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An efficient asymmetric desymmetrization of prochiral glutaric anhydrides with SuperQuat chiral oxazolidin-2-ones

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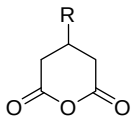
ABSTRACT

The asymmetric desymmetrization of 3-substituted glutaric anhydrides **1** bearing silyl, aryl and alkyl groups with the lithium salt of chiral oxazolidin-2-ones has been studied. The effects of the substituents at the 4- and 5-positions of the oxazolidin-2-ones on the diastereoselectivity of the anhydride opening were studied in detail. A SuperQuat chiral oxazolidin-2-one **2e** with 5,5-diaryl substituents showed optimum selectivity.

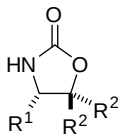
1. Introduction

The asymmetric desymmetrization (ADS) of symmetric molecules by enzymatic[1] and non-enzymatic methods[2] represents a powerful approach because it allows the generation of stereogenic centre(s) as well as permits simultaneous two-directional synthesis.[3,4] This makes ADS a powerful strategy,[5] and a large number of enantioselective total syntheses have been achieved based on this idea. The desymmetrization of anhydrides has been a particular focus of interest. Most investigations of this family of substrates have employed an achiral alcohol/thiol in combination with a chiral catalyst/enzymes[6–10] or chiral reagents such as alcohols[11] and amines.[12–17] Recently, carbon-based nucleophiles have also been used in the presence of chiral catalysts.[18–21] The enantioselectivity and the diastereoselectivity obtained in most of the cases using these reagents are moderate to good, while in many cases the selectivity is directly correlated to the substrate structure. The enantiomerically impure products often obtained with achiral reagents are not easily convertible to enantiopure forms. The purification is possible as diastereoisomers by attaching them to a chiral molecule[22,23] or an achiral bifunctional molecule.[24] Chiral reagents usually display high diastereoselectivities when reacted with bi- and tricyclic 2,3-disubstituted *meso*-carboxylic anhydrides. Although a few reagents[11–17] have been tested for the desymmetrization of 3-substituted glutaric anhydrides, the selectivity observed is not very high, and is also variable. The disadvantage of these methods is that the diastereomeric acids and their derivatives are generally inseparable. Moreover, in most cases, the chiral reagents are prepared in multistep reactions and so are not recoverable due to destruction during their removal.

We were in need of a suitable method for the desymmetrization of the prochiral 3-[dimethyl(phenyl)silyl]glutaric anhydride **1a** (Fig. 1) because it can easily lead to the asymmetric synthesis of various classes of small molecules, especially alkaloids possessing 3-hydroxypyrrolidine or piperidine moieties as the core structures.[25–27] These subgroups of alkaloids are frequently found in Nature,[28,29] many of which show a wide range of biological activities[30–32] for potential applications in medicine, and in the design of new drugs.[33–35] We have already shown the utility of **1a** for the syntheses of a pyrrolidine alkaloid, (+)-preussin,[36–38] and a piperidine alkaloid, (+)-carpamic acid.[39,40] Initially, we attempted the desymmetrization of anhydride **1a** with several chiral reagents including Heathcock's 1-(1′-naphthyl)ethanol.[11] The selectivities were moderate to poor while the diastereomeric half-acids or their esters were not separable by chromatography or crystallization. To overcome this problem, we introduced[41] a method for the desymmetrization of 3-substituted glutaric anhydrides **1** using the lithium salt of Evans' oxazolidin-2-one **2a**.[42] Thus, the reaction of **1a** with the lithium salt of **2a** provided a mixture of diastereoisomeric methyl esters **3a** and **4a** (Table 1) after esterification with diazomethane. Although the reaction was clean and quantitative, the



1a; R = $SiMe_2Ph$
1b; R = Ph
1c; R = 4-F-C_6H_5-
1d; R = Me_2CH-
1e; R = Me-



2a; R^1= $PhCH_2$-; R^2= H
2b; R^1= Me_2CH-; R^2= H
2c; R^1= Ph_2CH-; R^2= H
2d; R^1= Me_2CH-; R^2= Ph
2e; R^1= Me_2CH-;
R^2= 2-MeO-5-Me-C_6H_3-

Figure 1. Structures of anhydrides and oxazolidin-2-ones.

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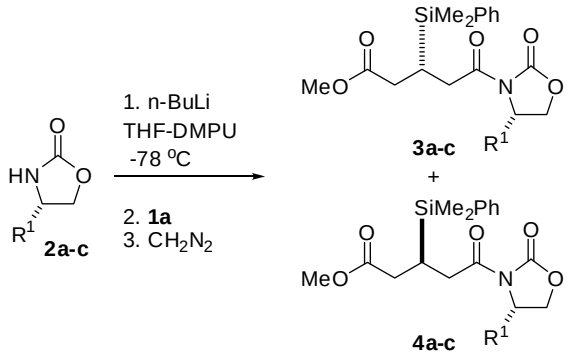
diastereoselectivity was poor (**3a**:**4a** = 2/1). Since then we were in search of a suitable chiral reagent for the desymmetrization of the **1a** with very high selectivity. Herein, we describe the development of a new SuperQuat[43] oxazolidin-2-one that can desymmetrize 3-substituted glutaric anhydrides with very high selectivity.

2. Results and discussion

As reported earlier,[41] desymmetrization of anhydride **1a** with Evans' oxazolidin-2-ones **2a** or **2b** (Table 1) showed poor selectivity providing esters **3a** or **3b** and **4a** or **4b**, respectively (**3**:**4** ~ 2/1). The parent acids of **3a** and **4a** were separable by fractional crystallization, while the methyl, benzyl and *tert*-butyl esters could be easily separated by conventional column chromatography on a preparative scale. Presently, we restricted ourselves with the oxazolidin-2-one class of chiral reagents because this fragment is widely used as a powerful auxiliary for controlling diastereoselective reactions[42] when attached to a carboxylic acid group. We, therefore, began our task by modifying the oxazolidin-2-one with various substituents. Sibi[44] had carried out modifications on Evans' original oxazolidin-2-one **2a** and had shown that the diphenyl-substituted oxazolidin-2-one **2c** (Fig. 1) was superior to **2a** in controlling the diastereoselectivity in radical and other reactions. Therefore, the oxazolidin-2-one **2c** was prepared following a reported procedure.[45] The lithium salt of this oxazolidin-2-one **2c** when reacted with anhydride **1a** in THF–DMPU [DMPU = 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one] (4/1) at −78 °C gave the diastereoisomeric acids with poor selectivity, as judged by converting them into their corresponding methyl esters **3c** and **4c** (**3c**:**4c** = 3/1) (Table 1, entry 3). This study indicated that the steric bulk of the substituent at the 4-position on the oxazolidin-2-one had virtually no effect on the diastereoselectivity of the anhydride opening.

Our next move was to examine the effect of the substituent(s) β to the nitrogen on the oxazolidin-2-one. There have been a number of research groups[46–48] which have independently introduced 5,5-disubstituted oxazolidin-2-ones called SuperQuats as chiral auxiliaries mainly to obviate the problems via purification of the products by crystallization, and limit the endocyclic cleavage during removal, which is known to be problematic with Evans' oxazolidin-2-ones.[49] It is also important to note the importance of these auxiliary types for the general chemist, with regard to their superior exo-cleavage,[43] conformational bias[50] and versatility.[51,52] More recently, other research groups have used these auxiliaries and have also shown them to be excellent and versatile. We prepared 4-isopropyl-5,5-diphenyloxazolidin-2-one **2d** from (*S*)-valine following the reported procedure.[53] The lithium salt of the oxazolidin-2-one **2d** in THF was made using *n*-BuLi at 0 °C and was reacted with anhydride **1a** at −78 °C in THF–DMPU (4/1) (Table 2, entry 1). We were able to see that a clean reaction took place, and the diastereoselectivity of the anhydride opening was significantly higher when compared to the earlier results with oxazolidin-2-ones **2a–c**. After diazomethane esterification, the diastereoisomeric methyl esters **3d** and **4d** were formed in a ratio of ca. 90:10, as determined by ^{1}H NMR spectroscopy. For further improvement of the diastereoselectivity, we prepared an oxazolidin-2-one **2e** with bulkier aryl groups at the 5,5-positions (Scheme 1) following a protocol similar to that used for the preparation of **2d**. The reaction of its lithium salt, as described above, with anhydride **1a** led to a mixture of diastereoisomeric acids which were esterified with diazomethane to give the methyl esters **3e** and **4e**

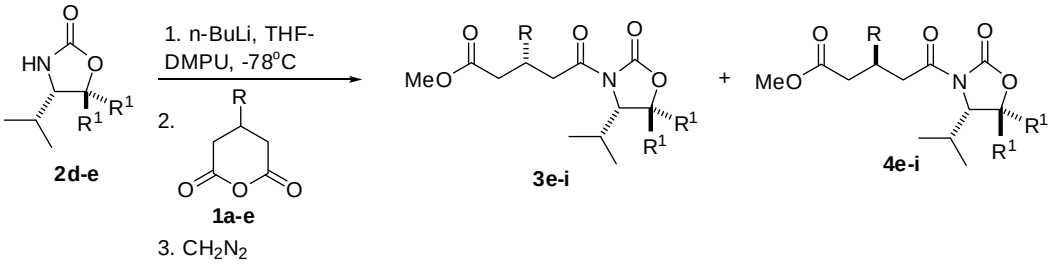
Table 1
Desymmetrization of anhydride **1a** with chiral oxazolidin-2-ones



Entry	R^1	2	3	4	Ratio[a] (**3**:**4**)	Yield (%)
1	$PhCH_2$–	**2a**	**3a**	**4a**	65:35	96[c]
2	Me_2CH–	**2b**	**3b**	**4b**	62:38[b]	95[c]
3	Ph_2CH–	**2c**	**3c**	**4c**	77:23[b]	89

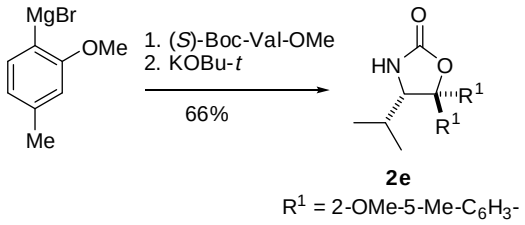
[a] Ratio determined by ^{1}H NMR of the crude product.
[b] Stereochemistry of methyl esters **3b**,**c** and **4b**,**c** was tentatively assigned in analogy with **3a** and **4a**.
[c] Results are from Ref. 41.

Table 2
Desymmetrization of anhydrides **1** with SuperQuat oxazolidin-2-one **2e**



Entry	R	R^1	1	3	4	Ratio[a] (**3**:**4**)	Yield (%)
1	$SiMe_2Ph$	Ph	**1a**	**3d**	**4d**	90:10	80
2	$SiMe_2Ph$	2-MeO–5-Me–C_6H_3–	**1a**	**3e**	**4e**	95:5	84
3	Ph	2-MeO–5-Me–C_6H_3–	**1b**	**3f**	**4f**	95:5[b]	80
4	4-F–C_6H_4–	2-MeO–5-Me–C_6H_3–	**1c**	**3g**	**4g**	95:5	70
5	Me_2CH–	2-MeO–5-Me–C_6H_3–	**1d**	**3h**	**4h**	90:10[b]	73
6	Me–	2-MeO–5-Me–C_6H_3–	**1e**	**3i**	**4i**	81:19[b]	74

[a] Ratio determined by ^{1}H NMR of the crude product.
[b] Stereochemistry of methyl esters **3d**,**f**,**h**,**i** and **4d**,**f**,**h**,**i** was tentatively assigned in analogy with **3e**/**3g** and **4e**/**4g**.



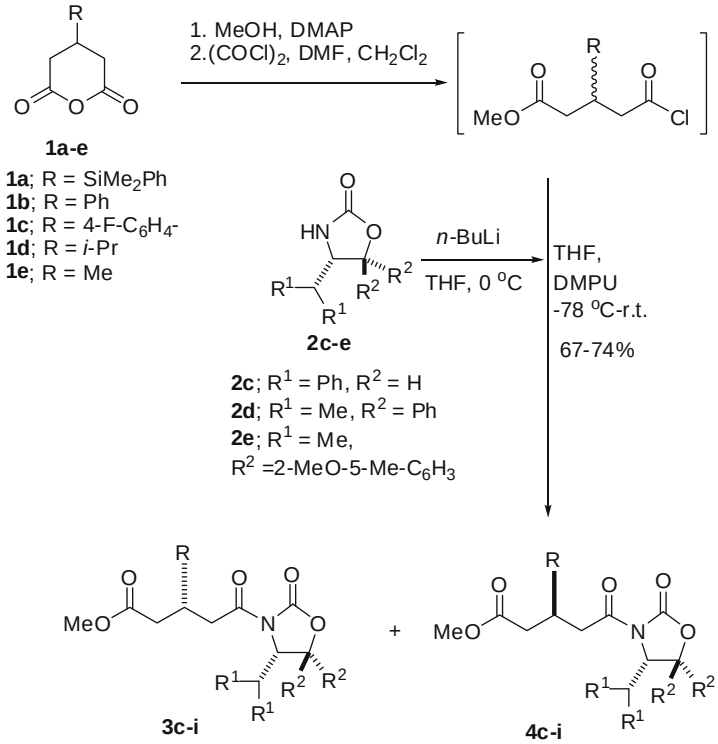
Scheme 1. Synthesis of SuperQuat oxazolidin-2-one **2e**.

in a 95:5 ratio (Table 2, entry 2). The high diastereoselectivity of the anhydride opening with **2e** is synthetically acceptable.

To examine the generality of this desymmetrization protocol, various prostereogenic 3-substituted glutaric anhydrides **1b**–**e** were treated with the Li-salt of **2e** under the standardized conditions (Table 2). The choices of the anhydrides were made based on their utility as key intermediates in the synthesis of various natural products. The diastereoselectivity of the anhydride opening of 3-aryl-substituted glutaric anhydrides **1b**,**c** was very high (95:5). For the isopropyl-substituted anhydride **1d**, the diastereoisomeric acids were formed in a ratio of 90:10. Although the methyl-substituted anhydride **1e** showed moderate diastereoselectivity (81:19), the diastereoisomeric ratio enrichment (dr = 94/6) could be easily improved to **3i**:**4i** = 94:6 by a single crystallization.

To determine the diastereoselectivity of the opening of anhydrides with oxazolidin-2-ones **2c**–**2e**, model mixtures of **3c**–**i** and **4c**–**i** were prepared. For this, anhydrides **1a**–**e** were opened up with methanol to give the racemic monomethyl esters (Scheme 2), which were then reacted with oxalyl chloride in the presence of catalytic amount of DMF to give the intermediate acid chlorides. The lithium salt of oxazolidin-2-ones **2c**–**2e** was prepared using butyl lithium and was reacted with the acid chlorides to give the corresponding diastereoisomeric mixtures of **3c**–**i** and **4c**–**i** in almost equal proportions and good yields. The ester methyl and/or silyl methyl protons of diastereomers **3c**–**e** and **4c**–**e**, while the isopropyl methyls and/or the ester methyls of the diastereoisomeric products **3f**–**i** and **4f**–**i** were discernable by ^{1}H NMR (Table 3), and thus used for diastereoisomer ratio determination.

To assess the sense of chiral induction in the anhydride opening reactions, it was essential to establish the absolute stereochemistry of the products. The mixture of acids obtained from the desymmetrization reaction of **1a** with **2e** was converted to a mixture of the



3c; R=SiMe$_2$Ph, R^1= Ph, R^2= H
3d; R=SiMe$_2$Ph, R^1=Me, R^2=Ph
3e; R=SiMe$_2$Ph, R^1=Me, R^2= 2-MeO-5-Me-C$_6$H$_3$
3f; R=Ph, R^1=Me, R^2= 2-MeO-5-Me-C$_6$H$_3$
3g; R=4-F-C$_6$H$_4$-, R^1=Me, R^2= 2-MeO-5-Me-C$_6$H$_3$
3h; R =*i*-Pr, R^1=Me, R^2= 2-MeO-5-Me-C$_6$H$_3$
3i; R=Me, R^1 =Me, R^2= MeO-5-Me-C$_6$H$_3$

4c; R=SiMe$_2$Ph, R^1= Ph, R^2= H
4d; R=SiMe$_2$Ph, R^1=Me, R^2=Ph
4e; R=SiMe$_2$Ph, R^1=Me, R^2= 2-MeO-5-Me-C$_6$H$_3$
4f; R=Ph, R^1=Me, R^2= 2-MeO-5-Me-C$_6$H$_3$
4g; R=4-F-C$_6$H$_4$-, R^1=Me, R^2= 2-MeO-5-Me-C$_6$H$_3$
4h; R =*i*-Pr, R^1=Me, R^2= 2-MeO-5-Me-C$_6$H$_3$
4i; R=Me, R^1 =Me, R^2= 2-MeO-5-Me-C$_6$H$_3$

Scheme 2. Preparation of model mixture of diastereomeric methyl esters **3c**–**i** and **4c**–**i**.

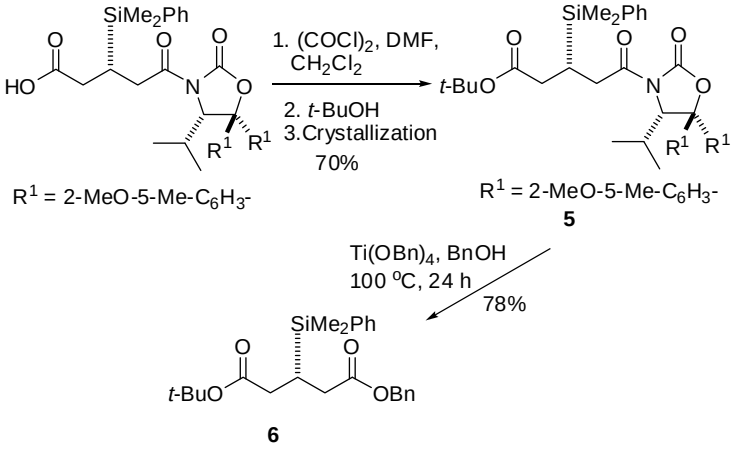
Table 3
Chemical shift values (δ) in ppm for selected group of protons of diastereoisomeric methyl esters **3c–i** and **4c–i**

Entry	**3**/**4**	CO_2Me of **3c–i**	CO_2Me of **4c–i**	$CHMe_2$ of **3d–i**	$CHMe_2$ of **4d–i**	Si*Me* of **3c–e**	Si*Me* of **4c–e**
1	**3c**/**4c**	3.58[a]	3.55[a]	—	—	0.32	0.32 and 0.33
2	**3d**/**4d**	3.47[a]	3.36[a]	0.72 and 0.86	0.71 and 0.84	0.18	0.27 and 0.30
3	**3e**/**4e**	3.47	—[b]	0.70 and 0.96	0.70 and 0.94	0.26 and 0.27[a]	0.31 and 0.34[a]
4	**3f**/**4f**	3.56	3.52	0.70 and 0.88[a]	0.50 and 0.63[a]	—	—
5	**3g**/**4g**	3.56	—[b]	0.69 and 0.88[a]	0.51 and 0.66[a]	—	—
6	**3h**/**4h**	3.62[a]	3.56[a]	0.71 and 0.82	—[b]	—	—
7	**3i**/**4i**	3.64[a]	3.58[a]	0.71 and 0.92	—[b]	—	—

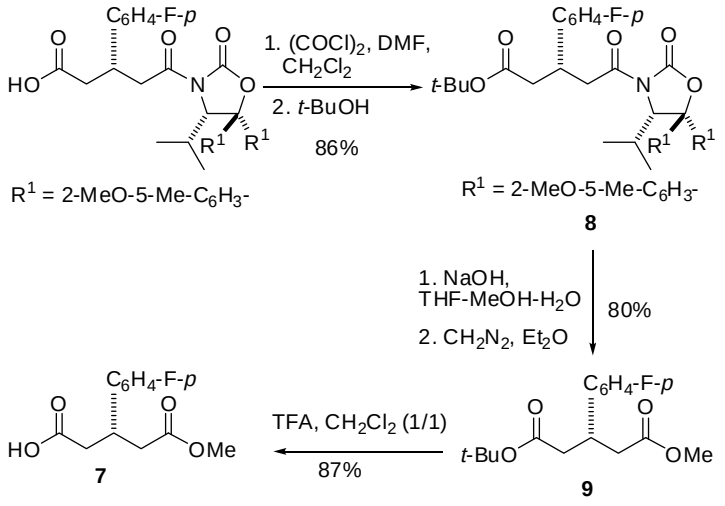
[a] Peaks at these positions were used for estimation of diastereoisomer ratio.
[b] Chemical shifts values could not be obtained with certainty due to overlap of peaks.

corresponding *t*-Bu esters (Scheme 3) which upon simple crystallization gave the pure diastereoisomeric ester **5**. The oxazolidin-2-one moiety from **5** was removed by transesterification using the benzyl alcohol and $Ti(OBn)_4$ catalyst to give the known diester **6**.[36] The (*R*)-configuration of the silicon-bearing asymmetric centre in **5** was confirmed from the specific rotation data of **6** {$[\alpha]_D^{22} = +1.15$ (*c* 2.08, MeOH); lit.:[36] $[\alpha]_D^{24} = +1.2$ (*c* 4.46, MeOH)}.

We also checked the facial selectivity for 3-fluorophenyl-substituted anhydride **1c** by converting it to the known derivative **7**. For this, the diastereoisomeric acid mixture from the desymmetrization reaction of **1c** with **2e** was converted to the *tert*-butyl ester **8**. Removal of the oxazolidin-2-one group was achieved by simple NaOH hydrolysis providing the acid which was esterified with diazomethane to give diester **9**. In this process also, the oxazolidin-2-one **2e** was recovered in 93% yield. The *tert*-butyl ester group in diester **9** was selectively hydrolyzed with TFA in dichloromethane to give the diacid monomethyl ester **7** in good yield (Scheme 4). The absolute stereochemistry of the aryl-bearing centre in **8** was ascertained to be (*R*) by comparing the specific rotation data of **7** {$[\alpha]_D^{22} = -3.4$ (*c* 1.54, $CHCl_3$)} with the reported value[10] {$[\alpha]_D^{20} = -4.3$ (*c* 1, $CHCl_3$)}.



Scheme 3. Determination of the sense of chiral induction for the desymmetrization of **1a** with **2e**.



Scheme 4. Determination of the sense of chiral induction for **1c** desymmetrization with **2e**.

The origin of the increase in diastereoselectivity of the anhydride opening with SuperQuat oxazolidin-2-ones **2d** and **2e** compared to that with Evans' type oxazolidin-2-ones **2a–c** can be explained on the basis of the conformational preferences of the oxazolidin-2-ones as shown in Figure 2. In the former type, the conformation **A-2** is favoured over conformation **B-2** due to the steric interaction between the 5-position aryl and isopropyl methyls, while in the latter type, both conformations **A-1** and **B-1** have similar steric interactions. The presence of geminal diaryl groups at the 5-position of **2d**,**e** would serve to direct the conformation of the stereocontrolling isopropyl group at the 4-position close to the point of the 3-position nitrogen as shown in **B-2**. The stereoinduction step is the kinetically controlled addition of the oxazolidin-2-one anion to the carbonyl of the prostereogenic anhydride. Of the two carbonyls in the anhydride, the one that has minimal steric hindrance provided by the oxazolidin-2-one anion and the substituent at the anhydride in the transition state underwent addition to give the observed product diastereoisomer.

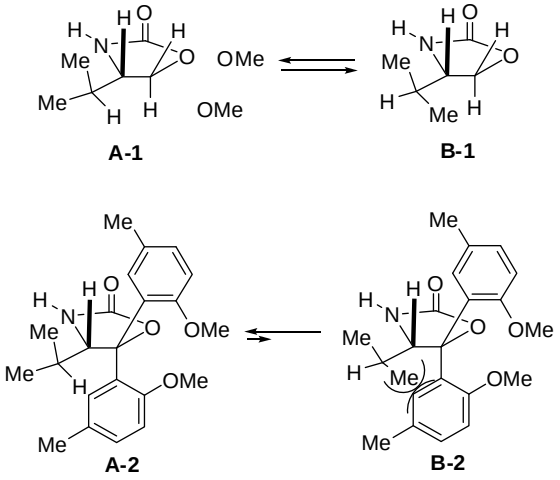


Figure 2. Conformational preferences of oxazolidin-2-ones.

3. Conclusion

In conclusion, the results of this investigation show that specially substituted diaryl SuperQuat oxazolidin-2-ones in stoichiometric amounts could be efficiently employed for the desymmetrization of prostereogenic anhydrides on a preparative scale with very high diastereoselectivity. Therefore, this could form a convenient method for both the enantioconvergent and enantiodivergent syntheses of differentially substituted glutaric acid derivatives. The diastereoselectivity depended significantly on the substituents β to the amino group, but not on the steric bulk of the α-substituents. The SuperQuat oxazolidin-2-ones could be easily prepared and can be detached from the products easily by NaOH hydrolysis or Ti(IV)-catalyzed transesterification with high recovery (>90%) without any loss of purity.

4. Experimental

All reactions were performed in oven-dried (120 °C) or flame-dried glass apparatus under a dry N_2 or argon atmosphere. Tetrahydrofuran (THF) was dried from sodium/benzophenone, while *t*-BuOH was dried from CaH_2 followed by storage over 4 Å molecular sieves. *n*-BuLi (1.5 M in hexane) was purchased from Aldrich. Anhydrides **1a**,[41] **1b–e**[11] and oxazolidin-2-ones **2a–b**,[54] **2c**,[45] **2d**[53] were prepared following the literature procedures. The column chromatography was performed on silica gel (230–400 mesh). The ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker 200 MHz spectrometer. The spectra were referenced to residual chloroform (δ 7.25 ppm, ^{1}H; δ 77.00 ppm, ^{13}C). The mass spectra were recorded on a Shimadzu GC–MS 2010 mass spectrometer (EI 70 eV). High resolution mass spectra were recorded at 60–70 eV with a Waters Micromass Q-TOF spectrometer (ESI, Ar). The IR spectra were recorded with a JASCO FT IR spectrophotometer in NaCl cells or in KBr discs. Peaks are reported in cm^{-1}. Melting points (mp) were determined on a Fischer John's melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-360 polarimeter. As the 5,5-aryl groups in oxazolidinones **2d** and **2e** are diastereotopic and magnetically nonequivalent, some of the aromatic protons and carbons for these aryls are discernable by NMR. Similar NMR differences of the aryl groups are also observed in case of acylated oxazolidinones **3d–i** and **4d–i** (vide infra).

4.1. (4*S*)-5,5-Di(2-methoxy-5-methylphenyl)-4-isopropyloxazolidin-2-one 2e

A solution of 2-methoxy-4-methylphenylmagnesium bromide was prepared in the usual way by using 2-bromo-4-methylanisole (30.4 g, 151 mmol), Mg turnings (3.7 g, 154 mmol) and THF (100 mL) under an argon atmosphere. A solution of *N*-(*tert*-butoxycarbonyl)-*S*-valine methyl ester (10 g, 43.2 mmol) in dry THF (50 mL) was added dropwise to the Grignard solution at 0 °C. After the addition was over, the reaction mixture was allowed to warm to room temperature and stirring was continued for 18 h. The reaction mixture was slowly poured into an ice-cold saturated NH_4Cl solution and extracted with ethyl acetate (2 × 150 mL). The combined organic phase was washed with brine (150 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed followed by crystallization from petroleum ether to give (2*S*)-2-*tert*-butyloxycarbonylamino-1,1-di(2-methoxy-5-methylphenyl)-3-methylbutanol (14.8 g, 77%). Mp 112–113 °C; $[\alpha]_D^{22} = -143.6$ (*c* 1, EtOH); R_f = 0.55 (hexane/ethyl acetate, 90/10); IR ($CHCl_3$ film): 3502, 3454, 1700, 1497 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.8 Hz, 6H, C*H*$_3$CHC*H*$_3$), 1.40 (s, 9H, *t*-BuO), 1.51–1.67 (m, 1H, CH$_3$C*H*CH$_3$), 2.28 (s, 3H, ArC*H*$_3$), 2.32 (s, 3H, ArC*H*$_3$), 3.47 (s, 3H, ArOC*H*$_3$), 3.48 (s, 3H, ArOC*H*$_3$), 5.05 (d, *J* = 10 Hz, 1H, NC*H*), 5.05 (d, *J* = 10.2 Hz, 1H, NH), 5.29 (s, br, 1H, OH), 6.60 (d, *J* = 7.8 Hz, 1H, Ar), 6.64 (d, *J* = 7.8 Hz, 1H, Ar), 6.90–6.98 (m, 2H, Ar), 7.52 (s, 1H, Ar), 7.58 (d, *J* = 2 Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.1 (CH*C*H$_3$), 20.6 (Ar*C*H$_3$), 20.8 (Ar*C*H$_3$), 22.6 (CH*C*H$_3$), 28.3 (3 × *C*H$_{3\text{-}t\text{-Bu}}$), 29.5 (*C*HMe$_2$), 55.2 (N*C*H), 55.3 (O*C*H$_3$), 55.9 (O*C*H$_3$), 78.2 (Me$_3$*C*O), 81.6 (Ar$_2$*C*OH), 111.7 (*C*H$_{\text{-Ar}}$), 112.3 (*C*H$_{\text{-Ar}}$), 127.4 (*C*H$_{\text{-Ar}}$), 127.9 (*C*H$_{\text{-Ar}}$), 128.1 (*C*H$_{\text{-Ar}}$), 128.8 (Me*C*$_{\text{-Ar}}$), 129.6 (Me*C*$_{\text{-Ar}}$), 129.7 (*C*H$_{\text{-Ar}}$), 132.5 (HOC*C*$_{\text{-Ar}}$), 133.0 (HOC*C*$_{\text{-Ar}}$), 153.8 (MeO*C*$_{\text{-Ar}}$), 154.8 (MeO*C*$_{\text{-Ar}}$), 156.2 (*C*=O). Anal. Calcd for $C_{26}H_{37}NO_5$: C, 70.40; H, 8.41; N, 3.16. Found: C, 70.45; H, 8.42; N, 3.02.

Potassium *tert*-butoxide (4.2 g, 37.8 mmol) was added to a stirred solution of the alcohol (2*S*)-2-*tert*-butyloxyamino-3-methyl-1,1-di(2-methoxy-5-methylphenyl)butanol (14.0 g, 31.5 mmol) in dry THF (205 mL) at 0 °C. After 2.5 h, the resulting suspension was poured into a 10% aqueous solution of NH_4Cl (350 mL) and extracted with $CHCl_3$ (2 × 200 mL). The extract was washed with water (2 × 100 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was crystallized from ethyl acetate to give oxazolidin-2-one **2e** (10.0 g, 86%). Mp 266–268 °C; $[\alpha]_D^{24} = -346.6$ (*c* 0.5, $CHCl_3$); R_f = 0.4 ($CHCl_3$); IR (KBr): 3359, 1764, 1503 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.66 (d, *J* = 6.6 Hz, 3H, C*H*$_3$CHCH$_3$), 0.92 (d, *J* = 7.2 Hz, 3H, CH$_3$CHC*H*$_3$), 1.51–1.67 (m, 1H, CH$_3$C*H*CH$_3$), 2.27 (s, 3H, ArC*H*$_3$), 2.32 (s, 3H, ArC*H*$_3$), 3.43 (s, 3H, OC*H*$_3$), 3.51 (s, 3H, OC*H*$_3$), 4.76 (d, *J* = 1.6 Hz, 1H, NC*H*), 6.22

(br, 1H, NH), 6.62 (d, J = 8.2 Hz, 1H, Ar), 6.69 (d, J = 8.2 Hz, 1H, Ar), 6.97–7.05 (m, 2H, Ar), 7.24 (s, d, J = 1 Hz, 1H, Ar), 7.67(d, J = 2 Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.0 ($CHCH_3$), 20.6 ($ArCH_3$), 20.8 ($ArCH_3$), 21.4 ($CHCH_3$), 29.2 ($CHMe_2$), 55.5 ($ArOCH_3$), 56.2 ($ArOCH_3$), 61.6 (NCH), 88.8 (Ar_2COCO), 111.3 (HC_{-Ar}), 114.0 (HC_{-Ar}), 127.9 (MeC_{-Ar}), 128.0 (HC_{-Ar}), 128.7 (HC_{-Ar}), 128.7 (MeC_{-Ar}), 129.0 (HC_{-Ar}), 129.1(O=COCC_{-Ar}), 129.5 (HC_{-Ar}), 129.6 (O=COCC_{-Ar}), 152.9 ($MeOC_{-Ar}$), 156.3 ($MeOC_{-Ar}$), 159.8 (C=O). Anal. Calcd for $C_{22}H_{27}NO_4$: C, 71.52; H, 7.37; N, 3.79. Found: C, 71.37; H, 7.17; N, 3.66.

4.2. (3′*R*,4*S*)-5,5-Di(2-methoxy-5-methylphenyl)-3-{3-[dimethyl-(phenyl)silyl]-4-methoxycarbonyl-1-oxobutyl}-4-isopropyl-oxazolidin-2-one 3e and its (3′*S*)-diastereoisomer 4e

n-Butyl lithium (1.8 mL, 1.5 M in hexane, 2.7 mmol) was slowly added to a suspension of oxazolidin-2-one **2e** (922 mg, 2.5 mmol) in dry THF (12.5 mL) at 0 °C under argon atmosphere until a clear solution resulted (30 min). The reaction mixture was cooled to −78 °C after which dry DMPU (6 mL) was added followed by a solution of the anhydride **1a** (670 mg, 2.7 mmol) in dry THF (12.5 mL). After 4 h at −78 °C, the reaction mixture was acidified with 5% citric acid solution and was extracted with ethyl acetate. The extract was concentrated under reduced pressure and the residue was dissolved in benzene. The benzene solution was washed several times with water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was treated with an ether solution of diazomethane and was concentrated under reduced pressure. The crude product was purified by column chromatography to give **3e** (1.32 g, 84%) as an inseparable mixture containing 5% of its diastereoisomer **4e** as a colourless oil. Data for **3e**: $[\alpha]_D^{23} = -165.7$ (*c* 1.68, MeOH); R_f = 0.56 (hexane/ethyl acetate, 85/15); IR ($CHCl_3$ film): 1778, 1735, 1698, 1613, 1503, 1256, 1113 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.26 (s, 3H, SiMe), 0.27 (s, 3H, SiMe), 0.70 (d, J = 6.6 Hz, 3H, CH_3CHCH_3), 0.96 (d, J = 7.2 Hz, 3H, CH_3CHCH_3), 1.58–1.75 (m, 1H, CH_3CHCH_3), 1.85–2.02 (m, 1H, SiCH), 2.22 (s, 3H, $ArCH_3$), 2.24 (dd, J = 8, 15.8 Hz, 1H, $CH_AH_BCO_2Me$), 2.33 (s, 3H, $ArCH_3$), 2.38 (dd, J = 6.4, 15.8 Hz, 1H, $CH_AH_BCO_2Me$), 2.95 (d, J = 6.4 Hz, 2H, $NCOCH_2$), 3.45 (s, 3H, $ArOCH_3$), 3.46 (s, 3H, $ArOCH_3$), 3.47 (s, 3H,$COOCH_3$), 5.77 (d, J = 1.8 Hz, 1H, NCH), 6.62 (d, J = 8.4Hz, 1H, Ar), 6.68 (d, J = 8.2 Hz, 1H, Ar), 6.95–7.06 (m, 2H, Ar), 7.20 (d, J = 2Hz, 1H, Ar), 7.28–7.33 (m, 3H, Ar), 7.42–7.49 (m, 2H, Ar), 7.68 (d, J = 1.8 Hz, 1H, Ar); ^{13} C NMR ($CDCl_3$, 50 MHz) δ −4.8 ($SiCH_3$), −4.2 ($SiCH_3$), 15.7 ($CHCH_3$), 17.1 (SiCH), 20.4 (2 × $ArCH_3$), 22.3 ($CHCH_3$), 29.6 ($CHMe_2$), 34.1 (CH_2CON), 35.1 (CH_2CO_2), 51.0 (CO_2CH_3), 55.0 ($ArOCH_3$), 55.6 ($ArOCH_3$), 61.9 (NCH), 88.7 (Ar_2COCO), 110.8 (HC_{-Ar}), 113.5 (HC_{-Ar}), 126.2 (C_{-Ar}), 127.1 (HC_{-Ar}), 127.5 (2 × HC_{-Ar}), 127.7 (C_{-Ar}), 128.5 (HC_{-Ar}), 128.6 (2 × C_{-Ar}), 128.9 (2 × HC_{-Ar}), 129.8 (HC_{-Ar}), 133.7 (2 × HC_{-Ar}), 136.7 (C_{-Ar}), 152.4 ($MeOC_{-Ar}$), 153.1 ($MeOC_{-Ar}$), 156.0 (NCO_2), 172.3 (CO_2CH_3), 173.2 (CON); ESI MS: m/z (%) = 632 (3) (M^++H), 555 (13), 554 (100), 510 (16); HRMS: Calcd for $C_{36}H_{46}NO_7Si$ (M^++H) 632.3044. Found: 632.3029.

A model diastereomeric mixture of methyl esters **3e** and **4e** was made by using the following procedure. A solution of the anhydride **1a** (124 mg, 0.5 mmol) and DMAP (12 mg, 0.1 mmol) in methanol (5 mL) was stirred at room temperature for 1 h. The solvent was evaporated and the residue was diluted with ethyl acetate. The ethyl acetate solution was washed with dil HCl, water and brine, dried over $MgSO_4$ and evaporated to give the half ester (140 mg, 0.5 mmol, 100%). The half ester was dissolved in dry dichloromethane (2 mL), after which dry DMF (6 μL, 0.08 mmol) was added followed by the addition of oxalyl chloride (107 μL, 1.23 mmol) at 0 °C under an argon atmosphere. After 2 h at room temperature, the reaction mixture was concentrated under reduced pressure followed by high vacuum (0.1 Torr) to give the crude acid chloride. In another flask, *n*-butyl lithium (0.35 mL, 1.5 M in hexane, 0.52 mmol) was slowly added to a suspension of oxazolidin-2-one **2e** (185 mg, 0.5 mmol) in dry THF (2 mL) at 0 °C under an argon atmosphere until a clear solution resulted (30 min). The reaction mixture was cooled to −78 °C, and dry DMPU (1 mL) was added followed by a solution of the crude acid chloride in dry THF (5 mL) which was prepared previously. The mixture was allowed to return to room temperature and was stirred for 2 h. The reaction mixture was diluted with water and extracted with ethyl acetate. The extract was washed with water and brine, dried and evaporated under reduced pressure. The residue was purified by column chromatography to give an inseparable 1:1 mixture of diastereoisomeric methyl esters **3e** and **4e** (212 mg, 67%) as a colourless oil. Data for **4e** (obtained from mixture): R_f = 0.56 (hexane/ethyl acetate, 85/15); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.31 (s, 3H, SiMe), 0.34 (s, 3H, SiMe), 0.70 (d, J = 6.6 Hz, 3H, CH_3CHCH_3), 0.94 (d, J = 7.2 Hz, 3H, CH_3CHCH_3), 1.58–1.75 (m, 1H, CH_3CHCH_3), 1.85–2.06 (m, 1H, SiCH), 2.23 (s, 3H, $ArCH_3$), 2.36 (s, 3H, $ArCH_3$), 2.23–2.39 (m, 2H, CH_2CO_2Me), 2.76 (dd, J = 9.6, 17.2 Hz, 1H, $NCOCH_AH_B$), 3.04 (dd, J = 4.2, 17.2 Hz, 1H, $NCOCH_AH_B$), 3.38 (s, 3H, $ArOCH_3$), 3.48 (s, 6H, $ArOCH_3$, $COOCH_3$), 5.78 (s, br, 1H, NCH), 6.62 (d, J = 8.4Hz, 1H, Ar), 6.68 (d, J = 8.2 Hz, 1H, Ar), 6.95–7.06 (m, 2H, Ar), 7.20 (d, J = 2Hz, 1H, Ar), 7.28–7.33 (m, 3H, Ar), 7.42–7.52 (m, 2H, Ar), 7.69 (s, br, 1H, Ar); ^{13}C NMR ($CDCl_3$, 50 MHz) δ −4.6 ($SiCH_3$), −4.2 ($SiCH_3$), 15.9 ($CHCH_3$), 17.9 (SiCH), 20.5 (2 × $ArCH_3$), 22.4 ($CHCH_3$), 29.8 ($CHMe_2$), 34.3 (CH_2CON), 35.3 (CH_2CO_2), 51.1 (CO_2CH_3), 55.3 ($ArOCH_3$), 55.9 ($ArOCH_3$), 62.1 (NCH), 88.9 (Ar_2COCO), 110.9 (HC_{-Ar}), 113.8 (HC_{-Ar}), 126.4 (C_{-Ar}), 127.2 (HC_{-Ar}), 127.6 (2 × HC_{-Ar}), 127.9 (C_{-Ar}), 128.7 (HC_{-Ar}), 128.8 (2 × C_{-Ar}), 129.0 (2 × HC_{-Ar}), 130.0 (HC_{-Ar}), 133.9 (2 × HC_{-Ar}), 136.9 (C_{-Ar}), 152.6 ($MeOC_{-Ar}$), 153.4 ($MeOC_{-Ar}$), 156.2 (NCO_2), 172.5 (CO_2CH_3), 173.3 (CON).

4.3. (3′*R*,4*S*)-5,5-Di(2-methoxy-5-methylphenyl)-4-isopropyl-3-(4-methoxycarbonyl-1-oxobutyl-3-phenyl)oxazolidin-2-one 3f and its (3′*S*)-diastereoisomer 4f

Following the general procedure described for the desymmetrization of **1a** with **2e**, anhydride **1b** (102 mg, 0.54 mmol) and oxazolidin-2-one **2e** (186 mg, 0.5 mmol) gave methyl esters **3f** (230 mg, 80%) as an inseparable mixture containing 5% of its diastereoisomer **4f** as a colourless oil. Data for **3f**: $[\alpha]_D^{23} = -172.8$ (*c* 1, MeOH); R_f = 0.6 (hexane/ethyl acetate, 85/15); IR ($CHCl_3$ film): 1777, 1737, 1702, 1612, 1503 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.70 (d, J = 6.6 Hz, 3H, CH_3CHCH_3), 0.88 (d, J = 7 Hz, 3H, CH_3CHCH_3), 1.58–1.72 (m, 1H, CH_3CHCH_3), 2.03 (s, 3H, $ArCH_3$), 2.34 (s, 3H, $ArCH_3$), 2.58 (dd, J = 8, 15.4 Hz, 1H, $CH_AH_BCO_2Me$), 2.68 (dd, J = 7.2, 15.4 Hz, 1H, $CH_AH_BCO_2Me$), 3.19–3.31 (m, 2H, $NCOCH_2$), 3.37 (s, 3H, $ArOCH_3$), 3.41 (s, 3H, $ArOCH_3$), 3.56 (s, 3H, $COOCH_3$), 3.65–3.83 (m, 1H, PhCH), 5.72 (d, J = 1.8 Hz, 1H, NCH), 6.59 (d, J = 8.2 Hz, 1H, Ar), 6.62 (d, J = 8.2 Hz, 1H, Ar), 6.90–7.05 (m, 3H, Ar), 7.12–7.21 (m, 5H, Ar), 7.66 (d, J = 2 Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.9 ($CHCH_3$), 20.5 (2 × $ArCH_3$), 22.3 ($CHCH_3$), 29.7 ($CHMe_2$), 37.3 (PhCH), 40.5 (CH_2CO_2), 40.9 (CH_2CON), 51.3 (CO_2CH_3), 55.2 ($ArOCH_3$), 55.7 ($ArOCH_3$), 62.0 (NCH), 89.1 (Ar_2COCO), 110.9 (HC_{-Ar}), 113.5 (HC_{-Ar}), 126.5 (C_{-Ar}, HC_{-Ar}), 127.2 (2 × HC_{-Ar}), 127.4 (HC_{-Ar}), 127.7 (C_{-Ar}), 128.3 (2 × HC_{-Ar}), 128.4 (HC_{-Ar}), 128.8 (C_{-Ar}), 128.9 (C_{-Ar}), 129.0 (HC_{-Ar}), 129.9 (HC_{-Ar}), 142.7 (*ipso*-C_{-Ph}), 152.5 ($MeOC_{-Ar}$), 153.5 ($MeOC_{-Ar}$), 155.9 (NCO_2), 170.7 (CO_2Me), 171.9 (CON). Anal. Calcd for $C_{34}H_{39}NO_7$: C, 71.18; H, 6.85; N, 2.44. Found: C, 71.08; H, 6.91; N, 2.29.

Following the general procedure described for the model synthesis of a mixture of **3e** and **4e** from **1a** and **2e**, anhydride **1b** (95 mg, 0.5 mmol) and oxazolidin-2-one **2e** (186 mg, 0.5 mmol) gave a 1:1 mixture of diastereoisomeric methyl esters **3f** and **4f** (203 mg, 71%) as a colourless oil. Data for **4f** (obtained

from mixture): R_f = 0.6 (hexane/ethyl acetate, 85/15); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.50 (d, J = 6.6 Hz, 3H, CH_3CHCH$_3$), 0.63 (d, J = 7 Hz, 3H, CH$_3$CHCH_3), 1.58–1.72 (m, 1H, CH$_3$CHCH$_3$), 2.24 (s, 3H, ArCH_3), 2.33 (s, 3H, ArCH_3), 2.54 (dd, J = 8.4, 15.6 Hz, 1H, CH_AH$_B$CO$_2$Me), 2.62 (dd, J = 6, 15.6 Hz, 1H, CH$_A$$H_BCO_2$Me), 3.00 (dd, J = 7, 16.6 Hz, 1H, CH_AH$_B$CON), 3.41 (dd, J = 10, 16.6 Hz, 1H, CH$_A$$H_B$CON), 3.44 (s, 3H, ArOC$H_3$), 3.47 (s, 3H, ArOC$H_3$), 3.52 (s, 3H, COOC$H_3$), 3.63–3.83 (m, 1H, PhC$H$), 5.72 (d, J = 1.8 Hz, 1H, NCH), 6.59 (d, J = 8.2 Hz, 1H, Ar), 6.68 (d, J = 8.2 Hz, 1H, Ar), 6.98–7.27 (m, 8H, Ar), 7.64 (d, J = 2 Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.6 (CHCH$_3$), 20.56 (2 × ArCH$_3$), 22.0 (CHCH$_3$), 29.6 (CHMe$_2$), 38.0 (PhCH), 40.2 (CH$_2$CO$_2$), 40.3 (CH$_2$CON), 51.3 (CO$_2$CH$_3$), 55.2 (ArOCH$_3$), 55.9 (ArOCH$_3$), 61.9 (NCH), 88.9 (Ar$_2$CO-CO), 110.9 (HC$_{-Ar}$), 113.9 (HC$_{-Ar}$), 126.3 (C$_{-Ar}$), 126.6 HC$_{-Ar}$), 127.2 (2 × HC$_{-Ar}$), 127.4 (HC$_{-Ar}$), 127.8 (C$_{-Ar}$), 128.3 (2 × HC$_{-Ar}$), 128.6 (HC$_{-Ar}$), 128.8 (C$_{-Ar}$), 128.9 (C$_{-Ar}$), 129.0 (HC$_{-Ar}$), 130.1 (HC$_{-Ar}$), 142.5 (*ipso*-C$_{-Ph}$), 152.6 (MeOC$_{-Ar}$), 153.3 (MeOC$_{-Ar}$), 156.2 (NCO$_2$), 171.0 (CO$_2$Me), 171.9 (CON).

4.4. (3′*R*,4*S*)-5,5-Di(2-methoxy-5-methylphenyl)-3-[3-(4-fluorophenyl)-4-methoxycarbonyl-1-oxobutyl]-4-isopropyloxazolidin-2-one 3g and its (3′*S*)-diastereoisomer 4g

Following the general procedure described for the desymmetrization of **1a** with **2e**, anhydride **1c** (167 mg, 0.8 mmol) and oxazolidin-2-one **2e** (275 mg, 0.75 mmol) gave a product which was crystallized from hexane–ethyl acetate to give methyl ester **3g** (308 mg, 70%) contaminated with 5% of its diastereoisomer **4g**. Data for **3g**: mp 95–98 °C; $[\alpha]_D^{23} = -173.1$ (c 0.84, MeOH); R_f = 0.46 (hexane/ethyl acetate 85/15); IR (KBr): 1765, 1736, 1706, 1504 cm^{-1}; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 0.69 (d, J = 6.6 Hz, 3H, CH_3CHCH$_3$), 0.88 (d, J = 6.6 Hz, 3H, CH$_3$CHCH_3), 1.55–1.70 (m, 1H, CH$_3$CHCH$_3$), 2.02 (s, 3H, ArCH_3), 2.34 (s, 3H, ArCH_3), 2.53 (dd, J = 8.2, 15.6 Hz,1H, CH_AH$_B$CO$_2$Me), 2.65 (dd, J = 6.8, 15.4 Hz, 1H, CH$_A$$H_BCO_2$Me), 3.16 (dd, J = 5.6, 17.2 Hz, 1H, NCOCH_AH$_B$), 3.36 (dd, J = 9.2, 17.2 Hz, 1H, NCOCH$_A$$H_B$), 3.39 (s, 3H, ArOC$H_3$), 3.42 (s, 3H, ArOC$H_3$), 3.56 (s, 3H, COOC$H_3$), 3.66–3.84 (m, 1H, ArC$H$), 5.70 (d, J = 1.8 Hz, 1H, NCH), 6.59 (d, J = 8.2 Hz, 1H, Ar), 6.62 (d, J = 8.4 Hz, 1H, Ar), 6.79–7.04 (m, 5H, Ar), 7.09–7.16 (m, 2H, Ar), 7.65 (d, J = 2Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.9 (CHCH$_3$), 20.4 (ArCH$_3$), 20.6 (ArCH$_3$), 22.4 (CHCH$_3$), 29.8 (CHMe$_2$), 36.8 (ArCH), 40.4 (CH$_2$CO$_2$), 41.0 (CH$_2$CON), 51.4 (CO$_2$$CH_3$), 55.3 (ArO$CH_3$), 55.8 (ArO$CH_3$), 62.0 (N$C$H), 89.2 (Ar$_2$$C$OCO), 111.0 (HC$_{-Ar}$), 113.6 (HC$_{-Ar}$), 115.1 (d, J = 21.1 Hz, 2 × HC$_{-Ar}$), 126.4 (C$_{-Ar}$), 127.3 (HC$_{-Ar}$), 127.6 (C$_{-Ar}$), 128.5 (HC$_{-Ar}$), 128.7 (HC$_{-Ar}$), 128.8 (C$_{-Ar}$), 128.9 (C$_{-Ar}$), 129.1 (2 × HC$_{-Ar}$), 130.0 (HC$_{-Ar}$), 138.3 (*ipso*-C$_{-Ar}$), 152.6 (MeOC$_{-Ar}$), 153.5 (MeOC$_{-Ar}$), 156.0 (NCO$_2$), 161.4 (d, J = 243 Hz, FC$_{-Ar}$), 170.6 (CO$_2$Me), 171.8 (CON); ESI MS: m/z (%) = 592 (10) (M$^+$+H), 548 (100); HRMS: Calcd for $C_{34}H_{39}NO_7F$ (M$^+$+H) 592.2711. Found: 592.2715.

Following the general procedure described for the model synthesis of a mixture of **3e** and **4e** from **1a** and **2e**, anhydride **1c** (208 mg, 1 mmol) and oxazolidin-2-one **2e** (369 mg, 1 mmol) gave an inseparable 1:1 mixture of diastereoisomeric methyl esters **3g** and **4g** (437 mg, 74%) as a colourless oil. Data for **4g** (obtained from the mixture): R_f = 0.46 (hexane/ethyl acetate 85/15); ^{1}H NMR (CDCl$_3$, 200 MHz) δ 0.51 (d, J = 6.8 Hz, 3H, CH_3CHCH$_3$), 0.66 (d, J = 6.8 Hz, 3H, CH$_3$CHCH_3), 1.48–1.70 (m, 1H, CH$_3$CHCH$_3$), 2.34 (s, 6H, 2 × ArCH_3), 2.47–2.68 (m, 2H, CH_2CO$_2$Me), 2.97 (dd, J = 6.8, 16.6 Hz, 1H, NCOCH_AH$_B$), 3.39–3.49 (dd, overlapped, 1H, NCOCH_AH$_B$), 3.45 (s, 3H, ArOCH_3), 3.48 (s, 3H, ArOCH_3), 3.52 (s, 3H, COOCH_3), 3.66–3.84 (m, 1H, ArCH), 5.73 (d, J = 1.8 Hz, 1H, NCH), 6.57–7.26 (m, 9H, Ar), 7.65 (d, J = 2Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.3 (CHCH$_3$), 20.3 (2 × ArCH$_3$), 21.8 (CHCH$_3$), 29.3 (CHMe$_2$), 37.2 (ArCH), 40.1 (CH$_2$CO$_2$, CH$_2$CON), 51.1 (CO$_2$CH$_3$), 54.9 (ArOCH$_3$), 55.5 (ArOCH$_3$), 61.7 (NCH), 88.9 (Ar$_2$$C$OCO), 110.7 (HC$_{-Ar}$), 113.5 (HC$_{-Ar}$), 114.8 (d, J = 21.1 Hz, 2 × HC$_{-Ar}$), 126.0 (C$_{-Ar}$), 127.0 (HC$_{-Ar}$), 127.3 (C$_{-Ar}$), 128.5 (HC$_{-Ar}$), 128.7 (HC$_{-Ar}$), 128.6 (2 × C$_{-Ar}$), 128.9 (2 × HC$_{-Ar}$), 129.9 (HC$_{-Ar}$), 138.1 (*ipso*-C$_{-Ar}$), 152.4 (MeOC$_{-Ar}$), 153.1 (MeOC$_{-Ar}$), 156.0 (NCO$_2$), 161.3 (d, J = 243 Hz, FC$_{-Ar}$), 170.6 (CO$_2$Me), 171.4 (CON).

4.5. (3′*R*,4*S*)-5,5-Di(2-methoxy-5-methylphenyl)-3-(3-isopropyl-4-methoxycarbonyl-1-oxobutyl)-4-isopropyloxazolidin-2-one 3h and its (3′*S*)-diastereoisomer 4h

Following the general procedure described for the desymmetrization of **1a** with **2e**, anhydride **1d** (125 mg, 0.8 mmol) and oxazolidin-2-one **2e** (275 mg, 0.75 mmol) gave methyl ester **3h** (295 mg, 73%) as an inseparable mixture containing 10% of its diastereoisomer **4h**. Data for **3h**: $[\alpha]_D^{24} = -188.3$ (c 0.44, EtOH); R_f = 0.45 (hexane/ethyl acetate 85/15); IR ($CHCl_3$ film): 1777, 1735, 1700, 1502 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.67 (d, J = 7 Hz, 3H, CH_3CHCH$_3$), 0.71 (d, J = 6.6 Hz, 3H, CH$_3$CHCH_3), 0.82 (d, J = 6.8 Hz, 3H, CH_3CHCH$_3$), 0.96 (d, J = 7 Hz, 3H, CH$_3$CHCH_3), 1.56–1.80 (m, 2H, 2 × CH$_3$CHCH$_3$), 2.19–2.25 (m, 1H, Me$_2$CHCH), 2.22 (s, 3H, ArCH$_3$), 2.31–2.49 (m, 2H, CH_2CO$_2$Me), 2.34 (s, 3H, ArCH$_3$), 2.80 (dd, J = 6.2 Hz, J = 17.2 Hz, 1H, CH_AH$_B$CON), 2.92 (dd, J = 6.8 Hz, J = 17.2 Hz, 1H, CH$_A$$H_B$CON), 3.46 (s, 3H, ArOC$H_3$), 3.47 (s, 3H, ArOC$H_3$), 3.62 (s, 3H, CO$_2CH_3$), 5.76 (d, J = 2 Hz, 1H, NCH), 6.61 (d, J = 8.2 Hz, 1H, Ar), 6.67 (d, J = 8.4 Hz, 1H, Ar), 6.96–7.06 (m, 2H, Ar), 7.18 (d, J = 2.2 Hz, 1H, Ar), 7.68 (d, J = 1.8 Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.0 (CHCH$_3$), 18.2 (CHCH$_3$), 19.4 (CHCH$_3$), 20.6 (2 × ArCH$_3$), 22.5 (CHCH$_3$), 29.8 (CHMe$_2$), 29.9 (CHMe$_2$), 35.3 (CH$_2$CO$_2$), 36.4 (CH$_2$CON), 36.7 (CHCHMe$_2$), 51.5 (CO$_2$$CH_3$), 55.4 (ArO$CH_3$), 56.0 (ArO$CH_3$), 62.3 (N$C$H), 89.2 (Ar$_2$$C$OCO), 111.0 (HC$_{-Ar}$), 114.0 (HC$_{-Ar}$), 126.4 (C$_{-Ar}$), 127.2 (HC$_{-Ar}$), 128.0 (C$_{-Ar}$), 128.8 (HC$_{-Ar}$), 129.0 (2 × C$_{-Ar}$), 129.1 (HC$_{-Ar}$), 130.1 (HC$_{-Ar}$), 152.7 (MeOC$_{-Ar}$), 153.6 (MeOC$_{-Ar}$), 156.3 (NCO$_2$), 172.3 (CO$_2$Me), 173.5 (CON). ESI MS: m/z (%) = 540 (43) (M$^+$+H), 496 (100). HRMS: Calcd for $C_{31}H_{42}NO_7$ (M$^+$+H) 540.2961. Found: 540.2946.

Following the general procedure described for the model synthesis of a mixture of **3e** and **4e** from **1a** and **2e**, anhydride **1d** (156 mg, 1 mmol) and oxazolidin-2-one **2e** (369 mg, 1 mmol) gave an inseparable 1:1 mixture of diastereoisomeric methyl esters **3h** and **4h** (399 mg, 74%) as a colourless oil. Data for **4h** (obtained from mixture): R_f = 0.45 (hexane/ethyl acetate 85/15); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.71 (d, J = 6.8 Hz, 3H, CH_3CHCH$_3$), 0.80 (d, J = 6.8 Hz, 3H, CH$_3$CHCH_3), 0.89 (d, J = 7.2 Hz, 3H, CH_3CHCH$_3$), 0.95 (d, J = 7.2 Hz, 3H, CH$_3$CHCH_3), 1.56–1.80 (m, 2H, 2 × CH$_3$CHCH$_3$), 2.19–2.25 (m, 1H, Me$_2$CHCH), 2.22 (s, 3H, ArCH$_3$), 2.31–2.49 (m, 2H, CH_2CO$_2$Me), 2.34 (s, 3H, ArCH$_3$), 2.65–2.98 (m, 2H, CH_2CON), 3.46 (s, 3H, ArOCH_3), 3.47 (s, 3H, ArOCH_3), 3.56 (s, 3H, CO$_2$CH$_3$), 5.77 (d, J = 2 Hz, 1H, NCH), 6.61 (d, J = 8.2 Hz, 1H, Ar), 6.67 (d, J = 8.4 Hz, 1H, Ar), 6.96–7.06 (m, 2H, Ar), 7.18 (d, J = 2.2 Hz, 1H, Ar), 7.68 (d, J = 1.8 Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.8 (CHCH$_3$), 18.6 (CHCH$_3$), 19.2 (CHCH$_3$), 20.4 (2 × ArCH$_3$), 22.3 (CHCH$_3$), 29.6 (CHMe$_2$), 29.8 (CHMe$_2$), 35.2 (CH$_2$CO$_2$), 35.8 (CH$_2$CON), 37.0 (CHCHMe$_2$), 51.1 (CO$_2$$CH_3$), 55.1 (ArO$CH_3$), 55.7 (ArO$CH_3$), 62.0 (N$C$H), 88.9 (Ar$_2$$C$OCO), 110.8 (HC$_{-Ar}$), 113.6 (HC$_{-Ar}$), 126.2 (C$_{-Ar}$), 127.1 (HC$_{-Ar}$), 127.7 (C$_{-Ar}$), 128.5 (HC$_{-Ar}$), 128.7 (2 × C$_{-Ar}$), 129.0 (HC$_{-Ar}$), 129.9 (HC$_{-Ar}$), 152.5 (MeOC$_{-Ar}$), 153.3 (MeOC$_{-Ar}$), 156.1 (NCO$_2$), 172.2 (CO$_2$Me), 173.0 (CON).

4.6. (3′*R*,4*S*)-5,5-Di(2-methoxy-5-methylphenyl)-3-(4-methoxycarbonyl-3-methyl-1-oxobutyl)-4-isopropyloxazolidin-2-one 3i and its (3′*S*)-diastereoisomer 4i

Following the general procedure described for the desymmetrization of **1a** with **2e**, anhydride **1e** (70 mg, 0.55 mmol) and

oxazolidin-2-one **2e** (185 mg, 0.5 mmol) gave methyl ester **3i** (188 mg, 74%) as an inseparable mixture containing 19% of its diastereoisomer **4i**. Recrystallization from hexane–ethyl acetate gave the methyl ester **3i** (124 mg, 49%) as an inseparable mixture containing 6% of its diastereoisomer **4i**. Data for **3i**: mp 82–84 °C; $[\alpha]_D^{23} = -198.55$ (*c* 0.69, EtOH); $R_f = 0.53$ (hexane/ethyl acetate 85/15); IR ($CHCl_3$ film): 1779, 1736, 1698, 1503 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.71 (d, $J = 6.8$ Hz, 3H, CH_3CHCH$_3$), 0.92 (d, $J = 6.8$ Hz, 3H, CH$_3$CHCH_3), 0.95 (d, $J = 7.2$ Hz, 3H, CHCH_3) 1.63–1.77 (m, 1H, CH$_3$CHCH$_3$), 2.18–2.60 (m, 3H, CH_2CO$_2$Me, MeCH), 2.23 (s, 3H, ArCH_3), 2.34 (s, 3H, ArCH_3), 2.75 (dd, $J = 7.4$, 16.6 Hz, 1H, NCOCH_AH$_B$), 2.90 (dd, $J = 6$, 16.6 Hz, 1H, NCOCH$_A$$H_B$), 3.47 (s, 3H, ArOC$H_3$), 3.48 (s, 3H, ArOC$H_3$), 3.64 (s, 3H, COOC$H_3$), 5.77 (d, $J = 1.2$ Hz, 1H, NCH), 6.62 (d, $J = 8.2$ Hz, 1H, Ar), 6.68 (d, $J = 8.4$ Hz, 1H, Ar), 6.97–7.07 (m, 2H, Ar), 7.18 (d, $J = 2$Hz, 1H, Ar), 7.68 (d, $J = 2$ Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.1 (CHCH_3), 19.5 (CHCH_3), 20.7 (2 × ArCH_3), 22.6 (CHCH_3), 26.9 (CHMe), 29.8 (CHMe$_2$), 40.7 (CH_2CO$_2$), 41.2 (CH_2CON), 51.4 (CO$_2$CH_3), 55.4 (ArOCH_3), 56.0 (ArOCH_3), 62.1 (NCH), 89.2 (Ar$_2$CO-CO), 111.1 (HC$_{-Ar}$), 114.0 (HC$_{-Ar}$), 126.5 (C$_{-Ar}$), 127.3 (HC$_{-Ar}$), 128.0 (HC$_{-Ar}$), 128.8 (C$_{-Ar}$), 129.0 (C$_{-Ar}$, HC$_{-Ar}$), 129.2 (C$_{-Ar}$), 130.1 (HC$_{-Ar}$), 152.7 (MeOC$_{-Ar}$), 153.5 (MeOC$_{-Ar}$), 156.3 (NCO$_2$), 171.8 (CO$_2$Me), 172.8 (CON). Anal. Calcd for $C_{29}H_{37}NO_7$: C, 68.08; H, 7.29; N, 2.74. Found: C, 67.81; H, 7.23; N, 2.68.

Following the general procedure described for the model synthesis of a mixture of **3e** and **4e** from **1a** and **2e**, anhydride **1e** (128 mg, 1 mmol) and oxazolidin-2-one **2e** (369 mg, 1 mmol) gave an inseparable 1:1 mixture of diastereoisomeric methyl esters **3i** and **4i** (368 mg, 72%) as a colourless oil. Data for **4i** (obtained from mixture): $R_f = 0.53$ (hexane/ethyl acetate 85/15); ^1H NMR (200 MHz, $CDCl_3$) δ 0.71 (d, $J = 6.8$ Hz, 3H, CH_3CHCH$_3$), 0.95 (d, $J = 6.8$ Hz, 3H, CH$_3$CHCH_3), 0.97 (d, $J = 7.2$ Hz, 3H, CHCH_3) 1.63–1.77 (m, 1H, CH$_3$CHCH$_3$), 2.18–2.60 (m, 3H, CH_2CO$_2$Me, MeCH), 2.23 (s, 3H, ArCH_3), 2.34 (s, 3H, ArCH_3), 2.75 (dd, $J = 7.4$, 16.6 Hz, 1H, NCOCH_AH$_B$), 2.90 (dd, $J = 6$, 16.6 Hz, 1H, NCOCH$_A$$H_B$), 3.47 (s, 6H, 2 × ArOC$H_3$), 3.58 (s, 3H, COOC$H_3$), 5.78 (d, $J = 1.2$ Hz, 1H, NCH), 6.62 (d, $J = 8.2$ Hz, 1H, Ar), 6.68 (d, $J = 8.4$ Hz, 1H, Ar), 6.97–7.07 (m, 2H, Ar), 7.18 (d, $J = 2$Hz, 1H, Ar), 7.68 (d, $J = 2$ Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.9 (CHCH_3), 19.5 (CHCH_3), 20.5 (2 × ArCH_3), 22.4 (CHCH_3), 26.9 (CHMe), 29.7 (CHMe$_2$), 40.2 (CH_2CO$_2$), 40.9 (CH_2CON), 51.2 (CO$_2$CH_3), 55.3 (ArOCH_3), 55.9 (ArOCH_3), 62.0 (NCH), 89.0 (Ar$_2$COCO), 110.9 (HC$_{-Ar}$), 113.8 (HC$_{-Ar}$), 127.2, 128.15 (2C), 128.6, 128.9 (2C), 129.0, 130.0, 152.6 (MeOC$_{-Ar}$), 153.4 (MeOC$_{-Ar}$), 156.2 (NCO$_2$), 171.7 (CO$_2$Me), 172.6 (CON).

4.7. (3′*R*,4*S*)-3-{3-[Dimethyl(phenyl)silyl]-4-methoxycarbonyl-1-oxobutyl}-5,5-diphenyl-4-isopropyloxazolidin-2-one 3d and its (3′*S*)-diastereoisomer 4d

Following the general procedure described for the desymmetrization of **1a** with **2e**, anhydride **1a** (1.36 g, 5.5 mmol) and oxazolidin-2-one **2d** (1.405 g, 5 mmol) gave methyl esters **3d** (2.17 g, 80%) as an inseparable mixture containing 10% of its diastereoisomer **4d** as colourless oil. Data for **3d**: $[\alpha]_D^{25} = -92.85$ (*c* 0.28, EtOH); $R_f = 0.56$ (hexane/ethyl acetate, 85/15); IR ($CHCl_3$ film): 1780, 1733, 1714, 1253, 1111 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.18 (s, 6H, Me$_2$Si), 0.72 (d, $J = 6.6$ Hz, 3H, CH_3CHCH$_3$), 0.86 (d, $J = 6.8$ Hz, 3H, CH$_3$CHCH_3), 1.80–2.00 (m, 2H, CH$_3$CHCH$_3$ and SiCH), 2.15 (dd, $J = 8$, 15.8 Hz, 1H, CH_AH$_B$CO$_2$Me), 2.32 (dd, $J = 6.2$, 15.8 Hz, 1H, CH$_A$$H_BCO_2$Me), 2.82–3.00 (m, 2H, NCOCH_2), 3.47 (s, 3H, COOCH_3), 5.34 (d, $J = 3.4$ Hz, 1H, NCH), 7.22–7.49 (m, 15H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.8 (SiCH$_3$), −4.2 (SiCH$_3$), 16.3 (SiCH), 17.3 (CHCH$_3$), 21.6 (CHCH$_3$), 29.8 (CHMe$_2$), 34.3 (CH$_2$CO$_2$), 35.3 (CH$_2$CON), 51.3 (CO$_2$CH$_3$), 64.8 (NCH), 89.3 (Ar$_2$COCO), 125.5 (2 × HC$_{-Ar}$), 125.9 (2 × HC$_{-Ar}$), 127.7 (2 × HC$_{-Ar}$), 127.9 (HC$_{-Ar}$), 128.3 (2 × HC$_{-Ar}$), 128.5 (HC$_{-Ar}$), 128.8 (2 × HC$_{-Ar}$), 129.2 (HC$_{-Ar}$), 133.9 (2 × HC$_{-Ar}$), 136.7 (SiC$_{-Ar}$), 138.1 (*ipso*-C$_{-Ar}$), 142.4 (*ipso*-C$_{-Ar}$), 153.0 (NCO$_2$), 172.4 (CO$_2$Me), 173.5 (CON). Anal. Calcd for $C_{32}H_{37}NO_5Si$: C, 70.69; H, 6.86; N, 2.54. Found: C, 70.84; H, 6.94; N, 2.33.

Following the general procedure described for the model synthesis of a mixture of **3e** and **4e** from **1a** and **2e**, anhydride **1a** (124 mg, 0.5 mmol) and oxazolidin-2-one **2d** (141 mg, 0.5 mmol) gave an inseparable 1:1 mixture of diastereoisomeric methyl esters **3d** and **4d** (193 mg, 71%) as colourless oil. Data for **4i** (obtained from mixture): $R_f = 0.56$ (hexane/ethyl acetate, 85/15); ^1H NMR (200 MHz, $CDCl_3$) δ 0.27 (s, 3H, MeSi), 0.30 (s, 3H, MeSi), 0.71 (d, $J = 6.6$ Hz, 3H, CH_3CHCH$_3$), 0.84 (d, $J = 6.8$ Hz, 3H, CH$_3$CHCH_3), 1.80–2.00 (m, 2H, CH$_3$CHCH$_3$ and SiCH), 2.18–2.40 (m, 2H, CH_2CO$_2$Me), 2.72 (dd, $J = 9.2$, 17.2 Hz, 1H, CH_AH$_B$CON), 3.0 (dd, $J = 4$, 17.2 Hz, 1H, CH$_A$$H_B$CON), 3.36 (s, 3H, COOC$H_3$), 5.35 (d, $J = 3.2$ Hz, 1H, NCH), 7.22–7.49 (m, 15H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.7 (SiCH$_3$), −4.3 (SiCH$_3$), 16.2 (SiCH), 17.9 (CHCH$_3$), 21.6 (CHCH$_3$), 29.8 (CHMe$_2$), 34.1 (CH$_2$CO$_2$), 35.1 (CH$_2$CON), 51.1 (CO$_2$CH$_3$), 64.5 (NCH), 89.2 (Ar$_2$COCO), 125.4 (2 × HC$_{-Ar}$), 125.8 (2 × HC$_{-Ar}$), 127.7 (2 × HC$_{-Ar}$), 127.9 (HC$_{-Ar}$), 128.3 (2 × HC$_{-Ar}$), 128.5 (HC$_{-Ar}$), 128.8 (2 × HC$_{-Ar}$), 129.2 (HC$_{-Ar}$), 133.9 (2 × HC$_{-Ar}$), 136.7 (SiC$_{-Ar}$), 138.1 (*ipso*-C$_{-Ar}$), 142.2 (*ipso*-C$_{-Ar}$), 153.0 (NCO$_2$), 172.5 (CO$_2$Me), 173.3 (CON).

4.8. (3′*R*,4*S*)-3-{3-[Dimethyl(phenyl)silyl]-4-methoxycarbonyl-1-oxobutyl}-4-(diphenylmethyl) oxazolidin-2-one 3c and its (3′*S*)-diastereoisomer 4c

Following the general procedure described for the desymmetrization of **1a** with **2e**, anhydride **1a** (160 mg, 0.64 mmol) and oxazolidin-2-one **2c** (165 mg, 0.65 mmol) gave methyl esters **3c** (294 mg, 89%) as an inseparable mixture containing 23% of its diastereoisomer **4c**. The major and minor diastereoisomers were separated by chromatography to give pure major diastereoisomer **3c** (218 mg, 66%) and minor isomer **4c** (71 mg, 22%). Data for major diastereoisomer **3c**: mp 113–114 °C; $[\alpha]_D^{23} = -91.8$ (*c* 1, EtOH); $R_f = 0.25$ (hexane/ethyl acetate 90/10); IR ($CHCl_3$ film): 1782, 1732, 1698, 1251, 1112 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.32 (s, 6H, Me$_2$Si), 1.88–2.02 (m, 1H, SiCH), 2.20 (dd, $J = 8.6$, 16.2 Hz, 1H, CH_AH$_B$CO$_2$Me), 2.36 (dd, $J = 5.2$, 16.2 Hz, 1H, CH$_A$$H_BCO_2$Me), 2.50 (dd, $J = 9.4$, 16.4 Hz, 1H, NCOCH_AH$_B$), 3.24 (dd, $J = 4.6$, 16.4 Hz, 1H, NCOCH$_A$$H_B$), 3.58 (s, 3H, COOC$H_3$), 4.31 (dd, $J = 2.8$, 9 Hz, 1H, OCH_AH$_B$CH), 4.39 (dd, $J = 9$, 9 Hz, 1H, OCH$_A$$H_B$CH), 4.61 (d, $J = 5.6$ Hz, 1H, PhCHPh), 5.06–5.14 (m, 1H, CONCH), 7.06–7.11 (m, 4H, Ar), 7.25–7.37 (m, 9H, Ar), 7.46–7.52 (m, 2H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.8 (2 × SiCH$_3$), 17.5 (SiCH), 33.9 (CH$_2$CO$_2$), 35.8 (CH$_2$CON), 50.8 (Ph$_2$CH), 51.4 (CO$_2$CH$_3$), 56.3 (OCH$_2$), 64.9 (NCH), 126.8 (HC$_{-Ar}$), 127.6 (HC$_{-Ar}$), 127.7 (2 × HC$_{-Ar}$), 128.2 (2 × HC$_{-Ar}$), 128.5 (2 × HC$_{-Ar}$), 128.7 (2 × HC$_{-Ar}$), 129.1 (3 × HC$_{-Ar}$), 134.0 (2 × HC$_{-Ar}$), 136.5 (SiC$_{-Ar}$), 138.2 (*ipso*-C$_{-Ar}$), 139.7 (*ipso*-C$_{-Ar}$), 153.3 (NCO$_2$), 172.4 (CO$_2$Me), 173.8 (CON). HRMS: Calcd for $C_{30}H_{33}NO_5NaSi$ (M^++Na) 538.2026. Found: 538.2031. Data for minor diastereoisomer **4c**: $[\alpha]_D^{26} = -118$ (*c* 1.56, EtOH), $R_f = 0.19$ (hexane/ethyl acetate 90/10); IR ($CHCl_3$ film): 1782, 1732, 1699, 1251, 1112 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.32 (s, 3H, MeSi), 0.33 (s, 3H, MeSi), 1.88–2.04 (m, 1H, SiCH), 2.21 (dd, $J = 8$, 15.4 Hz, 1H, CH_AH$_B$CO$_2$Me), 2.39 (dd, $J = 6$, 15.4 Hz, 1H, CH$_A$$H_BCO_2$Me), 2.76 (dd, $J = 3.8$, 17.6 Hz, 1H, NCOCH_AH$_B$), 3.05 (dd, $J = 9.2$, 17.6 Hz, 1H, NCOCH$_A$$H_B$), 3.55 (s, 3H, COOC$H_3$), 4.29–4.42 (m, 2H, C$H_2$OCO), 4.62 (d, $J = 5.6$ Hz, 1H, Ph$_2$CH), 5.16–5.24 (m, 1H, CHN), 7.03–7.08 (m, 4H, Ar), 7.22–7.28 (m, 6H, Ar), 7.35–7.40 (m, 3H, Ar), 7.48–7.52 (m, 2H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.6 (SiCH$_3$), −4.4 (SiCH$_3$), 17.6 (SiCH), 34.6 (CH$_2$CO$_2$), 35.4 (CH$_2$CON), 50.7 (Ph$_2$CH), 51.5 (CO$_2$CH$_3$), 56.3 (OCH$_2$), 65.0 (NCH), 127.0 (HC$_{-Ar}$), 127.7 (HC$_{-Ar}$), 127.8 (2 × HC$_{-Ar}$), 128.3 (2 × HC$_{-Ar}$),

128.6 (2 × HC$_{-Ar}$), 128.8 (2 × HC$_{-Ar}$), 129.2 (2 × HC$_{-Ar}$), 129.3 (HC$_{-Ar}$), 134.1 (2 × HC$_{-Ar}$), 136.8 (SiC$_{-Ar}$), 138.1 (*ipso*-C$_{-Ar}$), 139.6 (*ipso*-C$_{-Ar}$), 153.4 (NCO$_2$), 172.6 (CO$_2$Me), 173.9 (CON). Calcd for $C_{30}H_{33}NO_5NaSi$ (M^++Na) 538.2026. Found: 538.2021.

4.9. (3′*R*,4*S*)-3-{4-*tert*-Butoxyoxycarbonyl-3-[dimethyl(phenyl)-silyl]-1-oxobutyl}-5,5-di(2-methoxy-5-methylphenyl)-4-isopropyloxazolidin-2-one 5

Dry DMF (0.01 mL, 0.13 mmol) was added to a solution of the mixture of acids corresponding to methyl esters **3e** and **4e** (**3e**/**4e** = 95/5) (0.62 g, 1 mmol) in dry dichloromethane (10 mL) followed by the addition of oxalyl chloride (0.26 mL, 3 mmol) at 0 °C under an argon atmosphere. After 2 h at room temperature, the reaction mixture was concentrated under reduced pressure followed by high vacuum (0.1 Torr) to remove any excess of reagents and solvents. The residue was dissolved in dry *tert*-butanol (5 mL), cooled on ice-water bath and a solution of DMAP (0.18 g, 1.5 mmol) in dry *tert*-butanol (5 mL) was cannulated into it. The mixture was stirred overnight at room temperature and was evaporated under reduced pressure. The residue was purified by column chromatography followed by crystallization from hexane–ethyl acetate to give the ester **5** (0.47 g, 70%) as colourless crystals (de = >95% from NMR). Mp 125–128 °C; $[\alpha]_D^{21} = -165.9$ (*c* 0.64, $CHCl_3$); R_f = 0.65 (hexane/ethyl acetate 85/15); IR ($CHCl_3$ film): 1774, 1724, 1705, 1503, 1255, 1114 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.24 (s, 3H, SiMe), 0.25 (s, 3H, SiMe), 0.68 (d, *J* = 6.8 Hz, 3H, C*H*$_3$CHCH$_3$), 0.96 (d, *J* = 7 Hz, 3H, CH$_3$CHC*H*$_3$), 1.35 (s, 9H, *t*-Bu), 1.62–1.80 (m, 1H, CH$_3$C*H*CH$_3$), 1.90–2.07 (m, 1H, SiCH), 2.14 (dd, *J* = 8.4, 15.8 Hz, 1H, C*H*$_A$H$_B$CO$_2$Bu-*t*), 2.22 (s, 3H, ArC*H*$_3$), 2.31 (dd, *J* = 5.4, 15.8 Hz, 1H, CH$_A$*H*$_B$CO$_2$Bu-*t*), 2.34 (s, 3H, ArC*H*$_3$), 2.91 (dd, *J* = 6, 18.6 Hz, 1H, NCOC*H*$_A$H$_B$), 3.02 (dd, *J* = 6, 18.6 Hz, 1H, NCOCH$_A$*H*$_B$), 3.46 (s, 6H, ArOC*H*$_3$), 5.77 (d, *J* = 2 Hz, 1H, NC*H*), 6.62 (d, *J* = 8 Hz, 1H, Ar), 6.68 (d, *J* = 8 Hz, 1H, Ar), 7.01 (dt, *J* = 1.8, 8 Hz, 2H, Ar), 7.21 (d, *J* = 1.8 Hz, 1H, Ar), 7.27–7.31 (m, 3H, Ar), 7.43–7.49 (m, 2H, Ar), 7.68 (d, *J* = 1.8 Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.4 (Si*C*H$_3$), −3.8 (Si*C*H$_3$), 15.9 (Si*C*H), 16.7 (CH*C*H$_3$), 20.6 (Ar*C*H$_3$), 20.7 (Ar*C*H$_3$), 22.5 (CH*C*H$_3$), 27.9 (3 × *C*H$_{3\text{-}t\text{-}Bu}$), 29.9 (*C*HMe$_2$), 35.3 (*C*H$_2$CO$_2$), 35.7 (*C*H$_2$CON), 55.3 (ArOCH$_3$), 55.9 (ArOCH$_3$), 62.1 (N*C*H), 80.0 (Me$_3$*C*O), 88.8 (Ar$_2$*C*O-CO), 111.0 (HC$_{-Ar}$), 113.9 (HC$_{-Ar}$), 126.5 (C$_{-Ar}$), 127.3 (HC$_{-Ar}$), 127.7 (HC$_{-Ar}$, C$_{-Ar}$), 128.0 (HC$_{-Ar}$), 128.8 (HC$_{-Ar}$), 128.9 (C$_{-Ar}$, 2 × HC$_{-Ar}$), 129.0 (C$_{-Ar}$), 130.0 (HC$_{-Ar}$), 133.9 (2 × HC$_{-Ar}$), 137.4 (SiC$_{-Ar}$), 152.6 (MeOC$_{-Ar}$), 153.3 (MeOC$_{-Ar}$), 156.2 (NCO$_2$), 172.5 (*C*O$_2$Bu-*t*), 172.6 (*C*ON). Anal. Calcd for $C_{39}H_{51}NO_7Si$: C, 69.51; H, 7.63; N, 2.08. Found: C, 69.66; H, 7.66; N, 2.04.

4.10. (3*R*)-Benzyl *tert*-butyl 3-[dimethyl(phenyl)silyl]pentane-1,5-dioate 6

Titanium tetrakis benzyl alkoxide (0.375 M in benzyl alcohol, 2 mL, 0.75 mmol) was added to the *tert*-butyl ester **5** (336 mg, 0.5 mmol) and the mixture was heated at 100 °C for 28 h. The mixture was cooled to room temperature and water was added under stirring. The resulting mixture was filtered through a pad of Celite and the filtrate was evaporated. The benzyl alcohol was removed under reduced pressure and the residue was chromatographed to give ester **6**[36] (160 mg, 78%); R_f = 0.64 (hexane/ethyl acetate, 95/5); $[\alpha]_D^{22} = +1.15$ (*c* 2.08, MeOH); IR ($CHCl_3$ film): 1733, 1251, 1112 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.32 (s, 6H, SiMe$_2$), 1.42 (s, 9H, *t*-Bu), 1.85–1.99 (m, 1H, SiCH), 2.16–2.53 (m, 4H, 2 × CH$_2$COO), 5.03 (s, 2H, ArC*H*$_2$), 7.34–7.37 (m, 8H, Ar), 7.49–7.54 (m, 2H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.5 (Si*C*H$_3$), −4.3 (Si*C*H$_3$), 18.5 (Si*C*H), 28.1 (3 × *C*H$_{3\text{-}t\text{-}Bu}$), 34.6 (*C*H$_2$CO$_2$), 35.6 (*C*H$_2$CO$_2$), 66.2 (PhCH$_2$O), 80.3 (Me$_3$*C*O), 127.9 (2 × HC$_{-Ar}$), 128.1 (HC$_{-Ar}$), 128.3 (2 × HC$_{-Ar}$), 128.5 (2 × HC$_{-Ar}$), 129.3 (HC$_{-Ar}$), 134.0 (2 × HC$_{-Ar}$), 136.0 (C$_{-Ar}$), 136.9 (C$_{-Ar}$), 172.5 (*C*O$_2$Bu-*t*), 173.1 (*C*O$_2$Bn).

4.11. (3′*R*,4*S*)-3-{4-*tert*-Butoxyoxycarbonyl-3-(4-fluorophenyl)-1-oxobutyl}-5,5-di(2-methoxy-5-methylphenyl)-4-isopropyloxazolidin-2-one 8

Following the procedure described for the preparation of *tert*-butyl ester **5**, a mixture of acids corresponding to methyl esters **3g** and **4g** (415 mg, 0.71 mmol, **3g**:**4g** = 95:5) gave the *tert*-butyl ester **8** (0.39 g, 86%) after crystallization from hexane. Mp 71–73 °C; $[\alpha]_D^{23} = -157$ (*c* 1, EtOH); R_f = 0.63 (hexane/ethyl acetate, 85/15); IR ($CHCl_3$ film): 1775, 1724, 1704, 1606, 1510 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.68 (d, *J* = 6.6 Hz, 3H, C*H*$_3$CHCH$_3$), 0.89 (d, *J* = 7 Hz, 3H, CH$_3$CHC*H*$_3$), 1.27 (s, 9H, *t*-Bu), 1.52–1.74 (m, 1H, CH$_3$C*H*CH$_3$), 2.02 (s, 3H, ArC*H*$_3$), 2.33 (s, 3H, ArC*H*$_3$), 2.43 (dd, *J* = 8.8, 15 Hz, 1H, C*H*$_A$H$_B$CO$_2$Bu-*t*), 2.57 (dd, *J* = 6.6, 15 Hz, 1H, CH$_A$*H*$_B$CO$_2$Bu-*t*), 3.12 (dd, *J* = 5.4, 17 Hz, 1H, NCOC*H*$_A$H$_B$), 3.34 (dd, *J* = 9 Hz,17 Hz, 1H, NCOCH$_A$*H*$_B$), 3.37 (s, 3H, ArOC*H*$_3$), 3.40 (s, 3H, ArOC*H*$_3$), 3.56–3.76 (m, 1H, 4-F-PhC*H*), 5.70 (s, 1H, NCH), 6.58 (d, *J* = 8.2 Hz, 1H, Ar), 6.61 (d, *J* = 8.6 Hz, 1H, Ar), 6.78–7.03 (m, 5H, Ar), 7.09–7.16 (m, 2H, Ar), 7.64 (d, *J* = 1.8 Hz, 1H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.0 (CH*C*H$_3$), 20.4 (Ar*C*H$_3$), 20.6 (Ar*C*H$_3$), 22.4 (CH*C*H$_3$), 27.8 (3 × *C*H$_{3\text{-}t\text{-}Bu}$), 29.8 (*C*HMe$_2$), 37.1 (Ar*C*H), 40.7 (*C*H$_2$CO$_2$), 42.4 (*C*H$_2$CON), 55.3 (ArOCH$_3$), 55.8 (ArOCH$_3$), 62.0 (N*C*H), 80.5 (Me$_3$*C*O), 89.2 (Ar$_2$*C*OCO), 111.0 (HC$_{-Ar}$), 113.7 (HC$_{-Ar}$), 114.9 (d, *J* = 21 Hz, 2 × HC$_{-ArF}$), 126.5 (C$_{-Ar}$), 126.9 (C$_{-Ar}$), 127.3 (HC$_{-Ar}$), 127.7 (C$_{-Ar}$), 128.6 (HC$_{-Ar}$), 129.00 (C$_{-Ar}$, HC$_{-Ar}$), 129.1 (2 × HC$_{-Ar}$), 130.0 (HC$_{-Ar}$), 138.4 (d, *J* = 2.6 Hz, C$_{-Ar}$), 152.6 (MeOC$_{-Ar}$), 153.5 (MeOC$_{-Ar}$), 156.0 (NCO$_2$), 161.4 (d, *J* = 242 Hz, FC$_{-ArF}$), 170.7 (CON, *C*O$_2$Bu-*t*). HRMS: Calcd for $C_{37}H_{45}NO_7F$ (M^++H) 634.3180. Found: 634.3200.

4.12. (3*R*)-*tert*-Butyl methyl 3-(4-fluorophenyl)pentane-1,5-dioate 9

Aqueous sodium hydroxide solution (1 mL, 1 M, 1 mmol) was added to a stirred solution of ester **8** (0.37 g, 0.58 mmol) in MeOH–THF (1/1) (2.4 mL) at room temperature. After 2.5 h, the reaction mixture was concentrated and the residue was diluted with water (2 mL), acidified with dilute HCl and extracted with chloroform. The extract was washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was diluted with ether and the precipitate was filtered to give the oxazolidin-2-one **2e** (0.2 g, 93%). The filtrate was concentrated, esterified with an ether solution of diazomethane and concentrated under reduced pressure. The residue was purified by column chromatography followed by crystallization to give the diester **9** (0.14 g, 80%). Mp 67–69 °C; $[\alpha]_D^{24} = -1.2$ (*c* 1.17, MeOH); R_f = 0.53 (hexane/ethyl acetate, 90/10); IR ($CHCl_3$ film): 1733, 1606, 1511 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.30 (s, 9H, *t*-Bu), 2.42–2.73 (m, 4H, 2 × CH$_2$COO), 3.57 (s, 3H, OC*H*$_3$), 3.52–3.66 (m, 1H, ArC*H*), 6.91–7.01 (m, 2H, Ar), 7.14–7.26 (m, 2H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 27.7 (3 × *C*H$_{3\text{-}t\text{-}Bu}$), 37.8 (ArCH), 40.6 (*C*H$_2$CO$_2$), 41.7 (*C*H$_2$CO$_2$), 51.4 (CO$_2$*C*H$_3$), 80.5 (Me$_3$*C*O), 115.1 (d, *J* = 21.1 Hz, 2 × HC$_{-ArF}$), 128.8 (d, *J* = 7.9 Hz, 2 × HC$_{-ArF}$), 138.1 (*ipso*-C$_{-ArF}$), 161.5 (d, *J* = 243.2 Hz, FC$_{-ArF}$), 170.5 (*C*O$_2$CH$_3$), 171.8 (*C*O$_2$Bu-*t*). HRMS: Calcd for $C_{16}H_{21}O_4FNa$ (M^++Na) 319.1322. Found: 319.1323.

4.13. (3*R*)-Methyl hydrogen 3-(4-fluorophenyl)pentane-1,5-dioate 7

Trifluoroacetic acid (3.25 mL, 42.4 mmol) was added to a stirred solution of *t*-butyl ester **9** (95 mg, 0.32 mmol) in dry dichloromethane (3.25 mL) at 0 °C. After 2 h at 0 °C, the reaction mixture was concentrated under reduced pressure and the residue was purified

by column chromatography to give monomethyl ester **7**[10] (67 mg, 87%). $[\alpha]_D^{22} = -3.4$ (*c* 1.54, $CHCl_3$); IR ($CHCl_3$ film): 3460–3010 (br), 1734, 1605, 1511 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.52–2.80 (m, 4H, 2 × CH_2COO), 3.51–3.69 (m, 1H, ArC*H*), 3.56 (s, 3H, OCH_3), 6.91–7.00 (m, 2H, Ar), 7.13–7.22 (m, 2H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ 37.2 (ArCH), 40.2 (CH_2CO_2), 40.4 (CH_2CO_2), 51.7 (CO_2CH_3), 115.5 (d, J = 21.2 Hz, 2 × HC_{-ArF}), 128.7 (d, J = 7.9 Hz, 2 × HC_{-ArF}), 137.8 (d, J = 2.7 Hz, *ipso*-C_{-ArF}), 161.7 (d, J = 243.8 Hz, FC_{-ArF}), 171.9 (CO_2CH_3), 177.36 (CO_2H).

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