20 mm × 200 mm column, 12:1 hexanes/EtOAc as eluent, flash column) afforded an *N*-Boc aziridinecarboxylamide as a colorless oil. The Boc-protected aziridine was then reacted with *n*-butyllithium (0.52 mL, 1.6 *M* in hexanes, 0.84 mmol, 2.2 equiv) and ethanol (111 μL, 1.90 mmol, 5.00 equiv). Purification of the crude ester by silica gel chromatography (20 mm × 200 mm column, 9:1 hexanes/EtOAc as eluent, flash column) afforded aziridine (2*S*,3*S*)-**31** as a white foam in 64% yield (136 mg, 0.290 mmol) over two steps. This compound was identical in all respects to that obtained from *ent*-**25a**.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b02184.

Spectroscopic data for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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