Asymmetric Synthesis of 2,3-Disubstituted Succinates via Chiral Oxazolidinone Controlled Displacement of α-Trifluoromethanesulfonate Substituted Esters

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The addition of chiral imides to α-trifluoromethanesulfonate esters gave chiral 2,3-disubstituted succinates with moderate to excellent diastereoselectivity and in good overall chemical yields. Both *syn* and *anti* chiral products are attainable via this methodology, with generally better diastereoselectivity and chemical yields observed in the production of the *syn* products. The reactions proceed through the predicted S_N2 displacement of the triflate leaving group, as inferred from the absolute configuration of the products.

Introduction

The chiral oxazolidinone methodology pioneered by Evans[1] is now recognized as an exceedingly valuable and practical tool for the production of optically pure compounds. Of particular note, and relevance to this study, is the excellent stereocontrol observed in the alkylation of α-bromo esters[2,3] (Scheme 1). These investigations have led to success in the enantiocontrolled production of chiral monosubstituted succinates.[4,5] However, a restriction of this methodology is the inherent unreactive nature of simple primary alkyl halides and secondary α-halo and α-tosyl esters to imide enolates, which would otherwise allow access to a broad range of chiral compounds.[6,7] Studies employing chiral imide enolates have shown that primary and secondary halides, tosylates, and mesylate are not sufficiently reactive (R^2 = alkyl, product **A**, Scheme 1) to facilitate low temperature conversion to products with appreciable stereocontrol.[7]

The poor yields obtained with alkyl halide substrates has been attributed to the inherent lack of reactivity of these electrophiles to the relatively stable imide enolates. Better yields (and stereochemical control) are observed when activating groups are employed, such as allyl and benzyl[8] which suggested to us that the use of a better leaving group should lead to higher reactivity of the electrophile, and hence to a more efficient conversion to products. Indeed, Chamberlin *et. al.* have exemplified with three examples that primary and secondary triflates efficiently add to lithiated ketene dithioacetals with good diastereoselectivity and in excellent chemical yields.[9] Hoffman and Kim have also shown that lithiated β-keto esters add to chiral trifluoromethanesulfonyl lactate esters in moderate to excellent diastereoselectivity and with synthetically useful yields.[10] In addition, enolate alkylation of triflates has recently been demonstrated,[11] and the asymmetric alkylation of primary triflates has been employed in two recent total syntheses.[12]

Crimmins *et. al.*, have demonstrated that the alkylation of dianions of chiral monosubstituted succinate half esters with various alkyl bromides proceeds with moderate to good *syn* selectivity to give the corresponding chiral disubstituted succinates.[3] The *anti* derivatives are accessible through this methodology via epimerization of the newly introduced center with strong base treatment and low temperature quenching. We desired a more direct route to both *syn* and *anti* disubstituted products with predictable and efficient stereocontrol.

Herein, we report the results of our study on the asymmetric nucleophilic addition of chiral imide enolates to *chiral secondary triflates* derived from α-hydroxy acids. The products of these reactions provide a useful source of chiral building blocks well suited for further synthetic elaboration. In particular, chiral disubstituted succinates have gained increasing utility as amino acid replacements in a wide variety of inhibitors of Zn based metalloenzymes.[13] In these inhibitors, the succinate moiety has been shown to be a practical and effective surrogate for natural amino acid substrates. In most

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(2) Fadel, A.; Salaun, J. *Tetrahedron Lett.* **1988**, *29*, 6257.

(3) Becket, R. P.; Crimmins, M. J.; Davis, M. H.; Spavold, Z. *Synlett* **1993**, 137.

(4) For related methods of chiral auxiliary control in the synthesis of succinates see Bashiardes, G.; Collingwood, S. P.; Davies, S. G.; Preston, S. C. *J. Organomet. Chem.* **1989**, 364, C29. Bashiardes, G.; Collingwood, S. P.; Davies, S. G.; Preston, S. C. *J. Chem. Soc. Perkin Trans. 1* **1989**, 1162.

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(6) The displacement of α-tosyl esters with sodium enolates of malonate diesters has been reported using HMPA/THF solvent mixtures, requiring 48 h reaction times; see Larcheveque, M.; Petit, Y. *Synthesis* **1991**, 162.

(7) Ennis, M. D. Ph.D. thesis, California Institute of Technology, 1983. Ziegler, F. E.; Stirchak, E. P.; Wester, R. T. *Tetrahedron Lett.* **1986**, *27*, 1229. Mori, K. *Tetrahedron* **1983**, *39*, 3107.

(8) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am Chem. Soc.* **1982**, *104*, 1737. Bisaha, J. Research Report (D. Evans); Harvard University, 1983.

(9) Canan Koch, S. S.; Chamberlin, A. R. *J. Org. Chem.* **1993**, *58*, 2725.

(10) Hoffman, R. V.; Kim, H.-O. *Tetrahedron Lett.* **1993**, *34*, 2051.

(11) Bates, R. B.; Taylor, S. R. *J. Org. Chem.* **1994**, *59*, 245. Bates, R. B.; Taylor, S. R. *J. Org. Chem.* **1993**, *58*, 4469.

(12) Wipf, P.; Kim, Y.; Fritch, P. C. *J. Org. Chem.* **1993**, *58*, 7195. Williams, D. R.; McGill, J. M. *J. Org. Chem.* **1990**, *55*, 3457.

(13) For reviews of metalloproteinase inhibitor development and the use of chiral succinates as amino acid surrogates see Schwartz, M. A.; Van Wart, H. E. *Progress Med. Chem.* **1992**, *29*, 271. Johnson, W. H.; Roberts, N. A.; Borkakoti, N. *J. Enzyme Inhib.* **1987**, *2*, 1.

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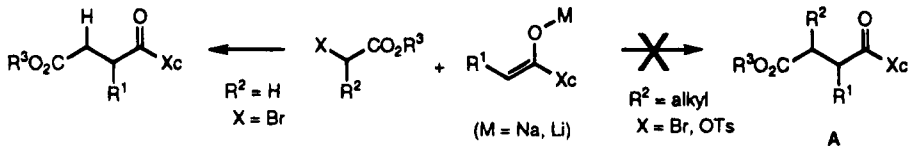
Scheme 1



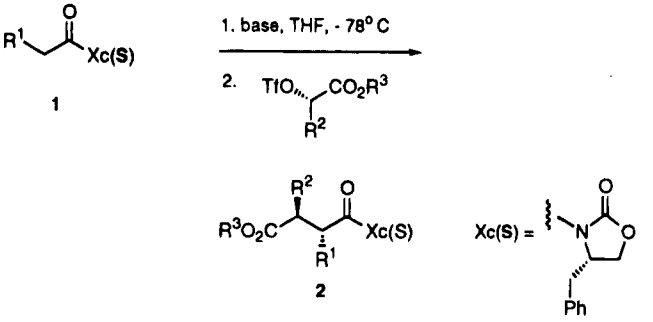
cases it is imperative to have the correct absolute stereochemistry of the succinate fragment to get optimum enzyme binding. Our selection of starting materials for this study was guided by the practical applicability of the chiral products of our reactions and subsequent derivatives, as leucine and homophenylalanine peptide mimics.

Results

Preparation of Secondary Chiral Triflates from Lactates. To allow us to selectively differentiate between the succinate "ester" groups in our addition products, we chose to explore the benzyl[14] and *tert*-butyl lactate triflates. While preparation of benzyl lactate triflates was straightforward, standard methods of *tert*-butyl protection of lactates using isobutylene and catalytic H_2SO_4 gave a mixture of the desired ester and *tert*-butyl ether. We found that *tert*-butyl 2-(*S*)-trifluoromethanesulfonyl lactates (phenyllactic or lactic acid) are efficiently prepared by reacting the corresponding α-hydroxy acids with 3 equiv of *O-tert*-butyl-*N,N*-diisopropylisourea and catalytic $CuCl_2$ at 0 °C for 48 h.[15,16] The triflates were then formed by treating *tert*-butyl lactate at −78 °C in THF with triflic anhydride and 1.17 equiv of pyridine, followed by flash chromatography on SiO_2. We found that these triflates did not degrade on storing neat at −20 °C over 6 months.

Asymmetric Displacements To Give Chiral Succinates. The results of this study are summarized in Tables 1 and 2. Reactions were carried out in dry THF using 1.3 equiv of the corresponding triflates. By employing the (*R*)- and (*S*)-4-(phenylmethyl)oxazolidinones, both *syn* and *anti* products, respectively, are attainable via this methodology. From a temperature study, it was found that reactions using the *tert*-butyl ester triflate (entries 1 and 6) were found to react slowly at −78 °C (7−10% conversion to product after 2 h) to produce *anti* products **2**. Temperatures above −20 °C to 0 °C were found to be optimum to effect this conversion. The creation of *anti* products (Table 1) was observed to proceed with less diastereoselectivity for *tert*-butyl ester cases (entries 1 and 6). However, the major diastereomer was easily separable by SiO_2 flash chromatography facilitating straightforward purification of products. Diastereoselectivity improved markedly when the benzyl ester triflates were used (entries 2 and 7), and in these cases the reactions were found to proceed smoothly at −40 °C. The effect of counterion was also examined in the *anti* case, and quite clearly, a pronounced decrease in selectivity was observed when sodium and potassium enolates were used (entries 3 and 4) with a reversal in selectivity observed in the case of potassium. In addition,

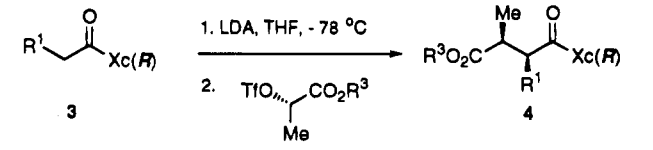
Table 1. Triflate Alkylations with (*S*)-4-(Phenylmethyl)oxazolidinones Imides



entry	R^1	R^2	R^3	base	yield, **2** (%)	diast ratio[c]
1	$CH_2CH(CH_3)_2$	CH_3	t-Bu	LDA	61[a]	79:21
2	$CH_2CH(CH_3)_2$	CH_3	Bn	LDA	63[a]	>98:2
3	$CH_2CH(CH_3)_2$	CH_3	t-Bu	NaHMDA	60[b]	70:30
4	$CH_2CH(CH_3)_2$	CH_3	t-Bu	KHMDS	60[b]	42:58
5	$CH_2CH(CH_3)_2$	Bn	t-Bu	LDA	28[d]	ND
6	$(CH_2)_2Ph$	CH_3	t-Bu	LDA	70[a]	79:21
7	$(CH_2)_2Ph$	CH_3	Bn	LDA	70[a]	>98:2

[a] Yield of purified major diasteromer. [b] Yield of mixture of diastereomers. [c] Determined by ^1H NMR of crude reaction mixture and confirmed by chiral HPLC. Pirkle DNPBG col. 220 nm, 1.0 mL/min, 95/4.5/0.5 hexane/ethanol/CH_2Cl_2. [d] 30% t-butyl cinnamate isolated.

Table 2. Triflate Alkylations with (*R*)-4-(Phenylmethyl)oxazolidinone Imides[a]



entry	R1	R3	yield, **4** (%)	diast ratio[b]
8	$CH_2CH(CH_3)_2$	t-Bu	88	>98:2
9	$CH_2CH(CH_3)_2$	Bn	79	>98:2
10	$(CH_2)_2Ph$	t-Bu	80	>98:2
11	$(CH_2)_2Ph$	Bn	88	>98:2
12[c]	$CH_2CH(CH_3)_2$	t-Bu	58	>98:2

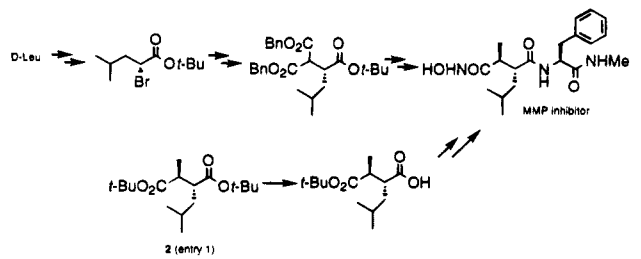
[a] Xc(*R*) = 4-(phenylmethyl)oxazolidinone. [b] Determined by ^1H NMR and confirmed by chiral HPLC (see Table 1). [c] This reaction was done with *tert*-butyl trifluoromethanesulfonyl phenyllactate as alkylating agent.

(14) The starting R^1-acyl-oxazolidinones were prepared from the corresponding acid chlorides (4-methylvaleryl or 4-phenylbutyryl) and lithium anion of either the (*R*)- or (*S*)-4-benzyloxazolidinone using standard conditions (see reference 1). Benzyl 2(*S*)-[(trifluoromethansulfonyl)oxypropionate was prepared by reacting (*S*)-benzyl lactate and triflic anhydride at −78 to −20 °C over 1 h, with 1.17 equiv of pyridine followed by SiO_2 chromatography.

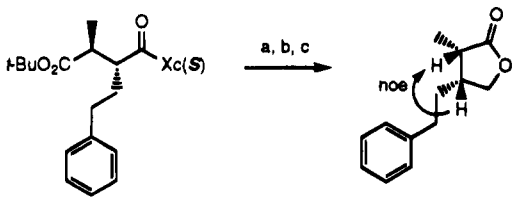
(15) Henry, R. A. *J. Heterocycl. Chem.* **1976**, *13*, 391.

(16) Mathias, L. J. *Synthesis* **1979**, 561. The MP and yield of *t*-butyl lactate are reported in a table in this reference but without experimental details. As part of our experimental we have included a detailed description for the preparation of this compound.

(17) Davidson, A. H.; Dickens, J. P.; Crimmins, M. J. World Patent 9005716, 1990. See for example the preparation of MMP inhibitors from D-leucine.



Scheme 2



2 (entry 7)

Reaction conditions: (a) $LiOH/H_2O_2$, THF-H_2O, 0 °C to RT, 18 h 80% (b) B_2H_6, THF 0 °C to RT 4h, 77% (c) TFA, RT, 4h 68%.

the alkylation attempt on the triflate of *tert*-butyl phenyllactate (entry 5) gave *tert*-butyl cinnamate as a major elimination derived byproduct of the reaction (run at 0 °C, as the reaction did not proceed to a significant extent at lower temperatures). However 28% of the *anti* diastereomer product was recovered as the major addition product.

In contrast, the reaction proceeds in higher yield and with greater stereocontrol to produce the *syn* products **4** (Table 2). Synthetically useful yields on the order of 80% and above (entries 8–10) were observed, with excellent diastereoselectivity in the addition and less sensitivity displayed toward the nature of the ester group. Interestingly, it was found that when employing the (*R*)-oxazolidinone in the starting imide, displacement of the triflate of *tert*-butyl (*S*)-phenyllactate was possible in the *syn* case (entry 12), giving a 58% yield of one diastereomer without the competing elimination reaction that was observed in the *anti* case described in entry 5.

Determination of Stereochemistry. The relative stereochemistry of selected cases was inferred by examining the NOESY spectrum of the corresponding lactone derivatives (these derivatives prepared as described by Crimmins[3]) as represented by the example in Scheme 2. The NOESY spectra revealed that the major products of the reactions studied resulted from the expected S_N2 displacement of the triflates. The absolute configuration of the asymmetric addition products was determined by comparing the spectral properties of reported metalloproteinase inhibitors derived from these intermediates, with those of known absolute configuration derived from leucine or homophenylalanine through published procedures.[14] Further work is in progress to determine the absolute configuration of the minor products and to further delineate the scope of this reaction.

Discussion

From the results of this study, we propose that the reactions to give the *anti* products (entries 1–7, employing the (*S*)-oxazolidinone as the chiral auxiliary) with (*S*)-lactates, results in "mismatched" asymmetric induction leading to products.[18] This is indicated by the generally lower yields, higher temperature required for conversion to products and reduced diastereoselectivity observed for *anti* selection in the case of the bulky *tert*-butyl ester lactate (entry 1). The benzyl trifluoromethanesulfonyl lactate (entry 2) however does allow for excellent diastereoselectivity and would therefore be the ester of choice in the *anti* selective transformation.

(18) For a discussion of matched and mismatched asymmetric induction see Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; pp 967 to 969 and references cited therein.

In contrast, it is suggested that *syn* selective products (Table 2) result from "matched" asymmetric induction. Excellent diastereoselectivity and chemical yields are observed with both *tert*-butyl and benzyl ester substrates, allowing more flexibility in the choice of reactants in targeting scalemic *syn* products. In general, these reactions were found to proceed efficiently at −78 °C with relatively short (~2 h) reaction times; however, better yields were obtained by letting the reaction temperature slowly increase to room temperature, without an appreciable change in de.

From the absolute configuration of the products, it is clear that the dominant mechanism of the reaction proceeds through the expected S_N2 route. However it is not clear to what degree chelation control of the approaching electrophile is important. One consideration is the decrease in stereoselectivity observed in the mismatched case (*anti*) when the counterion is changed from Li to Na to K. From an examination of molecular models, it is difficult to invoke a chelation control argument involving the enolate anion, counterion (Li, Na or K), and carbonyl oxygen of the approaching ester of the electrophile, as the complex would involve a highly strained six-membered ring transition state with geometry of approach that appears to be suboptimal. The de differences observed in the mismatched case in varying the counterion may simply be rationalized by loss of the enolate geometry through reaction at higher temperature. The matched asymmetric induction leading to *syn* products involves a sterically less congested transition state. This is reflected in the lower temperature at which the reaction proceeds and the generally better de's and chemical yields observed for the process.

Conclusion

It is clear from these findings that the addition reaction described is a useful methodology for the production of optically pure *syn*- and *anti*-disubstituted chiral succinates. We have demonstrated the utility of the triflate attached to a stereogenic center as a reactive leaving group for the S_N2 displacement by chiral lithium imides. We are currently examining the mechanistic aspects of this reaction as it relates to the differences observed in selectivity and yield for the *syn* vs *anti* products and the use of alkyl triflates as alkylating agents in related systems.

Experimental Section

Melting points were determined using a Meltemp apparatus and are uncorrected. ^1H NMR spectra were determined at 300 or 400 MHz, and ^{13}C NMR were determined at 75 MHz. Chemical shifts are reported in ppm relative to TMS in the solvents specified. Column chromatography was performed on silica gel 60 (230–400 mesh) using the specified eluants. THF was distilled from a potassium–benzophenone still. For each reaction, LDA was made fresh from anhydrous diisopropylamine and 2.5 M *n*-BuLi in hexanes. NaHMDS and KHMDS were used as preformed 1 M commercial solutions from Aldrich Chemical Co.

(*S*)-*tert*-Butyl lactate [A 3.5 M solution of *O*-*tert*-butyl-*N*,*N*-diisopropylisourea, cat. CuCl was first prepared as follows: Under a nitrogen atmosphere, diisopropylcarbodiimide (300g, 2.37 mol) was combined with CuCl (4.69 g, 0.0474 mol) in a 1 L round bottomed flask. *tert*-butyl alcohol (194.9 g, 2.63 mol) was added via an addition funnel over 30 min, and the mixture was allowed to stir for 4 days in the dark. This stock solution (approximately 3.5 M) could be stored at −20 °C for extended periods.] To a stirred suspension of L-(+)-lactic acid

(55 g, 0.610 mol) in 1000 mL anhydrous CH_2Cl_2 at 0 °C was added *O*-*tert*-butyl-*N*,*N*-diisopropylisourea·CuCl (174.4 mL, 3.5 M solution) dropwise over 30 min. The solution was allowed to reach room temperature and stirred for an additional 18 h. Acetic acid (75 mL) was added over 20 min and stirred for an additional 30 min. The solid diisopropyl urea that precipitated was filtered and washed with cold CH_2Cl_2. An ice–water mixture (1 L) was added and the solution basified to pH 8.0 with solid $NaHCO_3$, under vigorous stirring conditions. The solid material was filtered, and the phases were separated. The aqueous phase was washed with CH_2Cl_2 (2 × 350 mL), and the combined organics were washed with $NaHCO_3$ (sat.), water, and brine and then dried over $MgSO_4$. Following filtration, the solvent was evaporated at 10 °C. To the resulting oil was added 400 mL of pentane, and the resulting additional diisopropyl urea that precipitated was filtered off. The pentane solution was stored at −20 °C overnight, and the resulting product (needles) was collected and dried over a stream of N_2. (Note: the solid product sublimes readily at room temperature under vacuum) A second crop was also taken to provide 37 g (42%) of pure product: $[\alpha]_D$ −7.1 (*c* 1.116, methanol); identical to literature spectra, see Brown, H. C.; Pai, G. G. *J. Org. Chem.* **1985**, *50*, 1384.

(*S*)-*tert*-Butyl phenyllactate was prepared in the same manner as above. Purification by SiO_2 chromatography, 20% ether/hexane, 85% yield; mp 42–42.5 °C; $[\alpha]_D$ = 14.3 (*c* 0.54, methanol); IR (KBr) 3426, 3030, 3004, 1744, 1724, 1606 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.3 (5H, m); 4.4 (1H, m), 3.1 (2H, ddd, J = 6.6, 7.5, 13.9), 2.95 (1H, OH, d, J = 5.9 Hz), 1.53 (9H, s).

General Procedure. 2(*R*)-Isobutyl-3(*S*)-methylsuccinic Acid 1-[4(*S*)-(Phenylmethyl)-2-oxooxazolidinamide)]-4-(*tert*-Butyl Ester) (2, entry 1). *N*-(4-Methylvaleryl)-4(*S*)-(phenylmethyl)-2-oxazolidinone (1 g, 3.64 mmol) was dissolved in 15 mL of anhydrous THF and cooled to −78 °C under N_2. LDA (3.64 mmol, 1 M solution) was added over 10 min, and the solution was stirred at −78 °C for an additional 30 min. (*S*)-*tert*-butyl trifluoromethanesulfonyl lactate (1.47 g, 4.73 mmol) dissolved in 30 mL of THF was added over 20 min, and the resulting mixture was allowed to stir at −78 °C for 2 h and then slowly warmed to ambient temperature by removal of the cooling bath. After 16 h, the solution was concentrated on a rotary evaporator to 1/4 volume. Ethyl acetate was added followed by washing with 10% citric acid, water, then brine and dried over $MgSO_4$. Solvent evaporation gave an oil containing a 79:21 mixture of major products. Purification by SiO_2 chromatography 15% ethyl acetate/hexane to give 0.965 g (61%) of the major addition product. $[\alpha]_D$ = 62.2 (*c* 0.22 methanol); IR (KBr) 3025, 2958, 2872, 1782, 1728, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) major diastereomer δ 7.4–7.2 (5H, m), 4.7 (1H, m), 4.15 (2H, d), 4.1 (1H, m), 3.45 (1H, dd, J = 3.5, 13 Hz), 2.7 (2H, m), 1.8 (1H, m), 1.43 (9H, s), 1.25 (3H, d, J = 7.5 Hz) 0.9 (3H, d, J = 7.5 Hz), 0.85 (3H, d, J = 7.5 Hz); MS (*m*/*z*) 404 (M + H, 10), 348 (100). Anal. Calcd for $C_{23}H_{33}NO_5$: C, H, N, 68.46, 8.24, 3.47. Found: 68.09, 8.18, 3.62. Minor diastereomer δ 4.23 (1H, m), 3.3 (dd, J = 4.5, 13 Hz), 1.9 (3H, d, J = 7.5 Hz), 0.98 (3H, d, J = 7.5), 0.95 (3H, d, J = 7.5 Hz).

2(*R*)-Isobutyl-3(*S*)-methylsuccinic Acid 1-[4(*S*)-(Phenylmethyl)-2-oxooxazolidinamide]-4-(Benzyl Ester) (2, entry 2). Same procedure as above starting with *N*-(4-methylvaleryl)-4(*S*)-phenylmethyl)-2-oxazolidinone and (*S*)-benzyl trifluoromethanesulfonyl lactate (63%); $[\alpha]_D$ = 50.2 (*c* 0.65 methanol); IR (KBr) 3025, 2956, 2870, 1780, 1734, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4–7.19 (10H, m), 5.1 (2H, AB, J = 8.0, 15 Hz), 4.65 (1H, m), 4.2 (1H, m), 4.1 (2H, m), 3.3 (1H, dd, J = 3.5, 9 Hz), 2.9 (1H, m), 2.48 (1H, dd, J = 9, 12 Hz), 1.8 (1H, m), 1.45 (1H, m), 1.3 (3H, d, J = 8 Hz), 1.25 (1H, m), 0.9 (3H, d, 7.5 Hz), 0.85 (3H, d, J = 7.5 Hz); CI-MS 455 (M + NH_4^+), 438 (M + H). Anal. Calcd for $C_{27}H_{33}NO_5$: C, H, N, 71.54, 6.94, 3.22. Found: 71.32, 7.15, 3.19.

2(*R*)-Phenethyl-3(*S*)-methylsuccinic Acid 1-[4(*S*)-(Phenylmethyl)-2-oxooxazolidinamide]-4-(*tert*-Butyl Ester) (2, entry 6). Same procedure as above starting with N-(4-phenylbutanoyl)-4(*S*)-(phenylmethyl)-2-oxazolidinone and (*S*)-*tert*-butyl trifluoromethanesulfonyl lactate (70%): $[\alpha]_D$ = 62.5 (*c* 0.57 methanol); IR (KBr) 3025, 2978, 2934, 1780, 1726, 1696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4–7.1 (10H, m), 4.5 (1H, m), 4.1 (3H, m), 3.35 (1H, dd, J = 3.5, 13 Hz), 2.79 (1H, m), 2.6 (2H, m), 2.2 (1H, m), 1.9 (1H, m), 1.45 (9H, s), 1.2 (3H, s); CI-MS 469 (M + NH_4^+), 452 (M + H). Anal. Calcd for $C_{28}H_{33}NO_5$: C, H, N, 71.82, 7.38, 3.10. Found: C 71.70, H, 7.19, N, 2.98.

2(*S*)-Isobutyl-3(*S*)-methylsuccinic Acid 1-[4(*R*)-(Phenylmethyl)-2-oxooxazolidinamide]-4-(*tert*-Butyl Ester) (4, entry 8). Same procedure as above starting with *N*-4-(methylvaleryl)-4*R*-(phenylmethyl)-2-oxazolidinone and (*S*)-*tert*-butyl trifluoromethanesulfonyl lactate (88%): $[\alpha]_D$ = −49.3 (*c* 0.60 methanol); IR (KBr) 3025, 2958, 2872, 1784, 1724, 1696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4–7.2 (5H, m), 4.68 (1H, m), 4.25 (1H, m), 4.19 (2H, m), 3.35 (1H, dd, J = 2.0, 10.0 Hz), 2.8 (1H, m), 2.7 (1H, dd, 8.0, 10.0 Hz), 1.79 (1H, m), 1.5 (1H, m), 1.45 (9H, s), 1.09 (3H, d, J = 7.5 Hz), 0.9 (6H, d, J = 7.5 Hz); CI-MS 421 (M + NH_4^+), 404 (M + H). Anal. Calcd for $C_{23}H_{33}NO_5$: C, H, N 68.46, 8.24, 3.47. Found: 68.51, 8.14, 3.40.

2(*S*)-Phenethyl-3(*S*)-methylsuccinic Acid 1-[4(*R*)-(Phenylmethyl)-2-oxooxazolidinamide]-4-(*tert*-Butyl Ester) (4, entry 10). Same procedure as above starting with *N*-(4-phenylbutanoyl-4(*R*)-(phenylmethyl)-2-oxazolidinone and (*S*)-*tert*-butyl trifluoromethanesulfonyl phenyllactate (80%): $[\alpha]_D$ = −59.9 (*c* 0.29, methanol); IR (KBr) 3026, 2958, 2932, 1784, 1722, 1694 cm^{-1}; ^1H NMR ($CDCl_3$) 7.4–7.15 (10H, m), 4.65 (1H, m) 4.35 (1H, m), 4.15 (2H, m), 3.35 (1H, dd, J = 3.5, 15.0 Hz), 3.0 (3H, m), 2.65 (1H, dd, J = 15.0, 10.0 Hz), 1.85 (1H, m), 1.5 (1H, m), 1.28 (9H, s), 0.9 (3H, d, J = 7.5 Hz); CI-MS 497 (M + NH_4^+), 480 (M + H). Anal. Calcd for $C_{29}H_{37}NO_5$: C, H, N 71.82, 7.38, 3.10. Found: 71.44, 7.50, 2.98.

2(*S*)-Isobutyl-3(*S*)-methylsuccinic Acid 1-[4(*R*)-(Phenylmethyl)-2-oxooxazolidinamide]-4-(*tert*-Butyl Ester) (4, entry 12). Same procedure as above starting with *N*-(4-phenylbutanoyl)-4(*R*)-(phenylmethyl)-2-oxazolidinone and (*S*)-benzyl trifluoromethanesulfonyl lactate (58%); $[\alpha]_D$ = −50.0 (*c* 0.15, methanol); IR (KBr) 3025, 2978, 2982, 1782, 1722, 1694 cm^{-1}; ^1H NMR ($CDCl_3$) 7.4–7.1 (10H, m), 4.5 (1H, m), 4.2 (1H, ddd, J = 6.0, 9.0, 13.0 Hz), 4.1 (2H, m), 3.3 (1H, dd, J = 4.0, 15.0 Hz), 2.9 (1H, m), 2.65 (3H, m), 2.1–1.9 (2H, m), 1.41 (9H, s), 1.22 (3H, d, J = 7.5); CI-MS 469.2 (M + NH_4^+), 452 (M + H). Anal. Calcd for $C_{27}H_{33}NO_5$: C, H, N, 72.62, 7.79, 2.92. Found: 72.61, 7.91, 2.88.

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