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Synthesis of C_2–Symmetric Compounds *via* Double Alkylation of (α,ω–Dioxo–alkanediyl)bis–2–oxazolidinone Derivatives

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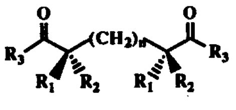
Abstract: A series of chiral C_2–symmetric compounds was prepared from readily available α,ω–diacyl chlorides and optically pure 2–oxazolidinone derivatives. Following preparation of the asymmetrically pure bis–oxazolidinone derivatives (6a–d, 11, 13, and 20), we prepared the dienolate of these compounds and quenched the reaction mixture with electrophiles such as iodomethane, allyl iodide, and benzyl bromide. Compounds 14a–e, and 15 were isolated with diastereomer ratios in excess of 9.8:1. If the chain length between the two carbonyl atoms was sufficiently small, dialkylation did not occur, but instead, provided cyclization products 18, 19, and 21. Mono–alkylated products 22a–c were prepared from 6c or 6d in modest yield. Unsymmetrical dialkylated compound 23 was prepared in 50% yield from 22b.

Compounds with a high degree of symmetry have been the subject of considerable synthetic effort in recent years;[1] several C_2–symmetric compounds are currently used as chiral ligands, and as chiral auxillaries in synthesis.[2] Recently, several groups have disclosed C_2– or pseudo C_2–symmetric compounds that have potential utility as pharmaceutical agents.[3]



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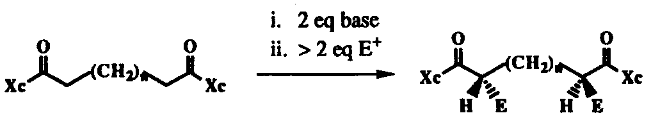
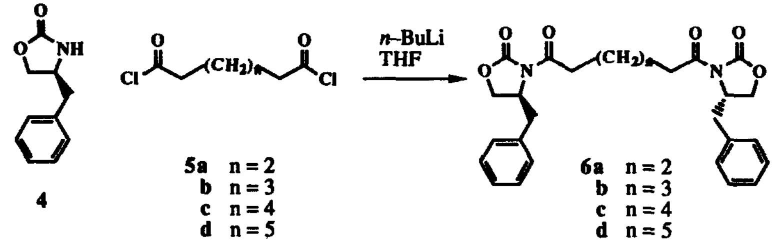
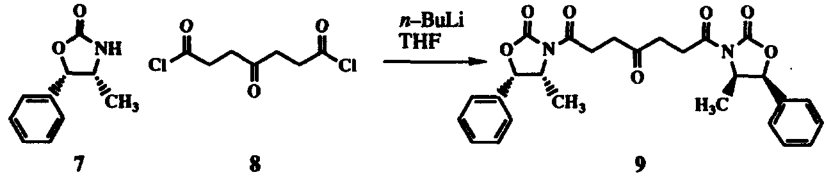
In connection with another ongoing program in our laboratories, the synthesis of HIV–1 protease inhibitors,[4] we were interested in the ready synthesis of C_2–symmetric compounds of general type **1**. It occurred to us that such compounds might be prepared by an asymmetric double alkylation of compound **2** utilizing a removable chiral auxillary (Xc) at both ends. The products of this reaction, **3**, could, in principle, be manipulated further in a wide variety of ways.



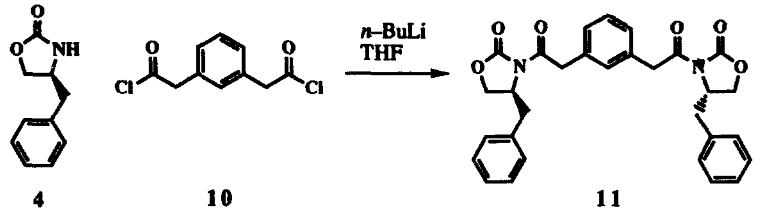
2 **3**

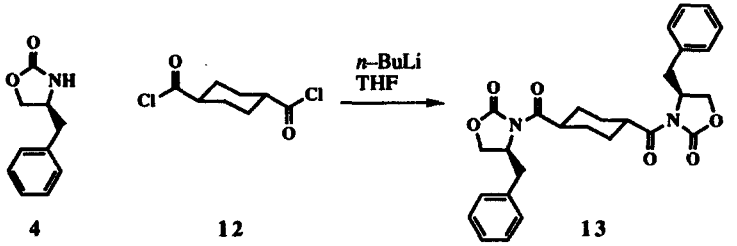
Because of the widespread use and superior results obtained in the asymmetric alkylation of chiral oxazolidinone derived enolates,[5] we chose to adapt this methodology to our own needs. The anion derived from oxazolidinone **4** was allowed to react with a variety of α,ω–diacyl chlorides (**5a–d**); compounds **6a–d** were obtained in moderate yield. Diacyl chlorides **8**, **10**, and **12** were prepared from the corresponding commercially available diacids by reaction with oxalyl chloride, and catalytic dimethylformamide (DMF), in methylene chloride (CH_2Cl_2) solution. Bis-oxazolidinones **9**, **11**, and **13** were synthesized from **8**, **10**, and **12**, respectively, by the method of Evans, *et. al.*[5] With these



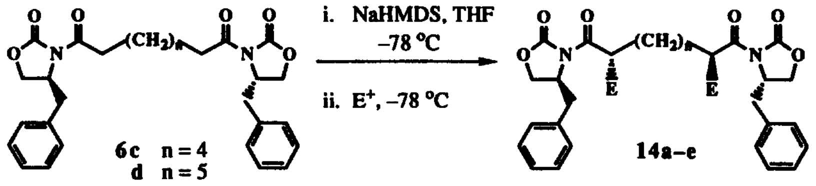


compounds in hand, we were now able to ask what level of asymmetric induction would occur in the double alkylation of **6a–d**, **9**, **11**, and **13**. Would the two enolates act independently of one another, or would the asymmetry induced in the first alkylation affect the subsequent alkylation? What is the influence of the chain length and geometry of the bridge between the enolates on the asymmetric induction?





Formation of the bis-enolates of **6c**, **6d**, and **11** with sodium bis(trimethylsilyl)amide (NaHMDS) in tetrahydrofuran (THF) at –78 °C occurred smoothly. Addition of various electrophiles to the cold solution provided adducts **14a–e**, and **15** (**Table 1**). That the major diastereomer of **14a–e**, and **15** has C_2-symmetry was immediately evident from its ^1H nmr, and especially, its ^{13}C NMR spectra. The ratio of diastereomers isolated was >9.8:1. We assign, as the minor diastereomer, compound **16** wherein *one* of the newly formed centers is inverted; we felt it highly unlikely, in light of Evans work,[5] that we would see *both* of the newly formed centers with the configuration opposite to that expected, *ie*. compound **17**. Additionally, the minor diastereomer exhibited spectral characteristics that were consistent with a compound that lacked C_2-symmetry. There was no evidence in the reaction mixture for the existence of compound **17**, which should exhibit C_2-symmetry. The yields and analytical data reported herein are for the mixture of diastereomers; the individual isomers were not separable on a preparative scale. The assignment of absolute stereochemistry followed from literature precedent;[5] diastereomer ratios were determined by HPLC.



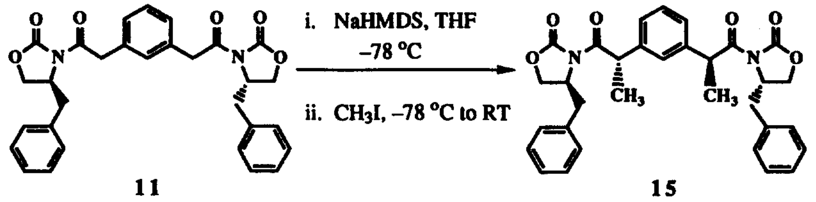
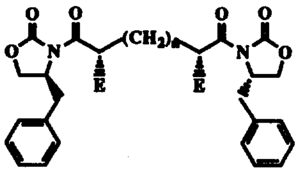


Table 1. Double Alkylation of **6c**, **6d**, **11**, and **23**.

Entry	Reactant	Electrophile	Product	% Yield	Diastereomer Ratio
1	**6c**	CH_3I	**14a**	48	≥ 20:1
2	**6c**	CH_2=$CHCH_2I$	**14b**	55	16:1
3	**6d**	CH_3I	**14c**	68	9.8:1
4	**6d**	CH_2=$CHCH_2I$	**14d**	69	≥ 20:1
5	**6d**	$PhCH_2Br$	**14e**	42	≥ 20:1
6	**11**	CH_3I	**15**	31	≥ 20:1
7	**25**	CH_3I	**26**	56	1:1



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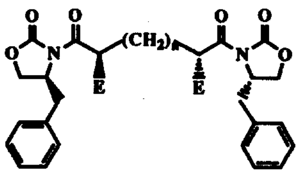

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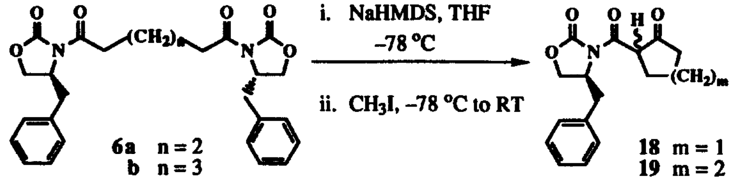
Interestingly, when **6a** and **6b** were allowed to react with NaHMDS at −78 °C, with or without the subsequent addition of iodomethane, compounds **18** and **19** were formed, respectively, in moderate yield. In the case of **18**, the two diastereomers were separated and isolated in a 1:1 ratio. Very little of the alleged dialkylated material could be seen (TLC analysis). Presumably, the initially formed mono–enolate attacks the neighboring carbonyl group with concomitant loss of **4** (which can be isolated from the reaction mixture); this process is reminiscent of the Dieckmann condensation. Cyclization of the mono–enolate is apparently faster than the second enolization. Attempts to suppress the cyclization by having the electrophile present during enolate formation were also unsuccessful. Not surprisingly, compound **20** (prepared from **9** and 1,2–ethanedithiol) gave **21** when allowed to react with NaHMDS in THF at −78 °C; a similar reaction pathway is in effect here.

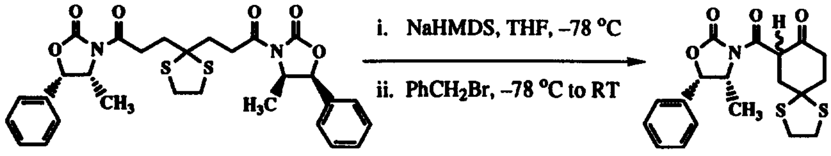


i. NaHMDS, THF −78 °C

ii. CH_3I, −78 °C to RT

6a n = 2
b n = 3

18 m = 1
19 m = 2



i. NaHMDS, THF, −78 °C

ii. $PhCH_2Br$, −78 °C to RT

20 **21**

It should be noted here that while **6b** and **20** cyclized to give **19** and **21**, respectively, after reaction with NaHMDS, dimethylation of **11** occurred in 31% yield to provide **15**. Each of these starting materials has a five carbon atom bridge between the carbonyl groups; in **6b** and **20** the five carbon atoms are sp^3–hybridized and unconstrained, while in **11**, the middle three carbon atoms are composed of a rigid aromatic ring. Simply having a small number of atoms between the reacting centers is not entirely sufficient for cyclization; when geometric constraints preclude a cyclization pathway the desired dialkylation proceeds well.

Attempts to alkylate the dianion of **13** with various electrophiles were also unsuccessful. It appears that either the dianion is never formed, or, if formed, the dianion is unreactive to electrophiles; this could be a manifestation of excessive steric hinderance. In a related result, we attempted to prepare the bis–enolate of adduct **14c** followed by quenching with allyl iodide. These experiments routinely returned starting material; apparently, formation of these compounds bearing quaternary centers with asymmetric control is not a straightforward process.

However, because of our unsuccessful attempts to prepare compounds with quaternary centers, we rationalized that if we could prepare mono–alkylated products of type **22**, then perhaps we could selectively introduce a second electrophile (E_2) with asymmetric induction *alpha* to the remaining carbonyl group to provide **23**. Compounds, **22a–c** were prepared in modest yield from 6c or 6d after reaction with NaHMDS (1.0 eq) followed by an electrophile (E_1) of choice (Table 2). We were then successful in preparing 23 by reaction of 22b first with NaHMDS (2.0 eq) followed by allyl iodide at –78 °C; compound 23 was isolated in 50% yield from the reaction mixture in a 80:10:4:4 ratio. It appears that excess base does partially epimerize the previously formed asymmetric center under these reaction conditions.

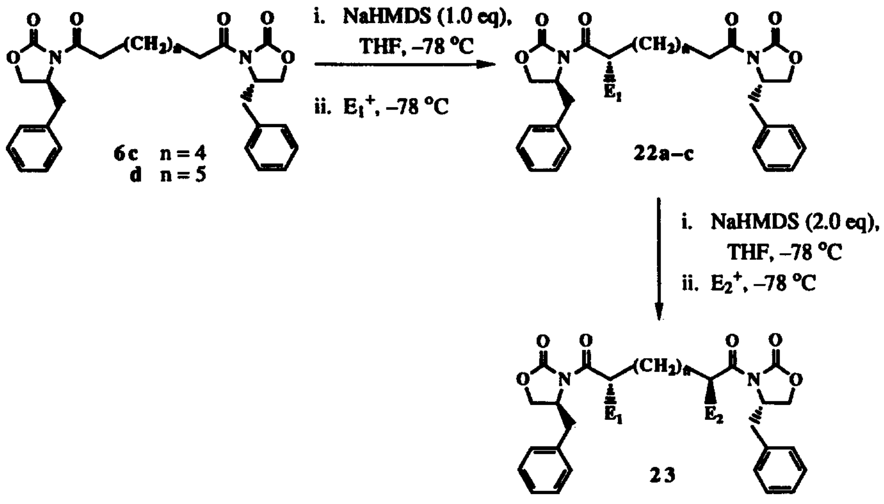
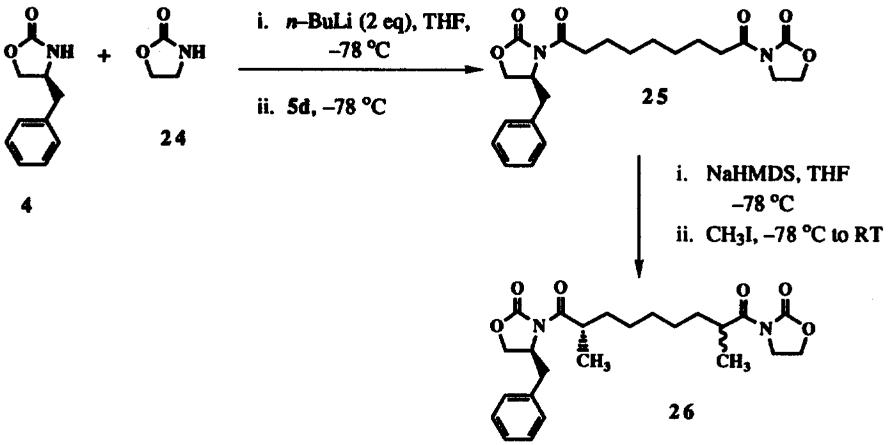


Table 2. Sequential Asymmetric Alkylation of **6c** and **6d**.

Entry	Reactant	Electrophile	Product	% Yield	Diastereomer Ratio
1	**6c**	CH_3I	**22a**	31	≥ 20:1
2	**6d**	CH_3I	**22b**	47	≥ 20:1
3	**6d**	$CH_2=CHCH_2I$	**22c**	35	≥ 20:1
4	**22b**	$CH_2=CHCH_2I$	**23**	50	80:10:4:4

To answer the question of whether any long range asymmetric induction is operative in the alkylation of **6d**, a control experiment was performed. We first prepared compound **25** from the reaction of 1 eq each of diacyl chloride **5d**, oxazolidinone **4**, and oxazolidinone **24**, in the presence of 2 eq of *n*–BuLi in THF. The desired bis–oxazolidinone **25** was isolated in 28% yield from the expected mixture of three products; the remaining two symmetrical coupled products could also be isolated by chromatography. Reaction of the derived bis–enolate of **25** with iodomethane gave dimethyl compound **26** in a 1:1 ratio of diastereomers. It is quite obvious in this case that there is little asymmetric induction from one end of compound **25** to the other; a statistical mixture of methylated products were obtained. From this result, it appears that asymmetric control in the alkylation of **6c–d** and **22b** is a direct result of local asymmetric control without any long distance control.



In conclusion, we have demonstrated the synthesis of a series of chiral bis-oxazolidinone derived diacids (**6a–d**, **11**, **13**, and **20**). Several of the oxazolidinone compounds **6c**, **6d**, and **11** were successfully transformed into new C_2-symmetric and optically active adducts **14a–e**, and **15**. These adducts could, in principle, be transformed by known procedures into highly useful synthons for subsequent synthesis. For example, transformation of the derived diacids of **14a–e**, and **15** into primary amides, and subsequent reaction with lithium aluminium hydride or Hofmann rearrangement conditions could provide optically active α,ω-diamines. These diamines, diacids, or derived diols could be very useful in organic synthesis or polymerization reactions. Additionally, one could imagine utilization of the opposite enantiomer of **4**, or **7** to access the opposite diastereomer of **14a–e**, and **15**. Mono-alkylated products **22a–c** were prepared in modest yield from **6c**, and **6d**. Unsymmetrical dialkylated compound **23** was prepared from **22b** in 50% yield. If this two-step experimental protocol is general, it expands the methodology described above considerably, and permits the synthesis of compounds that would have been difficult to prepare otherwise. Oxazolidinones **6a**, **6b**, **13**, and **20** all cyclized upon treatment with base at –78 °C; no alkylation products could be isolated from the reaction mixture.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Fast atom bombardment (FAB) mass spectra were determined on a VG-ZAB SE mass spectrometer. Electron impact (EI) and chemical ionization (CI) mass spectra were determined on a Finnigan MAT-90 mass spectrometer. IR spectra were recorded on a Nicolet 20SXB FT-IR spectrometer. ^{1}H NMR spectra were determined at 300 MHz, and ^{13}C NMR spectra were determined at 75 MHz, using a Nicolet QE-300 WB spectrometer; chemical shifts (δ) are in parts per million relative to tetramethylsilane. Apparent couplings are given in hertz. Specific rotations were recorded on a Perkin Elmer 241 Polarimeter. Elemental analyses were performed by Robertson Microlit Laboratories, Inc.; Madison, New Jersey. Unless otherwise noted all reagents and solvents obtained from commercial suppliers were of the highest possible purity and used without further purification. All non-aqueous reactions were performed in dry glassware under an inert atmosphere of dry argon or nitrogen.

Diastereomer ratios were determined by HPLC utilizing a Bakerbond DNBPG covalent chiral column (5 μm spherical, 4.6 mm x 250 mm) with n-hexane/2-propanol (9/1) mobile phase. Approximately 100 μg/mL of sample was prepared; 20 μL of this solution was injected onto the column. Ultraviolet detection (250 nm) was carried out on an ABI Model 785A Absorbance detector. A Hewlett-Packard LAS 3354A with HP 18652A A/D Converter was used to integrate the HPLC peaks.

[S–(R*,R*)]–3,3'–(1,6–Dioxo–1,6–hexanediyl)bis[4–(phenylmethyl)–2–oxazolidinone] (6a). To a solution of (S)–(–)–4–benzyl–2–oxazolidinone (4, 5.8 g, 32.8 mmol) and THF (30 mL) at –78 °C was added *n*–butyllithium (13.4 mL of a 2.5 M hexane solution, 33.6 mmol) dropwise; the yellow slurry was stirred at –78 °C for 25 min. To the slurry was added adipoyl chloride (2.4 mL, 16.4 mmol) dissolved in THF (5 mL) dropwise. The light yellow solution was stirred at –78 °C for 4 h. The reaction mixture was poured into saturated aqueous ammonium chloride solution (50 mL), diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 70 mL). The combined organic phases were washed with brine (3 x 70 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified on silica gel (elution with 45% EtOAc/hex) to provide **6a** as a colorless solid, 4.98 g (65%): mp 162–165 °C; $[\alpha]^{26}{}_D$ +65° (*c* 1.29, $CHCl_3$); IR (KBr) 1785, 1693, 1395, 1213 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.19 (m, 10H, aromatic), 4.72–4.64 (m, 2H, 2(NCH)), 4.24–4.14 (m, 4H, 2(OCH_2)), 3.31 (dd, 2H, *J* = 13.4, 3.3 Hz, 2(PhCH)), 3.03–2.94 (m, 4H, 2($COCH_2$)), 2.77 (dd, 2H, *J* = 13.3, 9.7 Hz, 2(PhCH)), 1.84–1.78 (m, 4H, 2($COCH_2CH_2$)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.74, 153.37, 135.23, 129.46, 128.85, 127.22, 66.12, 55.07, 37.82, 35.04, 23.42 ppm; MS (FAB) m/e 465 (M^+ + H). Anal. Calcd. for $C_{26}H_{28}N_2O_6$: C, 67.23; H, 6.08; N, 6.02. Found: C, 67.11; H, 6.19; N, 6.06.

[S–(R*,R*)]–3,3'–(1,7–Dioxo–1,7–heptanediyl)bis[4–(phenylmethyl)–2–oxazolidinone] (6b). Prepared by the same procedure as described for **6a** by reaction of **4** with pimeloyl chloride. Isolate **6b** as a yellow oil (55%): $[\alpha]^{26}{}_D$ +64° (*c* 1.18, $CHCl_3$); IR (neat) 1780, 1699, 1388, 1352, 1212 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.18 (m, 10H, aromatic), 4.71–4.63 (m, 2H, 2(NCH)), 4.24–4.14 (m, 4H, 2(OCH_2)), 3.30 (dd, 2H, *J* = 13.3, 3.3 Hz, 2(PhCH)), 3.03–2.90 (m, 4H, 2($COCH_2$)), 2.77 (dd, 2H, *J* = 13.3, 9.6 Hz, 2(PhCH)), 1.81–1.71 (m, 4H, 2($COCH_2CH_2$)), 1.52–1.46 (m, 2H, $COCH_2CH_2CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.04, 153.38, 135.25, 129.35, 128.87, 66.12, 55.08, 37.88, 35.23, 28.42, 23.89 ppm; MS (FAB) m/e 479 (M^+ + H). Anal. Calcd. for $C_{27}H_{30}N_2O_6$: C, 67.77; H, 6.32; N, 5.85. Found: C, 67.52; H, 6.39; N, 5.74.

[S–(R*,R*)]–3,3'–(1,8–Dioxo–1,8–octanediyl)bis[4–(phenylmethyl)–2–oxazolidinone] (6c). Prepared by the same procedure as described for **6a** by reaction of **4** with suberoyl chloride. Isolate **6c** as a colorless solid (76%): mp 122–123 °C; $[\alpha]^{26}{}_D$ +59° (*c* 1.08, $CHCl_3$); IR (KBr) 1786, 1704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.20 (m, 10H, aromatic), 4.72–4.64 (m, 2H, 2(NCH)), 4.24–4.14 (m, 4H, 2(OCH_2)), 3.31 (dd, 2H, *J* = 13.3, 3.3 Hz, 2(PhCH)), 3.01–2.88 (m, 4H, 2($COCH_2$)), 2.77 (dd, 2H, *J* = 13.3, 9.6 Hz, 2(PhCH)), 1.78–1.68 (m, 4H, 2($COCH_2CH_2$)), 1.48–1.42 (m, 4H, 2($COCH_2CH_2CH_2$)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.20, 153.75, 135.28, 129.37, 128.89, 127.27, 66.12, 55.15, 37.89, 35.38, 28.78, 24.03 ppm; MS (FAB) m/e 493 (M^+ + H). Anal. Calcd. for $C_{28}H_{32}N_2O_6$: C, 68.28; H, 6.55; N, 5.69. Found: C, 68.37; H, 6.53; N, 5.47.

[S–(R*,R*)]–3,3'–(1,9–Dioxo–1,9–nonanediyl)bis[4–(phenylmethyl)–2–oxazolidinone] (6d). Prepared by the same procedure as described for **6a** by reaction of **4** with azelaoyl chloride. Isolate **6d** as a colorless solid (65%): mp 90–91 °C; $[\alpha]^{26}{}_D$ +58° (*c* 1.10, $CHCl_3$); IR (KBr) 1785, 1781, 1708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.20 (m, 10H, aromatic), 4.70–4.65 (m, 2H, 2(NCH)), 4.23–4.14 (m, 4H, 2(OCH_2)), 3.31 (dd, 2H, *J* = 13.3, 3.4 Hz, 2(PhCH)), 3.03–2.84 (m, 4H, 2($COCH_2$)), 2.77 (dd, 2H, *J* = 13.3, 9.6 Hz, 2 (PhCH)), 1.77–1.64 (m, 4H, 2($COCH_2CH_2$), 1.41 (br s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.27, 153.39, 135.32, 129.37, 128.88, 127.26, 66.11, 55.10, 37.91, 35.42, 29.03, 28.87, 24.15 ppm; MS (EI) m/e 506 (M^+). Anal. Calcd. for $C_{29}H_{34}N_2O_6$: C, 68.76; H, 6.76; N, 5.53. Found: C, 68.54; H, 6.45; N, 5.35.

[4R–[3(4R*,5S*),4α,5α]]–3,3'–(1,4,7–Trioxo–1,7–heptanediyl)bis[4–methyl–5–phenyl–2–oxazolidinone] (9). To a slurry of 4–ketopimelic acid (1.5 g, 8.6 mmol) dissolved in dry CH_2Cl_2 (15 mL) was added DMF (0.03 mL) followed by oxalyl chloride (2.0 mL, 23 mmol) dropwise. The reaction mixture was stirred at room temperature for 3 h and concentrated *in vacuo* to provide diacyl chloride **8** which was used directly in the next reaction. Compound **9** was prepared by the same procedure as described for **6a** by reaction of **7** with **8**. Isolate **9** as a colorless solid (36%): mp 74–78 °C; $[\alpha]^{26}{}_D$ +30° (*c* 1.15, $CHCl_3$); IR (KBr) 1782, 1701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47–7.27 (m, 10H, aromatic), 5.69 (d, 2H, *J* = 7.3 Hz, 2(OCHPh)), 4.78–4.69 (m, 2H, 2(NCH)), 3.35–3.15 (m, 4H, 2($COCH_2$)), 2.98–2.77 (m, 4H, 2($COCH_2$)), 0.88 (d, 6H, *J* = 6.6 Hz, 2(CH_3)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.08, 171.79, 153.01, 133.26, 128.68, 128.63, 125.60, 79.07, 54.74, 36.21, 29.93, 14.46 ppm; MS (FAB) m/e 493 (M$^+$ + H). Anal. Calcd. for $C_{27}H_{28}N_2O_7$: C, 65.84; H, 5.73; N, 5.69. Found: C, 65.64; H, 5.75; N, 5.45.

[S-(R*,R*)]-3,3'-[1,3-Phenylenebis(1-oxo-2,1-ethanediyl)]bis[4-(phenylmethyl)-2-oxazolidinone] (11). To a solution of 1,3-phenylenediacetic acid (3.0 g, 15.5 mmol) dissolved in dry CH_2Cl_2 (15 mL) was added DMF (0.1 mL) followed by oxalyl chloride (4.0 mL, 46.4 mmol) dropwise. The reaction mixture was stirred at room temperature for 18 h and concentrated *in vacuo* to provide diacyl chloride **10** which was used directly in the next reaction. Compound **11** was prepared by the same procedure as described for **6a** by reaction of **4** with **10**. Isolate **11** as a colorless solid (27%): mp 54–60 °C; $[\alpha]^{26}_D$ +54° (*c* 1.10, $CHCl_3$); IR (KBr) 1779, 1698, 1391 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.22 (m, 10H, aromatic), 7.16–7.11 (m, 4H, aromatic), 4.70–4.62 (m, 2H, 2(NCH)), 4.37–4.22 (m, 4H, 2(OCH_2)), 4.19–4.08 (m, 4H, 2($COCH_2$)), 3.27 (dd, 2H, *J* = 13.4, 3.3 Hz, 2(PhCH)), 2.75 (dd, 2H, *J* = 13.4, 9.5 Hz, 2(PhCH)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.00, 153.32, 135.13, 133.78, 131.10, 129.37, 129.18, 128.89, 128.72, 66.09, 55.29, 41.45, 37.69 ppm; HRMS (FAB) m/e Calcd (M$^+$ + H): 513.2025. Found: 513.2018. Anal. Calcd. for $C_{30}H_{28}N_2O_6$: C, 70.30; H, 5.51; N, 5.47. Found: C, 70.03; H, 5.52; N, 5.26.

[4S-(R*,R*-*trans*)]-3,3'-(1,4-Cyclohexanediyldicarbonyl)bis[4-(phenylmethyl)-2-oxazolidinone] (13). To a solution of *trans*-1,4-cyclohexanedicarboxylic acid (3.0 g, 17.4 mmol) dissolved in dry CH_2Cl_2 (15 mL) was added DMF (0.1 mL) followed by oxalyl chloride (4.6 mL, 52.3 mmol) dropwise. The reaction mixture was stirred at room temperature for 18 h and concentrated *in vacuo* to provide diacyl chloride **12** which was used directly in the next reaction. Compound **13** was prepared by the same procedure as described for **6a** by reaction of **4** with **12**. Isolate **13** as a colorless solid (21%): mp 184–188 °C; $[\alpha]^{26}_D$ +66° (*c* 1.20, $CHCl_3$); IR (KBr) 1775, 1701, 1376 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.20 (m, 10H, aromatic), 4.71–4.65 (m, 2H, 2(NCH)), 4.24–4.16 (m, 4H, 2(OCH_2)), 3.64–3.48 (m, 2H, 2(COCH)), 3.24 (dd, 2H, *J* = 13.4, 3.2 Hz, 2(PhCH)), 2.78 (dd, 2H, *J* = 13.4, 9.4 Hz, 2(PhCH)), 2.15–1.96 (m, 4H), 1.70–1.61 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.67, 153.03, 135.17, 129.40, 128.87, 127.30, 66.06, 55.14, 41.51, 37.87, 28.29, 27.49 ppm; MS (FAB) m/e 491 (M$^+$ + H). Anal. Calcd. for $C_{28}H_{30}N_2O_6$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.51; H, 6.12; N, 5.52.

[2S-[2R*(R*),2[7R*(R*)]]]-3,3'-(2,7-Dimethyl-1,8-dioxo-1,8-octanediyl)bis[4-(phenylmethyl)-2-oxazolidinone] (14a). To a solution of NaHMDS (2.1 mL of a 1.0 M THF solution, 2.1 mmol) and THF (3 mL) at –78 °C was added **6c** (0.5 g, 1.0 mmol) dissolved in THF (5 mL). Stirring was continued at –78 °C for 30 min. To the –78 °C solution was added iodomethane (0.3 mL, 5.1 mmol); the resulting yellow solution was stirred at –78 °C for 4.5 h. Saturated aqueous ammonium chloride (25 mL) was added to the reaction mixture, allowed to warm to room temperature, diluted with water (30 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were washed with brine (3 x 50 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified on silica gel (elution with 35% EtOAc/hex) to provide **14a** as a yellow oil, 0.24 g (48%): $[\alpha]^{26}_D$ +81° (*c* 1.00, $CHCl_3$); IR (neat) 2974, 2934, 1780, 1695 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.20 (m, 10H, aromatic), 4.72–4.64 (m, 2H, 2(NCH)), 4.25–4.13 (m, 4H, 2(OCH_2)), 3.74–3.67 (m, 2H, 2(COCH)), 3.26 (dd, 2H, *J* = 13.3, 3.2 Hz, 2(PhCH)), 2.76 (dd, 2H, *J* = 13.3, 9.6 Hz, 2(PhCH)), 1.77–1.71 (m, 2H, 2($COCH_2CH$)), 1.45–1.26 (m, 6H), 1.21 (d, 6H, *J* = 6.8 Hz, 2(CH_3)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.18, 153.08, 135.33, 129.42, 128.89, 127.29, 66.01, 55.33, 37.92, 37.47, 33.18, 27.01, 17.34 ppm; MS (FAB) m/e 521 (M$^+$ + H). Anal. Calcd. for $C_{30}H_{36}N_2O_6$: C, 69.21; H, 6.97; N, 5.38. Found: C, 69.50; H, 6.95; N, 5.24.

[2S-[2R*(R*),2[8R*(R*)]]]-3,3'-(1,8-Dioxo-2,7-di-2-propenyl-1,8-octanediyl)bis[4-(phenylmethyl)-2-oxazolidinone] (14b). Prepared by the same procedure as described for **14a** by reaction of **6c** with allyl iodide. Isolate **14b** as a yellow oil (55%): $[\alpha]^{26}_D$ +70° (*c* 0.99, $CHCl_3$); IR (neat) 2978, 2928, 2860, 1778, 1695 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.20 (m, 10H, aromatic), 5.86–5.77 (m, 2H, 2(CH_2=C*H*)), 5.12–5.01 (m, 4H, 2(CH=C*H*$_2$)), 4.72–4.67 (m, 2H, 2(NCH)), 4.23–4.11 (m, 4H, 2(OCH_2)), 3.93–3.88 (m, 2H, 2(COCH)), 3.29 (dd, 2H, *J* = 13.3, 3.1 Hz, 2(PhCH)), 2.66 (dd, 2H, *J* = 13.3, 10.0 Hz, 2(PhCH)), 2.52–2.27 (m, 4H, 2(CH_2=CHC*H*$_2$)), 1.79–1.65 (m, 2H, 2(COCHC*H*)), 1.55–1.44 (m, 2H, 2(COCHC*H*)), 1.38–1.24 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

175.96, 153.17, 135.43, 135.22, 129.37, 128.88, 127.25, 117.12, 65.92, 55.48, 42.03, 38.06, 36.78, 31.28, 27.00 ppm; MS (FAB) m/e 573 (M^+ + H). Anal. Calcd. for $C_{34}H_{40}N_2O_6$: C, 71.31; H, 7.04; N, 4.89. Found: C, 71.49; H, 7.11; N, 4.60.

[2S–[2R*(R*),2[8R*(R*)]]]–3,3'–(2,8–Dimethyl–1,9–dioxo–1,9–nonanediyl)bis[4–(phenylmethyl)–2-oxazolidinone] (14c). Prepared by the same procedure as described for **14a** by reaction of **6d** with iodomethane. Isolate **14c** as a yellow oil (68%): $[\alpha]^{26}_D$ +81° (*c* 1.10, $CHCl_3$); IR (neat) 2977, 1779, 1699, 1455, 1386, 1350, 1291, 1237, 1211 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.20 (m, 10H, aromatic), 4.73–4.64 (m, 2H, 2(NCH)), 4.26–4.12 (m, 4H, 2(OCH_2)), 3.75–3.25 (m, 2H, 2(COCH)), 3.26 (dd, 2H, *J* = 13.3, 3.3 Hz, 2(PhCH)), 2.76 (dd, 2H, *J* = 13.3, 9.6 Hz, 2(PhCH)), 1.78–1.66 (m, 2H, 2($COCH_2CH$), 1.42–1.25 (m, 8H), 1.21 (d, 6H, *J* = 6.8 Hz, 2(CH_3)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.25, 153.06, 135.35, 129.43, 128.90, 127.30, 66.01, 55.33, 37.92, 37.64, 33.32, 29.55, 27.08, 17.37 ppm; MS (FAB) m/e 535 (M^+ + H). Anal. Calcd. for $C_{31}H_{38}N_2O_6$: C, 69.64; H, 7.16; N, 5.24. Found: C, 69.40; H, 7.16; N, 5.22.

[2S–[2R*(R*),2[8R*(R*)]]]–3,3'–(1,9–Dioxo–2,8–di–2–propenyl–1,9–nonanediyl)bis[4–(phenylmethyl)–2–oxazolidinone] (14d). Prepared by the same procedure as described for **14a** by reaction of **6d** with allyl iodide. Isolate **14d** as a yellow oil (69%): $[\alpha]^{26}_D$ +59° (*c* 1.00, $CHCl_3$); IR (neat) 2928, 2859, 1779, 1696, 1650, 1388, 1350 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.21 (m, 10H, aromatic), 5.89–5.75 (m, 2H, 2(CH_2=C*H*)), 5.11–5.02 (m, 4H, 2(CH=CH_2)), 4.74–4.65 (m, 2H, 2(NCH)), 4.19–4.13 (m, 4H, 2(OCH_2)), 3.95–3.85 (m, 2H, 2(COCH)), 3.29 (dd, 2H, *J* = 13.3, 3.1 Hz, 2(PhCH)), 2.66 (dd, 2H, *J* = 13.3, 10.0 Hz, 2(PhCH)), 2.5–2.25 (m, 4H, 2(CH_2=CHCH_2)), 1.78–1.65 (m, 2H, 2(COCHC*H*)), 1.51–1.41 (m, 2H, 2(COCHC*H*)), 1.28 (br s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.10, 153.22, 135.44, 135.26, 129.39, 128.91, 127.28, 117.13, 65.92, 55.50, 42.29, 38.10, 36.78, 31.42, 29.62, 27.06 ppm; MS (FAB) m/e 587 (M^+ + H). Anal. Calcd. for $C_{35}H_{42}N_2O_6$: C, 71.65; H, 7.21; N, 4.77. Found: C, 71.59; H, 6.92; N, 4.46.

[2S–[2R*(R*),2[8R*(R*)]]]–3,3'–[1,9–Dioxo–2,8–bis(phenylmethyl)–1,9–nonanediyl]bis[4–(phenylmethyl)–2–oxazolidinone] (14e). Prepared by the same procedure as described for **14a** by reaction of **6d** with benzyl bromide. Isolate **14e** as a colorless solid (42%): mp 118–120 °C; $[\alpha]^{26}_D$ +34° (*c* 1.00, $CHCl_3$); IR (KBr) 2926, 1769, 1692, 1393 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–6.98 (m, 20H, aromatic), 4.67–4.60 (m, 2H, 2(NCH)), 4.25–4.11 (m, 4H, 2(OCH_2)), 4.05–4.02 (m, 2H, 2(COCH)), 3.06–2.95 (m, 4H, 2(COCHCH_2Ph)), 2.78 (dd, 2H, *J* = 13.3, 6.7 Hz, 2(PhCH)), 2.38 (dd, 2H, *J* = 13.5, 9.4 Hz, 2(PhCH)), 1.77–1.42 (m, 4H, 2(COCHCH_2)), 1.33–1.26 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.03, 153.00, 139.06, 135.22, 129.64, 129.31, 129.04, 128.51, 128.28, 98.15, 65.68, 55.05, 44.45, 38.72, 37.48, 31.39, 29.55, 27.04 ppm; MS (FAB) m/e 687 (M^+ + H). Anal. Calcd. for $C_{43}H_{46}N_2O_6$: C, 75.19; H, 6.75; N, 4.08. Found: C, 74.92; H, 6.90; N, 4.00.

[2S–[2R*(R*),2[2R*(R*)]]]–3,3'–[1,3–Phenylenebis(2–methyl–1–oxo–2,1–ethanediyl)]bis[4–(phenylmethyl)–2-oxazolidinone] (15). Prepared by the same procedure as described for **14a** by reaction of **11** with iodomethane. Isolate **15** as a colorless solid (31%): mp 190–192 °C; $[\alpha]^{26}_D$ + 183° (*c* 1.0, $CHCl_3$); IR (KBr) 2967, 1785, 1694 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.19 (m, 14H, aromatic), 4.97 (q, 2H, *J* = 7.0 Hz, 2(C*H*CH_3)), 4.65–4.60 (m, 2H, 2(NCH)), 4.13–4.03 (m, 4H, 2(OCH_2), 3.34 (dd, 2H, *J* =13.3, 3.2 Hz, 2(PhCH)), 2.79 (dd, 2H, *J* = 13.3, 9.7 Hz, 2(PhCH)), 1.51 (d, 6H, *J* = 7.0 Hz, 2(CH_3)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.29, 152.90, 140.69, 135.41, 129.43, 128.92, 127.95, 127.30, 126.65, 65.97, 55.81, 43.81, 38.00, 19.50 ppm; HRMS (FAB) m/e Calcd (M^+ + H): 541.2338. Found: 541.2335. Anal. Calcd. for $C_{32}H_{32}N_2O_6$: C, 71.10; H, 5.97; N, 5.18. Found: C, 70.95; H, 5.92; N, 4.98.

(4S)–3–[(2–Oxocyclopentyl)carbonyl]–4–(phenylmethyl)–2–oxazolidinone (18). To a solution of NaHMDS (2.3 mL of a 1.0 M THF solution, 2.3 mmol) and THF (2 mL) at –78 °C was added **6a** (0.5 g, 1.1 mmol) dissolved in THF (14 mL). The mixture was stirred at –78 °C for 2 h, allowed to warm to room temperature, and stirred for 2 h. Saturated aqueous ammonium chloride (75 mL) was added to the reaction mixture and allowed to warm to room temperature, diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were washed with brine (3 x 50 mL), dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified on silica gel (elution with 40% EtOAc/hex) to provide **18** as a yellow oil, 0.17 g (55%): $[\alpha]^{26}_D$ +50° (*c* 1.25, $CHCl_3$); IR (neat) 2969, 1689, 1480, 1454 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.20 (m, 5H, aromatic), 4.76–4.64 (m, 2H, (NCH, N(CO)CH)), 4.31–4.17 (m, 2H, OCH_2), 3.35–3.27 (m, 1H, PhCH), 2.84–2.76 (m, 1H, PhCH), 2.45–2.13 (m, 4H), 2.06–1.91 (m, 1H), 1.61 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.84, 211.72, 169.54, 169.02, 153.65, 153.53, 135.23, 135.13, 129.44, 129.40, 128.95, 128.85, 127.38, 127.28, 67.96, 66.22, 66.08, 65.78, 55.23, 54.44, 54.25, 38.02, 37.90, 37.74, 26.65, 26.51, 20.66, 20.64 ppm; MS (FAB) m/e 288 (M^+ + H). Anal. Calcd. for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88. Found: C, 66.74; H, 5.89; N, 5.09.

(4S)-3-[(2-Oxocyclohexyl)carbonyl]-4-(phenylmethyl)-2-oxazolidinone (19). To a solution of NaHMDS (0.9 mL of a 1.0 M THF solution, 0.9 mmol) and THF (2 mL) at –78 °C was added **6b** (0.2 g, 0.4 mmol) dissolved in THF (5 mL). The mixture was stirred at –78 °C for 2.5 h. Saturated aqueous ammonium chloride (75 mL) was added to the reaction mixture, allowed to warm to room temperature, diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were washed with brine (3 x 50 mL), dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified on silica gel (elution with 30% EtOAc/hex) to provide **19** as a yellow oil, 0.074 g (55%): $[\alpha]^{26}_D$ +48° (*c* 1.00, $CHCl_3$); IR (neat) 2942, 1775, 1718, 1700, 1353 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.19 (m, 5H, aromatic), 4.80–4.51 (m, 2H, (NCH, N(CO)CH)), 4.30–4.14 (m, 2H, OCH_2), 3.47 (dd, 0.5H, *J* = 13.6, 3.4 Hz, 1 diastereomer (PhCH)), 3.30 (dd, 0.5H, *J* = 13.4, 3.3 Hz, 1 diastereomer (PhCH)), 2.83 (dd, 0.5H, *J* = 13.6, 10.0 Hz, 1 diastereomer (PhCH)), 2.77 (dd, 0.5H, *J* = 13.4, 9.6 Hz, 1 diastereomer (PhCH)), 2.65–2.41 (m, 2H), 2.32–1.90 (m, 4H), 1.81–1.26 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.70, 206.66, 169.90, 169.74, 153.75, 153.48, 135.60, 135.18, 129.46, 129.33, 129.03, 128.87, 127.29, 127.12, 66.36, 66.20, 56.83, 56.62, 55.30, 55.10, 42.11, 42.04, 38.08, 37.49, 29.39, 29.32, 27.74, 27.64, 24.21, 24.17 ppm; MS (FAB) m/e 302 (M^+ + H). Anal. Calcd. for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.35; N, 4.65. Found: C, 67.50; H, 6.22; N, 4.45.

[4R-[3(4R*,5S*),4α,5α]]-3,3'-[1,3-Dithiolan-2-ylidenebis(1-oxo-3,1-propanediyl)]bis[4-methyl-5-phenyl-2-oxazolidinone] (20). To a 0 °C solution of ketone **9** (1.38 g, 2.8 mmol) and 1,2-ethanedithiol (5.88 mL, 70.1 mmol) was added boron trifluoride etherate (1.03 mL, 8.4 mmol) dropwise. The resulting yellow colored solution was stirred at 0 °C for 30 min prior to dilution with EtOAc (150 mL). The organic phase was washed with 1 N NaOH (2 x 70 mL), water (70 mL), and brine (70 mL) prior to drying over anhydrous $MgSO_4$, filtration, and concentration. The residue was purified on silica gel (elution with 30% EtOAc/hex) to give **20** as a colorless foam, 1.59 g (100%): mp 58–64 °C; $[\alpha]^{26}_D$ +39° (*c* 0.85, $CHCl_3$); IR (KBr) 1781, 1700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.30 (m, 10H, aromatic), 5.68 (d, 2H, *J* = 7.3 Hz, 2(OCHPh)), 4.82–4.73 (m, 2H, 2(NCH)), 3.46–3.24 (m, 8H, 2(SCH_2), 2($COCH_2$)), 2.40–2.27 (m, 4H, 2($COCH_2CH_2$)), 0.91 (d, 6H, *J* = 6.6 Hz, 2(CH_3)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.53, 153.01, 133.30, 128.66, 125.64, 78.99, 70.26, 54.78, 40.72, 37.91, 33.16, 14.54 ppm; HRMS (FAB) m/e Calcd (M^+ + H): 569.1780. Found: 569.1771. Anal. Calcd. for $C_{29}H_{32}N_2S_2O_6$: C, 61.25; H, 5.67; N, 4.93; S, 11.28. Found: C, 60.98; H, 5.53; N, 4.75; S, 11.04.

[4R-[3(R* and S*),4α,5α]]-4-Methyl-3-[(8-oxo-1,4-dithiaspiro[4.5]dec-7-yl)carbonyl]-5-phenyl-2-oxazolidinone (21). Prepared by the same procedure as described for **18** by reaction of **20** with NaHMDS. Isolate **20** as a colorless foam (63%): mp 60–64 °C; $[\alpha]^{26}_D$ +13° (*c* 0.7, $CHCl_3$); IR (KBr) 1781, 1700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.29 (m, 5H, aromatic), 5.76 (d, 0.5H, *J* = 7.4 Hz, OCHPh), 5.67 (d, 0.5H, *J* = 7.3 Hz, OCHPh), 5.07–4.76 (m, 2H, (NCH, N(C=O)CH)), 3.46–3.39 (m, 4H, SCH_2CH_2S), 2.97–2.71 (m, 2H), 2.62–2.44 (m, 4H), 0.98 (d, 1.5H, *J* = 6.6 Hz, CH_3), 0.90 (d, 1.5H, *J* = 6.6 Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.67, 204.59, 168.51, 168.15, 153.15, 152.90, 133.12, 133.08, 128.77, 128.68, 125.67, 79.23, 65.85, 65.82, 55.89, 55.72, 54.90, 54.79, 44.22, 42.71, 42.54, 41.23, 41.18, 39.39, 38.69, 14.76, 14.14 ppm; HRMS (FAB) m/e Calcd (M^+ + H): 392.0990. Found: 392.0997.

[2S-[1(R*),2R*,8(R*)]]-3,3'-(2-Methyl-1,8-dioxo-1,8-octanediyl)bis[4-(phenylmethyl)-2-oxazolidinone] (22a). To a solution of **6c** (0.5 g, 1.0 mmol) and THF (7.5 mL) at –78 °C was added NaHMDS (1.0 mL of a 1.0 M THF solution, 1.0 mmol) dropwise and stirred for 45 min. To the –78 °C solution was added methyl iodide (0.3 mL, 5.0 mmol) by syringe; stirring was continued for 5 h. A saturated aqueous solution of ammonium chloride (25 mL) was added to the reaction mixture, diluted with water (20 mL), and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were washed with brine (3 x 50 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified on silica gel (elution with 30% EtOAc/hex) to provide **22a**, as a colorless oil, 0.16 g (31%): $[\alpha]^{26}_D$ +69° (*c* 0.5, $CHCl_3$); IR (neat) 2933, 2859, 1777, 1696, 1386, 1351, 1210 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.20 (m, 10H, aromatic), 4.71–4.64 (m, 2H, 2(NCH)), 4.26–4.13 (m, 4H, 2(OCH$_2$)), 3.73–3.71 (m, 1H, COCH), 3.32–3.24 (m, 2H, 2(PhCH)), 2.96–2.88 (m, 2H, COCH$_2$), 2.81–2.73 (m, 2H, 2(PhCH)), 1.75–1.63 (m, 4H), 1.45–1.37 (m, 4H), 1.22 (d, 3H, J = 6.8 Hz, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 177.18, 173.25, 153.43, 153.07, 135.30, 129.40, 128.90, 127.29, 66.14, 66.01, 55.32, 55.13, 37.88, 37.55, 35.34, 33.16, 28.95, 26.88, 24.06, 17.38 ppm; HRMS (FAB) m/e Calcd. (M$^+$ + H): 507.2495. Found: 507.2502.

[2S–[1(R*),2R*,8(R*)]]–3,3'–(2–Methyl–1,9–dioxo–1,9–nonanediyl)bis[4–(phenylmethyl)–2–oxazolidinone] (22b). Prepared by the same procedure as described for **22a** by reaction of **6d** with methyl iodide. Isolate **22b** as a colorless oil (45%): $[\alpha]^{26}_{D}$ +69° (c 1.0, CHCl$_3$); IR (neat) 2932, 1781, 1698, 1387, 1212 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.36–7.20 (m, 10H, aromatic), 4.70–4.67 (m, 2H, 2(NCH)), 4.21–4.15 (m, 4H, 2(OCH$_2$)), 3.76–3.65 (m, 1H, COCH), 3.32–3.25 (m, 2H, 2(PhCH)), 3.05–2.85 (m, 2H, COCH$_2$), 2.82–2.73 (m, 2H, 2(PhCH)), 1.81–1.63 (m, 4H), 1.49–1.29 (m, 6H), 1.22 (d, 3H, J = 6.8 Hz, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 177.21, 173.30, 153.41, 153.30, 129.39, 128.89, 127.27, 66.12, 65.97, 55.30, 55.11, 37.87, 37.64, 35.43, 33.29, 29.28, 28.88, 27.02, 24.10, 17.37 ppm; HRMS (FAB) m/e Calcd. (M$^+$ + H): 521.2651. Found: 521.2647. Anal. Calcd. for $C_{30}H_{36}N_2O_6$: C, 69.21; H, 6.97; N, 5.38. Found: C, 68.93; H, 6.99; N, 5.15.

[2R–[2R*(S*),2(S*)]]–3,3'–(1,9–Dioxo–2–propenyl–1,9–nonanediyl)bis[4–(phenylmethyl)–2–oxazolidinone] (22c). Prepared by the same procedure as described for **22a** by reaction of **6d** with allyl iodide. Isolate **22c** as a colorless oil (35%): $[\alpha]^{26}_{D}$ +58° (c 1.0, CHCl$_3$); IR (neat) 2976, 1779, 1697, 1387, 1210 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.38–7.20 (m, 10H, aromatic), 5.90–5.76 (m, 1H, CH$_2$=C*H*), 5.13–5.03 (m, 2H, CH=C*H*$_2$), 4.73–4.64 (m, 2H, 2(NCH)), 4.23–4.12 (m, 4H, 2(OCH$_2$)), 3.94–3.89 (m, 1H, COCH), 3.32–3.27 (m, 2H, 2(PhCH)), 3.03–2.85 (m, 2H, COCH$_2$), 2.76 (dd, 1H, J = 13.3, 9.6 Hz, PhCH), 2.66 (dd, 1H, J = 13.3, 10.0 Hz, PhCH), 2.50–2.32 (m, 2H, CH$_2$=CHC*H*$_2$), 1.80–1.45 (m, 4H), 1.42–1.28 (bs, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 176.04, 173.32, 153.50, 153.25, 135.45, 135.27, 129.40, 128.92, 127.28, 117.13, 66.14, 65.92, 55.51, 42.27, 38.10, 37.92, 36.82, 35.44, 31.44, 29.32, 28.87, 27.03, 24.11 ppm; HRMS (FAB) m/e Calcd. (M$^+$ + H): 547.2808. Found: 547.2811. Anal. Calcd. for $C_{32}H_{38}N_2O_6$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.35; H, 7.13; N, 4.96.

[2S–[2R*(R*),8S*(R*)]]–3,3'–[2–Methyl–1,9–dioxo–8–(2–propenyl)–1,9–nonanediyl]bis[4–(phenylmethyl)–2–oxazolidinone] (23). To a –78 °C solution of **22b** (0.28 g, 0.54 mmol) and THF (4 mL) was added NaHMDS (1.1 mL of a 1.0 M THF solution, 1.1 mmol) dropwise. The mixture was stirred at –78 °C for 45 min. To the cold solution was added allyl iodide (0.25 mL, 2.7 mmol) by syringe; stirring was continued at –78 °C for 2.5 h. A saturated aqueous solution of ammonium chloride (25 mL) was added to the reaction mixture, diluted with water (20 mL), and extracted with CH$_2$Cl$_2$ (3 x 50 mL). The combined organic phases were washed with brine (3 x 50 mL), dried with anhydrous Na$_2$SO$_4$, filtered, and concentrated *in vacuo*. The residue was purified on silica gel (elution with 20% EtOAc/hex) to provide **23**, as a colorless oil, 0.15 g (50%): $[\alpha]^{26}_{D}$ +74° (c 0.9, CHCl$_3$); IR (neat) 2859, 1779, 1697 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.35–7.20 (m, 10H, aromatic), 5.84–5.78 (m, 1H, C*H*=CH$_2$), 5.12–5.02 (m, 2H, CH=C*H*$_2$), 4.72–4.65 (m, 2H, 2(NCH)), 4.25–4.12 (m, 4H, 2(COCH$_2$)), 3.98–3.85 (m, 1H, COCH), 3.75–3.65 (m, 1H, COCH), 3.32–3.23 (m, 2H, 2(PhCH)), 2.80–2.62 (m, 2H, 2(PhCH)), 2.52–2.25 (m, 2H, C*H*$_2$CH=CH$_2$), 1.80–1.63 (m, 4H), 1.51–1.25 (m, 6H), 1.21 (d, 3H, J = 6.8 Hz, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) δ 177.20, 176.04, 153.14, 153.03, 135.42, 135.24, 129.39, 128.88, 127.27, 117.11, 65.98, 65.89, 55.48, 55.30, 42.23, 38.06, 37.85, 37.60, 36.78, 33.25, 31.41, 29.56, 27.05, 17.33 ppm; HRMS (FAB) m/e (M$^+$ + H): 561.2964. Found: 561.2955. Anal. Calcd. for $C_{33}H_{40}N_2O_6$: C, 70.69; H, 7.19; N, 5.00. Found: C, 70.66; H, 7.22; N, 4.82.

(S)–3–[1,9–Dioxo–9–(2–oxo–3–oxazolidinyl)nonyl]–4–(phenylmethyl)–2–oxazolidinone (25). To a solution of **4** (4.7 g, 26.7 mmol), 2–oxazolidinone (**24**, 2.3 g, 26.7 mmol) and THF (25 mL) at –78 °C was added *n*–butyllithium (21.3 mL of a 2.0 M hexane solution, 53.3 mmol) dropwise; the resulting orange slurry was stirred at –78 °C for 25 min. To the slurry was added azelaoyl chloride (5.3 mL, 26.7 mmol) dissolved in THF (5 mL), stirred at –78 °C for 2 h, allowed to warm to room temperature, and stirred for an additional 3 h. The reaction mixture was poured into a saturated aqueous ammonium chloride solution (100 mL), diluted with water (50 mL) and extracted with CH$_2$Cl$_2$ (3 x 75 mL). The combined organic phases were washed with brine (3 x 75 mL), dried with anhydrous Na$_2$SO$_4$ and filtered, and concentrated *in vacuo*. The residue was purified on silica gel (elution with 50% EtOAc/hex) to provide **25** as a white solid, 1.0 g (28%): mp 64–65 °C; $[\alpha]^{26}_D$ +34° (*c* 1.00, $CHCl_3$); IR (KBr) 1786, 1692, 1390 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.20 (m, 5H, aromatic), 4.72–4.63 (m, 1H, NCH), 4.45–4.35 (m, 2H, $OC\mathit{H}_2CH$), 4.25–4.13 (m, 2H, $OC\mathit{H}_2CH_2$), 4.05–3.98 (m, 2H, NCH_2), 3.29 (dd, 1H, *J* = 13.3, 3.3 Hz, PhCH), 2.94–2.87 (m, 4H, $2(COCH_2)$), 2.75 (dd, 1H, *J* = 13.3, 9.6 Hz, PhCH), 1.70–1.62 (m, 4H), 1.43 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.41, 173.24, 153.38, 135.28, 129.35, 128.86, 127.24, 66.09, 61.94, 55.07, 42.45, 37.85, 35.39, 34.96, 28.97, 28.82, 24.09 ppm; MS (FAB) m/e 417 (M^+ + H). Anal. Calcd. for $C_{22}H_{28}N_2O_6$: C, 63.45; H, 6.78; N, 6.73. Found: C, 63.31; H, 6.83; N, 6.86.

[2S-[2R*(R*),2(8R* and 8S*)]]-3[2,8-Dimethyl-1,9-dioxo-9-(2-oxo-3-oxazolidinyl)nonyl]-4-(phenylmethyl)-2-oxazolidinone (26). Prepared by the same procedure as described for **14a** by reaction of **25** with iodomethane. Isolate as an inseparable mixture of diastereomers **26** as a yellow oil (56%): $[\alpha]^{26}_D$ +47° (*c* 1.10, $CHCl_3$); IR (neat) 2974, 1777, 1696, 1387, 1287 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.20 (m, 5H, aromatic), 4.71–4.66 (m, 1H, NCH), 4.43–4.37 (m, 2H, OCH_2), 4.25–4.14 (m, 2H, OCH_2CH_2), 4.04–4.00 (m, 2H, NCH_2), 3.75–3.66 (m, 2H, 2(COCH)), 3.26 (dd, 1H, *J* = 13.3, 3.2 Hz, PhCH), 2.77 (dd, 1H, *J* = 13.3, 9.5 Hz, 2(PhCH)), 1.77–1.68 (m, 2H), 1.42–1.26 (m, 8H), 1.21 (d, 3H, *J* = 6.81 Hz, CH_3), 1.15 (d, 3H, *J* = 6.8 Hz, CH_3): ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.26, 177.28, 153.86, 152.93, 135.26, 129.31, 128.77, 127.16, 65.91, 61.73, 55.29, 42.70, 37.89, 37.53, 37.50, 33.42, 33.36, 33.22, 33.18, 29.42, 29.30, 26.97, 26.87, 26.77, 17.27, 16.91, 16.89 ppm; MS (FAB) m/e 447 (M^+ + H). Anal. Calcd. for $C_{24}H_{32}N_2O_6$: C, 64.85; H, 7.26; N, 6.30. Found: C, 64.55; H, 7.09; N, 6.17.

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References

1. For some reviews on interesting symmetrical compounds consult: Eaton, P. E. *Tetrahedron* **1979**, *35*, 2189–2223. Paquette, L. A. *Chem. Rev.* **1989**, *89*, 1051–1065. Kroto, H. W.; Allaf, A. W.; Balm, S. P. *Chem. Rev.* **1991**, *91*, 1213–1235.
2. (a) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581–1590. (b) Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503–516.
3. (a) Kempf, D. J.; Norbeck, D. W.; Codacovi, L. M.; Wang, X. C.; Kohlbrenner, W. E.; Wideburg, N. E.; Paul, D. A.; Knigge, M. F.; Vasavanonda, S.; Craig-Kennard, A.; Saldivar, A.; Rosenbrook, W. Jr.; Clement, J. J.; Plattner, J. J.; Erickson, J. *J. Med. Chem.* **1990**, *33*, 2687–2689. (b) Chenera, B.; Boehm, J. C.; Dreyer, G. B. *Bioorg. and Med. Chem. Lett.* **1991**, *1*, 219–222. (c) Askin, D.; Wallace, M. A.; Vacca, J. P.; Reamer, R. A.; Volante, R. P.; Shinkai, I. *J. Org. Chem.* **1992**, *57*, 2771–2773.
4. Babine, R. E.; Zhang, N.; Jurgens, A.; Schow, S. R.; Desai, P. R.; James, J. C.; Semmelhack, M. *Bioorg. and Med. Chem. Lett.* **1992**, *2*, 541–546.
5. Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737–1739. Evans, D. A. *Aldrichimica Acta.* **1982**, *15*, 23–32.