Compound 4:
Merrifield-OH resin (10 g, 14.4 mmol, Novabiochem) was swelled in 1:1 tetrahydrofuran (THF) /dichloromethane (DCM). To this was added triphenylphosphine (7.9 g, 30 mmol, Aldrich) and N_{α}-Boc-N_{β}-Fmoc-L-Diaminopropionic acid (12.7 g, 30 mmol) and the slurrry was cooled to 0 °C under Argon. To this gently agitating solution was added diethylazodicarboxylate (5.22 g, 30 mmol, Aldrich) slowly over a period of 5 minutes. This reaction was kept at 0 °C for 60 minutes then allowed to gradually warm to room temperature while agitating for 60 h. The off-white colored resin was filtered and washed with THF (5X), DCM (5X), then alternating DCM/methanol (MTH) washes (6 each). The resin was vacuum dried for 18 h. Yield: 14.3 g (90%), CHN: %N 2.263 (obs.), 2.5 (calc.), IR (cm^{-1}): 1731, 1716, 1695

Compound 6:
N_{α}-Boc-N_{β}-Fmoc-L-Diaminopropionic acid loaded hydroxymethyl Merifield-PS resin (1.72 g, 1.4 mmol) was rinsed three times with (DCM) then treated with a solution of 25% piperidine in N,N-dimethylformamide (DMF). The reaction was allowed to agitate for 30 minutes. The resin was filtered and washed liberally with DMF (6X) followed by MeOH (3X), DCM (3X) and alternating MeOH-DCM washes (3X each). (Ninhydrin testing[1] of resin 4 gave a strong positive result.) The deprotected resin (**4**) was rinsed a final time with a 4:1 solution of chloroform (CHL)/MeOH. Resin **4** was swelled in 4:1 CHL/MTH (20-25 mL) and to this was added hydrocinnamaldehyde (5 eq., 7.5 mmol, Aldrich). The resin was agitated for 5 minutes before adding 2,6-dimethylphenyl isocyanide (5 eq., 7.5 mmol, Fluka) followed by R(+)-2-bromopropionic acid (5 eq., 7.5 mmol, Fluka). The resin mixture was agitated for 2.5 h before filtering and washing with 4:1 CHL/MeOH (5X). The reaction was repeated in an identical manner for 3.5 h. The resin was filtered and washed with 4:1 CHL/MeOH (5X) followed by alternating DCM/MeOH washes (3X each). Ninhydrin testing of resin 5 was negative. Resin **5** was treated with 25% trifluoroacetic acid (TFA) in DCM for 1 h. The resin was filtered and washed with DCM (6X) followed by alternating DCM/MeOH (3X each) washes. The Boc deprotected resin **5b** was swelled in 10% diisopropylethylamine (DiPEA)/DCM and agitated for 18 h then filtered and washed with DMF (3X) followed by alternating DCM/MeOH (3X each) washes.

Preparation of the isobutylcarbonic acid mixed anhydride[2] of Boc-Phe-OH
Boc-Phe-OH (5eq., 7.5 mmol, Advanced Chemtech) was dissolved in dry THF (20 mL) under an Argon atmosphere and cooled to 0 °C using an ice bath while being magnetically stirred. To the cooled solution was added N-methylmorpholine (5.5 eq., 8.25 mmol) followed by the *slow* addition of isobutylchloroformate (5 eq., 7.5 mmol, Aldrich) over a period of 10 minutes. A white precipitate was observed immediately. The heterogeneous solution was allowed to stir at 0 °C for 15 minutes.

Compound 7a and 7b:
Resin **6** was swelled in DMF (5 mL) and to this was added the heterogeneous mixed anhydride solution prepared previously. The reaction was allowed to agitate for 6 h. before filtering and washing with DMF (5X). The reaction was repeated in an identical manner except that it was allowed to agitate for 72 hr. The resin was filtered and washed with DMF (5X) followed by alternating DCM/MeOH (3X each) washes. The resin **6d** was agitated with a solution of 25 % TFA/DCM for 1 h. The resin **6e** was filtered and washed with alternating DCM/MeOH (5X each) followed by DCM (2X) then taken up in a 2M solution of acetic acid (AcOH)/2-propanol (iPrOH) and heated to 50 °C for 18 h. The resin was filtered and washed with MeOH (4X) and the filtrate and washings were collected and combined before evaporating to dryness under reduced pressure. The crude, yellowish-orange, solid was co-evaporated with CHL (3X) then vacuum dried for 18 h. Crude yield: 0.327 g (42%), MS APCI: 553=[M+H] The crude sample was purified by RP-HPLC (C_4 column, 55 min linear gradient start: 95% water with 0.1% TFA added / 5% acetonitrile to 100 % acetonitrile) to give 0.167 g (22% from **4**) of a white solid.

References
1) Kaiser, E.; Colescott, R.L.; Bossinger, C.D.; Cook, P.I. *Anal. Biochem*. **1970**, *34*, 595-598
2) Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*, 2nd ed.; Springer-Verlag, New York, 1994, pp. 93-94.

Separation and characterization of diastereomers 7a and 7b:
The purified mixture of C^* diastereomers (0.167 g) was separated by RP-HPLC (Inertsil ODS-3, 50x250mm, C_{18}) using a 60 min gradient at 50 mL/min. Mobile phase: 50% methanol; 50% water; 0.1% trifluoracetic acid (v/v/v) to 100% methanol. The individual diastereomers had retention times of 25 min and 32 min respectively. **Early fraction:** ^{1}H NMR (500 MHz, $CDCl_3$, δ) 1.44 (d, J_{fe}=7.2 Hz, 3H), 2.12 (m, 1H), 2.17 (s, 6H), 2.44 (m, 1H), 2.66 (m, 1H), 2.78 (m, 1H), 2.90 (dd, $J_{a'a}$=14.4 Hz, $J_{a'b}$=9.4 Hz, 1H), 3.55 (dd, $J_{aa'}$=14.4 Hz, J_{ab}=3.2 Hz, 1H), 4.18 (dd, $J_{ba'}$=9.4 Hz, J_{ba}=3.2 Hz, 1H), 3.78 (dd, $J_{cd'}$=11.2 Hz, J_{cd}=3.6 Hz, 1H), 4.08 (dd, $J_{dd'}$=14.4 Hz, J_{dc}=3.6 Hz, 1H), 3.46 (dd, $J_{d'd}$=14.4 Hz, $J_{d'c}$=11.2 Hz, 1H), 4.83 (q, J_{ef}=7.2 Hz, 1H), 5.21 (t, J=7.5 Hz, 1H), 7.04-7.40 (m, 13H). $^{13}C\{^1H\}$ (125 MHz, $CDCl_3$, δ) 18.8, 19.7, 30.0, 32.9, 37.2, 41.5, 53.6, 55.2, 55.4, 56.7, 126.7, 127.9, 128.0, 128.5, 128.7, 129.0, 129.5, 129.6, 133.3, 135.2, 135.4, 140.6, 165.9, 166.3, 168.0, 170.4 MS (DCI): m/z 553 $[M+H]^+$ **Late fraction:** ^{1}H NMR (500 MHz, $CDCl_3$, δ) 1.43 (d, J_{fe}=6.9 Hz, 3H), 2.14 (m, 1H), 2.13 (s, 6H), 2.39 (m, 1H), 2.68 (m, 2H), 2.94 (dd, $J_{a'a}$=14.7 Hz, $J_{a'b}$=9.0 Hz, 1H), 3.48 (dd, $J_{aa'}$=14.7 Hz, J_{ab}=3.4 Hz, 1H), 4.24 (dd, $J_{ba'}$=9.0 Hz, J_{ba}=3.4 Hz, 1H), 4.35 (dd, $J_{cd'}$=11.2 Hz, J_{cd}=3.3 Hz, 1H), 4.28 (dd, $J_{dd'}$=13.8 Hz, J_{dc}=3.3 Hz, 1H), 3.35 (dd, $J_{d'd}$=13.8 Hz, $J_{d'c}$=11.2 Hz, 1H), 4.78 (q, J_{ef}=6.7 Hz, 1H), 5.25 (dd, $J_{gh/h'}$=8.9, 6.4 Hz, 1H), 7.00-7.35 (m, 13H). $^{13}C\{^1H\}$ (125 MHz, $CDCl_3$, δ) 18.7, 19.8, 30.9, 32.8, 37.2, 42.5, 54.1, 55.2, 55.3, 56.3, 126.8, 127.8, 127.9, 128.5, 128.6, 129.0, 129.4, 129.6, 133.3, 135.2, 135.4, 140.3, 166.2, 166.6, 169.0, 170.4 MS (DCI): m/z 553 $[M+H]^+$

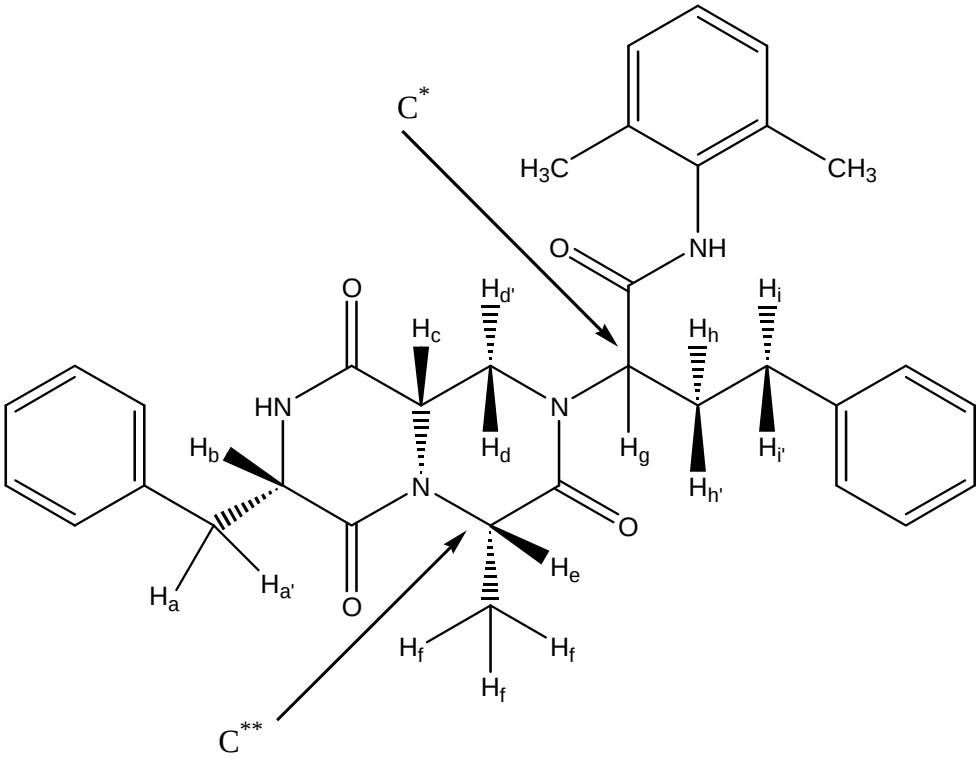

Table of Proton Assignments for Separated Diastereomers

Proton (H_x)	Chemical Shift (δ) Early Fraction	Chemical Shift (δ) Late Fraction
a'	2.90	2.94
a	3.55	3.48
b	4.18	4.24
c	3.78	4.35
d	4.08	4.28
d'	3.46	3.35
e	4.83	4.78
f	1.44	1.43
g	5.21	5.25
h	2.44	2.39
h'	2.12	2.14
I	2.78	2.68
I'	2.66	2.68
aromatic dimethyl	2.17	2.13
aromatic	7.04-7.40	7.0-7.35

NOESY Interpretation and Mechanism of Bromide Displacement

The relative stereochemistry at C** for each of the separated C* isomers (**7a** & **7b**) was determined by NOE cross peak correlation. In each case, the CH_3 (H_f) resonance at 1.44/1.43 ppm shows a cross peak to $H_{d'}$ at 3.46/3.35 ppm. This would strongly indicate that these two groups are in close proximity (co-facial). The $H_{d'}$ assignment was confirmed by measurement of the 11.2 Hz vicinal coupling constant to H_c. This is consistent with a dihedral angle of approximately 180° between these two protons. This direct evidence coupled with a lack of cross peak correlation of H_e with $H_{d'}$ would strongly suggest that the resulting C** stereochemistry is **S** and a result of S_n2 displacement of bromine with inversion of configuration at C**.

2D-NOESY 500 MHz NMR Experiments
Early fraction

```
HCS1719-68
4/18/00

Pulse Sequence: noesy
 Solvent: CDCl3
 Ambient temperature
File: hcs1719-68earlynoesyproc
INOVA-500  "freeman"
PULSE SEQUENCE: noesy
 Relax. delay 7.000 sec
 Mixing 0.700 sec
 Acq. time 0.226 sec
 Width     4530.8 Hz
 2D Width 4530.8 Hz
 16 repetitions
 2 x 256 increments
OBSERVE    H1, 499.7413949 MHz
DATA PROCESSING
 Line broadening 0.1 Hz
 Gauss apodization 0.125 sec
F1 DATA PROCESSING
 Gauss apodization 0.018 sec
FT size 2048 x 2048
Total time 18 hr, 8 min, 41 sec
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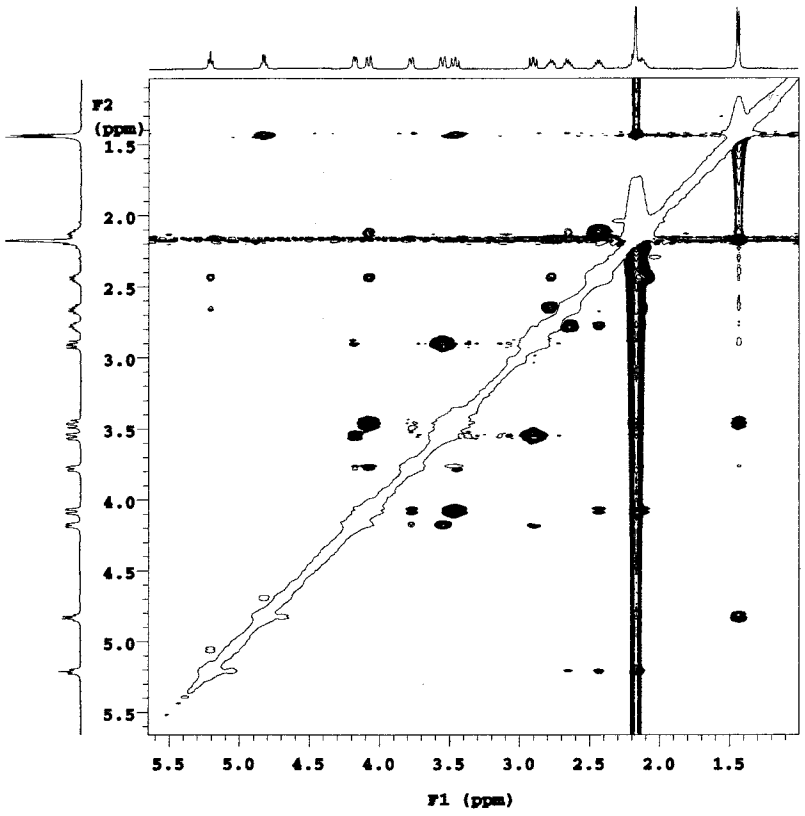

Late Fraction

HCS1719-68
late fraction 4/20/00

Pulse Sequence: noesy
Solvent: CDCl3
Ambient temperature
File: seanproc
INOVA-500 "freeman"

PULSE SEQUENCE: noesy
Relax. delay 7.000 sec
Mixing 0.700 sec
Acq. time 0.226 sec
Width 4530.8 Hz
2D Width 4530.8 Hz
16 repetitions
2 x 256 increments
OBSERVE H1, 499.7413949 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
Gauss apodization 0.127 sec
F1 DATA PROCESSING
Gauss apodization 0.125 sec
FT size 2048 x 2048
Total time 18 hr, 8 min, 41 sec