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Asymmetric Dihydroxylation of Esters and Amides of Methacrylic, Tiglic, and Angelic Acid: No Exception to the Sharpless Mnemonic!

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Literature findings on the facial selectivity of the Sharpless asymmetric dihydroxylation (SAD) of isobutyl angelate are contradictory and partly in conflict with the Sharpless mnemonic. We systematically screened the SAD of esters and amides of angelic, tiglic, and methacrylic acid. Enantiocontrol arose in 14 of the 15 reactions, culminating at 99 % *ee* for the Weinreb amide of tiglic acid. The absolute configurations of all the nonracemic products were established by (stereo)chemical correlations. Without exception, they conform to the Sharpless mnemonic.

Introduction

The Sharpless asymmetric dihydroxylation (SAD) of olefins[1] is a major asset for accessing enantiomerically pure 1,2-diols, enantiomerically pure functionalized 1,2-diols, and enantiomerically pure follow-up products thereof.[2–4] The number of applications of the SAD reaction in synthesis is impressive, which underlines that this transformation is rightfully considered an extremely reliable, and hence prize-worthy,[3] tool in asymmetric synthesis in general.

An appealing feature of SADs is that the absolute configurations of the resulting diols are easily predicted by the so-called "Sharpless mnemonic".[5] Assignments based thereupon were corroborated by independent evidence in many instances. Therefore, more often than not, the mnemonic has assumed a further-going role: It is used for "deriving" the configuration of a SAD product. Whether so much confidence is warranted must be gauged against the number of exceptions to the predictions. In essence, we are unaware of any such exception at all, exempting, of course, the SADs of geminally disubstituted,[6] *cis*-disubstituted,[7] and tetrasubstituted C=C bonds;[8] these all provide disproportionately little orientational bias if scrutinized by the mnemonic. A few SADs that engaged trisubstituted C=C bonds in certain enynes were once associated with counter-mnemonic facial selectivities,[9] however, these assignments have been corrected recently.[10]

To the best of our knowledge, the trisubstituted C=C bond of angelic acid esters **3** (Figure 1), and derivatives thereof, is the only SAD site at which, according to the literature, configurational control was incongruent, at least in one instance contradictory, and in part in conflict with the Sharpless mnemonic (Scheme 1, see below).[11–19] This investigation unravels the steric course of the SAD of esters and amides of methacrylic acid,[20] tiglic acid,[21] and angelicacid[22]unambiguously(seebelow);enantiomericallypure (in most cases) or enriched (occasionally) 1,2-diols obtained from such substrates were used in the construction of complex natural products,[20k,21b,21c] represented drug candidates,[20h,20j] served as building blocks for peptides[20a,20c,20e–20g,21a,22b] or became the progenitor of other diverse products.[20b,20d,20i,21d,22a,22c] Our central finding was that angelate SADs proceed in full accordance with the Sharpless mnemonic.

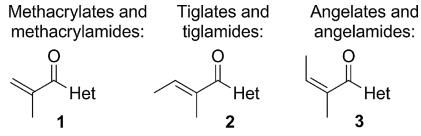

Figure 1. Methacrylates **1**, tiglates **2**, and angelates **3**, and their respective amides, the substrates used for SADs in this investigation and in many earlier studies.[20–22]

The first SAD of an alkyl angelate was executed in the context of the synthesis of "what should have been (2*S*,3*R*)-α-methylthreonine"[11] [(2*S*,3*R*)-**6**]: Dihydroxylating isobutyl angelate (**3b**) with Sharpless' AD-mix β[1] gave the diol (*R*,*R*)-**7b** (60% *ee*;[11] Scheme 1, line 2). Six steps down the road they achieved α-methylthreonine (**6**), but were surprised to find that its specific rotation "was of the opposite sign from the literature value".[11] The latter stemmed from a specimen of (2*S*,3*R*)-**6**, the precursor (**5**) of which had been analyzed by X-ray diffraction[23] (Scheme 1, line 1). Later, the outcome of the SAD of isobutyl angelate (**3b**) was re-interpreted and the configurational assignment of the earlier study[11] altered from (2*S*,3*R*)-**6** to (2*R*,3*S*)-**6** (Scheme 1, line 3).[12] Based on force field calculations and

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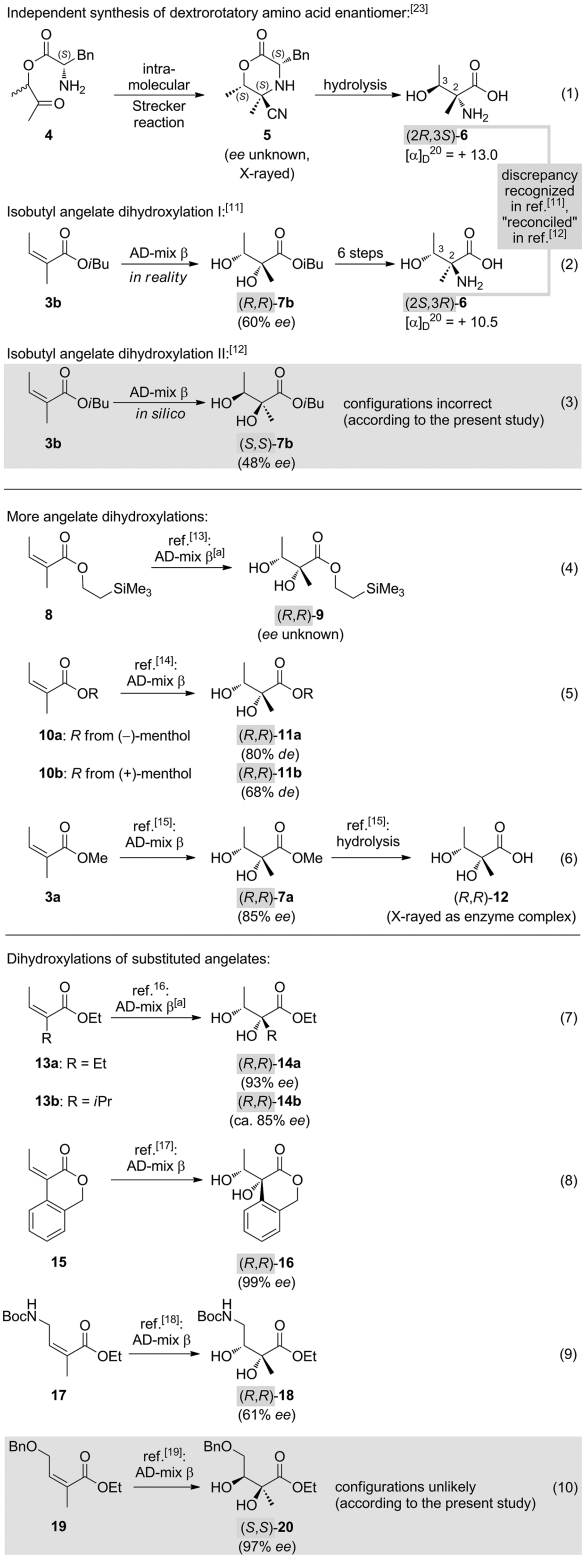


Scheme 1. Literature findings and/or claims concerning the SAD of alkyl angelates **3** and substituted alkyl angelates. The emphasis is on the contradictions and/or doubts that are contained therein or evoked thereby. Dihydroxylations that gave products for which the configurational assignments must be reversed in the light of results of this study are depicted on a light-grey background. [a] This SAD was performed with AD-mix α[1] and led to the mirror-image of the diol depicted in this scheme. For the sake of easier comparison with the facial selectivity of AD-mix β-mediated SADs, the genuine result is replaced by the outcome (fictitious, yet predictable) of the corresponding SAD with AD-mix β[1].

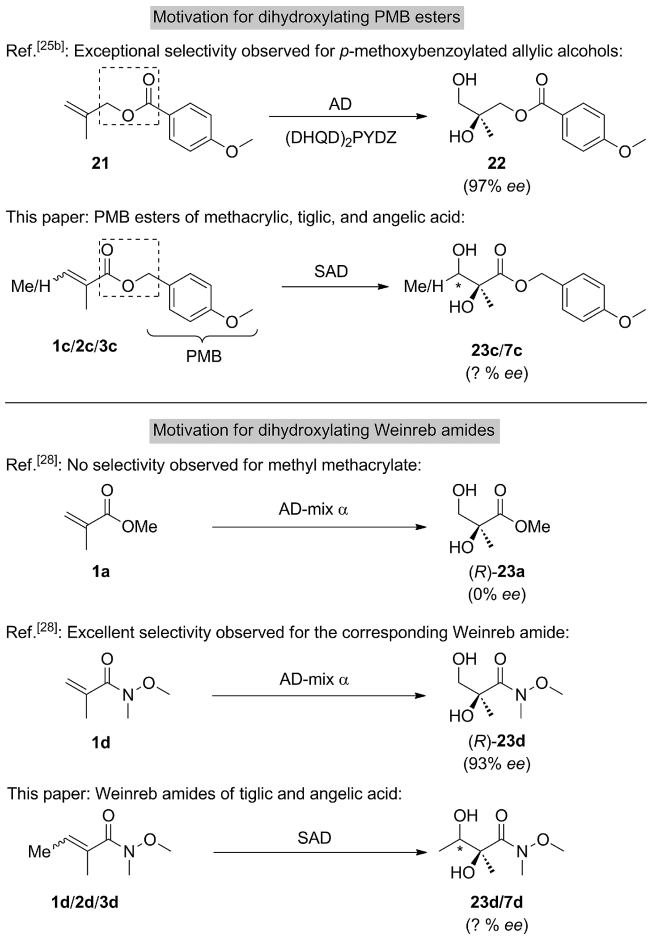
a genetic algorithm for searching transition structures reasons were forwarded as to why this particular SAD would comply with a transition state ("Chapleur transition state"[12]) that is at odds with the Sharpless mnemonic. In contrast, we felt that additional experiments should be performed before one dismantles an otherwise utterly reliable predictive tool like the Sharpless mnemonic.

The absolute configurations of the major diol enantiomers obtained by the SAD of other esters of angelic acid[13–15] (Scheme 1, lines 4–6) and by the SAD of esters of substituted angelic acids (Scheme 1, lines 7–10) were also published. The configurations of diol (*R*,*R*)-**9** (line 4),[13] diols (*R*,*R*)-**14a** and (*R*,*R*)-**14b** (line 7),[16] diol (*R*,*R*)-**18** (line 9),[18] and diol (*S*,*S*)-**20** (line 10)[19] were not established experimentally but "simply" drawn such that they do (lines 4, 7, and 9) or do not (line 10) comply with the Sharpless mnemonic. In contrast, the absolute configurations of diols (*R*,*R*)-**11a** and (*R*,*R*)-**11b** (line 5),[14] diol (*R*,*R*)-**7a** (line 6),[15] and diol (*R*,*R*)-**16** (line 8)[17] were proven by chemical correlations[14a] and by an X-ray analysis of the product obtained after a further 10 synthetic steps,[14b] an X-ray analysis of the underlying dihydroxycarboxylic acid (*R*,*R*)-**12** as an enzyme complex,[15] and by correlating the diol (*R*,*R*)-**16** chemically with a molecule, the absolute configuration of which is known from X-ray crystallography,[17] respectively.

In the context of a natural product synthesis project,[24] we considered enantiomerically enriched diols like diol **7** as a building block. For type-**7** diols emerging from the SAD of derivatives of angelic acid (**3**; Figure 1), a literature survey revealed that we would face variable enantiomeric excesses (60–99% *ee*) and that there was no consensus about the stereochemical outcome (Scheme 1[19]). This led us to diverge from the target-oriented work to study the SAD reactions of angelic acid derivatives in some depth. We also scrutinized their *E* isomers likewise, that is, tiglic acid derivatives (**2**; Figure 1), and certain "nor-compounds", namely methacrylic acid derivatives (**1**; Figure 1). This approach was chosen to gather insights firstly into effects of the double bond configuration and secondly into the role of the methyl group at C-3.

In more detail, our study comprised the SAD reactions of isobutyl esters **1b**–**3b** (Figure 1). This was done mainly in order to re-investigate the SAD of isobutyl angelate (**3b**), for which Scheme 1 juxtaposes conflicting literature results (lines 2[11] and 3[12]). Methyl esters **1a**–**3a** (Figure 1) were included in our study because of their commercial availability and PMB esters **1c**–**3c** (Scheme 2) because they resemble, to some extent, PMBz-protected allyl alcohol **21**. The latter shows exceptional selectivity in the SAD reaction (e.g., Scheme 2, top),[25] which may be attributed to the strong interactions of the PMBz group with the methoxyquinoline moiety of the ligand,[26] or, speaking in terms of the Sharpless mnemonic, a strong prevalence for the PMBz group to lie in the SW corner. Weinreb amides (**d**) were of interest because of the exceptional selectivity observed in the dihydroxylation of the Weinreb amide of methacrylic acid (**1d**).[27,28] Pyrrolidine-derived amides (**e**; not depicted

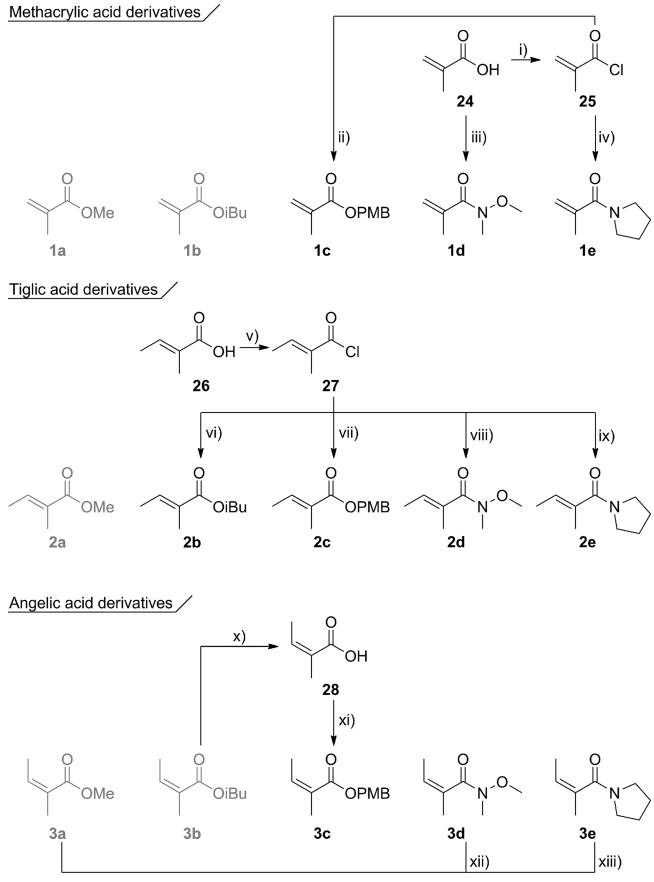
in Scheme 2) complement our spectrum of esters/amides and allowed us to verify whether Weinreb amides behave as ordinary amides under SAD conditions.



Scheme 2. Results of SAD reactions from the literature, which led us to include PMB esters and Weinreb amides in our study. Top: SAD of allylic 4-methoxybenzoates (e.g., **21**) display considerably more enantiocontrol than if the acyl group was different.[25b] Our PMB esters **1c**–**3c** exhibit the same distance between the methoxyphenyl group and the C=C bond as in "favored substrates" **21**, even if the CH_2–O–C(=O) motif is inverted. Bottom: SAD of methyl methacrylate (**1a**) shows no enantiocontrol whereas the corresponding Weinreb amide (**1d**) is dihydroxylated with 93% *ee*.[28]

Synthesis of the Substrates

Five of the ester substrates used in our study were commercially available: **1a**, **1b**, **2a**, **3a**, and **3b** (Scheme 3, grey color). This left 10 substrates to be synthesized (Scheme 3, black color). The derivatives of methacrylic and tiglic acid were prepared from the corresponding carboxylic acids **24** and **26**. They were first activated as the acid chlorides **25** and **27**, respectively. These were then treated with an appropriate nucleophile/base pair. This delivered the esters **1c** (72%), **2b** (86%), and **2c** (72%), and the amides **1d**[29] (82%), **1e** (84%), **2d** (78%), and **2e** (81%). Angelic acid (**28**) was prepared by hydrolyzing its isobutyl ester (**3b**; 44% yield after separating from some tiglic acid by crystallization). We attempted to activate angelic acid (**28**) as an acid chloride and treated the latter with nucleophile/base pairs, which had served well in the methacrylic and tiglic acid series, but we could not suppress the systems' tendency to undergo $E \rightarrow Z$ isomerizations. We circumvented this obstacle as follows: PMB angelate (**3c**) was obtained in 90% yield by combining angelic acid as a nucleophile with PMB-Cl as an electrophile. The amides **3d** (76%) and **3e** (70%) were derived from the magnesium salts of the underlying amines and their acylation with methyl angelate (**3a**).



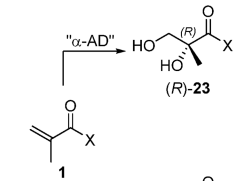
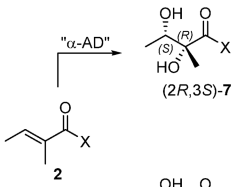
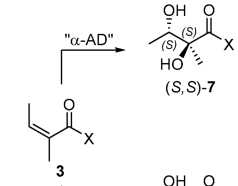
Scheme 3. Origin of the substrates (**1a**–**e** to **3a**–**e**) of this study; grey: commercially available, black: synthesized as specified below. Reagents and conditions: i) $SOCl_2$ (1.5 equiv.), DMF (2 drops), reflux, 2 h, 75%; ii) PMB-OH (1.05 equiv.), pyridine (1.2 equiv.), CH_2Cl_2, room temp., 18 h, 72%; iii) $SOCl_2$ (1.3 equiv.), CH_2Cl_2, reflux, 1 h; HNMe(OMe)·HCl (2.0 equiv.), pyridine (4.0 equiv.), 0 °C, 1 h; room temp., 18 h, 82% (ref.[29]: 94%); iv) pyrrolidine (2.0 equiv.), CH_2Cl_2, room temp., 4 h, 84%; v) $SOCl_2$ (1.2 equiv.), DMF (2 drops), reflux, 2.5 h, 96%; vi) *i*BuOH (1.5 equiv.), pyridine (1.5 equiv.), CH_2Cl_2, 0 °C → room temp., 18 h, 86%; vii) PMB-OH (1.05 equiv.), pyridine (1.2 equiv.), CH_2Cl_2, 0 °C → room temp., 18 h, 72%; viii) HNMe(OMe)·HCl (1.05 equiv.), pyridine (2.4 equiv.), CH_2Cl_2, 0 °C → room temp., 18 h, 78%; ix) pyrrolidine (2.2 equiv.), CH_2Cl_2, 0 °C → room temp., 18 h, 81%; x) LiOH·H_2O (1.1 equiv.), MeOH/H_2O (1:1), reflux, 4 h, 88% of a E/Z = 10:90 mixture, which was recrystallized from EtOH giving the pure Z isomer in 44% yield; xi) PMB-Cl (1.01 equiv.), Cs_2CO_3 (1.0 equiv.), DMF, 0 °C, 1 h; room temp., 2 h, 90%; xii) HNMe(OMe)·HCl (1.55 equiv.), THF, –20 °C, 30 min; *i*PrMgCl (3.0 equiv.), THF, –20 °C, 30 min, 76%; xiii) pyrrolidine (1.55 equiv.), THF, –20 °C, 30 min; *i*PrMgCl (1.5 equiv.), THF, –20 °C, 30 min, 70%.

Results and Discussion

As expected,[28] the SAD of methyl methacrylate (**1a**) yielded racemic material (Table 1, entries 1 and 2). The isobutyl ester **1b** performed only slightly better, delivering 10 and 16% *ee* with "α-AD" and "β-AD", respectively (entries 3 and 4). The SADs of PMB methacrylate (**1c**) yielded diols with 61 and 72% *ee* (entries 5 and 6). The Weinreb amide **1d** of methacrylic acid was dihydroxylated asymmetrically exceptionally well, as reported previously,[27,28] providing the corresponding diols with 95 and 98% *ee* (with "α-AD" and "β-AD", entries 7 and 8, respectively). The "normal" methacrylic amide **1e** performed not quite as well in terms of enantiomeric excess (74 and 88% *ee*), and the yields remained somewhat lower in the α and β series (60 and 88%; entries 9 and 10, respectively) even though we employed more $K_2OsO_2(OH)_4$ and more ligand.

The extended reaction time of 5 d, which was required for the SADs of the Weinreb amide **1d** and the pyrrolidide **1e** (Table 1, entries 7–10), already included a trick. It might be useful, in general, for conducting sluggish SADs. Initially we observed that in these reactions a significant amount of $K_3[Fe(CN)_6]$ stuck to the wall of the reaction flask after two days. This decreased the amount of $K_3[Fe(CN)_6]$ left in the reaction mixture so much that the dihydroxylation reaction virtually stopped. As a conse-

Table 1. SADs of methacrylic, tiglic, and angelic acid derivatives.

Dihydroxylation[a]	Entry	1	X	Conditions[a]	Time	23	Optical Activity	$[\alpha]_D^{20}$	Yield	*ee*[b]
	1	**1a**	-OMe	"α-AD"[c]	2 d	(*R*)-**23a**	—[d]	—[d]	85%	—[d]
	2			"β-AD"[c]	2 d	(*S*)-**23a**	—[d]	—[d]	90%	—[d]
	3	**1b**	-O*i*Bu	"α-AD"	1 d	(*R*)-**23b**	(+)	+1.3	92%	10%
	4			"β-AD"	1 d	(*S*)-**23b**	(−)	−2.3	94%	16%
	5	**1c**	-OPMB	"α-AD"	3 d	(*R*)-**23c**	(−)	−0.3	90%	61%
	6			"β-AD"	3 d	(*S*)-**23c**	(+)	+0.3	90%	72%
	7	**1d**	-N(OMe)Me	"α-AD"[c,e]	5 d	(*R*)-**23d**	(+)	+13.2[32]	83%	95%
	8			"β-AD"[c,e]	5 d	(*S*)-**23d**	(−)	−13.1[32]	93%	98%
	9	**1e**	-N(CH$_2$)$_4$	"α-AD"[c,e]	5 d	(*R*)-**23e**	(+)	+11.1	60%	74%
	10			"β-AD"[c,e]	5 d	(*S*)-**23e**	(−)	−13.1	88%	83%
	11	**2a**	-OMe	"α-AD"	4 d	(2*R*,3*S*)-**7a**	(+)	+0.3[31,33]	85%	87%
	12			"β-AD"	4 d	(2*S*,3*R*)-**7a**	(−)	−0.4[31,33]	84%	92%
	13	**2b**	-O*i*Bu	"α-AD"	1 d	(2*R*,3*S*)-**7b**	(+)	+5.5	86%	81%
	14			"β-AD"	1 d	(2*S*,3*R*)-**7b**	(−)	−7.2	86%	85%
	15	**2c**	-OPMB	"α-AD"	5 d	(2*R*,3*S*)-**7c**	(−)	−1.1	81%	93%
	16			"β-AD"	5 d	(2*S*,3*R*)-**7c**	(+)	+1.4	81%	95%
	17	**2d**	-N(OMe)Me	"α-AD"[c,e]	4 d	(2*R*,3*S*)-**7d**	(+)	+17.6	81%	98%
	18			"β-AD"[c,e]	4 d	(2*S*,3*R*)-**7d**	(−)	−17.7	89%	99%
	19	**2e**	-N(CH$_2$)$_4$	"α-AD"[c,e]	6 d	(2*R*,3*S*)-**7e**	(+)	+33.4	59%	97%
	20			"β-AD"[c,e]	6 d	(2*S*,3*R*)-**7e**	(−)	−35.9	76%	98%
	21	**3a**	-OMe	"α-AD"	1 d	(*S*,*S*)-**7a**	(+)	+4.7[33]	82%	77%
	22			"β-AD"	1 d	(*R*,*R*)-**7a**	(−)	−5.1[33]	86%	90%
	23	**3b**	-O*i*Bu	"α-AD"	6 d	(*S*,*S*)-**7b**	(−)	−6.8	92%	67%
	24			"β-AD"	6 d	(*R*,*R*)-**7b**	(+)	+7.8	84%	82%
	25	**3c**	-OPMB	"α-AD"	5 d	(*S*,*S*)-**7c**	(−)	−2.3	78%	60%
	26			"β-AD"	5 d	(*R*,*R*)-**7c**	(+)	+2.8	78%	80%
	27	**3d**	-N(OMe)Me	"α-AD"[c,e]	5 d	(*S*,*S*)-**7d**	(−)	−14.6	68%	62%
	28			"β-AD"[c,e]	5 d	(*R*,*R*)-**7d**	(+)	+17.2	80%	71%
	29	**3e**	-N(CH$_2$)$_4$	"α-AD"[c,e]	6 d	(*S*,*S*)-**7e**	(+)	+11.9	58%	34%
	30			"β-AD"[c,e]	6 d	(*R*,*R*)-**7e**	(−)	−15.7	69%	27%

[a] α-AD: $K_3[Fe(CN)_6]$ (3.0 equiv.), K_2CO_3 (3.0 equiv.), $MeSO_2NH_2$ (1.0 equiv.), $(DHQ)_2PHAL$ (2.0 mol-%), $K_2OsO_2(OH)_4$ (1.0 mol-%), *t*BuOH/H_2O (1:1), 0 °C, time. β-AD: $K_3[Fe(CN)_6]$ (3.0 equiv.), K_2CO_3 (3.0 equiv.), $MeSO_2NH_2$ (1.0 equiv.), $(DHQD)_2PHAL$ (2.0 mol-%), $K_2OsO_2(OH)_4$ (1.0 mol-%), *t*BuOH/H_2O (1:1), 0 °C, time. [b] Determined by analytical HPLC. To calibrate the respective HPLC analysis, the corresponding racemic diol was also prepared by using the modified Upjohn reaction described by Sharpless and coworkers.[30] [c] $PhSO_2NH_2$ was used instead of $MeSO_2NH_2$ to facilitate separation of the product by flash chromatography. [d] These products are racemic. [e] 3.0 mol-% of the respective ligand and 2.0 mol-% of $K_2OsO_2(OH)_4$ were used.

quence, the yields fell to 21–45%. This impediment was remedied by siliconizing the inside of the reaction flask prior to conducting the SAD. This was considered as a potential improvement for all the SAD reactions. So, from then on, we routinely siliconized the reaction flask before each SAD (for details, see the Exp. Sect.).

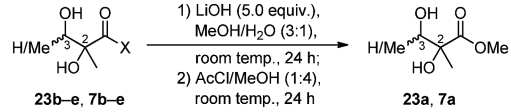
The SADs of the tiglic acid based esters and amides **2a**–**e** (Table 1, entries 11–20) succeeded with good or very good enantiocontrol. The Weinreb amide **2d** performed best (98 and 99% *ee*, entries 17 and 18) and the isobutyl ester worst (81 and 85% *ee*, entries 13 and 14). All in all, we obtained higher or much higher *ee* values than with the methacrylic analogues (entries 1–10). Qualitatively, the dependency of the *ee* value on the substituent was similar: Weinreb amide > pyrrolidide > PMB ester > the two aliphatic esters. However, isobutyl tiglate (**2b**) reacted with less enantiocontrol (entries 13 and 14) than methyl tiglate (**2a**; entries 11 and 12) whereas for isobutyl (**1b**) and methyl methacrylate (**1a**) the opposite was true (entries 3 and 4 vs. entries 1 and 2).

The *ee* values of the SADs of the angelic acid based esters **3a**–**c** and the Weinreb amide **3d** (Table 1, entries 21–28) ranged from 90% [methyl angelate (**3a**) + "β-AD", entry 22] to 60% [PMB ester of angelic acid (**3c**) + "α-AD", entry 25]. Curiously, the pyrrolidide **3e** reacted with exceptionally low *ee* values (entries 29 and 30) and was the only substrate for which the $(DHQ)_2PHAL$ ligand outperformed the $(DHQD)_2PHAL$ ligand.[34] Methyl angelate (**3a**) was dihydroxylated nearly as enantioselectively (entries 21 and 22) as methyl tiglate (**2a**; entries 11 and 12). All the other derivatives of angelic acid (**3b**–**e**) were dihydroxylated with less enantiocontrol than their tiglic acid based congeners (**2b**–**e**). Remarkably, the aliphatic esters of angelic acid (**3a**,**b**) underwent SADs with higher enantioselectivity than the analogous amides (**3d**,**e**). The opposite observation was made for the methacrylic acid based ester/amide pairs (**1a**,**b** vs. **1d**,**e**) and their tiglic acid analogues (**2a**,**b** vs. **2d**,**e**). The "spread" between the five pairs of *ee* values for the "β-AD" and "α-AD" reactions of the derivatives **3a**–**e** of angelic acid (–7 to +20%; mean absolute value: 13%) is larger than usual. For example, the analogous spreads for the tiglic acid analogues **2a**–**e** are +1 to +5% (mean value: 3%) and for the methacrylic acid analogues **1a**–**e** 0 to +11% (mean value: 7%).

Measuring the *ee* values of the 15 diols, which are compiled in Table 1 as pairs of enantiomers (except for the diols from methyl methacrylate; entries 1 and 2), was the prelude to determining their favored absolute configurations (Table 2; if any, cf. entries 1 and 2 of Table 1). In doing so, we turned to the 15 diols obtained by "α-AD"-mediated SADs (Table 1), considering their counterparts from the "β-AD"-mediated SADs as their mirror images.

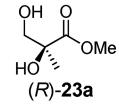
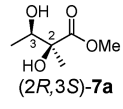
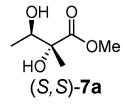
Five of the "α-AD"-based diols contain the carbon framework of methacrylic acid (**23a**–**e**; "methacrylic diols"), another five that of tiglic acid (*syn*-diols **7a**–**e**; "tiglic diols"), and the remaining five that of angelic acid (*anti*-diols **7a**–**e**; "angelic diols"). We facilitated their analysis by converting the methacrylic diols **23b**–**e** into the methyl ester **23a**, the tiglic diols *syn*-**7b**–**e** into the methyl ester *syn*-**7a**, and the angelic diols *anti*-**7b**–**e** into the methyl ester *anti*-**7a** (Table 2). This was achieved by successive hydrolysis and esterification reactions. It worked well for the isobutyl esters, PMB esters, and Weinreb amides (average yield: 87% over the two steps), but badly for the pyrrolidides (average yield: 24% over the two steps).[35] Chiral GC revealed that the four nonracemic "methacrylic diols" had identical configurations.[36] The same was true for the five "tiglic diols" and likewise for the five "angelic diols".[36] This consolidation of the product portfolio obviated the need of attributing the absolute configurations of all 15 diols of Table 2 individually. Instead, we clarified their absolute configurations group-wise (by GC and the experiments of Scheme 4).

Table 2. Conversion, by saponification and esterification, of the diols **23b**–**e** and **7b**–**e** from the "α-AD"-mediated SADs presented in Table 1, that is, of the diols with a butyl ester (**b**), a PMB ester (**c**), a Weinreb amide (**d**), or a pyrrolidide moiety (**e**), into the methyl ester containing diols **23a**, *syn*-**7a**, and *anti*-**7a**. This set of transformations reduced the number of diols to which an absolute configuration had to be (re)assigned from 15 to 3.



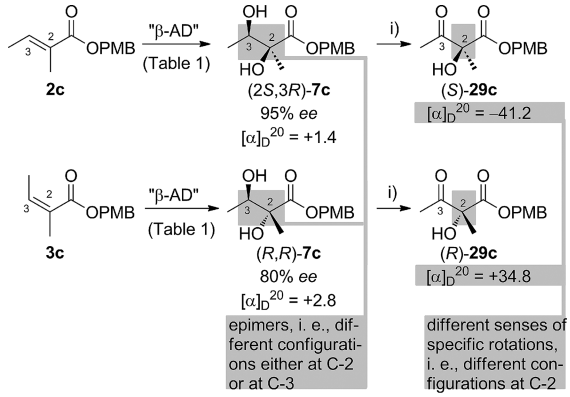
23b–e, 7b–e **23a, 7a**

X =	-O*i*Bu	-OPMB	-N(OMe)Me	-N(CH$_2$)$_4$	
	(*R*)-**23b**	(*R*)-**23c**	(*R*)-**23d**	(*R*)-**23e**	(*R*)-**23a**
	(2*R*,2*S*)-**7b**	(2*R*,3*S*)-**7c**	(2*R*,3*S*)-**7d**	(2*R*,3*S*)-**7e**	(2*R*,3*S*)-**7a** ("*syn*")
	(*S*,*S*)-**7b**	(*S*,*S*)-**7c**	(*S*,*S*)-**7d**	(*S*,*S*)-**7e**	(*S*,*S*)-**7a** ("*anti*")

Entry	X	Reactant	*ee*	Product	*ee*[a]	Yield
1	-O*i*Bu	(*R*)-**23b**	10	 (*R*)-**23a**	(5%)	90%
2	-OPMB	(*R*)-**23c**	61		(55%)	91%
3	-N(OMe)Me	(*R*)-**23d**	95		(87%)	87%
4	-N(CH$_2$)$_4$	(*R*)-**23e**	74		(89%)	10%
5	-O*i*Bu	(2*R*,3*S*)-**7b**	81	 (2*R*,3*S*)-**7a**	83%	59%
6	-OPMB	(2*R*,3*S*)-**7c**	93		93%	91%
7	-N(OMe)Me	(2*R*,3*S*)-**7d**	98		99%	75%
8	-N(CH$_2$)$_4$	(2*R*,3*S*)-**7e**	97		96%	27%
9	-O*i*Bu	(*S*,*S*)-**7b**	67	 (*S*,*S*)-**7a**	(68%)	96%
10	-OPMB	(*S*,*S*)-**7c**	60		(59%)	100%
11	-N(OMe)Me	(*S*,*S*)-**7d**	62		(71%)	90%
12	-N(CH$_2$)$_4$	(*S*,*S*)-**7e**	34		(30%)	34%

[a] The *ee* values were determined by chiral GC (see the Supporting Information). The *ee* values for (*R*)-**23a** (entries 1–4) and (*S*,*S*)-**7a** (entries 9–12) are given in parentheses; they are approximate values because our analyses did not baseline-separate the enantiomers.

The methyl ester containing diol **23a** and its progenitors **23b**–**e** are *R* enantiomers[37] because the absolute configuration of the SAD-based Weinreb amide **23d** is known.[20a,20c,20f,20k] The methyl ester containing diol *syn*-**7a** and its progenitors **7b**–**e** are 2*R*,3*S*-configured because this is the absolute configuration of the carboxylic acid obtained by hydrolysis of this *syn*-diol; this configuration was established by X-ray structural analysis of an enzyme complex of that acid.[21d] Finally, the methyl ester containing



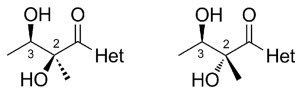
Scheme 4. Proof that the SAD of the isomeric PMB esters **2c** (tiglate) and **3c** (angelate) hydroxylates C-3 with identical facial selectivity (i.e., from the *Re* side) but C-2 with opposite facial selectivity (i.e., **2c** from the *Si* side but **3c** from the *Re* side). This proves that these diols are configured in accordance with the predictions from Sharpless' mnemonic (see main text). Reagents and conditions: i) Bleach (total content of chlorine approx. 10%, approx. 1.6 M, 1.65 equiv.), KBr (1.0 equiv.), TEMPO (0.5 equiv.), saturated aqueous $NaHCO_3$ solution/CH_2Cl_2 (1:1), 0 °C, 15 min; 76% for (*S*)-**29c**, 90% for (*R*)-**29c**.

diol *anti*-**7a** and its progenitors **7b**–**e** are the C-2 epimers of the aforementioned diols. We proved this by the stereochemical correlations presented in Scheme 4. They destroy the stereocenters at C-3 of diols (2*S*,3*R*)-**7c** (from PMB tiglate and "β-AD", cf. entry 16 of Table 1) and (*R*,*R*)-**7c** (from PMB angelate and "β-AD", cf. entry 26 of Table 1) by oxidizing the respective hydroxy groups to oxo substituents. Conversely, the stereocenters at C-2 are preserved. Hence, the methyl ester containing diol *anti*-**7a** originating (Table 2) from our "α-AD"-mediated SADs of esters and amides of angelic acid of Table 1 must be *S*,*S*-configured. The same is concluded from the identity of our diol *anti*-**7a** from Table 2 with an independently prepared specimen, which was subjected to X-ray analysis as an enzyme complex.[15,38]

It is worthwhile (re)turning to the stereochemical correlations in Scheme 4 in some detail. The dihydroxy esters (2*S*,3*R*)-**7c** from the "β-AD"-based SAD of PMB tiglate (**2c**) and (*S*,*S*)-**7c** from the "β-AD"-based SAD of PMB angelate (**3c**), which had been prepared according to Table 1 (entries 16 and 26, respectively), must be epimers. Their oxidations provided the antipodal forms of the hydroxy keto ester **29c**. The dihydroxy ester (2*S*,3*R*)-**7c** led to the hydroxy keto ester (*S*)-**29c**, which is levorotatory, and the dihydroxy ester (*S*,*S*)-**7c** gave the hydroxy keto ester (*R*)-**29c**, which is dextrotatory. This proves that their dihydroxy ester precursors (2*S*,3*R*)- and (*S*,*S*)-**7c** are C-2 and not C-3 epimers (as was briefly mentioned above). These oxidations were unexpectedly difficult with respect to their chemoselectivity. Treatment of CH_2Cl_2 solutions of a dihydroxy ester **7c** with pyridinium dichromate (PDC) or with 10 mol-% 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO)/stoichiometric $PhI(OAc)_2$ resulted in glycol cleavages, even with 1 equiv. of the respective oxidant. Treatment of our dihydroxy esters **7c** with the Dess–Martin reagent gave no bias at all between glycol cleavage and the desired oxidation. Only 50 mol-% TEMPO combined with a stoichiometric amount of bleach furnished the hydroxy keto esters **29c** in a clean reaction. In fact, the crude product was essentially pure.

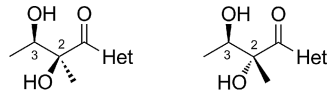
The "*syn*"-diols (2*S*,3*R*)- and (2*R*,3*S*)-**7a**–**e** and their "*anti*" diastereomers (*R*,*R*)- and (*S*,*S*)-**7a**–**e** reveal ^{1}H NMR shifts or ^{1}H NMR shift differences (Table 3) as well as ^{13}C NMR shift differences, which might be indicators of their relative configurations. In this regard, the bottom line of Table 3 illustrates three seemingly characteristic ^{1}H NMR shift orderings: (1)·δ(2-CH_3) is smaller in the *syn* isomers than in the *anti* isomers and the respective δ ranges do not overlap (δ_{syn} = 1.31–1.37 ppm, δ_{anti} = 1.43–1.50 ppm). (2) δ(3-H) is larger in the *syn* isomers than in the *anti* isomers with a $\delta_{syn} - \delta_{anti}$ maximum of +0.46 for the Weinreb amide (**7d**). δ(4-H_3) is larger in the *syn* isomers than in the *anti* isomers (again, the respective δ ranges do not overlap: δ_{syn} = 1.20–1.25 ppm, δ_{anti} = 0.99–1.17 ppm). Moreover, the bottom line of Table 3 indicates that two of the mentioned characteristics can be combined to give an improved criterion for distinguishing the *syn*- and *anti*-configured diols: The methyl groups 2-CH_3 and 4-H_3 display a smaller differ-

Table 3. ^{1}H NMR shifts of 4-H_3, 2-CH_3, and 3-H in the diastereomeric diols (2*S*,3*R*)-**7a**–**e** ("*syn*"-**7a**–**e**) and (*R*,*R*)-**7a**–**e** ("*anti*"-**7a**–**e**) at 400 MHz in $CDCl_3$.



7	Het	δ(2-CH_3) [ppm]		δ(3-H) [ppm]		δ(4-H_3) [ppm]		δ(2-CH_3) – δ(4-H_3) [ppm]	
		syn	*anti*	*syn*	*anti*	*syn*	*anti*	*syn*	*anti*
a	OMe	1.32	1.44	3.94	3.80	1.23	1.15	0.09	0.29
b	O*i*Bu	1.31	1.45	3.93	3.81	1.22	1.17	0.09	0.28
c	OPMB	1.31	1.43	3.94	3.78	1.20	1.08	0.11	0.35
d	NMe(OMe)	1.37	1.49	4.15	3.69	1.25	0.99	0.12	0.50
e	$N(CH_2)_4$	1.33	1.50	4.19	3.93	1.21	1.09	0.12	0.41
		$\Delta\delta_{syn-anti}$ = –0.13 ppm		$\Delta\delta_{syn-anti}$ = +0.23 ppm		$\Delta\delta_{syn-anti}$ = +0.13 ppm		$\Delta\Delta\delta_{syn-anti}$ = +0.26 ppm	

Table 4. ^{13}C NMR shifts of C-1, C-2, 2-CH_3, C-3, and C-4 in the diastereomeric diols (2*S*,3*R*)-**7a–e** ("*syn*"-**7a–e**) and (*R*,*R*)-**7a–e** ("*anti*"-**7a–e**) at 101 MHz in $CDCl_3$.



(2*S*,3*R*)-**7a–e** "*syn*" (*R*,*R*)-**7a–e** "*anti*"

7	Het	δ(C-1) [ppm]		δ(C-2) [ppm]		δ(2-CH_3) [ppm]		δ(C-3) [ppm]		δ(C-4) [ppm]	
		syn	*anti*	*syn*	*anti*	*syn*	*anti*	*syn*	*anti*	*syn*	*anti*
a	OMe	176.83	176.00	77.37	77.27	21.80	22.35	71.71	72.31	16.76	17.79
b	O*i*Bu	176.38	175.70	77.31	77.19	21.77	22.46	71.71	72.26	16.77	17.80
c	OPMB	176.25	175.45	77.32	77.13	21.74	22.32	71.71	72.26	16.76	17.71
d	NMe(OMe)	175.51	175.72	77.67	77.23	21.84	22.13	70.38	70.04	17.17	18.33
e	$N(CH_2)_4$	173.63	173.35	77.47	76.53	21.21	21.39	70.74	70.89	16.16	18.02
		$\Delta\delta_{syn-anti}$ is positive or negative		$\Delta\delta_{syn-anti}$ is positive or negative		$\Delta\delta_{syn-anti}$ = –0.46 ppm		$\Delta\delta_{syn-anti}$ is positive or negative		$\Delta\delta_{syn-anti}$ = –1.21 ppm	

ence in shift in the *syn* series [δ(2-CH_3) – δ(4-H_3) = 0.09–0.12 ppm] than in the *anti* series [δ(2-CH_3) – δ(4-H_3) = 0.28–0.50 ppm].[39] Similarly, the bottom line of Table 4 reveals two seemingly characteristic ^{13}C NMR shift orderings: (1) δ(2-CH_3) is smaller in the *syn* isomers than in the *anti* isomers. (2) δ(C-4) is smaller in the *syn* isomers than in the *anti* isomers with no overlap between the δ ranges (δ_{syn} = 16.16–17.17 ppm, δ_{anti} = 17.71–18.33 ppm).

The key question behind this study was the following: Do asymmetric dihydroxylations of the prototypical α,β-unsaturated substrate scaffolds **1**–**3** take a different steric course than the Sharpless mnemonic predicts? Exempting methyl methacrylate (**9a**), which reacted without enantiocontrol (Table 1, entries 1 and 2) and thereby is the only exception, the stereochemical assignments of Table 2 give an easy answer: The SAD reactions of the methacrylic (**1**), tiglic (**2**), and angelic backbones (**3**) each proceeded in accordance with the Sharpless mnemonic.[40] This is true (Figure 2) both for the methacrylic backbone **1** if the C=O-containing substituent at C-α resides in the moderately stabilizing SW corner,[41] and for the tiglic and angelic backbones **2** and **3** if the methyl substituent at C-β is kept at a distance by the destabilizing SE corner.

Tiglic acid derivatives **2** allow, in order of decreasing importance, for nondestabilizing interactions of their β-substituent and for stabilizing interactions of their α-substituent in the SAD transition state concomitantly. Angelic acid derivatives **3** enjoy only the former effect, being deprived of the latter. This difference fits with the observation that our tiglic acid derivatives **2a–e** were dihydroxylated with higher *ee* values (Table 1, entries 11–20) than their angelic acid analogues **3a–e** (Table 1, entries 21–30).

With respect to our re-examination of the facial selectivity of isobutyl angelate (**3b**) with "β-AD" (as defined in footnote a of Table 1), our result (Table 1, entry 14) debunks the suggestion[12] that it is engaged by AD-mix β in

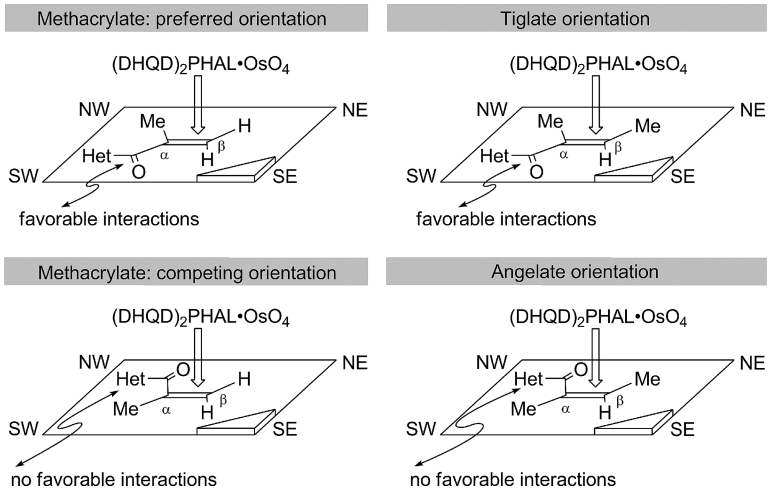


Figure 2. Sharpless mnemonic[40] analysis of the orientation of the substrates of this study (Het represents OR or NR_2[40]) in the transition state of SADs mediated by AD-mix β or β-AD (as defined in footnote a of Table 1). The facial selectivities [if existing, cf. the exception of methyl methacrylate (**9a**; entries 1 and 2 of Table 1)] shown here follow from the stereochemical correlations of Table 2.

a "Chapleur transition state", reacting allegedly[12] as depicted in line 3 of Scheme 1. By the same token the identical facial selectivities of methyl angelate (**3a**) and isobutyl angelate (**3b**) with "β-AD" make the published[19] 3D course of the SAD of the benzyloxy-substituted ethyl angelate **19**, which is shown as line 10 of Scheme 1, untrustworthy.

Conclusions

We subjected five different derivatives each of methacrylic, tiglic, and angelic acid to asymmetric dihydroxylation by using a modified Sharpless asymmetric dihydroxylation protocol. Among the methacrylic acid derivatives, the Weinreb amide **1d** stood out in terms of yield and enantiomeric excess (Table 1, entries 7 and 8): 83% yield and 95% *ee* with $(DHQ)_2PHAL$; 93% yield and 98% *ee* with $(DHQD)_2PHAL$. Most of the tiglic acid derivatives reacted in over 80% yield (Table 1, entries 11–20) and the enantiomeric excesses for both amides were excellent (97–99% *ee*). The derivatives of angelic acid reacted somewhat less satisfyingly (Table 1, entries 21–30). Nonetheless methyl angelate was dihydroxylated in 82% yield and with 77% *ee* by using $(DHQ)_2PHAL$ or in 86% yield and with 90% *ee* by using $(DHQD)_2PHAL$.

Our most important finding is that each substrate scaffold delivered the same diol enantiomer no matter whether it reacted as an ester or an amide. In addition, the stereostructures of all the diols were in agreement with the Sharpless mnemonic. Therefore we consider the latter as fully rehabilitated with regard to the doubts that were raised some time ago[9,12] but have not persisted (ref.[10] and the current work; Figure 2).

Experimental Section

General Methods and Analytic Techniques: All reactions that did not require the presence of water were carried out under dry N_2. Reaction flasks were dried in an oven (65 °C) and under reduced pressure with a heat gun prior to use. Liquids were added by syringe or through a cannula through a rubber septum. Solids were added in a counter-current of dry N_2. Reactions that required or allowed the presence of water were carried out in the laboratory atmosphere. Solvents: THF was distilled from potassium, and CH_2Cl_2 over CaH_2 under dry N_2 prior to use. Other solvents that were obtained commercially as "dry" or "extra dry" solvents were used without further purification. *c*-C_6H_{12}, EtOAc, MeOH, EtOH, CH_2Cl_2, and *tert*-butyl methyl ether (TBME) for work-up and column chromatography were distilled prior to use by using a rotary evaporator to remove high-boiling fractions. Et_2O, pentane, and $CHCl_3$ for work-up and column chromatography were obtained as p.a. grade solvents and used without further purification. Grignard reagents were stored in a freezer in Schlenk flasks with PTFE screw caps and PTFE valves. Prior to use, they were titrated by using salicylaldehyde phenylhydrazone.[42] Chromatography: TLC on Merck silica plates with glass as supporting material (TLC Silicagel 60 F_{254}) was used to monitor reactions and assess purification procedures. If possible, chromatograms were marked in UV light at 254 nm and subsequently stained by using permanganate (2 g $KMnO_4$, 4 g $NaHCO_3$, 100 mL of H_2O) or vanillin stain (4.5 g vanillin, 75 mL of EtOH, 4 mL conc. H_2SO_4). Macherey–Nagel & Co silica gel 60® (230–400 mesh) was used for flash column chromatography.[43] Chromatography conditions are documented for the respective experiment in the following manner: ($d \times h$ cm, V mL, solv1:solv2, *a*:*b*–*c*:*d*, F_x–F_y), which means: a column with the inner diameter of d cm was packed with h cm silica gel, fractions of V mL were collected, the product was eluted with the solvents solv1 and solv2 in the ratio *a*:*b*, the ratio, if not stated otherwise, was changed every 12 fractions in the following series (the first ratio marks the starting point, the last ratio marks the end point): 100:0, 100:1, 50:1, 20:1, 10:1, 5:1, 3:1, 2:1, 1:1, 1:2, 1:3, 0:100, F_x–F_y are the fractions containing the product. NMR spectra were recorded with a Bruker AM 400 spectrometer [^1H (400 MHz), ^{13}C (100 MHz), DQF-COSY, edHSQC, and HMBC experiments], a Bruker DRX 500 spectrometer [^1H (500 MHz), ^{13}C (126 MHz), DQF-COSY, edHSQC ("C,H-COSY"), and HMBC experiments], or an automated Varian Mercury VX 300 spectrometer [^1H (300 MHz)]. Spectra were referenced internally by the ^1H and ^{13}C NMR solvent signals [$CDCl_3$: 7.26 ppm (^1H) and 77.10 ppm (^{13}C)]. The ^1H NMR spectroscopic data are reported as follows: Chemical shift (δ in ppm), multiplicity (s for singlet, d for doublet, t for triplet; m for multiplet, m_c for symmetrical multiplet, br. for broad), coupling constant(s) (Hz; ^3J couplings unless otherwise noted), integral, and assignment. The ^{13}C NMR spectroscopic data are reported in terms of chemical shift and assignment. For AB signals the high-field part is named A and the low-field part B. The atom numbering used for NMR assignments follows the IUPAC nomenclature. Primed nuclei refer to substituents. Specifically, the locants "*i*", "*o*", "*m*", and "*p*" refer to the *ipso*, *ortho*, *meta*, and *para* positions of the *p*-methoxyphenyl groups; these locants are assigned such that the CH_2-substituted aromatic carbon is designated as the *ipso* carbon. High-resolution mass spectra were recorded with a Thermo Exactive mass spectrometer equipped with an orbitrap analyzer and by using the electron spray ionization (ESI; spray voltage: 4–5 kV) or atmospheric pressure chemical ionization (APCI; spray current: 5 μA) technique. Elemental analyses were performed with an Elementar Vario El CHNS analyzer. Melting points were determined with a Büchi melting point apparatus using open glass capillaries.[44] IR spectra were recorded with a Perkin–Elmer Paragon 1000 FT-IR spectrometer on films of the sample on an NaCl plate. HPLC: The enantiomeric excesses (*ee*s) were determined by using a Merck Hitachi LaChrom L 7100 HPLC instrument; for further details, see individual experimental descriptions. Optical rotations were measured with a Perkin–Elmer 341 polarimeter at 598 nm (Na lamp) and/or 587, 546, 436, and 365 nm (Hg lamp). The values of $[\alpha]_\lambda^{20}$ were calculated by using the expression $[\alpha]_\lambda^{20} = (100\alpha_{exp.})/(cd)$, in which λ [nm] is the wavelength, $\alpha_{exp.}$ [°] the experimental result, c [g/100 mL] the concentration, and d [dm] the length of the optical cell. $[\alpha]_\lambda^{20}$ values are given as the arithmetic mean of five measurements.

General Procedure A – Racemic Dihydroxylations: Citric acid (0.75 equiv.) and the respective olefin were dissolved in *t*BuOH/H_2O (1:1, 1 M). $K_2OsO_2(OH)_4$ (0.25 mol-%) and *N*-methylmorpholine *N*-oxide[45] ("NMO", 50% in H_2O, 1.2 equiv.) were added. The resulting green solution was stirred at room temp. until the green color disappeared. The reaction was then quenched by the addition of a saturated aqueous Na_2SO_3 solution. The phases were separated and the aqueous phase was extracted with EtOAc (3×). The combined organic phases were washed with brine and dried with $MgSO_4$. The solvent was removed under reduced pressure. The product was purified by flash chromatography on silica gel.[43]

General Procedure B – Asymmetric Dihydroxylations: Finely powdered $K_3[Fe(CN)_6]$ (3.0 equiv.), K_2CO_3 (3.0 equiv.), $(DHQ)_2PHAL$ or $(DHQD)_2PHAL$ (2.0 mol-%), and $K_2OsO_2(OH)_4$ (1.0 mol-%) were added to precooled *t*BuOH/H_2O (1:1, 0.1 M) at 0 °C.[46] $MeSO_2NH_2$ or $PhSO_2NH_2$ (1.0 equiv.) and the respective olefin were added to the suspension. The mixture was stirred at 0 °C until the olefin could no longer be detected by TLC. The reaction was quenched by the addition of a saturated aqueous Na_2SO_3 solution. The phases were separated and the aqueous phase was extracted with EtOAc (3×). The combined organic phases were washed with brine, dried with $MgSO_4$, and the solvent was removed under reduced pressure. The product was purified by flash chromatography on silica gel.[43]

4-Methoxybenzyl Methacrylate (1b): A solution of (4-methoxyphenyl)methanol ("PMB-OH", 3.74 mL, 4.16 g, 30.1 mmol, 1.05 equiv.) in pyridine (2.78 mL, 2.72 g, 34.4 mmol, 1.2 equiv.) was added dropwise to a solution of **25** (2.80 mL, 3.00 g, 28.7 mmol) in CH_2Cl_2 (25 mL) and the mixture was stirred overnight at room temp. (a white precipitate formed). The reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (10 mL). H_2O (approx. 5 mL) was added until the precipitate dissolved, the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried with $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel[43] (5.5 × 5.5 cm, 50 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 15–26). The product was obtained as a colorless oil (4.30 g, 72%). IR (film): $\tilde{\nu}$ = 2960, 2840, 1715, 1635, 1615, 1585, 1515, 1455, 1375, 1320, 1295, 1250, 1160, 1110, 1035, 1010 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.95 [dd, $^4J_{2\text{-Me},3\text{-H}(E)}$ = 1.6, $^4J_{2\text{-Me},3\text{-H}(Z)}$ = 1.0 Hz, 3 H, 2-Me], 3.81 (s, 3 H, *p*-OMe), 5.13 (s, 2 H, 1′-H_2), 5.56 [dq, J_{gem} = $^4J_{3\text{-H}(E),2\text{-Me}}$ = 1.6 Hz, 1 H, 3-H^E], 6.13 [dq, J_{gem} = 1.7, $^4J_{3\text{-H}(Z),2\text{-Me}}$ = 1.0 Hz, 1 H, 3-H^Z], 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.32 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 18.42 (2-Me), 55.36 (*p*-OMe), 66.31 (C-1′), 114.01 (2 C-*m*), 125.69 (C-3), 128.35 (C-*i*)*, 129.99 (2 C-*o*), 136.45 (C-2)*, 159.67 (C-*p*), 167.42 (C-1) ppm. *Assignments interchangeable. edHSQC: ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 18.42 (2-Me) ↔ δ = 1.95 (2-Me); δ = 55.36 (*p*-OMe) ↔ δ = 3.81 (*p*-OMe); δ = 66.31 (C-1′) ↔ δ = 5.13 (1′-H_2); δ = 114.01 (2 C-*m*) ↔ δ = 6.89 (2 *m*-H); δ = 125.69 (C-3) ↔ δ = 5.56 (3-H^E) and 6.13 (3-H^Z); δ = 129.99 (2 C-*o*) ↔ δ = 7.32 (2 *o*-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_{12}H_{18}NO_3$ $[M + NH_4]^+$ 224.12867; found 224.12870 (+0.1 ppm). $C_{12}H_{14}O_3$ (206.24): calcd. C 69.89, H 6.84; found C 69.65, H 6.67.

Isobutyl (*E*)-2-Methylbut-2-enoate (2b): A solution of **27** (2.50 mL, 2.70 g, 22.8 mmol) in CH_2Cl_2 (11 mL) was added dropwise to a solution of isobutanol (3.17 mL, 2.38 g, 34.2 mmol, 1.5 equiv.) and pyridine (2.76 mL, 2.70 g, 34.2 mmol, 1.5 equiv.) in CH_2Cl_2 (11 mL) at 0 °C and the mixture was stirred overnight at room temp. (a white precipitate formed). The reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (10 mL). H_2O (ca. 5 mL) was added until the precipitate dissolved, the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried with $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was distilled under reduced pressure (b.p. 160 °C). The product was obtained as a colorless oil (3.06 g, 86%). IR (film): $\tilde{\nu}$ = 2965, 2915, 2875, 2850, 1710, 1655, 1560, 1470, 1380, 1370, 1345, 1270, 1210, 1140, 1080, 1030 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 0.94 (d, $J_{3',2'}$ = $J_{2'\text{-Me},2'}$ = 6.7 Hz, 6 H, 2′-Me, 3′-H_3), 1.77 (dq, $J_{4,3}$ = 7.2, $^5J_{4,2\text{-Me}}$ = 1.2 Hz, 3 H, 4-H_3), 1.82 (dq, $^4J_{2\text{-Me},3}$ = $^5J_{2\text{-Me},4}$ = 1.4 Hz, 3 H, 2-Me), 1.95 (dqq, $J_{2',1'}$ = $J_{2',2'\text{-Me}}$ = $J_{2',3'}$ = 6.7 Hz, 1 H, 2′-H), 3.89 (d, $J_{1',2'}$ = 6.7 Hz, 2 H, 1′-H_2), 6.84 (qq, $J_{3,4}$ = 7.1, $^4J_{3,2\text{-Me}}$ = 1.4 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 12.03 (2-Me), 14.29 (C-4), 19.20 (2′-Me, C-3′), 27.91 (C-2′), 70.55 (C-1′), 128.90 (C-2), 136.77 (C-3), 168.19 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 12.03 (2-Me) ↔ δ = 1.82 (2-Me); δ = 14.29 (C-4) ↔ δ = 1.77 (4-H_3); δ = 19.20 (2′-Me, C-3′) ↔ δ = 0.94 (2′-Me, 3′-H_3); δ = 27.91 (C-2′) ↔ δ = 1.95 (2′-H); δ = 70.55 (C-1′) ↔ δ = 3.89 (1′-H_2); δ = 136.77 (C-3) ↔ δ = 6.84 (3-H) ppm. HRMS (pos. APCI, CH_2Cl_2): calcd. for $C_9H_{17}O_2$ $[M + H]^+$ 157.12285; found 157.12280 (–0.3 ppm).

4-Methoxybenzyl (*E*)-2-Methylbut-2-enoate (2c): A solution of (4-methoxyphenyl)methanol ("PMB-OH", 6.63 mL, 7.38 g, 53.4 mmol, 1.05 equiv.) in pyridine (4.93 mL, 4.83 g, 61.0 mmol, 1.2 equiv.) was added dropwise to a solution of **27** (6.03 g, 50.9 mmol) in CH_2Cl_2 (50 mL) and the mixture was stirred overnight at room temp. (a white precipitate formed). The reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (20 mL). H_2O (ca. 10 mL) was added until the precipitate dissolved, the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic phases were dried with $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was distilled under reduced pressure ($b.p._{0.1mbar}$ = 63 °C). The product was obtained as a colorless oil (7.92 g, 72%). IR (film): $\tilde{\nu}$ = 2955, 2840, 2060, 1710, 1650, 1615, 1515, 1460, 1385, 1250, 1135, 1075, 1035, 970, 825, 735 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.78 (dq, $J_{4,3}$ = 7.1, $^5J_{4,2\text{-Me}}$ = 1.0 Hz, 3 H, 4-H_3), 1.84 (dq, $^4J_{2\text{-Me},3}$ = $^5J_{2\text{-Me},4}$ = 1.1 Hz, 3 H, 2-Me), 3.81 (s, 3 H, OMe), 5.11 (s, 2 H, 1′-H_2), 6.84–6.91 [m, 3 H, possibly interpretable as 6.88 (qq, $J_{3,4}$ = 7.1, $^4J_{3,2\text{-Me}}$ = 1.5 Hz, 1 H, 3-H) superimposed by 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H)], 7.31 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 12.15 (2-Me), 14.42 (C-4), 55.37 (C-OMe), 66.07 (C-1′), 113.99 (2 C-*m*), 128.68 (C-*i*)*, 128.71 (C-2)*, 129.94 (2 C-*o*), 137.49 (C-3), 159.59 (C-*p*), 168.08 (C-1) ppm. *Assignments interchangeable. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 12.15 (2-Me) ↔ δ = 1.84 (2-Me); δ = 14.42 (C-4) ↔ δ = 1.78 (4-H_3); δ = 55.37 (C-OMe) ↔ δ = 3.81 (OMe); δ = 66.07 (C-1′) ↔ δ = 5.11 (1′-H_2); δ = 113.99 (2 C-*m*) ↔ δ = 6.89 (2 *m*-H); δ = 129.94 (2 C-*o*) ↔ δ = 7.31 (2 *o*-H); δ = 137.49 (C-3) ↔ δ = 6.88 (3-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_{13}H_{20}NO_3$ $[M + NH_4]^+$ 238.14432; found 238.14440 (+0.3 ppm). $C_{13}H_{16}O_3$ (220.27): calcd. C 70.89, H 7.32; found C 70.71, H 7.22.

(*E*)-2-Methyl-1-(pyrrolidin-1-yl)but-2-en-1-one (2e):[47] Pyrrolidine (7.62 mL, 6.60 g, 92.8 mmol, 2.2 equiv.) was added slowly to a solution of **27** (5.00 g, 42.1 mmol) in CH_2Cl_2 (35 mL) at 0 °C. The solution was stirred at room temp. overnight. The reaction was quenched by the addition of a saturated aqueous NH_4Cl solution (50 mL). The phases were separated and the aqueous phase extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were dried with $MgSO_4$ and the solvent evaporated under reduced pressure. The residue was distilled under reduced pressure ($b.p._{0.1mbar}$ 85 °C). The product was obtained as a colorless oil (5.24 g, 81%). IR (film): $\tilde{\nu}$ = 3490, 2970, 2875, 1660, 1615, 1425, 1375, 1340, 1250, 1230, 1185, 1165, 1115, 1085, 1035, 1015, 9660,

915, 840 cm^{-1}. ^1H NMR (500.42 MHz, $CDCl_3$, 263 K): δ = 1.62 (m_c, possibly interpretable as dq, $J_{4,3}$ = 6.9, $^5J_{4,2\text{-Me}}$ = 0.9 Hz, 3 H, 4-H_3), 1.77 (m_c, 3 H, 2-Me), 1.81 (m_c, 4 H, 3′-H_2, 4′-H_2), 3.38 (m_c, 4 H, 2′-H_2, 5′-H_2), 5.68 (qq, $J_{3,4}$ = 6.8, $^4J_{3,2\text{-Me}}$ = 1.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125.83 MHz, $CDCl_3$, 263 K): δ = 13.33 (C-4), 13.51 (2-Me), 24.34 (C-3′)*, 26.07 (C-4′)*, 45.48 (C-2′)**, 48.71 (C-5′)**, 126.46 (C-3), 133.23 (C-2), 171.98 (C-1) ppm. *,** Assignments interchangeable. edHSQC ("C,H-COSY", 125.83/500.42 MHz, $CDCl_3$, 263 K): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 13.33 (C-4) ↔ δ = 1.62 (4-H_3); δ = 13.51 (2-Me) ↔ δ = 1.77 (2-Me); δ = 24.34 (C-3′) and 26.07 (C-4′) ↔ δ = 1.81 (3′-H_2, 4′-H_2); δ = 45.48 (C-2′) and 48.71 (C-5′) ↔ δ = 3.38 (2′-H_2, 5′-H_2); δ = 126.46 (C-3) ↔ δ = 5.68 (3-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_9H_{16}NO$ $[M + H]^+$ 154.12319; found 154.12330 (+0.7 ppm).

4-Methoxybenzyl (*Z*)-2-Methylbut-2-enoate (3c): Compound **28** (1.80 g, 18.0 mmol) and Cs_2CO_3 (5.86 g, 18.0 mmol, 1.0 equiv.) were dissolved in DMF (36 mL) and the solution was cooled to 0 °C. 1-(Chloromethyl)-4-methoxybenzene (2.84 g, 18.2 mmol, 1.01 equiv.) was added to the solution and the mixture was stirred for 1 h at 0 °C and 2 h at room temp. The reaction was quenched by the addition of H_2O (30 mL). The phases were separated and the aqueous phase extracted with TBME (3 × 30 mL). The combined organic phases were dried with $MgSO_4$ and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography (3.5 × 20 cm, 50 mL, 10:1–3:1, 14–25). The product was obtained as a colorless liquid (3.56 g, 90%). IR (film): $\tilde{\nu}$ = 2955, 2840, 1710, 1615, 1515, 1360, 1385, 1350, 1300, 1250, 1150, 1085, 1040, 965, 825, 760 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.90 (dq, $^4J_{2\text{-Me},3} = {}^5J_{2\text{-Me},4}$ = 1.6 Hz, 3 H, 2-Me), 1.97 (dq, $J_{4,3}$ = 7.2, $^5J_{4,2\text{-Me}}$ = 1.5 Hz, 3 H, 4-H_3), 3.81 (s, 3 H, OMe), 5.13 (s, 2 H, 1′-H_2), 6.06 (qq, $J_{3,4}$ = 7.2, $^4J_{3,2\text{-Me}}$ = 1.5 Hz, 1 H, 3-H), 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.32 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 15.87 (C-4), 20.69 (2-Me), 55.37 (C-OMe), 65.74 (C-1′), 113.99 (2 C-*m*), 127.97 (C-*i*)*, 128.56 (C-2)*, 129.95 (2 C-*o*), 138.03 (C-3), 159.59 (C-*p*), 168.04 (C-1) ppm. *Assignments interchangeable. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 15.87 (C-4) ↔ δ = 1.97 (4-H_3); δ = 20.69 (2-Me) ↔ δ = 1.90 (2-Me); δ = 55.37 (C-OMe) ↔ δ = 3.81 (OMe); δ = 65.74 (C-1′) ↔ δ = 5.13 (1′-H_2); δ = 113.99 (2 C-*m*) ↔ δ = 6.89 (2 *m*-H); δ = 129.95 (2 C-*o*) ↔ δ = 7.32 (2 *o*-H); δ = 138.03 (C-3) ↔ δ = 6.06 (3-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_{13}H_{20}NO_3$ $[M + NH_4]^+$ 238.14432; found 238.14430 (–0.1 ppm). $C_{13}H_{16}O_3$ (220.27): calcd. C 70.89, H 7.32; found C 70.64, H 7.14.

(*Z*)-*N*-Methoxy-*N*,2-dimethylbut-2-enamide (3d):[47] HNMe(OMe)·HCl (2.08 g, 21.2 mmol, 1.55 equiv.) was dissolved in THF (30 mL) and the solution was cooled to –20 °C. Methyl (*Z*)-2-methylbut-2-enoate (**3a**; 1.86 mL, 1.75 g, 13.7 mmol) was added and the solution was stirred for 30 min at –20 °C. *i*PrMgCl (1.5 M in THF, 27.4 mL, 41.2 mmol, 3.0 equiv.) was added dropwise to the solution and the mixture was stirred for 30 min at –20 °C. The reaction was quenched by the addition of a saturated aqueous NH_4Cl solution (30 mL). The precipitate (Mg salts) was filtered and washed with EtOAc (30 mL). The phases were separated and the aqueous phase extracted with EtOAc (3 × 30 mL). The combined organic phases were dried with $MgSO_4$ and the solvent evaporated under reduced pressure. The residue was distilled under reduced pressure ($b.p._{0.1mbar}$ 70 °C). The product was obtained as a colorless oil (1.50 g, 76%). IR (film): $\tilde{\nu}$ = 3490, 2970, 2940, 1655, 1650, 1460, 1435, 1385, 1320, 1210, 1175, 1100, 1070, 1040, 1015, 995, 915, 870, 835 cm^{-1}.

For this compound most signals in the room temp. 125 MHz ^{13}C NMR spectrum ($CDCl_3$) appear as very broad signals or are broadened to such an extent that they do not appear at all. The cause of this seems to be the hindered rotation around the amide bond. The 333 K 500 MHz ^1H NMR spectrum ($CDCl_3$) shows very clear signals, the 333 K 125 MHz ^{13}C NMR spectrum ($CDCl_3$), however, lacks the signal of the carboxy-carbon (see below). Lowering the temperature to 263 K seems to slow the rotation around the amide bond that much that almost every ^{13}C signal in the 263 K 125 MHz ^{13}C NMR spectrum ($CDCl_3$) appears twice (see below). ^1H NMR (500.42 MHz, $CDCl_3$, 333 K): δ = 1.59 (dq, $J_{4,3}$ = 6.9, $^5J_{4,2\text{-Me}}$ = 1.6 Hz, 3 H, 4-H_3), 1.82 (dq, $^4J_{2\text{-Me},3} = {}^5J_{2\text{-Me},4}$ = 1.6 Hz, 3 H, 2-Me), 3.16 (s, 3 H, NMe), 3.60 (s, 3 H, OMe), 5.41 (qq, $J_{3,4}$ = 6.9, $^4J_{3,2\text{-Me}}$ = 1.6 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125.83 MHz, $CDCl_3$, 333 K): δ = 14.76 (C-4), 19.78 (2-Me), 32.97 (C-NMe)*, 61.20 (C-OMe), 124.56 (C-3), 132.59 (C-2). Although two HMBC cross-peaks, namely δ^{13C} = 171.25 (C-1) ↔ δ^{1H} = 1.82 (2-Me) and δ^{13C} = 171.25 (C-1) ↔ δ^{1H} = 3.16 (NMe) ppm, can be observed at this temperature, no ^{13}C signal for C-1 can be found. * This signal appears as a broad singlet. edHSQC ("C,H-COSY", 125.83/500.42 MHz, $CDCl_3$, 333 K): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 14.76 (C-4) ↔ δ = 1.59 (4-H_3); δ = 19.78 (2-Me) ↔ δ = 1.82 (2-Me); δ = 32.97 (C-NMe) ↔ δ = 3.16 (NMe); δ = 61.20 (C-OMe) ↔ δ = 3.60 (OMe); δ = 124.56 (C-3) ↔ δ = 5.41 (3-H) ppm. ^1H NMR (500.42 MHz, $CDCl_3$, 263 K): δ = 1.51–1.57 (m, 3 H, 4-H_3), 1.74–1.80 (m, 3 H, 2-Me), 3.14 (s, 3 H, NMe), 3.51 [s, 3 H, OMe (major rotamer)]*, 3.68 [s, 3 H, OMe (minor rotamer)]*, 5.34–5.44 (m, 1 H, 3-H) ppm. *A NOESY spectrum shows cross-peaks between these signals with the same phase as the homo-cross-peaks. This proves that these signals belong to the same protons in two rotamers. ^{13}C NMR (125.83 MHz, $CDCl_3$, 263 K): δ = 14.59 [C-4 (minor rotamer)], 15.13 [C-4 (major rotamer)], 19.86 [2-Me (both rotamers)], 31.66 [C-NMe (major rotamer)], 35.10 [C-NMe (minor rotamer)], 60.40 [C-OMe (minor rotamer)], 61.51 [C-OMe (major rotamer)], 124.08 [C-3 (major rotamer)], 125.27 [C-3 (minor rotamer)], 131.17 [C-2 (minor rotamer)], 132.40 [C-2 (major rotamer)], 167.79 [C-1 (minor rotamer)], 171.89 [C-1 (major rotamer)] ppm. edHSQC ("C,H-COSY", 125.83/500.42 MHz, $CDCl_3$, 263 K): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 14.59 [C-4 (minor rotamer)] and 15.13 [C-4 (major rotamer)] ↔ δ = 1.51–1.57 (4-H_3); δ = 19.86 [2-Me (both rotamers)] ↔ δ = 1.74–1.80 (2-Me); δ = 31.66 [C-NMe (major rotamer)] and 35.10 [C-NMe (minor rotamer)] ↔ δ = 3.14 (NMe); δ = 60.40 [C-OMe (minor rotamer)] ↔ δ = 3.68 [OMe (minor rotamer)]; δ = 61.51 [C-OMe (major rotamer)] ↔ δ = 3.51 [OMe (major rotamer)]; δ = 124.08 [C-3 (major rotamer)] and 125.27 [C-3 (minor rotamer)] ↔ δ = 5.34–5.44 (3-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_7H_{14}NO_2$ $[M + H]^+$ 144.10245; found 144.10250 (+0.3 ppm).

(*Z*)-2-Methyl-1-(pyrrolidin-1-yl)but-2-en-1-one (3e):[47] Pyrrolidine (1.74 mL, 1.51 g, 21.2 mmol, 1.55 equiv.) was dissolved in THF (30 mL) and the solution was cooled to –20 °C. Methyl (*Z*)-2-methylbut-2-enoate (1.86 mL, 1.75 g, 13.7 mmol) was added and the solution was stirred for 30 min at –20 °C. *i*PrMgCl (1.5 M in THF, 13.7 mL, 20.5 mmol, 1.5 equiv.) was added dropwise to the solution and the mixture was stirred for 30 min at –20 °C. The reaction was quenched by the addition of a saturated aqueous NH_4Cl solution (30 mL). The precipitate (Mg salts) was filtered and washed with

EtOAc (30 mL). The phases of the filtrate were separated and the aqueous phase extracted with EtOAc (3 × 30 mL). The combined organic phases were dried with $MgSO_4$ and the solvent evaporated under reduced pressure. The residue was distilled under reduced pressure ($b.p._{0.1mbar}$ 65 °C). The product was obtained as a colorless oil (2.46 g, 70%). IR (film): $\tilde{\nu}$ = 3480, 2970, 2920, 2875, 1625, 1560, 1525, 1455, 1435, 1380, 1345, 1320, 1250, 1225, 1185, 1170, 1115, 1080, 1035, 980, 960, 915, 880, 845 cm^{-1}. ^1H NMR (500.42 MHz, $CDCl_3$, 333 K): δ = 1.50 (dq, $J_{4,3}$ = 6.9, $^5J_{4,2\text{-Me}}$ = 1.6 Hz, 3 H, 4-H_3), 1.76 (dq, $^4J_{2\text{-Me},3}$ = $^5J_{2\text{-Me},4}$ = 1.6 Hz, 3 H, 2-Me), 1.81 (m_c, 4 H, 3′-H_2, 4′-H_2), 3.24 (m_c, 2 H, 2′-H_2)*, 3.41 (m_c, 2 H, 5′-H_2)*, 5.29 (qq, $J_{3,4}$ = 6.8, $^4J_{3,2\text{-Me}}$ = 1.5 Hz, 1 H, 3-H) ppm. * Assignments interchangeable. ^{13}C NMR (125.83 MHz, $CDCl_3$, 333 K): δ = 14.48 (C-4), 19.60 (2-Me), 24.37 (C-3′)*, 25.82 (C-4′)*, 44.68 (C-5′)**, 46.69 (C-2′)**, 122.55 (C-3), 134.28 (C-2), 170.52 (C-1) ppm. *,** Assignments interchangeable. edHSQC ("C,H-COSY", 125.83/500.42 MHz, $CDCl_3$, 333 K): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 14.48 (C-4) ↔ δ = 1.50 (4-H_3); δ = 19.60 (2-Me) ↔ δ = 1.76 (2-Me); δ = 24.37 (C-3′) ↔ δ = 1.81 (3′-H_2, 4′-H_2); δ = 25.82 (C-4′) ↔ δ = 1.81 (3′-H_2, 4′-H_2); δ = 44.68 (C-5′) ↔ δ = 3.41 (5′-H_2); δ = 46.69 (C-2′) ↔ δ = 3.24 (2′-H_2); δ = 122.55 (C-3) ↔ δ = 5.29 (3-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_9H_{16}NO$ $[M + H]^+$ 154.12319; found 154.12320 (+0.1 ppm).

Methyl *rel*-(2*R*,3*S*)-2,3-Dihydroxy-2-methylbutanoate (*syn*-7a):[48] Following the general procedure A, the title compound was prepared from methyl (*E*)-2-methylbut-2-enoate (**2a**; 0.50 g, 4.4 mmol), citric acid (0.63 g, 3.3 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (4.0 mg, 11 µmol, 0.25 mol-%), and NMO (50% in H_2O, 1.2 g, 5.3 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 13–22) rendered the product as a colorless oil (0.57 g, 88%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.23 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.32 (s, 3 H, 2-Me), 2.03 (br. s, 1 H, 3-OH), 3.33 (br. s, 1 H, 2-OH), 3.82 (s, 3 H, OMe), 3.95 (q, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H) ppm.

Methyl (2*R*,3*S*)-2,3-Dihydroxy-2-methylbutanoate [(2*R*,3*S*)-7a]:[48] Following the general procedure B, the title compound was prepared from methyl (*E*)-2-methylbut-2-enoate (**2a;** 0.50 g, 4.4 mmol), $K_3[Fe(CN)_6]$ (4.3 g, 13 mmol, 3.0 equiv.), K_2CO_3 (1.8 g, 13 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.42 g, 4.4 mmol, 1.0 equiv.), $(DHQ)_2$-PHAL (68 mg, 88 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (16 mg, 44 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, c-C_6H_{12}/EtOAc = 3:1–1:1, 13–22) rendered the product as a colorless oil (0.55 g, 85%; 87% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 90:10, 210 nm, t_R = 7.51 (2*S*,3*R*), 8.35 min (2*R*,3*S*). $[\alpha]_D^{20}$ = +0.3 (*c* = 1.16 g/100 mL, $CHCl_3$); $[\alpha]_{546}^{20}$ = –0.2 (*c* = 1.16 g/100 mL, $CHCl_3$); $[\alpha]_{436}^{20}$ = –1.9 (*c* = 1.16 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –7.6 (*c* = 1.16 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.23 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.32 (s, 3 H, 2-Me), 2.02 (br. s, 1 H, 3-OH), 3.34 (s, 1 H, 2-OH), 3.82 (s, 3 H, OMe), 3.94 (br. s, 1 H, 3-H) ppm.

Methyl (2*S*,3*R*)-2,3-Dihydroxy-2-methylbutanoate [(2*S*,3*R*)-7a]: Following the general procedure B, the title compound was prepared from methyl (*E*)-2-methylbut-2-enoate (**2a**; 0.50 g, 4.4 mmol), $K_3[Fe(CN)_6]$ (4.3 g, 13 mmol, 3.0 equiv.), K_2CO_3 (1.8 g, 13 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.42 g, 4.4 mmol, 1.0 equiv.), $(DHQD)_2$-PHAL (68 mg, 88 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (16 mg, 44 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 15–24) rendered the product as a colorless oil (0.54 g, 84%; 92% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 90:10, 210 nm, t_R = 7.39 (2*S*,3*R*), 8.69 min (2*R*,3*S*). $[\alpha]_D^{20}$ = –0.4 (*c* = 1.10 g/100 mL, $CHCl_3$); $[\alpha]_{546}^{20}$ = ±0.0 (*c* = 1.10 g/100 mL, $CHCl_3$); $[\alpha]_{436}^{20}$ = +2.3 (*c* = 1.10 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +8.5 (*c* = 1.10 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3465, 2985, 2950, 1735, 1450, 1380, 1265, 1190, 1135, 1090, 1015, 980, 945, 915, 870, 795, 750, 680 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.23 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.32 (s, 3 H, 2-Me), 2.03 (br. s, 1 H, 3-OH), 3.36 (s, 1 H, 2-OH), 3.82 (s, 3 H, OMe), 3.94 (br. q, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 16.76 (C-4), 21.80 (2-Me), 53.12 (OMe), 71.71 (C-3), 77.37 (C-2), 176.83 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 16.76 (C-4) ↔ δ = 1.23 (4-H_3); δ = 21.80 (2-Me) ↔ δ = 1.32 (2-Me); δ = 53.12 (OMe) ↔ δ = 3.82 (OMe); δ = 71.71 (C-3) ↔ δ = 3.94 (3-H) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_6H_{12}O_4Na$ $[M + Na]^+$ 171.06330; found 171.06333 (+0.2 ppm). $C_6H_{12}O_4$ (148.16): calcd. C 48.64, H 8.16; found C 48.37, H 8.00.

Isobutyl *rel*-(2*R*,3*S*)-2,3-Dihydroxy-2-methylbutanoate (*syn*-7b):[48] Following the general procedure A, the title compound was prepared from isobutyl (*E*)-2-methylbut-2-enoate (**2b**; 0.30 g, 1.9 mmol), citric acid (0.28 g, 1.4 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (1.8 mg, 4.8 µmol, 0.25 mol-%), and NMO (50% in H_2O, 0.54 g, 2.3 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 9–17) rendered the product as a colorless oil (0.33 g, 89%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 0.95 (d, $J_{3',2'}$ = $J_{2'\text{-Me},2'}$ = 6.7 Hz, 6 H, 3′-H_3, 2′-Me), 1.24 (d, $J_{4,3}$ = 6.3 Hz, 3 H, 4-H_3), 1.33 (s, 3 H, 2-Me), 1.98 (d, $J_{3\text{-OH},3}$ = 7.5 Hz, 1 H, 3-OH), 2.00 (tqq, $J_{2',1'}$ = $J_{2',3'}$ = $J_{2',2'\text{-Me}}$ = 6.7 Hz, 1 H, 2′-H), 3.39 (s, 1 H, 2-OH), 3.95 (dq, $J_{3,3\text{-OH}}$ = 8.5, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H), 4.01 (d, $J_{1',2'}$ = 6.7 Hz, 2 H, 1′-H_2) ppm.

Isobutyl (2*R*,3*S*)-2,3-Dihydroxy-2-methylbutanoate [(2*R*,3*S*)-7b]:[48] Following the general procedure B, the title compound was prepared from isobutyl (*E*)-2-methylbut-2-enoate (**2b**; 0.25 g, 1.6 mmol), $K_3[Fe(CN)_6]$ (1.6 g, 4.8 mmol, 3.0 equiv.), K_2CO_3 (0.66 g, 4.8 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.15 g, 1.6 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (25 mg, 32 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (5.9 mg, 16 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 9–11) rendered the product as a colorless oil (0.26 g, 86%; 81% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 10.29 (2*S*,3*R*), 11.43 min (2*R*,3*S*). $[\alpha]_D^{20}$ = +5.5 (*c* = 0.96 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +27.0 (*c* = 0.96 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 0.958 (d, $J_{3',2'}$ = 6.7 Hz, 3 H, 3′-H_3) superimposed by 0.960 (d, $J_{2'\text{-Me},2'}$ = 6.7 Hz, 3 H, 2′-Me), 1.23 (d, $J_{4,3}$ = 6.3 Hz, 3 H, 4-H_3), 1.33 (s, 3 H, 2-Me), 1.98 (d, $J_{3\text{-OH},3}$ = 9.2 Hz, 3-OH) superimposed by 1.99 (tqq, $J_{2',1'}$ = $J_{2',3'}$ = $J_{2',2'\text{-Me}}$ = 6.7 Hz, 1 H, 2′-H), 3.38 (s, 1 H, 2-OH), 3.94 (dq, $J_{3,3\text{-OH}}$ = 9.2, $J_{3,4}$ = 6.5 Hz, 1 H, 3-H), 4.01 (d, $J_{1',2'}$ = 6.4, 1′-H_2) ppm.

Isobutyl (2*S*,3*R*)-2,3-Dihydroxy-2-methylbutanoate [(2*S*,3*R*)-7b]: Following the general procedure B, the title compound was prepared from isobutyl (*E*)-2-methylbut-2-enoate (**2b**; 0.25 g, 1.6 mmol), $K_3[Fe(CN)_6]$ (1.6 g, 4.8 mmol, 3.0 equiv.), K_2CO_3 (0.66 g, 4.8 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.15 g, 1.6 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (25 mg, 32 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (5.9 mg, 16 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 11–20) rendered the product as a colorless oil (0.27 g, 86%; 85% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 10.05 (2*S*,3*R*), 11.65 min (2*R*,3*S*).

$[\alpha]_D^{20}$ = –7.2 (*c* = 0.91 g/100 mL, $CHCl_3$). $[\alpha]_{365}^{20}$ = –35.0 (*c* = 0.91 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3475, 2970, 2880, 1735, 1465, 1380, 1255, 1190, 1130, 1090, 1015, 985, 945, 790, 750, 680 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 0.938 (d, $J_{3',2'}$ = 6.7 Hz, 3 H, 3′-H_3) superimposed by 0.941 (d, $J_{2'\text{-Me},2'}$ = 6.7 Hz, 3 H, 2′-Me), 1.22 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.31 (s, 3 H, 2-Me), 1.98 (tqq, $J_{2',1'}$ = $J_{2',3'}$ = $J_{2',2'\text{-Me}}$ = 6.7 Hz, 1 H, 2′-H), 3.93 (q, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H), 3.98 (d, $J_{1',2'}$ = 6.7 Hz, 2 H, 1′-H_2). The OH groups were not visible in this spectrum. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 16.77 (C-4), 18.97, 19.01 (C-3′, 2′-Me), 21.77 (2-Me), 27.82 (C-2′), 71.71 (C-3), 72.15 (C-1′), 77.31 (C-2), 176.38 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 16.77 (C-4) ↔ δ = 1.22 (4-H_3); δ = 18.97, 19.01 (C-3′, 2′-Me) ↔ δ = 0.935 (3′-H_3) and 0.941 (2′-Me); δ = 21.77 (2-Me) ↔ δ = 1.31 (2-Me); δ = 27.82 (C-2′) ↔ δ = 1.98 (2′-H); δ = 71.71 (C-3) ↔ δ = 3.93 (3-H); δ = 72.15 (C-1′) ↔ δ = 3.98 (1′-H_2) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_9H_{19}NO_4$ $[M + H]^+$ 191.12833; found 191.12830 (–0.2 ppm). $C_9H_{18}O_4$ (190.24): calcd. C 56.82, H 9.54; found C 56.46, H 9.44.

4-Methoxybenzyl *rel*-(2*R*,3*S*)-2,3-Dihydroxy-2-methylbutanoate (*syn*-7c):[48] Following the general procedure A, the title compound was prepared from **2c** (0.50 g, 2.3 mmol), citric acid (0.33 g, 1.7 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (2.1 mg, 5.7 µmol, 0.25 mol-%), and NMO (50% in H_2O, 0.64 g, 2.7 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:3, 21–46) rendered the product as a colorless oil (0.54 g, 94%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.20 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.31 (s, 3 H, 2-Me), 1.94 (br. s, 1 H, 3-OH), 3.34 (br. s, 1 H, 2-OH), 3.81 (s, 3 H, *p*-OMe), 3.94 (q, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H), 5.18 (s, 2 H, 1′-H_2), 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.30 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm.

4-Methoxybenzyl (2*R*,3*S*)-2,3-Dihydroxy-2-methylbutanoate [(2*R*,3*S*)-7c]:[48] Following the general procedure B, the title compound was prepared from **2c** (0.50 g, 2.3 mmol), $K_3[Fe(CN)_6]$ (2.2 g, 6.8 mmol, 3.0 equiv.), K_2CO_3 (0.94 g, 6.8 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.21 g, 2.2 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (35 mg, 45 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (8.4 mg, 22 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 11–26) rendered the product as a colorless oil (0.47 g, 81%; 93% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 90:10, 229 nm, t_R = 15.37 (2*S*,3*R*), 17.69 min (2*R*,3*S*). $[\alpha]_D^{20}$ = –1.1 (*c* = 1.03 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –12.8 (*c* = 1.03 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.20 (d, $J_{4,3}$ = 6.3 Hz, 3 H, 4-H_3), 1.31 (s, 3 H, 2-Me), 1.94 (d, $J_{3\text{-OH},3\text{-H}}$ = 8.8 Hz, 1 H, 3-OH), 3.34 (s, 1 H, 2-OH), 3.81 (s, 3 H, *p*-OMe), 3.94 (dq, $J_{3,3\text{-OH}}$ = 7.8, $J_{3,4}$ = 6.7 Hz, 1 H, 3-H), 5.18 (s, 2 H, 1′-H_2), 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.30 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm.

4-Methoxybenzyl (2*S*,3*R*)-2,3-Dihydroxy-2-methylbutanoate [(2*S*,3*R*)-7c]: Following the general procedure B, the title compound was prepared from **2c** (0.50 g, 2.3 mmol), $K_3[Fe(CN)_6]$ (2.2 g, 6.8 mmol, 3.0 equiv.), K_2CO_3 (0.94 g, 6.8 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.21 g, 2.2 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (35 mg, 45 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (8.4 mg, 22 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 11–26) rendered the product as a colorless oil (0.47 g, 81%; 95% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 90:10, 229 nm, t_R = 15.07 (2*S*,3*R*), 17.64 min (2*R*,3*S*). $[\alpha]_D^{20}$ = +1.4 (*c* = 1.05 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +14.3 (*c* = 1.05 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3500, 2985, 2840, 2060, 1730, 1615, 1515, 1455, 1375, 1250, 1180, 1130, 1035, 950, 825, 765, 675 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.20 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.31 (s, 3 H, 2-Me), 1.98 (d, $J_{3\text{-OH},3}$ = 8.5 Hz, 1 H, 3-OH), 3.36 (s, 1 H, 2-OH), 3.81 (s, 3 H, *p*-OMe), 3.94 (qd, $J_{3,4}$ = $J_{3,3\text{-OH}}$ = 6.6 Hz, 1 H, 3-H), 5.18 (s, 2 H, 1′-H_2), 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.29 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *m*-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 16.76 (C-4), 21.74 (2-Me), 55.37 (*p*-OMe), 67.74 (C-1′), 71.71 (C-3), 77.32 (C-2), 114.13 (2 C-*m*), 127.40 (C-*i*), 130.10 (2 C-*o*), 159.94 (C-*p*), 176.25 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 16.76 (C-4) ↔ δ = 1.20 (4-H_3); δ = 21.74 (2-Me) ↔ δ = 1.31 (2-Me); δ = 55.37 (*p*-OMe) ↔ δ = 3.81 (*p*-OMe); δ = 67.74 (C-1′) ↔ δ = 5.18 (1′-H_2); δ = 71.71 (C-3) ↔ δ = 3.94 (3-H); δ = 114.13 (2 C-*m*) ↔ δ = 6.89 (2 *m*-H); δ = 130.10 (2 C-*o*) ↔ δ = 7.29 (2 *m*-H) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_{13}H_{18}O_5Na$ $[M + Na]^+$ 277.10520; found 277.10519 (±0.0 ppm). $C_{13}H_{14}O_5$ (250.25): calcd. C 61.41, H 7.13; found C 61.38, H 7.14.

***rel*-(2*R*,3*S*)-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylbutanamide (*syn*-7d):**[48] Following the general procedure A, the title compound was prepared from **2d** (0.30 g, 2.1 mmol), citric acid (0.30 g, 1.6 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (7.7 mg, 21 µmol, 1.0 mol-%), and NMO (50% in H_2O, 0.59 g, 2.5 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 2:1–1:3, 28–36) rendered the product as a colorless oil (0.31 g, 84%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.26 (d, $J_{4,3}$ = 6.3 Hz, 3 H, 4-H_3), 1.37 (s, 3 H, 2-Me), 2.02 (d, $J_{3\text{-OH},3}$ = 10.5 Hz, 1 H, 3-OH), 3.31 (s, 3 H, N-Me), 3.75 (s, 3 H, O-Me), 4.16 (dq, $J_{3,3\text{-OH}}$ = 10.6, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H), 4.43 (s, 1 H, 2-OH) ppm.

(2*R*,3*S*)-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylbutanamide [(2*R*,3*S*)-7d]:[48] Following the general procedure B, the title compound was prepared from **2d** (0.30 g, 2.1 mmol), $K_3[Fe(CN)_6]$ (2.1 g, 6.3 mmol, 3.0 equiv.), K_2CO_3 (0.87 g, 6.3 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.33 g, 2.1 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (49 mg, 63 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (16 mg, 42 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 2:1–1:3, 23–34) rendered the product as a colorless oil (0.30 g; 81%; 98% *ee*). Analytical HPLC: Chiralpak OD-H, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 19.27 (*S*), 24.74 min (*R*). $[\alpha]_D^{20}$ = +17.6 (*c* = 1.12 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +54.9 (*c* = 1.12 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.25 (d, $J_{4,3}$ = 6.3 Hz, 3 H, 4-H_3), 1.37 (s, 3 H, 2-Me), 2.02 (br. s, 1 H, 3-OH), 3.31 (s, 3 H, N-Me), 3.75 (s, 3 H, O-Me), 4.16 (br. s, 1 H, 3-H), 4.44 (br. s, 1 H, 2-OH) ppm.

(2*S*,3*R*)-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylbutanamide [(2*S*,3*R*)-7d]: Following the general procedure B, the title compound was prepared from **2d** (0.30 g, 2.1 mmol), $K_3[Fe(CN)_6]$ (2.1 g, 6.3 mmol, 3.0 equiv.), K_2CO_3 (0.87 g, 6.3 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.33 g, 2.1 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (49 mg, 63 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (16 mg, 42 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 2:1–1:3, 27–35) rendered the product as a colorless oil (0.33 g, 89%; 99% *ee*). Analytical HPLC: Chiralpak OD-H, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 19.84 (*S*), 24.39 min (*R*). $[\alpha]_D^{20}$ = –17.7 (*c* = 1.34 g/100 mL, $CHCl_3$);

$[\alpha]_{365}^{20}$ = –52.0 (*c* = 1.34 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3430, 2985, 2945, 2915, 2850, 2835, 1640, 1460, 1450, 1370, 1260, 1210, 1180, 1090, 1015, 995 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.25 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.37 (s, 3 H, 2-Me), 2.03 (d, $J_{3\text{-}OH,3}$ = 10.0 Hz, 1 H, 3-OH), 3.31 (s, 3 H, N-Me), 3.75 (s, 3 H, O-Me), 4.15 (m_c, possibly interpretable as dq, $J_{3,3\text{-}OH}$ = 9.2, $J_{3,4}$ = 6.6 Hz, 1 H, 3-H), 4.44 (s, 1 H, 2-OH) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 17.17 (C-4), 21.84 (2-Me), 33.90 (N-Me), 61.04 (O-Me), 70.38 (C-3), 77.67 (C-2), 175.51 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 17.17 (C-4) ↔ 1.25 (4-H_3); δ = 21.84 (2-Me) ↔ 1.37 (2-Me); δ = 33.90 (N-Me) ↔ 3.31 (N-Me); δ = 61.04 (O-Me) ↔ 3.75 (O-Me); δ = 70.38 (C-3) ↔ 4.15 (3-H) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_7H_{15}NO_4Na$ $[M + Na]^+$ 200.08988; found 200.08990 (+0.1 ppm).

***rel*-(2*R*,3*S*)-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)butan-1-one (*syn*-7e):**[48] Following the general procedure A, the title compound was prepared from **2e** (0.17 g, 1.1 mmol), citric acid (0.16 g, 0.82 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (4.0 mg, 11 µmol, 1.0 mol-%), and NMO (50% in H_2O, 0.31 g, 1.3 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 19–25) rendered the product as a colorless oil (0.21 g, 100%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.22 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.34 (s, 3 H, 2-Me), 1.86 (br. m_c, 2 H, 3′-H_2)*, 1.93 (br. m_c, 2 H, 4′-H_2)*, 3.55 (br. m_c, 2 H, 2′-H_2)** superimposed by 3.65 (br. m_c, 1 H, 5′-H)** superimposed by 3.75 (br. m_c, 1 H, 5′-H)**, 4.20 (q, $J_{3,4}$ = 6.3 Hz, 1 H, 3-H) ppm. *,** The assignments of 3′-H and 4′-H, and of 2′-H and 5′-H are arbitrary. The OH groups were not visible in this spectrum.

(2*R*,3*S*)-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)butan-1-one [(2*R*,3*S*)-7e]:[48] Following the general procedure B, the title compound was prepared from **2e** (0.30 g, 2.0 mmol), $K_3[Fe(CN)_6]$ (1.9 g, 5.9 mmol, 3.0 equiv.), K_2CO_3 (0.81 g, 5.9 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.31 g, 2.0 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (46 mg, 59 µmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (14 mg, 39 µmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:3, 45–51) rendered the product as a colorless oil (0.22 g, 59%; 97% *ee*). Analytical HPLC: Chiralpak AD-3, *n*-heptane/*i*PrOH = 95:5, 230 nm, t_R = 12.95 (2*S*,3*R*), 15.60 min (2*R*,3*S*). $[\alpha]_D^{20}$ = +33.4 (*c* = 1.06 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +112.0 (*c* = 1.06 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.22 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.34 (s, 3 H, 2-Me), 1.86 (br. m_c, 2 H, 3′-H_2)*, 1.93 (br. m_c, 2 H, 4′-H_2)*, 2.58 (d, $J_{3\text{-}OH,3}$ = 7.5 Hz, 1 H, 3-OH), 3.55 (br. m_c, 2 H, 2′-H_2)** superimposed by 3.68 (br. m_c, 1 H, 5′-H)** superimposed by 3.76 (br. m_c, 1 H, 5′-H)**, 3.93 (s, 1 H, 2-OH), 4.20 (dq, $J_{3,3\text{-}OH}$ = $J_{3,4}$ = 6.6 Hz, 1 H, 3-H) ppm. *,** The assignments of 3′-H and 4′-H, and of 2′-H and 5′-H are arbitrary.

(2*S*,3*R*)-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)butan-1-one [(2*S*,3*R*)-7e]: Following the general procedure B, the title compound was prepared from **2e** (0.30 g, 2.0 mmol), $K_3[Fe(CN)_6]$ (1.9 g, 5.9 mmol, 3.0 equiv.), K_2CO_3 (0.81 g, 5.9 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.31 g, 2.0 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (46 mg, 59 µmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (14 mg, 39 µmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:3, 45–51) rendered the product as a colorless oil (0.28 g, 76%; 98% *ee*). Analytical HPLC: Chiralpak AD-3, *n*-heptane/*i*PrOH = 95:5, 230 nm, t_R = 12.41 (2*S*,3*R*), 16.15 min (2*R*,3*S*). $[\alpha]_D^{20}$ = –35.9 (*c* = 1.32 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –115.6 (*c* = 1.32 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3390, 2975, 2915, 2880, 2850, 1600, 1440, 1365, 1340, 1260, 1185, 1150, 1085, 1070 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.21 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.33 (s, 3 H, 2-Me), 1.84 (br. m_c, 2 H, 3′-H_2)*, 1.93 (br. m_c, 2 H, 4′-H_2)*, 2.70 (br. d, $J_{3\text{-}OH,3}$ = 6.8 Hz, 1 H, 3-OH), 3.54 (br. m_c, 2 H, 2′-H_2)** superimposed by 3.67 (br. m_c, 1 H, 5′-H)** superimposed by 3.75 (br. m_c, 1 H, 5′-H)**, 3.97 (s, 1 H, 2-OH), 4.19 (dq, $J_{3,3\text{-}OH}$ = $J_{3,4}$ = 6.2 Hz, 1 H, 3-H) ppm. *,** The assignments of 3′-H and 4′-H, and of 2′-H and 5′-H are arbitrary. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 16.16 (C-4), 21.21 (2-Me), 23.23 (C-3′)*, 27.01 (C-4′)*, 47.75 (C-5′)**, 48.03 (C-2′)**, 70.74 (C-3), 77.47 (C-2), 173.63 (C-1) ppm. *,** The assignments of 3′-H and 4′-H, and of 2′-H and 5′-H are arbitrary, but consistent with the assignment in the ^1H NMR spectrum. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 16.16 (C-4) ↔ δ = 1.21 (4-H_3); δ = 21.21 (2-Me) ↔ δ = 1.33 (2-Me); δ = 23.23 (C-3′)* ↔ δ = 1.84 (3′-H_2); δ = 27.01 (C-4′)* ↔ δ = 1.93 (4′-H_2); δ = 47.75 (C-5′) ↔ δ = 3.67 (5′-H) and 3.75 (5′-H); δ = 48.03 (C-2′) ↔ δ = 3.54 (2′-H_2); δ = 70.74 (C-3) ↔ δ = 4.19 (3-H) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_{12}H_{16}O_4Na$ $[M + Na]^+$ calcd. 210.11061; found 210.11070 (+0.4 ppm).

Methyl *rel*-(2*S*,3*S*)-2,3-Dihydroxy-2-methylbutanoate (*anti*-7a):[48] Following the general procedure A, the title compound was prepared from methyl (*Z*)-2-methylbut-2-enoate (**3a**; 0.50 g, 4.4 mmol), citric acid (0.63 g, 3.3 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (4.0 mg, 11 µmol, 0.25 mol-%), and NMO (50% in H_2O, 1.2 g, 5.3 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 8–20) rendered the product as a colorless oil (0.53 g, 82%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.16 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.44 (s, 3 H, 2-Me), 2.16 (d, $J_{3\text{-}OH,3}$ = 8.1, 1 H, 3-OH), 3.36 (s, 1 H, 2-OH), 3.73–3.87 (m, 1 H, 3-H) superimposed by 3.81 (s, 3 H, OMe) ppm.

Methyl (2*S*,3*S*)-2,3-Dihydroxy-2-methylbutanoate [(*S*,*S*)-7a]:[48] Following the general procedure B, the title compound was prepared from methyl (*Z*)-2-methylbut-2-enoate (**3a**; 0.50 g, 4.4 mmol), $K_3[Fe(CN)_6]$ (4.3 g, 13 mmol, 3.0 equiv.), K_2CO_3 (1.8 g, 13 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.42 g, 4.4 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (68 mg, 88 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (16 mg, 44 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 19–36) rendered the product as a colorless oil (0.53 g, 82%; 77% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 14.05 (*S*,*S*), 15.97 min (*R*,*R*). $[\alpha]_D^{20}$ = +4.7 (*c* = 0.94 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +17.4 (*c* = 0.94 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.16 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.44 (s, 3 H, 2-Me), 2.19 (d, $J_{3\text{-}OH,3}$ = 7.9, 1 H, 3-OH), 3.38 (s, 1 H, 2-OH), 3.75–3.86 (m, 1 H, 3-H) superimposed by 3.81 (s, 3 H, OMe) ppm.

Methyl (2*R*,3*R*)-2,3-Dihydroxy-2-methylbutanoate [(*R*,*R*)-7a]: Following the general procedure B, the title compound was prepared from methyl (*Z*)-2-methylbut-2-enoate (**3a**; 0.50 g, 4.4 mmol), $K_3[Fe(CN)_6]$ (4.3 g, 13 mmol, 3.0 equiv.), K_2CO_3 (1.8 g, 13 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.42 g, 4.4 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (68 mg, 88 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (16 mg, 44 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 13–22) rendered the product as a colorless oil (0.55 g, 86%; 90% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 14.56 (*S*,*S*), 15.46 min (*R*,*R*). $[\alpha]_D^{20}$ = –5.1 (*c* = 1.12 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –21.4 (*c* = 1.12 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3465, 2985, 2950, 1735, 1450, 1375, 1255, 1185, 1155,

1090, 1015, 980, 910, 870, 795, 750, 700 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.15 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.44 (s, 3 H, 2-Me), 2.20 (d, $J_{3\text{-}OH,3}$ = 8.0 Hz, 1 H, 3-OH), 3.39 (s, 1 H, 2-OH), 3.80 (dq, $J_{3,3\text{-}OH}$ = 8.0, $J_{3,4}$ = 6.5 Hz, 1 H, 3-H) superimposed by 3.81 (s, 3 H, OMe) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 17.79 (C-4), 22.35 (2-Me), 52.97 (OMe), 72.31 (C-3), 77.27 (C-2), 176.00 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 17.79 (C-4) $\leftrightarrow$ δ = 1.15 (4-H_3); δ = 22.35 (2-Me) $\leftrightarrow$ δ = 1.44 (2-Me); δ = 52.97 (OMe) $\leftrightarrow$ δ = 3.81 (OMe); δ = 72.31 (C-3) $\leftrightarrow$ δ = 3.80 (3-H) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_6H_{12}O_4Na$ $[M + Na]^+$ 171.06330; found 171.06333 (+0.2 ppm).

Isobutyl *rel*-(2*S*,3*S*)-2,3-Dihydroxy-2-methylbutanoate (*anti*-7b):[48] Following the general procedure A, the title compound was prepared from isobutyl (*Z*)-2-methylbut-2-enoate (**3b**; 0.50 g, 3.2 mmol), citric acid (0.46 g, 2.4 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (3.0 mg, 8.0 µmol, 0.25 mol-%), and NMO (50% in H_2O, 0.90 g, 3.8 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 8–14) rendered the product as a colorless oil (0.57 g, 92%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 0.96 (d, $J_{3',2'} = J_{2'\text{-}Me,2'}$ = 6.7 Hz, 6 H, 3′-H_3, 2′-Me), 1.17 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.45 (s, 3 H, 2-Me), 1.99 [ddqq, $J_{2',1'\text{-}H(A)} = J_{2',1'\text{-}H(B)} = J_{2',3'} = J_{2',2'\text{-}Me}$ = 6.7 Hz, 1 H, 2′-H], 2.17 (br. s, 1 H, 3-OH), 3.41 (br. s, 1 H, 2-OH), 3.81 (q, $J_{3,4}$ = 6.4 Hz, 1 H 3-H) ppm, AB signal [δ_A = 3.97, δ_B = 4.03 ppm, A part additionally split by $J_{1'\text{-}H(A),2'}$ = 6.6 Hz, B part additionally split by $J_{1'\text{-}H(B),2'}$ = 6.7, J_{AB} = 10.5 Hz, 2 H, 1′-H_2].

Isobutyl (2*S*,3*S*)-2,3-Dihydroxy-2-methylbutanoate [(*S*,*S*)-7b]:[48] Following the general procedure B, the title compound was prepared from isobutyl (*Z*)-2-methylbut-2-enoate (**3b**; 0.50 g, 3.2 mmol), $K_3[Fe(CN)_6]$ (3.2 g, 9.6 mmol, 3.0 equiv.), K_2CO_3 (1.3 g, 9.6 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.30 g, 3.2 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (50 mg, 64 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (12 mg, 32 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 2:1–1:2, 8–13) rendered the product as a colorless oil (0.56 g, 92%; 67% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 8.03 (*S*,*S*), 9.01 min (*R*,*R*). $[a]_D^{20}$ = –6.8 (*c* = 1.47 g/100 mL, $CHCl_3$); $[a]_{365}^{20}$ = –36.8 (*c* = 1.47 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 0.96 (d, $J_{3',2'} = J_{2'\text{-}Me,2'}$ = 6.7 Hz, 6 H, 3′-H_3, 2′-Me), 1.17 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.45 (s, 3 H, 2-Me), 1.99 [ddqq, $J_{2',1'\text{-}H(A)} = J_{2',1'\text{-}H(B)} = J_{2',3'} = J_{2',2'\text{-}Me}$ = 6.7 Hz, 1 H, 2′-H], 2.18 (br. d, $J_{3\text{-}OH,3}$ = 7.8 Hz, 1 H, 3-OH), 3.42 (s, 1 H, 2-OH), 3.81 (dq, $J_{3,3\text{-}OH} = J_{3,4}$ = 6.8 Hz, 1 H, 3-H) ppm, AB signal [δ_A = 3.96, δ_B = 4.02 ppm, A part additionally split by $J_{1'\text{-}H(A),2'}$ = 6.7 Hz, B part additionally split by $J_{1'\text{-}H(B),2'}$ = 6.7, J_{AB} = 10.6 Hz, 2 H, 1′-H_2].

Isobutyl (2*R*,3*R*)-2,3-Dihydroxy-2-methylbutanoate [(*R*,*R*)-7b]: Following the general procedure B, the title compound was prepared from isobutyl (*Z*)-2-methylbut-2-enoate (**3b**; 0.50 g, 3.2 mmol), $K_3[Fe(CN)_6]$ (3.2 g, 9.6 mmol, 3.0 equiv.), K_2CO_3 (1.3 g, 9.6 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.30 g, 3.2 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (50 mg, 64 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (12 mg, 32 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 2:1–1:2, 5–15) rendered the product as a colorless oil (0.51 g, 84%; 82% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 8.20 (*S*,*S*), 8.81 min (*R*,*R*). $[a]_D^{20}$ = +7.8 (*c* = 1.24 g/100 mL, $CHCl_3$); $[a]_{365}^{20}$ = +43.5 (*c* = 1.24 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3465, 2970, 2880, 1735, 1465, 1375, 1250, 1180, 1125, 1090, 1015, 985, 950, 920, 790, 750, 700 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 0.960 (d, $J_{3',2'}$ = 6.8 Hz, 3 H, 3′-H_3) superimposed by 0.961 (d, $J_{2'\text{-}Me,2'}$ = 6.8 Hz, 3 H, 2′-Me), 1.17 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.45 (s, 3 H, 2-Me), 1.99 [ddqq, $J_{2',1'\text{-}H(A)} = J_{2',1'\text{-}H(B)} = J_{2',3'} = J_{2',2'\text{-}Me}$ = 6.7 Hz, 1 H, 2′-H], 2.17 (s, 1 H, 3-OH), 3.42 (br. s, 1 H, 2-OH), 3.81 (q, $J_{3,3\text{-}OH}$ = 7.6, $J_{3,4}$ = 6.6 Hz, 1 H, 3-H) ppm, AB signal [δ_A = 3.96, δ_B = 4.02 ppm, A part additionally split by $J_{1'\text{-}H(A),2'}$ = 6.5 Hz, B part additionally split by $J_{1'\text{-}H(B),2'}$ = 6.6, J_{AB} = 10.5 Hz, 2 H, 1′-H_2]. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 17.80 (C-4), 19.05 (C-3′)*, 19.09 (2′-Me)*, 22.46 (2-Me), 27.79 (C-2′), 72.26 (C-3)**, 72.29 (C-1′)**, 77.19 (C-2), 175.70 (C-1) ppm. *,** Assignments interchangeable. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 17.80 (C-4) $\leftrightarrow$ δ = 1.17 (4-H_3); δ = 19.05 (C-3′) and 19.09 (2′-Me) $\leftrightarrow$ δ = 0.960 (3′-H_3) and 0.961 (2′-Me); δ = 22.46 (2-Me) $\leftrightarrow$ δ = 1.45 (2-Me); δ = 27.79 (C-2′) $\leftrightarrow$ δ = 1.99 (2′-H); δ = 72.26 (C-3) and 72.29 (C-1′) $\leftrightarrow$ δ = 3.81 (3-H) ppm, and AB signal (δ_A = 3.96, δ_B = 4.02 ppm, 1′-H_2). HRMS (pos. APCI, MeOH): calcd. for $C_9H_{19}O_4$ $[M + H]^+$ 191.12833; found 191.12830 (–0.2 ppm). $C_9H_{18}O_4$ (190.24): calcd. C 56.82, H 9.54; found C 56.43, H 9.40.

4-Methoxybenzyl *rel*-(2*S*,3*S*)-2,3-Dihydroxy-2-methylbutanoate (*anti*-7c):[48] Following the general procedure A, the title compound was prepared from **3c** (0.30 g, 1.4 mmol), citric acid (0.20 g, 1.0 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (1.3 mg, 3.4 µmol, 0.25 mol-%), and NMO (50% in H_2O, 0.38 g, 1.6 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 15–21) rendered the product as a colorless oil (0.31 g, 90%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.08 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.43 (s, 3 H, 2-Me), 2.10 (br. d, $J_{3\text{-}OH,3}$ = 8.2 Hz, 1 H, 3-OH), 3.36 (s, 1 H, 2-OH), 3.78 (dq, $J_{3\text{-}OH,3} = J_{3,4}$ = 6.7 Hz, 1 H, 3-H) superimposed by 3.82 (s, 3 H, *p*-OMe), AB signal (δ_A = 5.15, δ_B = 5.18 ppm, J_{AB} = 11.9 Hz, 2 H, 1′-H_2), 6.90 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.29 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm.

4-Methoxybenzyl (2*S*,3*S*)-2,3-Dihydroxy-2-methylbutanoate [(*S*,*S*)-7c]:[48] Following the general procedure B, the title compound was prepared from **3c** (0.30 g, 1.4 mmol), $K_3[Fe(CN)_6]$ (1.3 g, 4.1 mmol, 3.0 equiv.), K_2CO_3 (0.56 g, 4.1 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.13 g, 1.4 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (21 mg, 27 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (5.0 mg, 14 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 8–13) rendered the product as a colorless oil (0.27 g, 78%; 60% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 229 nm, t_R = 17.74 (*S*,*S*), 19.67 min (*R*,*R*). $[a]_D^{20}$ = –2.3 (*c* = 1.38 g/100 mL, $CHCl_3$); $[a]_{365}^{20}$ = –2.9 (*c* = 1.38 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.08 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.43 (s, 3 H, 2-Me), 2.10 (br. d, $J_{3\text{-}OH,3}$ = 7.6 Hz, 1 H, 3-OH), 3.35 (s, 1 H, 2-OH), 3.78 (dq, $J_{3\text{-}OH,3} = J_{3,4}$ = 6.9 Hz, 1 H, 3-H) superimposed by 3.82 (s, 3 H, *p*-OMe), AB signal (δ_A = 5.15, δ_B = 5.18 ppm, J_{AB} = 11.9 Hz, 2 H, 1′-H_2), 6.90 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.29 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm.

4-Methoxybenzyl (2*R*,3*R*)-2,3-Dihydroxy-2-methylbutanoate [(*R*,*R*)-7c]: Following the general procedure B, the title compound was prepared from **3c** (0.30 g, 1.4 mmol), $K_3[Fe(CN)_6]$ (1.3 g, 4.1 mmol, 3.0 equiv.), K_2CO_3 (0.56 g, 4.1 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.13 g, 1.4 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (21 mg, 27 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (5.0 mg, 14 µmol, 1.0 mol-

%). Purification by flash chromatography on silica gel[43] (2 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 9–16) rendered the product as a colorless oil (0.27 g, 78%; 80% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 229 nm, t_R = 18.05 (*S*,*S*), 19.58 min (*R*,*R*). $[\alpha]_D^{20}$ = +2.8 (*c* = 1.23 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +3.4 (*c* = 1.23 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3480, 2980, 2935, 2840, 2060, 1725, 1615, 1515, 1465, 1245, 1175, 1035, 820 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.08 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.43 (s, 3 H, 2-Me), 2.13 (br. d, $J_{3\text{-}OH,3}$ = 8.2 Hz, 1 H, 3-OH), 3.38 (s, 1 H, 2-OH), 3.78 (dq, $J_{3\text{-}OH,3}$ = $J_{3,4}$ = 7.1 Hz, 1 H, 3-H) superimposed by 3.81 (s, 3 H, *p*-OMe), AB signal (δ_A = 5.15, δ_B = 5.18 ppm, J_{AB} = 11.9 Hz, 2 H, 1′-H_2), 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.29 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 17.71 (C-4), 22.32 (2-Me), 55.38 (*p*-OMe), 67.72 (C-1′), 72.26 (C-3), 77.13 (C-2), 114.15 (2 C-*m*), 127.16 (C-*i*), 130.33 (2 C-*o*), 160.02 (C-*p*), 175.45 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 17.71 (C-4) ↔ δ = 1.08 (4-H_3); δ = 22.32 (2-Me) ↔ δ = 1.43 (2-Me); δ = 55.38 (*p*-OMe) ↔ δ = 3.81 (*p*-OMe); δ = 67.72 (C-1′) ↔ δ = AB signal (δ_A = 5.15, δ_B = 5.18 ppm, 1′-H_2); δ = 72.26 (C-3) ↔ δ = 3.78 (3-H); δ = 114.15 (2 C-*m*) ↔ δ = 6.89 (2 *m*-H); δ = 130.33 (2 C-*o*) ↔ δ = 7.29 (2 *o*-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_{13}H_{22}NO_5$ [M + NH_4]$^+$ 272.14980; found 272.14980 (±0.0 ppm). $C_{13}H_{18}O_5$ (254.28): calcd. C 61.41, H 7.14; found C 61.11, H 7.12.

***rel*-(2*S*,3*S*)-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylbutanamide (*anti*-7d):**[48] Following the general procedure A, the title compound was prepared from **3d** (0.60 g, 4.2 mmol), citric acid (0.60 g, 3.1 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (16 mg, 42 µmol, 1.0 mol-%), and NMO (50% in H_2O, 1.2 g, 5.0 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 21–33) rendered the product as a colorless oil (0.34 g, 86%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.03 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.53 (s, 3 H, 2-Me), 2.24 (d, $J_{3\text{-}OH,3}$ = 11.3 Hz, 1 H, 3-OH), 3.27 (s, 3 H, N-Me), 3.73 (s, 3 H, O-Me), 4.04 (dq, $J_{3,3\text{-}OH}$ = 11.1, $J_{3,4}$ = 6.3 Hz, 1 H, 3-H), 4.31 (s, 1 H, 2-OH) ppm.

(2*S*,3*S*)-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylbutanamide [(*S*,*S*)-7d]:[48] Following the general procedure B, the title compound was prepared from **3d** (0.20 g, 1.4 mmol), $K_3[Fe(CN)_6]$ (1.4 g, 4.2 mmol, 3.0 equiv.), K_2CO_3 (0.58 g, 4.2 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.22 g, 1.4 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (33 mg, 42 µmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (10 mg, 28 µmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 23–33) rendered the product as a colorless oil (0.17 g, 68%; 62% *ee*). Analytical HPLC: Chiralpak AD-H, *n*-heptane/EtOH = 95:5, 230 nm, t_R = 38.56 (*R*,*R*), 42.88 min (*S*,*S*). $[\alpha]_D^{20}$ = –14.6 (*c* = 1.11 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –37.2 (*c* = 1.11 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.03 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.53 (s, 3 H, 2-Me), 2.24 (d, $J_{3\text{-}OH,3}$ = 10.8 Hz, 1 H, 3-OH), 3.26 (s, 3 H, N-Me), 3.73 (s, 3 H, O-Me), 4.04 (dq, $J_{3,3\text{-}OH}$ = 10.5, $J_{3,4}$ = 6.2 Hz, 1 H, 3-H), 4.31 (s, 1 H, 2-OH) ppm.

(2*R*,3*R*)-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylbutanamide [(*R*,*R*)-7d]: Following the general procedure B, the title compound was prepared from **3d** (0.20 g, 1.4 mmol), $K_3[Fe(CN)_6]$ (1.4 g, 4.2 mmol, 3.0 equiv.), K_2CO_3 (0.58 g, 4.2 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.22 g, 1.4 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (33 mg, 42 µmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (10 mg, 28 µmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 23–31) rendered the product as a colorless oil (0.20 g, 80%; 71% *ee*). Analytical HPLC: Chiralpak AD-H, *n*-heptane/EtOH = 95:5, 230 nm, t_R = 38.37 (*R*,*R*), 43.18 min (*S*,*S*). $[\alpha]_D^{20}$ = +17.2 (*c* = 1.35 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +45.6 (*c* = 1.35 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3420, 2985, 2940, 2850, 1640, 1460, 1375, 1350, 11260, 1195, 1180, 1140, 1190, 1060, 995 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 0.99 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.49 (s, 3 H, 2-Me), 3.23 (s, 3 H, N-Me), 3.69 (s, 3 H, O-Me), 4.00 (q, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H) ppm. The OH groups were not visible in this spectrum. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 18.33 (C-4), 22.13 (2-Me), 33.71 (N-Me), 60.88 (O-Me), 70.04 (C-3), 77.23 (C-2), 175.72 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 18.33 (C-4) ↔ 0.99 (4-H_3); δ = 22.13 (2-Me) ↔ 1.49 (2-Me); δ = 33.71 (N-Me) ↔ 3.23 (N-Me); δ = 60.88 (O-Me) ↔ 3.69 (O-Me); δ = 70.04 (C-3) ↔ 4.00 (3-H) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_7H_{15}NO_4Na$ [M + Na]$^+$ 200.08988; found 200.08990 (+0.1 ppm).

***rel*-(2*S*,3*S*)-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)butan-1-one (*anti*-7e):**[48] Following the general procedure A, the title compound was prepared from **3e** (0.30 g, 2.0 mmol), citric acid (0.28 g, 1.5 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (7.2 mg, 20 µmol, 1.0 mol-%), and NMO (50% in H_2O, 0.55 g, 2.3 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–0:100, 13–20) rendered the product as a colorless oil (0.36 g, 99%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.09 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.50 (s, 3 H, 2-Me), 1.87 (br. m_c, 2 H, 3′-H_2)* superimposed by 1.96 (br. m_c, 2 H, 4′-H_2)*, 2.61 (d, $J_{3\text{-}OH,3}$ = 9.8 Hz, 1 H, 3-OH), 3.44–3.72 (m, 4 H, 2′-H_2, 5′-H_2), 3.93 (dq, $J_{3,3\text{-}OH}$ = 10.0, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H) 4.31 (s, 1 H, 2-OH) ppm. * The assignments of 3′-H and 4′-H are arbitrary.

(2*S*,3*S*)-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)butan-1-one [(*S*,*S*)-7e]:[48] Following the general procedure B, the title compound was prepared from **3e** (0.30 g, 2.0 mmol), $K_3[Fe(CN)_6]$ (1.9 g, 5.9 mmol, 3.0 equiv.), K_2CO_3 (0.81 g, 5.9 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.31 g, 2.0 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (46 mg, 59 µmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (14 mg, 39 µmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:3–0:100, 12–19) rendered the product as a colorless oil (0.21 g, 58%, 34% *ee*). Analytical HPLC: Chiralpak OD-H, *n*-heptane/EtOH = 100:1, 210 nm, 40 °C, t_R = 34.54 (*S*,*S*), 38.09 min (*R*,*R*). $[\alpha]_D^{20}$ = +11.9 (*c* = 0.73 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.10 (d, $J_{4,3}$ = 6.4 Hz, 3 H, 4-H_3), 1.51 (s, 3 H, 2-Me), 1.87 (br. m_c, 2 H, 3′-H_2)* superimposed by 1.96 (br. m_c, 2 H, 4′-H_2)*, 2.64 (d, $J_{3\text{-}OH,3}$ = 9.5 Hz, 1 H, 3-OH), 3.44–3.72 (m, 4 H, 2′-H_2, 5′-H_2), 3.93 (dq, $J_{3,3\text{-}OH}$ = 8.4, $J_{3,4}$ = 6.3 Hz, 1 H, 3-H), 4.32 (s, 1 H, 2-OH) ppm. * The assignments of 3′-H and 4′-H are arbitrary.

(2*R*,3*R*)-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)butan-1-one [(*R*,*R*)-7e]: Following the general procedure B, the title compound was prepared from **3e** (0.30 g, 2.0 mmol), $K_3[Fe(CN)_6]$ (1.9 g, 5.9 mmol, 3.0 equiv.), K_2CO_3 (0.81 g, 5.9 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.31 g, 2.0 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (46 mg, 59 µmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (14 mg, 39 µmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:3–0:100, 12–19) rendered the product as a colorless oil (0.25 g, 69%, 27% *ee*). Analytical HPLC: Chiralpak OD-H, *n*-heptane/EtOH = 100:1, 210 nm, 40 °C, t_R = 31.62 (*S*,*S*), 35.09 min (*R*,*R*). $[\alpha]_D^{20}$ = –15.7 (*c* = 1.25 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3380, 2975, 2880, 1595, 1455, 1365, 1295, 1185, 1150, 1095, 1015, 915, 745, 690 cm^{-1}. ^1H NMR (400.13 MHz,

$CDCl_3$): δ = 1.09 (d, $J_{4,3}$ = 6.3 Hz, 3 H, 4-H_3), 1.50 (s, 3 H, 2-Me), 1.86 (br. m_c, 2 H, 3′-H_2)* superimposed by 1.96 (br. m_c, 2 H, 4′-H_2)*, 2.66 (d, $J_{3\text{-OH},3}$ = 8.0 Hz, 1 H, 3-OH), 3.47–3.71 (m, 4 H, 2′-H_2, 5′-H_2), 3.93 (br. m_c, possibly interpretable as dq, $J_{3,3\text{-OH}}$ = $J_{3,4}$ = 6.5 Hz, 1 H, 3-H), 4.30 (s, 1 H, 2-OH) ppm. * The assignments of 3′-H and 4′-H are arbitrary. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 18.02 (C-4), 21.39 (2-Me), 23.26 (C-3′)*, 26.95 (C-4′)*, 47.51 (C-2′)**, 48.09 (C-5′)**, 70.89 (C-3), 76.53 (C-2), 173.35 (C-1) ppm. * The assignments of C-3′ and C-4′ are arbitrary, but consistent with the ^{1}H NMR spectrum. ** The assignments of C-2′ and C-5′ are arbitrary. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 18.02 (C-4) $\leftrightarrow$ δ = 1.09 (4-H_3); δ = 21.39 (2-Me) $\leftrightarrow$ δ = 1.50 (2-Me); δ = 23.26 (C-3′) $\leftrightarrow$ δ = 1.86 (3′-H_2); δ = 26.95 (C-4′) $\leftrightarrow$ δ = 1.96 (4′-H_2); δ = 47.51 (C-2′) and 48.09 (C-5′) $\leftrightarrow$ δ = 3.47–3.71 (2′-H_2, 5′-H_2); δ = 70.89 (C-3) $\leftrightarrow$ δ = 3.93 (3-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_9H_{18}NO_3Na$ [M + H]$^+$ 188.12812; found 188.12817 (+0.3 ppm).

Methyl *rac*-2,3-Dihydroxy-2-methylpropanoate (*rac*-23a):[48] Following the general procedure A, the title compound was prepared from methyl methacrylate (**1a**; 0.53 mL, 0.50 g, 5.0 mmol), citric acid (0.72 g, 3.7 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (4.6 mg, 13 µmol, 0.25 mol-%), and NMO (50% in H_2O, 1.4 g, 6.0 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 23–29) rendered the product as a colorless oil (0.57 g, 85%). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, 2-Me), 2.20 (br. s, 1 H, 3-OH), 3.50 (s, 1 H, 2-OH), 3.58 (d, J_{gem} = 11.3 Hz, 1 H, 3-H), 3.80 (br. d, J_{gem} = 11.6 Hz, 1 H, 3-H) superimposed by 3.82 (s, 3 H, OMe) ppm.

Surmised Preparation of Methyl (*R*)-2,3-Dihydroxy-2-methylpropanoate [(*R*)-23a]:[48] Following the general procedure B, the title compound was prepared from methyl methacrylate (**1a**; 0.30 g, 3.0 mmol), $K_3[Fe(CN)_6]$ (3.0 g, 9.0 mmol, 3.0 equiv.), K_2CO_3 (1.2 g, 9.0 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.29 g, 3.0 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (47 mg, 60 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (11 mg, 30 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 25–33) rendered the product as a colorless oil (0.34 g, 85%; although AD conditions were used this compound turned out to be racemic). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 12.55 (1st enantiomer), 13.59 min (2nd enantiomer). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, 2-Me), 2.17 [br. dd, $J_{3\text{-OH},3\text{-H}(2)}$ = 8.8, $J_{3\text{-OH},3\text{-H}(1)}$ = 4.3 Hz, 1 H, 3-OH], 3.49 (s, 1 H, 2-OH), 3.58 [dd, J_{gem} = 11.3, $J_{3\text{-H}(1),3\text{-OH}}$ = 4.3 Hz, 1 H, 3-H], 3.80 [dd, J_{gem} = 11.2, $J_{3\text{-H}(2),3\text{-OH}}$ = 9.2 Hz, 1 H, 3-H] superimposed by 3.82 (s, 3 H, OMe) ppm.

Surmised Preparation of Methyl (*S*)-2,3-Dihydroxy-2-methylpropanoate [(*S*)-23a]: Following the general procedure B, the title compound was prepared from methyl methacrylate (**1a**; 0.30 g, 3.0 mmol), $K_3[Fe(CN)_6]$ (3.0 g, 9.0 mmol, 3.0 equiv.), K_2CO_3 (1.2 g, 9.0 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.29 g, 3.0 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (47 mg, 60 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (11 mg, 30 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 26–33) rendered the product as a colorless oil (0.36 g, 90%; although AD conditions were used this compound turned out to be racemic). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/*i*PrOH = 95:5, 210 nm, t_R = 12.54 (1st enantiomer), 13.56 min (2nd enantiomer). IR (film): $\tilde{\nu}$ = 3445, 2985, 2955, 2880, 1735, 1455, 1380, 1280, 1230, 1135, 1055, 975, 940, 890, 815, 770, 705 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, 2-Me), 2.26 (br. s, 1 H, 3-OH), 3.53 (s, 1 H, 2-OH), 3.58 (dd, J_{gem} = 11.4 Hz, 1 H, 3-H), 3.80 [m_c, possibly interpretable as dd, J_{gem} = 11.0, $J_{3\text{-H}(2),3\text{-OH}}$ = 7.1 Hz, 1 H, 3-H] superimposed by 3.82 (s, 3 H, OMe) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 22.06 (2-Me), 53.19 (OMe), 68.45 (C-3), 75.64 (C-2), 176.20 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 22.06 (2-Me) $\leftrightarrow$ δ = 1.35 (2-Me); δ = 53.19 (OMe) $\leftrightarrow$ δ = 3.82 (OMe); δ = 68.45 (C-3) $\leftrightarrow$ δ = 3.58 (3-H) and 3.80 (3-H) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_5H_{10}O_4Na$ [M + Na]$^+$ 157.04770; found 157.04768 (–0.1 ppm).

Isobutyl *rac*-2,3-Dihydroxy-2-methylpropanoate (*rac*-23b):[48] Following the general procedure A, the title compound was prepared from isobutyl methacrylate (**1b**; 0.53 mL, 0.50 g, 3.5 mmol), citric acid (0.51 g, 2.6 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (3.2 mg, 8.8 µmol, 0.25 mol-%), and NMO (50% in H_2O, 0.99 g, 4.2 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 11–24) rendered the product as a colorless oil (0.57 g, 92%). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 0.95 (d, $J_{3',2'} = J_{2'\text{-Me},2'}$ = 6.7 Hz, 6 H, 3′-H_3, 2′-Me), 1.36 (s, 3 H, 2-Me), 1.99 (tqq, $J_{2',1'} = J_{2',3'} = J_{2',2'\text{-Me}}$ = 6.7 Hz, 1 H, 2′-H), 2.17 [dd, $J_{3\text{-OH},3\text{-H}(2)}$ = 9.2, $J_{3\text{-OH},3\text{-H}(1)}$ = 4.4 Hz, 1 H, 3-OH], 3.53 (s, 1 H, 2-OH), 3.58 [dd, J_{gem} = 11.2, $J_{3\text{-H}(1),3\text{-OH}}$ = 4.2 Hz, 1 H, 3-H], 3.80 [dd, J_{gem} = 11.1, $J_{3\text{-H}(2),3\text{-OH}}$ = 9.2 Hz, 1 H, 3-H], 4.00 (d, $J_{1',2'}$ = 6.7 Hz, 1′-H_2) ppm.

Isobutyl (*R*)-2,3-Dihydroxy-2-methylpropanoate [(*R*)-23b]:[48] Following the general procedure B, the title compound was prepared from isobutyl methacrylate (**1b**; 0.53 mL, 0.50 g, 3.5 mmol), $K_3[Fe(CN)_6]$ (3.5 g, 11 mmol, 3.0 equiv.), K_2CO_3 (1.5 g, 11 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.33 g, 3.5 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (55 mg, 70 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (13 mg, 35 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 8–23) rendered the product as a colorless oil (0.56 g, 92%; 10% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/EtOH = 90:10, 210 nm, t_R = 9.96 (*R*), 12.73 min (*S*). $[\alpha]_D^{20}$ = +1.3 (*c* = 1.16 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +3.9 (*c* = 1.16 g/100 mL, $CHCl_3$). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 0.95 (d, $J_{3',2'} = J_{2'\text{-Me},2'}$ = 6.7 Hz, 6 H, 3′-H_3, 2′-Me), 1.36 (s, 3 H, 2-Me), 1.99 (tqq, $J_{2',1'} = J_{2',3'} = J_{2',2'\text{-Me}}$ = 6.7 Hz, 1 H, 2′-H), 2.16 [br. dd, $J_{3\text{-OH},3\text{-H}(2)}$ = 7.3, $J_{3\text{-OH},3\text{-H}(1)}$ = 3.1 Hz, 1 H, 3-OH], 3.52 (s, 1 H, 2-OH), 3.58 (br. d, J_{gem} = 10.7 Hz, 1 H, 3-H), 3.79 [dd, J_{gem} = 10.6, $J_{3\text{-H}(2),3\text{-OH}}$ = 8.7 Hz, 1 H, 3-H], 4.00 (d, $J_{1',2'}$ = 6.6 Hz, 1′-H_2) ppm.

Isobutyl (*S*)-2,3-Dihydroxy-2-methylpropanoate [(*S*)-23b]: Following the general procedure B, the title compound was prepared from isobutyl methacrylate (**1b**; 0.53 mL, 0.50 g, 3.5 mmol), $K_3[Fe(CN)_6]$ (3.5 g, 11 mmol, 3.0 equiv.), K_2CO_3 (1.5 g, 11 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.33 g, 3.5 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (55 mg, 70 µmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (13 mg, 35 µmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 17–27) rendered the product as a colorless oil (0.58 g, 94%; 16% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/EtOH = 90:10, 210 nm, t_R = 10.03 (*R*), 12.69 min (*S*). $[\alpha]_D^{20}$ = –2.3 (*c* = 1.27 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –6.6 (*c* = 1.27 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3455, 2965, 2880, 1735, 1465, 1380, 1280, 1220, 1135, 1055, 985, 940 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 0.950 (d, $J_{3',2'}$ = 6.8 Hz, 3 H, 3′-H_3) superimposed by 0.952 (d, $J_{2'\text{-Me},2'}$ = 6.7 Hz, 3 H, 2′-Me), 1.36 (s, 3 H, 2-Me), 1.99 (tqq, $J_{2',1'} = J_{2',3'} = J_{2',2'\text{-Me}}$ = 6.7 Hz, 1 H, 2′-H), 2.21 [dd, $J_{3\text{-OH},3\text{-H}(2)}$ = 9.3,

$J_{3\text{-OH},3\text{-H}(1)}$ = 4.4 Hz, 1 H, 3-OH], 3.55 [d, $^4J_{2\text{-OH},3\text{-H}(2)}$ = 0.6 Hz, 1 H, 2-OH]*, 3.59 [dd, J_{gem} = 11.2, $J_{3\text{-H}(1),3\text{-OH}}$ = 4.3 Hz, 1 H, 3-H], 3.80 [dd, J_{gem} = 11.1, $J_{3\text{-H}(2),3\text{-OH}}$ = 9.0 Hz, 1 H, 3-H], 4.01 [m_c, possibly interpretable as AB signal, δ_A = 4.00, δ_B = 4.01 ppm, A part additionally split by $J_{1'\text{-H}(A),2'}$ = 6.7 Hz, B part additionally split by $J_{1'\text{-H}(B),2'}$ = 6.7, J_{AB} = 10.4 Hz, 2 H, 1′-H_2]. * No other signal shows a coupling of 0.6 Hz, however, the 3-H signal at δ = 3.80 ppm appears to be a little "broader" than all the other signals. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 18.96 (C-3′)*, 18.99 (2′-Me)*, 22.11 (2-Me), 27.84 (C-2′), 68.48 (C-3), 72.25 (C-1′), 75.55 (C-2), 175.81(C-1) ppm. * Assignments interchangeable. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 18.96 (C-3′) and 18.99 (2′-Me) $\leftrightarrow$ δ = 0.950 (3′-H_3) and 0.952 (2′-Me); δ = 22.11 (2-Me) $\leftrightarrow$ δ = 1.36 (2-Me); δ = 27.84 (C-2′) $\leftrightarrow$ δ = 1.99 (2′-H); δ = 68.48 (C-3) $\leftrightarrow$ δ = 3.59 (3-H) and 3.80 (3-H); δ = 72.25 (C-1′) $\leftrightarrow$ δ = 4.01 (1′-H_2) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_8H_{16}O_4Na$ $[M + Na]^+$ calcd. 199.09460; found 199.09463 (+0.2 ppm).

4-Methoxybenzyl *rac*-2,3-Dihydroxy-2-methylpropanoate (*rac*-23c):[48] Following the general procedure A, the title compound was prepared from **1b** (0.53 mL, 0.50 g, 2.4 mmol), citric acid (0.35 g, 1.8 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (2.2 mg, 6.1 μmol, 0.25 mol-%), and NMO (50% in H_2O, 0.68 g, 2.9 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 10–16) rendered the product as a colorless oil (0.55 g, 96%). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, 2-Me), 2.12 (br. s, 1 H, 3-OH), 3.48 (s, 1 H, 2-OH), 3.56 (d, J_{gem} = 11.3 Hz, 1 H, 3-H), 3.80 (d, J_{gem} = 9.5 Hz, 1 H, 3-H) superimposed by 3.81 (s, 3 H, *p*-OMe), 5.18 (m_c, 2 H, 1′-H_2), 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.29 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm.

4-Methoxybenzyl (*R*)-2,3-Dihydroxy-2-methylpropanoate [(*R*)-23c]:[48] Following the general procedure B, the title compound was prepared from **1b** (0.53 mL, 0.50 g, 2.4 mmol), $K_3[Fe(CN)_6]$ (2.4 g, 7.3 mmol, 3.0 equiv.), K_2CO_3 (1.0 g, 7.3 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.23 g, 2.4 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (38 mg, 49 μmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (8.9 mg, 24 μmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 13-21) rendered the product as a colorless oil (0.52 g, 90%; 61% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/EtOH = 90:10, 229 nm, t_R = 18.07 (*R*), 21.14 min (*S*). $[\alpha]_D^{20}$ = –0.3 (*c* = 0.50 g/100 mL, $CHCl_3$). $[\alpha]_{365}^{20}$ = –2.7 (*c* = 0.50 g/100 mL, $CHCl_3$). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, 2-Me), 2.10 [dd, $J_{3\text{-OH},3\text{-H}(2)}$ = 9.1, $J_{3\text{-OH},3\text{-H}(1)}$ = 4.6 Hz, 1 H, 3-OH], 3.47 (s, 1 H, 2-OH), 3.56 [dd, J_{gem} = 11.3, $J_{3\text{-H}(1),3\text{-OH}}$ = 4.5 Hz, 1 H, 3-H], 3.80 [dd, J_{gem} = 11.3, $J_{3\text{-H}(2),3\text{-OH}}$ = 8.8 Hz, 1 H, 3-H] superimposed by 3.81 (s, 3 H, *p*-OMe), 5.18 (m_c, 2 H, 1′-H_2), 6.89 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.29 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm.

4-Methoxybenzyl (*S*)-2,3-Dihydroxy-2-methylpropanoate [(*S*)-23c]: Following the general procedure B, the title compound was prepared from **1b** (0.53 mL, 0.50 g, 2.4 mmol), $K_3[Fe(CN)_6]$ (2.4 g, 7.3 mmol, 3.0 equiv.), K_2CO_3 (1.0 g, 7.3 mmol, 3.0 equiv.), $MeSO_2NH_2$ (0.23 g, 2.4 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (38 mg, 49 μmol, 2.0 mol-%), and $K_2OsO_2(OH)_4$ (8.9 mg, 24 μmol, 1.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 3:1–1:1, 10–17) rendered the product as a colorless oil (0.52 g, 90%; 72% *ee*). Analytical HPLC: Kromasil 3-AmyCoat, *n*-heptane/EtOH = 90:10, 210 nm, t_R = 18.18 (*R*), 20.99 min (*S*). $[\alpha]_D^{20}$ = +0.3 (*c* = 0.56 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +2.8 (*c* = 0.56 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3450, 2940, 2840, 1735, 1615, 1515, 1460, 1380, 1250, 1175, 1135, 1040, 920, 825, 735 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, 2-Me), 2.21 (br. s, 1 H, 3-OH), 3.51 (br. s, 1 H, 2-OH) superimposed by 3.57 (d, J_{gem} = 11.3 Hz, 1 H, 3-H), 3.80 (d, J_{gem} = 11.3 Hz, 1 H, 3-H) superimposed by 3.81 (s, 3 H, *p*-OMe), 5.18 (m_c, 2 H, 1′-H_2), 6.90 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.29 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *m*-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 22.00 (2-Me), 55.38 (*p*-OMe), 67.81 (C-1′), 68.43 (C-3), 75.61 (C-2), 114.14 (2 C-*m*), 127.34 (C-2′), 130.06 (2 C-*o*), 159.95 (C-*p*), 175.65 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 22.00 (2-Me) $\leftrightarrow$ δ = 1.34 (2-Me); δ = 55.38 (*p*-OMe) $\leftrightarrow$ δ = 3.81 (*p*-OMe); δ = 67.81 (C-1′) $\leftrightarrow$ δ = 5.18 (1′-H_2); δ = 68.43 (C-3) $\leftrightarrow$ δ = 3.57 (3-H) and 3.80 (3-H); δ = 114.14 (2 C-*m*) $\leftrightarrow$ δ = 6.90 (2 *m*-H); δ = 130.06 (2 C-*o*) $\leftrightarrow$ δ = 7.29 (2 *o*-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_{12}H_{20}NO_5$ $[M + NH_4]^+$ 258.13415; found 258.13430 (+0.6 ppm).

***rac*-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylpropanamide (*rac*-23d):**[48] Following the general procedure A, the title compound was prepared from **1d** (0.50 g, 3.9 mmol), citric acid (0.56 g, 2.9 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (3.6 mg, 9.7 μmol, 0.25 mol-%), and NMO (50% in H_2O, 1.1 g, 4.6 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 19–36) rendered the product as a colorless oil (0.52 g, 82%). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, 2-Me), 2.39 [br. dd, $J_{3\text{-OH},3\text{-H(B)}}$ = 8.4, $J_{3\text{-OH},3\text{-H(A)}}$ = 4.1 Hz, 1 H, 3-OH], 3.30 (s, 3 H, N-Me), 3.62 (br. d, J_{gem} = 11.7 Hz, 1 H, 3-H), 3.75 (s, 3 H, O-Me), 3.91 [dd, J_{gem} = 10.9, $J_{3\text{-H}(2),3\text{-OH}}$ = 8.9 Hz, 1 H, 3-H], 4.52 (s, 1 H, 2-OH) ppm.

(*R*)-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylpropanamide [(*R*)-23d]:[48] Following the general procedure B, the title compound was prepared from **1d** (0.30 g, 2.3 mmol), $K_3[Fe(CN)_6]$ (2.3 g, 7.0 mmol, 3.0 equiv.), K_2CO_3 (0.96 g, 7.0 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.37 g, 2.3 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (54 mg, 70 μmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (17 mg, 47 μmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 13–30) rendered the product as a colorless oil (0.32 g, 83%; 95% *ee*). Analytical HPLC: Chiralpak AD-3, *n*-heptane/*i*PrOH = 95:5, 230 nm, t_R = 19.86 (*S*), 22.67 min (*R*). $[\alpha]_D^{20}$ = +13.2 (*c* = 1.01 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +40.9 (*c* = 1.01 g/100 mL, $CHCl_3$). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 1.39 (s, 3 H, 2-Me), 2.34 [br. dd, $J_{3\text{-OH},3\text{-H(B)}}$ = 9.1, $J_{3\text{-OH},3\text{-H(A)}}$ = 4.4 Hz, 1 H, 3-OH], 3.31 (s, 3 H, N-Me), 3.63 [br. dd, J_{gem} = 11.4, $J_{3\text{-H}(1),3\text{-OH}}$ = 3.5 Hz, 1 H, 3-H], 3.76 (s, 3 H, O-Me), 3.92 [dd, J_{gem} = 11.1, $J_{3\text{-H}(2),3\text{-OH}}$ = 9.5 Hz, 1 H, 3-H], 4.52 (s, 1 H, 2-OH) ppm.

(*S*)-2,3-Dihydroxy-*N*-methoxy-*N*,2-dimethylpropanamide [(*S*)-23d]: Following the general procedure B, the title compound was prepared from **1d** (0.30 g, 2.3 mmol), $K_3[Fe(CN)_6]$ (2.3 g, 7.0 mmol, 3.0 equiv.), K_2CO_3 (0.96 g, 7.0 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.37 g, 2.3 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (54 mg, 70 μmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (17 mg, 47 μmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 14–25) rendered the product as a colorless oil (0.35 g, 93%; 98% *ee*). Analytical HPLC: Chiralpak AD-3, *n*-heptane/*i*PrOH = 95:5, 230 nm, t_R = 17.88 (*S*), 24.38 min (*R*). $[\alpha]_D^{20}$ = –13.1 (*c* = 1.17 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –40.1 (*c* =

1.17 g/100 mL, $CHCl_3$). IR (film): ṽ = 3430, 2980, 2940, 2880, 1640, 1460, 1365, 1180, 1110, 1055, 990, 935, 865, 735, 690 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, 2-Me), 2.39 [br. dd, $J_{3\text{-OH},3\text{-H(B)}}$ = 9.5, $J_{3\text{-OH},3\text{-H(A)}}$ = 4.7 Hz, 1 H, 3-OH], 3.30 (s, 3 H, N-Me), 3.62 [br. dd, J_{gem} = 11.4, $J_{3\text{-H(1)},3\text{-OH}}$ = 4.2 Hz, 1 H, 3-H], 3.75 (s, 3 H, O-Me), 3.92 [dd, J_{gem} = 11.1, $J_{3\text{-H(2)},3\text{-OH}}$ = 9.6 Hz, 1 H, 3-H], 4.53 (s, 1 H, 2-OH) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 21.57 (2-Me), 33.70 (C-*N*-Me), 61.15 (O-Me), 67.78 (C-3), 75.99 (C-2), 174.60 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 21.57 (2-Me) ↔ δ = 1.38 (2-Me); δ = 33.70 (C-*N*-Me) ↔ δ = 3.30 (N-Me); δ = 61.15 (O-Me) ↔ δ = 3.75 (O-Me); δ = 67.78 (C-3) ↔ δ = 3.62 (3-H) and 3.92 (3-H). HRMS: (pos. ESI, MeOH): calcd. for $C_6H_{13}NO_4Na$ $[M + Na]^+$ calcd. 186.07420; found 186.07423 (+0.1 ppm).

***rac*-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)propan-1-one (*rac*-23e):**[48] Following the general procedure A, the title compound was prepared from **1e** (0.50 g, 3.6 mmol), citric acid (0.52 g, 2.7 mmol, 0.75 equiv.), $K_2OsO_2(OH)_4$ (13 mg, 36 µmol, 1.0 mol-%), and NMO (50% in H_2O, 1.0 g, 4.3 mmol, 1.2 equiv.). Purification by flash chromatography on silica gel[43] (2.5 × 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 21–30) rendered the product as a colorless oil (0.61 g, 98%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, 2-Me), 1.86 (br. m_c, 2 H, 3′-H_2)*, 1.95 (br. m_c, 2 H, 4′-H_2)*, 2.64 (br. s, 1 H, 3-OH), 3.48 (br. d, J_{gem} = 11.4 Hz, 1 H, 3-H) superimposed by 3.44–3.66 (m, 3 H, 2′-H_2, 5′-H)**, 3.71–3.84 (m, 1 H, 5′-H)**, 3.99 (br. d, J_{gem} = 11.3 Hz, 1 H, 3-H), 4.17 (s, 1 H, 2-OH) ppm. *,** The assignments of 3′-H and 4′-H, and of 2′-H and 5′-H are arbitrary.

(*R*)-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)propan-1-one [(*R*)-23e]:[48] Following the general procedure B, the title compound was prepared from **1e** (0.30 g, 2.2 mmol), $K_3[Fe(CN)_6]$ (2.1 g, 6.5 mmol, 3.0 equiv.), K_2CO_3 (0.89 g, 6.5 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.34 g, 2.2 mmol, 1.0 equiv.), $(DHQ)_2PHAL$ (51 mg, 65 µmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (16 mg, 43 µmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 22–29) rendered the product as a colorless oil (0.22 g, 60%; 74% *ee*). Analytical HPLC: Chiralpak OJ-H, *n*-heptane/*i*PrOH = 98:2, 210 nm, t_R = 20.31 (*R*), 22.95 min (*S*). $[\alpha]_D^{20}$ = +11.1 (*c* = 1.01 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +35.4 (*c* = 1.01 g/100 mL, $CHCl_3$). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, 2-Me), 1.85 (br. m_c, 2 H, 3′-H_2)*, 1.95 (br. m_c, 2 H, 4′-H_2)*, 3.48 (d, J_{gem} = 11.4 Hz, 1 H, 3-H) superimposed by 3.48–3.66 (m, 3 H, 2′-H_2, 5′-H)**, 3.72–3.84 (m, 1 H, 5′-H)**, 3.99 (d, J_{gem} = 11.4 Hz, 1 H, 3-H) ppm. *,** The assignments of 3′-H and 4′-H, and of 2′-H and 5′-H are arbitrary. The OH groups are not visible in this spectrum.

(*S*)-2,3-Dihydroxy-2-methyl-1-(pyrrolidin-1-yl)propan-1-one [(*S*)-23e]: Following the general procedure B, the title compound was prepared from **1e** (0.30 g, 2.2 mmol), $K_3[Fe(CN)_6]$ (2.1 g, 6.5 mmol, 3.0 equiv.), K_2CO_3 (0.89 g, 6.5 mmol, 3.0 equiv.), $PhSO_2NH_2$ (0.34 g, 2.2 mmol, 1.0 equiv.), $(DHQD)_2PHAL$ (51 mg, 65 µmol, 3.0 mol-%), and $K_2OsO_2(OH)_4$ (16 mg, 43 µmol, 2.0 mol-%). Purification by flash chromatography on silica gel[43] (2 15 cm, 20 mL, *c*-C_6H_{12}/EtOAc = 1:1–1:3, 25–36) rendered the product as a colorless oil (0.33 g, 88%; 83% *ee*). Analytical HPLC: Chiralpak OJ-H, *n*-heptane/*i*PrOH = 98:2, 210 nm, t_R = 20.25 (*R*), 22.25 min (*S*). $[\alpha]_D^{20}$ = –13.1 (*c* = 1.17 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –40.1 (*c* = 1.17 g/100 mL, $CHCl_3$). IR (film): ṽ = 3385, 2970, 2880, 2240, 1600, 1445, 1370, 1340, 1250, 1235, 1180, 1145, 1055, 975, 925, 865, 730, 685 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, 2-Me), 1.84 (br. m_c, 2 H, 3′-H_2)*, 1.95 (br. m_c, 2 H, 4′-H_2)*, 2.82 (br. s, 1 H, 3-OH), 3.47 (d, J_{gem} = 11.4 Hz, 1 H, 3-H) superimposed by 3.53 (m_c, 2 H, 2′-H_2)** superimposed by 3.61 (m_c, 1 H, 5′-H)**, 3.78 (m_c, 1 H, 5′-H)**, 3.98 (d, J_{gem} = 11.5 Hz, 1 H, 3-H), 4.21 (s, 1 H, 2-OH) ppm. *,** The assignments of 3′-H and 4′-H, and of 2′-H and 5′-H are arbitrary. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 21.07 (2-Me), 23.29 (C-3′)*, 26.95 (C-4′)*, 47.55 (C-5′)**, 47.90 (C-2′)**, 68.49 (C-3), 75.73 (C-2), 172.84 (C-1) ppm. *,** The assignments of 3′-H and 4′-H, and of 2′-H and 5′-H are arbitrary, but consistent with the assignments in the ^1H NMR spectrum. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 21.07 (2-Me) ↔ δ = 1.35 (2-Me); δ = 23.29 (C-3′) ↔ δ = 1.84 (3′-H_2); δ = 26.95 (C-4′) ↔ δ = 1.95 (4′-H_2); δ = 47.55 (C-5′) ↔ δ = 3.61 (5′-H) and 3.78 (5′-H); δ = 47.90 (C-2′) ↔ δ = 3.53 (2′-H_2); δ = 68.49 (C-3) ↔ δ = 3.47 (3-H) and 3.98 (3-H) ppm. HRMS: (pos. ESI, MeOH): calcd. for $C_8H_{15}NO_3Na$ $[M + Na]^+$ 196.09496; found 196.09500 (+0.2 ppm).

(*Z*)-2-Methylbut-2-enoic Acid (28): Isobutyl (*Z*)-2-methylbut-2-enoate (**3b**; 10.0 mL, 8.90 g, 57.0 mmol) and $LiOH·H_2O$ (2.63 g, 62.7 mmol, 1.1 equiv.) were dissolved in MeOH/H_2O (1:1, 36 mL). The mixture was heated at reflux for 4 h. The reaction mixture was poured onto ice (20 g) and the resulting mixture was extracted with TBME (5 × 50 mL). The combined organic phases were dried with $MgSO_4$ and the solvent removed under reduced pressure. This furnished the product (5.03 g, 50.2 mmol, 88%) as an *E*/*Z* = 10:90 mixture of stereoisomers. Recrystallization from EtOH (5 mL) furnished the product as colorless crystals (2.50 g, 44%). IR (film): ṽ = 2930, 2590, 1810, 1673, 1651, 1635, 1460, 1415, 1380, 1350, 1285, 1265, 1185, 1165, 1085, 1045, 945 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.91 (dq, $^4J_{2\text{-Me},3}$ = $^5J_{2\text{-Me},4}$ = 1.5 Hz, 3 H, 2-Me), 2.04 (dq, $J_{4,3}$ = 7.3, $^5J_{4,2\text{-Me}}$ = 1.5 Hz, 3 H, 4-H_3), 6.23 (qq, $J_{3,4}$ = 7.3, $^4J_{3,2\text{-Me}}$ = 1.5 Hz, 1 H, 3-H), 12.36 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 16.08 (C-4), 20.38 (2-Me), 127.36 (C-2), 141.18 (C-3), 174.10 (C-1) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 16.08 (C-4) ↔ δ = 2.04 (4-H_3); δ = 20.38 (2-Me) ↔ δ = 1.91 (2-Me); δ = 141.18 (C-3) ↔ δ = 6.23 (3-H) ppm. HRMS: (neg. ESI, MeOH): calcd. for $C_5H_7O_2$ $[M - H]^-$ calcd. 99.04460; found 99.04450 (–1.1 ppm).

4-Methoxybenzyl *rac*-2-Hydroxy-2-methyl-3-oxobutanoate (*rac*-29c): Ester *syn*-**7c** (117 mg, 460 µmol) was dissolved in CH_2Cl_2 (3.7 mL) and the solution was cooled to 0 °C. Saturated aqueous $NaHCO_3$ solution (3.7 mL), KBr (54.8 mg, 460 µmol, 1.0 equiv.), and 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO, 35.9 mg, 230 µmol, 0.5 equiv.) were added successively. Bleach (total content of Cl ca. 10%, ca. 1.6 M, 158 µL, 253 µmol, 0.55 equiv.) was added[49] through a graduated pipette and the mixture was stirred vigorously at 0 °C for 2 min. This was repeated twice and the mixture was stirred vigorously at 0 °C for another 13 min. The reaction was quenched by the addition of a saturated aqueous Na_2SO_3 solution (1 mL). The phases were separated and the aqueous phase was washed with CH_2Cl_2 (2 × 4 mL). The combined organic phases were dried with $MgSO_4$ and the solvent evaporated under reduced pressure. Purification by flash chromatography on silica gel[43] (1.5 × 15 cm, 15 mL, *c*-C_6H_{12}/EtOAc = 3:1, 3–6) rendered the product as a colorless oil (92.1 mg, 79%). ^1H NMR (300.06 MHz, $CDCl_3$): δ = 1.58 (s, 3 H, 2-Me), 2.17 (s, 3 H, 4-H_3), 3.81 (s, 3 H, *p*-OMe), 4.15 (s, 1 H, 2-OH), AB signal (δ_A = 5.14, δ_B = 5.16 ppm,

J_{AB} = 11.9 Hz, 2 H, 1′-H_2), 6.88 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.27 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm.

4-Methoxybenzyl (*S*)-2-Hydroxy-2-methyl-3-oxobutanoate [(*S*)-29c]: Ester (2*S*,3*R*)-**7c** (121 mg, 476 μmol; 95% *ee*) was dissolved in CH_2Cl_2 (3.8 mL) and the solution was cooled to 0 °C. A saturated aqueous $NaHCO_3$ solution (3.8 mL), KBr (56.6 mg, 476 μmol, 1.0 equiv.), and TEMPO (37.2 mg, 238 μmol, 0.5 equiv.) were added successively. Bleach (total content of Cl ca. 10%, ca. 1.6 M, 164 μL, 262 μmol, 0.55 equiv.) was added[49] through a graduated pipette and the mixture was stirred vigorously at 0 °C for 2 min. This was repeated twice and the mixture was stirred vigorously at 0 °C for another 13 min. The reaction was quenched by the addition of a saturated aqueous Na_2SO_3 solution (1 mL). The phases were separated and the aqueous phase washed with CH_2Cl_2 (2 4 mL). The combined organic phases were dried with $MgSO_4$ and the solvent evaporated under reduced pressure. Purification by flash chromatography on silica gel[43] (1.5 × 15 cm, 15 mL, *c*-C_6H_{12}/EtOAc = 3:1, 3–5) rendered the product as a colorless oil (92.0 mg, 76%, 93% *ee*). Analytical HPLC: Chiralpak AD-3, *n*-heptane/*i*PrOH = 100:1, 230 nm, t_R = 40.34 (*R*), 42.18 min (*S*). $[\alpha]_D^{20}$ = –41.2 (*c* = 0.95 g/100 mL, $CHCl_3$); $[\alpha]_{546}^{20}$ = –50.4 (*c* = 0.73 g/100 mL, $CHCl_3$); $[\alpha]_{436}^{20}$ = –101.8 (*c* = 0.73 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = –210.6 (*c* = 0.73 g/100 mL, $CHCl_3$). ^{1}H NMR (300.06 MHz, $CDCl_3$): δ = 1.58 (s, 3 H, 2-Me), 2.17 (s, 3 H, 4-H_3), 3.81 (s, 3 H, *p*-OMe), 4.14 (s, 1 H, 2-OH), AB signal (δ_A = 5.14, δ_B = 5.16 ppm, J_{AB} = 11.9 Hz, 2 H, 1′-H_2), 6.88 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.27 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm.

4-Methoxybenzyl (*R*)-2-Hydroxy-2-methyl-3-oxobutanoate [(*R*)-29c]: Ester (*R*,*R*)-**7c** (111 mg, 437 μmol; 80% *ee*) was dissolved in CH_2Cl_2 (3.5 mL) and the solution was cooled to 0 °C. A saturated aqueous $NaHCO_3$ solution (3.5 mL), KBr (52.0 mg, 437 μmol, 1.0 equiv.), and TEMPO (34.1 mg, 218 μmol, 0.5 equiv.) were added successively. Bleach (total content of Cl ca. 10%, ca. 1.6 M , 150 μL, 240 μmol, 0.55 equiv.) was added[49] through a graduated pipette and the mixture was stirred vigorously at 0 °C for 2 min. This was repeated twice and the mixture was stirred vigorously at 0 °C for another 13 min. The reaction was quenched by the addition of a saturated aqueous Na_2SO_3 solution (1 mL). The phases were separated and the aqueous phase washed with CH_2Cl_2 (2 4 mL). The combined organic phases were dried with $MgSO_4$ and the solvent evaporated under reduced pressure. Purification by flash chromatography on silica gel[43] (1.5 × 15 cm, 15 mL, *c*-C_6H_{12}/EtOAc = 3:1, 2–4) rendered the product as a colorless oil (99.0 mg, 90%, 77% *ee*). Analytical HPLC: Chiralpak AD-3, *n*-heptane/*i*PrOH = 100:1, 230 nm, t_R = 40.01 (*R*), 43.35 min (*S*). $[\alpha]_D^{20}$ = +34.8 (*c* = 0.66 g/100 mL, $CHCl_3$); $[\alpha]_{546}^{20}$ = +42.0 (*c* = 0.77 g/100 mL, $CHCl_3$); $[\alpha]_{436}^{20}$ = +85.9 (*c* = 0.77 g/100 mL, $CHCl_3$); $[\alpha]_{365}^{20}$ = +176.5 (*c* = 0.77 g/100 mL, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3455, 2940, 1720, 1615, 1515, 1460, 1360, 1305, 1250, 1155, 1115, 1030, 915, 820, 745 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 1.56 (s, 3 H, 2-Me), 2.16 (s, 3 H, 4-H_3), 3.79 (s, 3 H, OMe), 4.17 (s, 1 H, 2-OH), AB signal (δ_A = 5.12, δ_B = 5.16 ppm, J_{AB} = 11.9 Hz, 2 H, 1′-H_2), 6.86 (m_c, possibly interpretable as AA′ part of an AA′BB′ signal, 2 H, 2 *m*-H), 7.26 (m_c, possibly interpretable as BB′ part of an AA′BB′ signal, 2 H, 2 *o*-H) ppm. ^{13}C NMR (100.63 MHz, $CDCl_3$): δ = 21.71 (2-Me), 24.09 (C-4), 55.28 (C-OMe), 67.92 (C-1′), 81.08 (C-2), 114.07 (2 C-*m*), 127.02 (C-*i*), 130.19 (2 C-*o*), 159.96 (C-*p*), 171.19 (C-1), 204.63 (C-3) ppm. edHSQC ("C,H-COSY", 100.62/400.13 MHz, $CDCl_3$): Allows the assignment of all nonquaternary carbon atoms by their cross-peaks with directly bonded protons [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 21.71 (2-Me) $\leftrightarrow$ δ = 1.56 (2-Me); δ = 24.09 (C-4) $\leftrightarrow$ δ = 2.16 (4-H_3); δ = 55.28 (C-OMe) $\leftrightarrow$ δ = 3.79 (OMe); δ = 67.92 (C-1′) $\leftrightarrow$ δ = AB signal (δ_A = 5.12, δ_B = 5.16 ppm, 1′-H_2); δ = 114.07 (2 C-*m*) $\leftrightarrow$ δ = 6.86 (2 *m*-H); δ = 130.19 (2 C-*o*) $\leftrightarrow$ δ = 7.26 (2 *o*-H) ppm. HRMS (pos. APCI, MeOH): calcd. for $C_{13}H_{20}NO_5$ $[M + NH_4)^+$ 270.13360; found 270.13376 (+0.6 ppm). HRMS: (neg. APCI, MeOH): calcd. for $C_{13}H_{16}O_5Cl$ $[M + Cl)^-$ calcd. 287.06917; found 287.06927 (+0.3 ppm).

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[31] Remarkably, the specific rotations of compounds (2*R*,3*S*)- and (2*S*,3*R*)-**7** are not only extremely small, but the algebraic sign changes at shorter wavelengths (see the Exp. Sect.).

[32] The specific rotations of Weinreb amides (*R*)-**23d** {$[a]_D^{20}$ = +13.2 (*c* = 1.01 g/100 mL, $CHCl_3$)} and (*S*)-**23d** {$[a]_D^{20}$ = –13.2 (*c* = 1.17 g/100 mL, $CHCl_3$)} have the same algebraic sign as those reported, in: the literature[20f] {(*R*)-**23d**: $[a]_D^{20}$ = +4.7 (*c* = 1.80 g/100 mL, MeOH); (*S*)-**23d**: $[a]_D^{20}$ = –4.6 (*c* = 1.80 g/100 mL, MeOH)}, however, they differ, in: magnitude. This may be due to the use of different solvents.

[33] Fülöp and co-workers; found quite different specific rotations for the four stereoisomers of **7a**:[15]

	$[\alpha]_D^{22}$ ($CHCl_3$) Fülöp et al.	$[\alpha]_D^{20}$ ($CHCl_3$) this paper	$[\alpha]_D^{20}$ ($CHCl_3$) literature
(2*R*,3*S*)-**7a**	+16.4 (75% *ee*)	+0.3[31] (87% *ee*)	–1.0[b]; +1.0[d]
(2*S*,3*R*)-**7a**	–17.9 (87% *ee*)	–0.4[31] (92% *ee*)	+1.0[c]
(*S*,*S*)-**7a**	+27.8[e] (75% *ee*)	+4.7 (77% *ee*)	+8.7[a]; +12.3[d]
(*R*,*R*)-**7a**	–24.8 (85% *ee*)	–5.1 (90% *ee*)	

[a] A. Battaglia, G. Barbaro, P. Giorgianni, A. Guerrini, C. Bertucci, S. Geremia, *Chem. Eur. J.* **2000**, *6*, 3551–3557. [b] A. Battaglia, E. Baldelli, G. Barbaro, P. Giorgianni, A. Guerrini, M. Monari, S. Selva, *Tetrahedron: Asymmetry* **2002**, *13*, 1825–1832. [c] W. Ladner, *Chem. Ber.* **1983**, *116*, 3413–3426. [d] A. R. Moen, K. Ruud, T. Anthonsen, *J. Mol. Catal. B: Enzym.* **2008**, *50*, 74–79. [e] Somewhat in contrast, see p. S9 of the Supporting Information of ref.[15]: $[\alpha]_D^{30}$ = +12.5 (*c* = 1.2 g/100 mL, $CHCl_3$) for (*S*,*S*)-**7a** with 96^% *ee*.

However, specific rotations similar to ours were reported by others (see above). It may be hypothesized that (2*R*,3*S*)-**7a** and (2*S*,3*R*)-**7a** are virtually optically inactive at 589 nm so that "their" specific rotations may be caused by contaminants. If that was true the specific rotations of Fülöp and co-workers[15] might be caused by contamination of their products by the corresponding AD ligand: The work-up, which they published, mentioned neither acidic washing nor achromatography, one of which measures would appear to be necessary for removing that ligand. The specific rotations of the pure ligands are: $(DHQ)_2PHAL$: $[a]_D$ = +336 (*c* = 1.22 g/100 mL, MeOH); $DHQD_2PHAL$: $[a]_D$ = –263 (*c* = 1.15 g/100 mL, MeOH).

[34] We considered the fact that the $(DHQ)_2PHAL$ ligand outperforms the $(DHQD)_2PHAL$ ligand as remarkable and also that the *ee* values were low. Therefore we performed these experiments twice and obtained identical results.

[35] None of the saponification/esterification sequences presented in Table 2 should have changed the enantiopurity of the compounds involved. This expectation is borne out by entries 5–8; there, the product enantiomers were separated well by chiral GC (cf. also footnote [a] of Table 2). Nonetheless, the data in Table 2 indicate decreases in *ee* by up to 8% (entry 3) and increases in *ee* by up to 15% (entry 4). These obvious contradictions to reasonable expectation may be due to our inability to separate entirely the product enantiomers by chiral GC; integrating overlapping elution peaks did not give better results.

[36] All GC traces can be found in the Supporting Information.

[37] This conclusion is corroborated by the identical signs of the specific rotations of the SAD-based Weinreb amide **23d** in our work[32] and elsewhere[20f].

[38] This conclusion is corroborated at least somewhat by the identities of the signs of the specific rotations of the *syn*-configured methyl ester-containing diols (*S*,*S*)- and (*R*,*R*)-**7a** in our work in comparison with ref.[15] (cf. ref.[32]). Disturbingly, the absolute values of these rotations differ by factors of around 5, i.e., some values must be wrong (cf. also footnote [e] to the table in ref.[32]).

[39] The authors of ref.[13] noticed the same shift difference and exploited it in a structure elucidation.

[40] The ester and amide moieties in Figure 2 are drawn with *s-cis* conformations whether or not these are preferred in the respective transition. It is even conceivable that the favorite conformation is substrate-dependent.

[41] Figure 2 shows two ways in which methacrylates **1** fit into the Sharpless mnemonic without substituents bigger than hydrogen interfering with the hindered SE corner. They are depicted on the left-hand side of Figure 2. If, as a consequence, no orientational bias at all results for the substrate, it reacts without enantiocontrol. This was the case for methyl methacrylate (**1a**): It gave the diol **23a** as a racemic mixture (Table 1,

entries 1 and 2). However, the SW corner of the SAD transition-state mnemonic was/is capable of interacting favorably with most substrates. This conjecture led to the first modification of the mnemonic[5b,5c] and is borne out in the attributes "preferred" versus "competing" of the alternative methacrylate orientations in Figure 2. If our SADs of the methacrylic derivatives **1b**–**e** (10–98% *ee*; Table 1, entries 3–10) are viewed from this perspective, the strengths of these SW interactions follow the order Weinreb amide > pyrrolidide > PMB ester >> *i*Bu ester.

[42] B. E. Love, E. G. Jones, *J. Org. Chem.* **1999**, *64*, 3755–3756.

[43] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923–2925.

[44] The melting points are neither corrected nor uncorrected as these terms refer to total immersion thermometers. In our laboratory partial immersion thermometers are used exclusively. By definition these need no correction for immersion depth: G. V. D. Tiers, *J. Chem. Educ.* **1990**, *67*, 258–259.

[45] In another context it was shown that transition-metal ions may promote the degradation of *N*-methylmorpholine *N*-oxide (NMO); T. Rosenau, A. Potthast, H. Sixta, P. Kosma, *Prog. Polym. Sci.* **2001**, *26*, 1763–1837. As a precaution, NMO was never handled with steel cannulas. This avoidance of transition-metal ion contact was hoped to leave stock solutions and aliquots thereof unaffected.

[46] To achieve good yields the flask should be siliconized by treatment with $SiMe_2Cl_2$ in the following manner: The flask is filled with a solution of $SiMe_2Cl_2$ in toluene (10% v/v) and sealed. After 30 min the flask is emptied (the $SiMe_2Cl_2$ solution can be recycled), rinsed successively with toluene (2×) to wash away excess $SiMe_2Cl_2$, MeOH (2×) to convert the remaining R_3SiCl groups into R_3SiOMe groups, and dried in an oven at 70 °C.

[47] Compounds **2e**, **3d**, and **3e** are described in the literature; the description of their formation is sparse, though, and the compounds were not fully characterized: O. Miyata, T. Shinada, I. Ninomiya, T. Naito, T. Date, K. Okamura, S. Inagaki, *J. Org. Chem.* **1991**, *56*, 6556–6564.

[48] All diols were prepared by a) a racemic dihydroxylation, b) a SAD by using the $(DHQ)_2PHAL$ ligand, and c) a SAD by using the $(DHQD)_2PHAL$ ligand. Full characterization data refer to the diol from the SAD performed with the $(DHQD)_2PHAL$ ligand.

[49] The slightly orange mixture turned bright red upon adding bleach; thereafter it gradually faded to orange again. However, there was no clear endpoint. This meant it was impossible to carry out this reaction as a titration.

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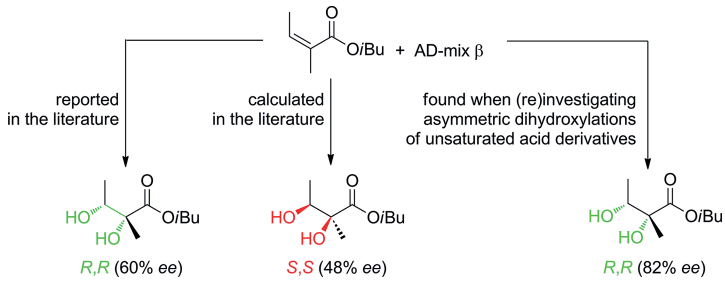
Dihydroxylations Revisited



Keywords: Asymmetric catalysis / Configuration determination / Dihydroxylation / 1,2-Diols / Enantioselectivity / Oxidation

The Sharpless mnemonic is generally accepted as a predictive tool for the stereochemical outcome of Sharpless asymmetric dihydroxylation reactions. However, it was claimed that isobutyl tiglate is dihydroxylated with the opposite facial selectivity because of a preference for a "Chapleur transition state". We have investigated this claim and proved it false.

