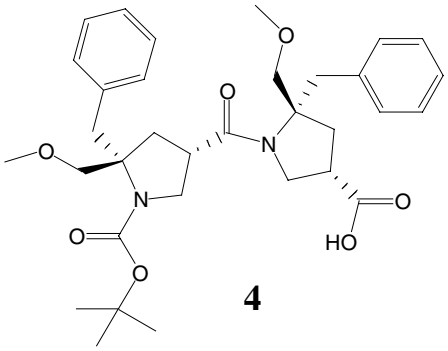
Supplementary Material: 17 pages

Section 1: Crystal Structure parameters for molecule **4:**

Data collection, structure refinement and references
Figure 1. The crystal structure of Molecule **4**
Figure 2. Packing diagram of Molecule **4** viewed along the b axis
Table 1. Crystal data and structure refinement for Molecule **4**
Table 2. Atomic coordinates and equivalent isotropic displacement parameters for Molecule **4**
Table 3. Bond lengths and angles for Molecule 4
Table 4. Anisotropic displacement parameters for Molecule 4
Table 5. Hydrogen coordinates and isotropic displacement parameters for Molecule 4
Table 6. Torsion angles for Molecule 4
Table 7. Hydrogen bonds for Molecule 4

Section 2: NMR experimental and Structure Calculations for Molecule **5:**

Data collection
Table 8. Resonance assignment of molecule **5** in CD_2Cl_2
Table 9. NOE derived restraints used in structure calculations
Structure Calculations
Figure 3. Overlay of structures before and after minimization
Table 10: Pairwise RMSD comparisons of minimized and unminimized structures



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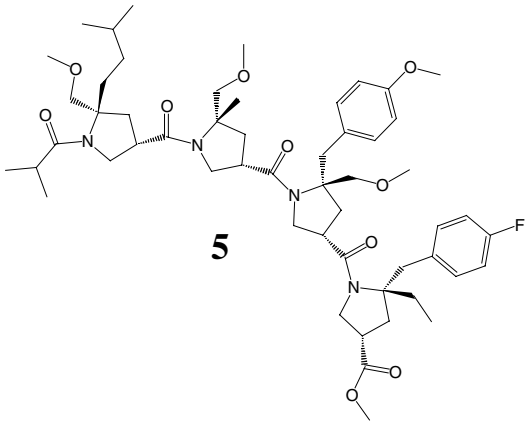


5

Crystallographic Experimental Section

Data Collection

A colorless crystal with approximate dimensions 0.81 x 0.16 x 0.15 mm^3 was selected under oil at ambient conditions and attached to the tip of a glass capillary. The crystal was mounted in a stream of cold nitrogen at 173(2) K and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed on a Bruker CCD-1000 diffractometer with Mo K_α (λ = 0.71073 Å) radiation and a diffractometer to crystal distance of 4.85 cm.

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 20 frames collected at intervals of 0.3º in a 6º range about ω with the exposure time of 10 seconds per frame. A total of 90 reflections was obtained. The reflections were successfully indexed by an automated indexing routine built in the SMART program. The final cell constants were calculated from a set of 5269 strong reflections from the actual data collection.

The data were collected by using the multirun data collection routine. The reciprocal space was surveyed to the extent of a full sphere to a resolution of 0.80 Å. A total of 22546 data were harvested by collecting two sets of 606 frames and one set of 357 frames with 0.3º scans in ω and an exposure time of 45 sec per frame. This highly redundant dataset was corrected for Lorentz and polarization effects. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements. [1]

Structure Solution and Refinement

The systematic absences in the diffraction data were uniquely consistent for the space group $P2_12_12_1$ that yielded chemically reasonable and computationally stable results of refinement.

A successful solution by the direct methods provided most non-hydrogen atoms from the *E*-map. The remaining non-hydrogen atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were included in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients. Intermolecular hydrogen bonding interactions are observed in the lattice and they form a series of one-dimensional chains in the *a* direction.

The final least-squares refinement of 385 parameters against 3159 data resulted in residuals R (based on F^2 for $I \geq 2\sigma$) and wR (based on F^2 for all data) of 0.0327 and 0.0845, respectively. The final difference Fourier map was featureless. The absolute structure could not be reliably determined from the structural data but is known from knowledge of the synthesis.

The ORTEP diagram is drawn with 30% probability ellipsoids.

References

[1] Blessing, R.H. *Acta Cryst*. **1995**, *A51*, 33-38.

[2] All software and sources of the scattering factors are contained in the SHELXTL (version 5.1) program library (G. Sheldrick, Bruker Analytical X-Ray Systems, Madison, WI).

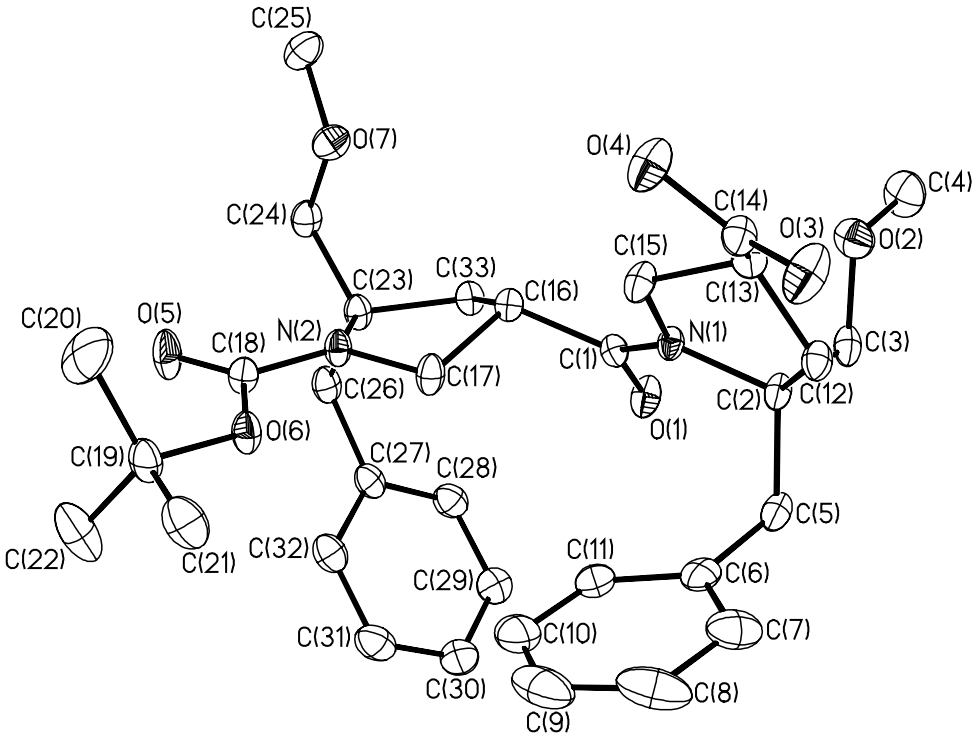


Figure 1. The crystal structure of Molecule 4.

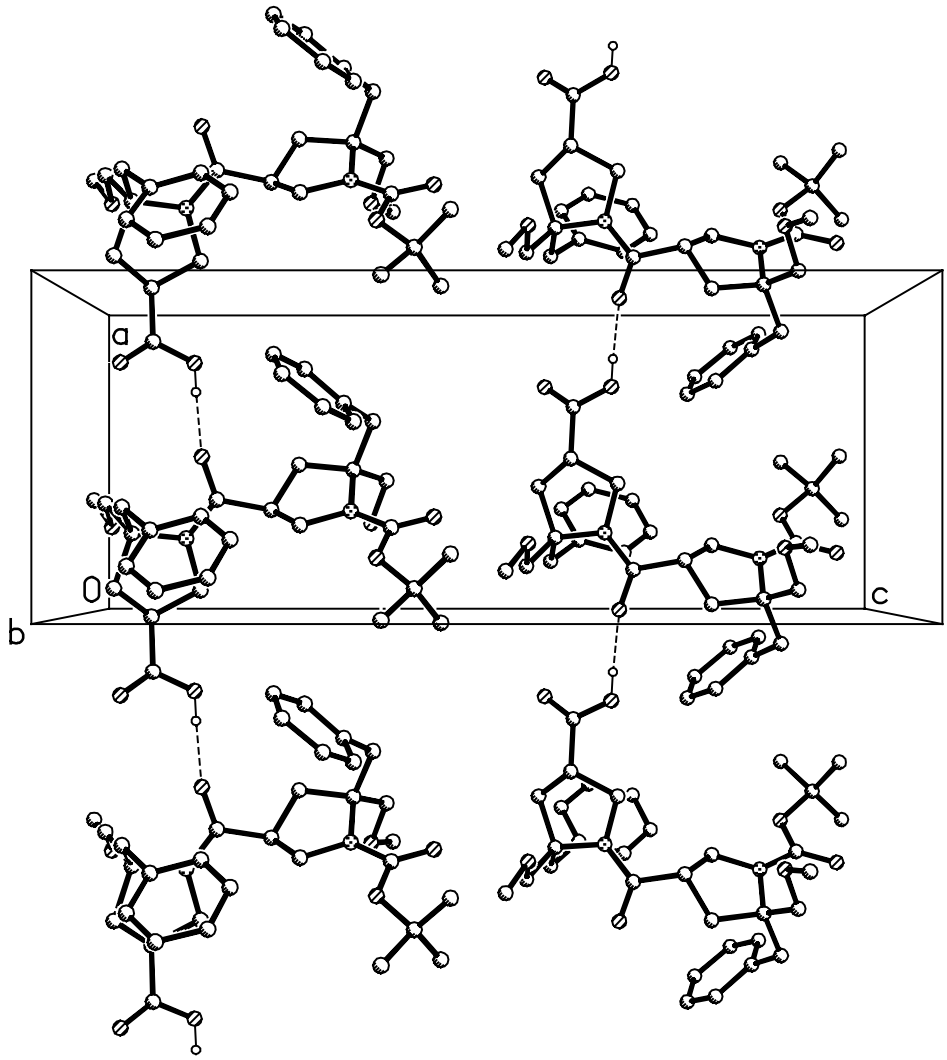


Figure 2. Packing diagram of Molecule 4 viewed along the *b* axis.

Table 1. Crystal data and structure refinement for Molecule **4**.

Empirical formula	$C_{33}H_{44}N_2O_7$	
Formula weight	580.70	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.9111(9) Å	α= 90°.
	b = 15.4387(15) Å	β= 90°.
	c = 22.970(2) Å	γ = 90°.
Volume	3160.1(5) $Å^3$	
Z	4	
Density (calculated)	1.221 Mg/m^3	
Absorption coefficient	0.085 mm^{-1}	
F(000)	1248	
Crystal size	0.81 x 0.16 x 0.15 mm^3	
Theta range for data collection	1.77 to 25.00°.	
Index ranges	0<=h<=10, 0<=k<=18, 0<=l<=27	
Reflections collected	22546	
Independent reflections	3159 [R(int) = 0.0396]	
Completeness to theta = 25.00°	99.9 %	
Absorption correction	Empirical with SADABS	
Max. and min. transmission	0.9873 and 0.9341	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3159 / 0 / 385	
Goodness-of-fit on F^2	0.999	
Final R indices [I>2sigma(I)]	R1 = 0.0327, wR2 = 0.0814	
R indices (all data)	R1 = 0.0389, wR2 = 0.0844	
Absolute structure parameter	N/A	
Largest diff. peak and hole	0.214 and -0.128 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Molecule **4**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	4882(2)	6569(1)	1649(1)	38(1)
O(2)	2753(2)	5433(1)	499(1)	46(1)
O(3)	-2299(2)	6950(1)	723(1)	52(1)
O(4)	-2241(2)	6167(1)	1538(1)	45(1)
O(5)	3057(2)	6894(1)	4380(1)	51(1)
O(6)	1836(2)	7755(1)	3730(1)	36(1)
O(7)	2886(2)	4843(1)	3595(1)	40(1)
N(1)	2409(2)	6573(1)	1467(1)	25(1)
N(2)	3236(2)	6676(1)	3403(1)	30(1)
C(1)	3587(2)	6431(1)	1818(1)	26(1)
C(2)	2563(2)	6894(2)	852(1)	29(1)
C(3)	3471(3)	6250(2)	489(1)	35(1)
C(4)	3604(4)	4775(2)	226(1)	56(1)
C(5)	3340(3)	7790(2)	810(1)	35(1)
C(6)	2657(3)	8489(2)	1185(1)	38(1)
C(7)	1613(3)	9067(2)	966(1)	56(1)
C(8)	929(4)	9676(2)	1336(2)	75(1)
C(9)	1300(4)	9700(2)	1916(2)	74(1)
C(10)	2380(4)	9154(2)	2130(1)	62(1)
C(11)	3059(3)	8558(2)	1767(1)	45(1)
C(12)	916(3)	6940(2)	647(1)	32(1)
C(13)	38(3)	6329(2)	1039(1)	32(1)
C(14)	-1623(2)	6532(2)	1074(1)	32(1)
C(15)	835(2)	6404(2)	1623(1)	33(1)
C(16)	3283(2)	6152(1)	2445(1)	26(1)
C(17)	2813(3)	6932(2)	2818(1)	35(1)
C(18)	2738(3)	7091(1)	3885(1)	33(1)
C(19)	946(3)	8219(2)	4171(1)	42(1)
C(20)	-92(5)	7578(2)	4468(2)	84(1)
C(21)	49(3)	8842(2)	3808(1)	55(1)
C(22)	1966(5)	8701(2)	4589(1)	74(1)
C(23)	4514(3)	6062(2)	3415(1)	31(1)
C(24)	4199(3)	5270(2)	3789(1)	36(1)
C(25)	2783(3)	3997(2)	3839(1)	48(1)
C(26)	5959(3)	6490(2)	3658(1)	36(1)
C(27)	6451(3)	7295(2)	3339(1)	35(1)
C(28)	7472(3)	7246(2)	2883(1)	42(1)
C(29)	7843(4)	7972(2)	2559(1)	51(1)
C(30)	7200(4)	8765(2)	2690(1)	52(1)
C(31)	6226(3)	8831(2)	3153(1)	50(1)
C(32)	5850(3)	8102(2)	3476(1)	42(1)
C(33)	4675(2)	5813(2)	2761(1)	30(1)

Table 3. Bond lengths [Å] and angles [°] for Molecule **4**.

O(1)-C(1)	1.237(3)	C(1)-N(1)-C(2)	123.17(17)
O(2)-C(4)	1.414(3)	C(15)-N(1)-C(2)	111.95(15)
O(2)-C(3)	1.415(3)	C(18)-N(2)-C(17)	122.92(18)
O(3)-C(14)	1.195(3)	C(18)-N(2)-C(23)	122.58(17)
O(4)-C(14)	1.324(3)	C(17)-N(2)-C(23)	113.08(16)
O(5)-C(18)	1.211(3)	O(1)-C(1)-N(1)	120.81(18)
O(6)-C(18)	1.350(3)	O(1)-C(1)-C(16)	120.78(19)
O(6)-C(19)	1.473(3)	N(1)-C(1)-C(16)	118.29(18)
O(7)-C(24)	1.416(3)	N(1)-C(2)-C(3)	110.34(17)
O(7)-C(25)	1.423(3)	N(1)-C(2)-C(12)	102.45(16)
N(1)-C(1)	1.342(3)	C(3)-C(2)-C(12)	111.47(18)
N(1)-C(15)	1.471(3)	N(1)-C(2)-C(5)	113.20(16)
N(1)-C(2)	1.503(3)	C(3)-C(2)-C(5)	108.02(17)
N(2)-C(18)	1.355(3)	C(12)-C(2)-C(5)	111.34(19)
N(2)-C(17)	1.451(3)	O(2)-C(3)-C(2)	109.35(18)
N(2)-C(23)	1.482(3)	C(6)-C(5)-C(2)	114.98(18)
C(1)-C(16)	1.527(3)	C(7)-C(6)-C(11)	118.3(3)
C(2)-C(3)	1.530(3)	C(7)-C(6)-C(5)	121.7(2)
C(2)-C(12)	1.543(3)	C(11)-C(6)-C(5)	120.0(2)
C(2)-C(5)	1.551(3)	C(6)-C(7)-C(8)	120.2(3)
C(5)-C(6)	1.508(3)	C(9)-C(8)-C(7)	120.0(3)
C(6)-C(7)	1.383(4)	C(10)-C(9)-C(8)	120.0(3)
C(6)-C(11)	1.390(3)	C(9)-C(10)-C(11)	120.1(3)
C(7)-C(8)	1.406(4)	C(10)-C(11)-C(6)	121.2(3)
C(8)-C(9)	1.374(5)	C(13)-C(12)-C(2)	106.25(17)
C(9)-C(10)	1.371(5)	C(14)-C(13)-C(12)	113.95(19)
C(10)-C(11)	1.381(4)	C(14)-C(13)-C(15)	113.08(19)
C(12)-C(13)	1.520(3)	C(12)-C(13)-C(15)	103.53(18)
C(13)-C(14)	1.516(3)	O(3)-C(14)-O(4)	124.2(2)
C(13)-C(15)	1.522(3)	O(3)-C(14)-C(13)	124.6(2)
C(16)-C(33)	1.529(3)	O(4)-C(14)-C(13)	111.17(19)
C(16)-C(17)	1.536(3)	N(1)-C(15)-C(13)	104.13(16)
C(19)-C(21)	1.503(4)	C(1)-C(16)-C(33)	113.53(17)
C(19)-C(22)	1.516(4)	C(1)-C(16)-C(17)	110.65(17)
C(19)-C(20)	1.517(4)	C(33)-C(16)-C(17)	103.08(17)
C(23)-C(24)	1.520(3)	N(2)-C(17)-C(16)	103.37(17)
C(23)-C(26)	1.551(3)	O(5)-C(18)-O(6)	125.4(2)
C(23)-C(33)	1.559(3)	O(5)-C(18)-N(2)	124.8(2)
C(26)-C(27)	1.508(3)	O(6)-C(18)-N(2)	109.78(17)
C(27)-C(28)	1.390(3)	O(6)-C(19)-C(21)	102.49(18)
C(27)-C(32)	1.392(3)	O(6)-C(19)-C(22)	110.6(2)
C(28)-C(29)	1.385(4)	C(21)-C(19)-C(22)	110.8(2)
C(29)-C(30)	1.385(4)	O(6)-C(19)-C(20)	108.7(2)
C(30)-C(31)	1.377(4)	C(21)-C(19)-C(20)	110.0(3)
C(31)-C(32)	1.389(4)	C(22)-C(19)-C(20)	113.7(3)
C(4)-O(2)-C(3)	113.0(2)	N(2)-C(23)-C(24)	112.53(19)
C(18)-O(6)-C(19)	120.57(16)	N(2)-C(23)-C(26)	111.90(18)
C(24)-O(7)-C(25)	110.95(19)	C(24)-C(23)-C(26)	106.99(18)
C(1)-N(1)-C(15)	124.83(17)	N(2)-C(23)-C(33)	102.14(16)

C(24)-C(23)-C(33)	111.31(19)	C(29)-C(28)-C(27)	121.2(2)
C(26)-C(23)-C(33)	112.06(18)	C(28)-C(29)-C(30)	120.0(3)
O(7)-C(24)-C(23)	110.49(18)	C(31)-C(30)-C(29)	119.6(3)
C(27)-C(26)-C(23)	114.64(18)	C(30)-C(31)-C(32)	120.3(2)
C(28)-C(27)-C(32)	118.1(2)	C(31)-C(32)-C(27)	120.8(2)
C(28)-C(27)-C(26)	120.8(2)	C(16)-C(33)-C(23)	107.30(17)
C(32)-C(27)-C(26)	121.1(2)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x 10^3$) for Molecule **4**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	20(1)	64(1)	28(1)	4(1)	1(1)	1(1)
O(2)	40(1)	48(1)	50(1)	-11(1)	14(1)	0(1)
O(3)	28(1)	85(1)	45(1)	23(1)	-1(1)	9(1)
O(4)	21(1)	74(1)	41(1)	17(1)	5(1)	5(1)
O(5)	69(1)	62(1)	22(1)	-2(1)	-5(1)	25(1)
O(6)	38(1)	44(1)	26(1)	-3(1)	3(1)	14(1)
O(7)	38(1)	38(1)	43(1)	8(1)	-1(1)	4(1)
N(1)	20(1)	36(1)	20(1)	1(1)	2(1)	-1(1)
N(2)	32(1)	37(1)	21(1)	1(1)	-2(1)	10(1)
C(1)	21(1)	32(1)	25(1)	-4(1)	1(1)	2(1)
C(2)	23(1)	44(1)	20(1)	3(1)	0(1)	-3(1)
C(3)	28(1)	56(2)	22(1)	-2(1)	2(1)	-3(1)
C(4)	57(2)	57(2)	54(2)	-6(1)	11(1)	15(2)
C(5)	27(1)	51(1)	26(1)	9(1)	-2(1)	-8(1)
C(6)	30(1)	39(1)	45(1)	6(1)	1(1)	-15(1)
C(7)	45(2)	43(2)	80(2)	2(1)	-18(2)	-9(1)
C(8)	42(2)	42(2)	141(4)	-14(2)	-11(2)	-2(2)
C(9)	63(2)	51(2)	109(3)	-26(2)	26(2)	-22(2)
C(10)	76(2)	47(2)	62(2)	-7(1)	20(2)	-21(2)
C(11)	52(2)	39(1)	45(1)	4(1)	6(1)	-15(1)
C(12)	25(1)	45(1)	24(1)	2(1)	-3(1)	-2(1)
C(13)	25(1)	39(1)	32(1)	-2(1)	0(1)	-1(1)
C(14)	24(1)	43(1)	28(1)	1(1)	-3(1)	-3(1)
C(15)	20(1)	53(2)	26(1)	7(1)	1(1)	-2(1)
C(16)	21(1)	33(1)	25(1)	0(1)	0(1)	5(1)
C(17)	37(1)	45(1)	23(1)	3(1)	-2(1)	13(1)
C(18)	35(1)	38(1)	27(1)	1(1)	2(1)	4(1)
C(19)	44(1)	45(1)	38(1)	-10(1)	9(1)	11(1)
C(20)	85(3)	74(2)	92(2)	11(2)	56(2)	18(2)
C(21)	49(2)	55(2)	61(2)	-15(1)	-2(2)	20(2)
C(22)	87(3)	74(2)	63(2)	-33(2)	-21(2)	27(2)
C(23)	32(1)	37(1)	25(1)	-1(1)	-3(1)	9(1)
C(24)	39(1)	39(1)	30(1)	4(1)	-3(1)	10(1)
C(25)	51(2)	43(1)	50(1)	13(1)	10(1)	6(1)
C(26)	38(1)	43(1)	27(1)	-1(1)	-8(1)	8(1)
C(27)	34(1)	39(1)	33(1)	-6(1)	-11(1)	3(1)
C(28)	44(2)	38(1)	45(1)	-4(1)	-3(1)	4(1)
C(29)	60(2)	47(2)	47(1)	-2(1)	5(1)	0(1)
C(30)	65(2)	43(1)	50(1)	4(1)	-2(2)	2(1)
C(31)	55(2)	37(1)	57(2)	-5(1)	-9(1)	8(1)
C(32)	39(1)	46(1)	42(1)	-9(1)	-6(1)	5(1)
C(33)	26(1)	35(1)	27(1)	-1(1)	-2(1)	6(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for Molecule **4**.

	x	y	z	U(eq)
H(4)	-3142	6322	1564	68
H(3A)	3548	6460	83	42
H(3B)	4498	6198	649	42
H(4A)	4576	4719	422	84
H(4B)	3766	4927	-184	84
H(4C)	3061	4225	250	84
H(5A)	4407	7722	921	42
H(5B)	3312	7984	399	42
H(7)	1358	9052	564	67
H(8)	211	10071	1184	90
H(9)	807	10096	2169	89
H(10)	2661	9186	2528	74
H(11)	3816	8188	1919	54
H(12A)	528	7538	683	38
H(12B)	833	6757	235	38
H(13)	163	5724	890	38
H(15A)	416	6887	1855	40
H(15B)	742	5860	1848	40
H(16)	2475	5703	2452	32
H(17A)	3354	7463	2697	42
H(17B)	1719	7037	2790	42
H(20A)	491	7209	4731	126
H(20B)	-585	7218	4174	126
H(20C)	-853	7894	4692	126
H(21A)	-511	8521	3512	82
H(21B)	728	9254	3619	82
H(21C)	-654	9158	4058	82
H(22A)	2691	9046	4367	112
H(22B)	2502	8284	4834	112
H(22C)	1362	9085	4835	112
H(24A)	5062	4868	3769	43
H(24B)	4070	5450	4200	43
H(25A)	2953	4028	4260	72
H(25B)	3543	3623	3661	72
H(25C)	1783	3759	3763	72
H(26A)	5791	6639	4072	43
H(26B)	6784	6060	3643	43
H(28)	7925	6706	2792	51
H(29)	8538	7925	2247	61
H(30)	7430	9261	2462	63
H(31)	5810	9378	3253	60
H(32)	5175	8154	3794	51
H(33A)	5593	6076	2594	36
H(33B)	4747	5176	2718	36

Table 6. Torsion angles [°] for Molecule **4**.

C(15)-N(1)-C(1)-O(1)	178.1(2)	N(1)-C(1)-C(16)-C(17)	-77.8(2)
C(2)-N(1)-C(1)-O(1)	0.7(3)	C(18)-N(2)-C(17)-C(16)	-165.4(2)
C(15)-N(1)-C(1)-C(16)	-5.9(3)	C(23)-N(2)-C(17)-C(16)	27.9(3)
C(2)-N(1)-C(1)-C(16)	176.70(18)	C(1)-C(16)-C(17)-N(2)	-154.65(19)
C(1)-N(1)-C(2)-C(3)	60.9(2)	C(33)-C(16)-C(17)-N(2)	-32.9(2)
C(15)-N(1)-C(2)-C(3)	-116.8(2)	C(19)-O(6)-C(18)-O(5)	-10.3(4)
C(1)-N(1)-C(2)-C(12)	179.70(19)	C(19)-O(6)-C(18)-N(2)	169.7(2)
C(15)-N(1)-C(2)-C(12)	2.0(2)	C(17)-N(2)-C(18)-O(5)	179.5(3)
C(1)-N(1)-C(2)-C(5)	-60.3(3)	C(23)-N(2)-C(18)-O(5)	-15.1(4)
C(15)-N(1)-C(2)-C(5)	122.0(2)	C(17)-N(2)-C(18)-O(6)	-0.5(3)
C(4)-O(2)-C(3)-C(2)	-173.47(19)	C(23)-N(2)-C(18)-O(6)	164.96(19)
N(1)-C(2)-C(3)-O(2)	58.2(2)	C(18)-O(6)-C(19)-C(21)	-176.0(2)
C(12)-C(2)-C(3)-O(2)	-54.9(2)	C(18)-O(6)-C(19)-C(22)	65.9(3)
C(5)-C(2)-C(3)-O(2)	-177.53(17)	C(18)-O(6)-C(19)-C(20)	-59.5(3)
N(1)-C(2)-C(5)-C(6)	-52.8(3)	C(18)-N(2)-C(23)-C(24)	63.4(3)
C(3)-C(2)-C(5)-C(6)	-175.30(18)	C(17)-N(2)-C(23)-C(24)	-129.9(2)
C(12)-C(2)-C(5)-C(6)	62.0(2)	C(18)-N(2)-C(23)-C(26)	-57.1(3)
C(2)-C(5)-C(6)-C(7)	-95.7(3)	C(17)-N(2)-C(23)-C(26)	109.6(2)
C(2)-C(5)-C(6)-C(11)	83.6(3)	C(18)-N(2)-C(23)-C(33)	-177.2(2)
C(11)-C(6)-C(7)-C(8)	-3.2(4)	C(17)-N(2)-C(23)-C(33)	-10.4(2)
C(5)-C(6)-C(7)-C(8)	176.1(2)	C(25)-O(7)-C(24)-C(23)	165.33(19)
C(6)-C(7)-C(8)-C(9)	0.2(4)	N(2)-C(23)-C(24)-O(7)	56.6(2)
C(7)-C(8)-C(9)-C(10)	2.6(5)	C(26)-C(23)-C(24)-O(7)	179.85(17)
C(8)-C(9)-C(10)-C(11)	-2.3(5)	C(33)-C(23)-C(24)-O(7)	-57.4(2)
C(9)-C(10)-C(11)-C(6)	-0.9(4)	N(2)-C(23)-C(26)-C(27)	-56.2(2)
C(7)-C(6)-C(11)-C(10)	3.6(4)	C(24)-C(23)-C(26)-C(27)	-179.89(19)
C(5)-C(6)-C(11)-C(10)	-175.7(2)	C(33)-C(23)-C(26)-C(27)	57.8(3)
N(1)-C(2)-C(12)-C(13)	-22.2(2)	C(23)-C(26)-C(27)-C(28)	-92.7(3)
C(3)-C(2)-C(12)-C(13)	95.8(2)	C(23)-C(26)-C(27)-C(32)	84.7(3)
C(5)-C(2)-C(12)-C(13)	-143.52(18)	C(32)-C(27)-C(28)-C(29)	-2.4(4)
C(2)-C(12)-C(13)-C(14)	157.13(19)	C(26)-C(27)-C(28)-C(29)	175.0(2)
C(2)-C(12)-C(13)-C(15)	33.9(2)	C(27)-C(28)-C(29)-C(30)	0.5(4)
C(12)-C(13)-C(14)-O(3)	20.5(3)	C(28)-C(29)-C(30)-C(31)	1.8(4)
C(15)-C(13)-C(14)-O(3)	138.3(2)	C(29)-C(30)-C(31)-C(32)	-2.2(4)
C(12)-C(13)-C(14)-O(4)	-161.29(19)	C(30)-C(31)-C(32)-C(27)	0.2(4)
C(15)-C(13)-C(14)-O(4)	-43.4(3)	C(28)-C(27)-C(32)-C(31)	2.0(4)
C(1)-N(1)-C(15)-C(13)	-158.9(2)	C(26)-C(27)-C(32)-C(31)	-175.4(2)
C(2)-N(1)-C(15)-C(13)	18.8(2)	C(1)-C(16)-C(33)-C(23)	147.40(18)
C(14)-C(13)-C(15)-N(1)	-155.6(2)	C(17)-C(16)-C(33)-C(23)	27.7(2)
C(12)-C(13)-C(15)-N(1)	-31.8(2)	N(2)-C(23)-C(33)-C(16)	-11.6(2)
O(1)-C(1)-C(16)-C(33)	-17.2(3)	C(24)-C(23)-C(33)-C(16)	108.7(2)
N(1)-C(1)-C(16)-C(33)	166.82(19)	C(26)-C(23)-C(33)-C(16)	-131.50(19
O(1)-C(1)-C(16)-C(17)	98.2(3)		

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for Molecule **4** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(4)-H(4)...O(1)#1	0.84	1.81	2.650(2)	175(1)

Symmetry transformations used to generate equivalent atoms:
#1 x-1,y,z

NMR experimental section

Data Collection: An approximately 10 mM NMR sample was prepared by dissolving 3 mg of lyophilized peptide **5** in 300 ul of CD_2Cl_2 (or CD_3OD) and placed in a 3mm NMR tube. A trace amount of tetramethylsilane (Aldrich) was added to the CD_2CL_2 sample and 2,2-dimethyl-2-silapentane-5-sulfonate (DSS; Merck, Rahway, NJ) was added to the CD_3OD sample as internal reference. NMR experiments were performed on a Varian INOVA 600 MHz spectrometer at 4, 14 and 24 ºC using a 3 mm Nalorac probe. COSY (Aue et al., 1976), TOCSY (Bax & Davies, 1985), NOE spectroscopy (NOESY; Jeener et al., 1979), and rotating frame Overhauser spectroscopy (ROESY; Bax & Davies, 1985; Bothner-by et al., 1984) experiments were performed using standard Varian pulse sequences. All two-dimensional spectra were acquired with a spectral window of 6600 Hz by collecting 2048 points in f2 and 400-600 points in f1. All spectra, with the exception of gCOSY experiments, were acquired in the phase-sensitive mode with hypercomplex phase cycling (States-Haberkorn method). TOCSY experiments employed a standard MLEV-17 spin lock sequence with a spin lock field of 7-8 kHz and mixing time of 60-80 ms. ROESY experiments utilized a 3 kHz spin lock field and mixing times of 250 and 300 ms. NOESY spectra were acquired with mixing times of 500, 550 and 600 ms. NOESY mixing times were chosen based on T1 measurements. Only positive NOEs were observed at all mixing times and ROESY and NOESY spectra were compared to ensure the absence of spin diffusion. All data was processed using Varian VNMR 6.3 software. Sine or cosine squared window functions were generally applied after baseline correction. The spectra were displayed and the assignment performed using SPARKY software (T. D. Goddard and D. G. Kneller, SPARKY 3, University of California, San Francisco).

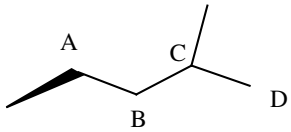
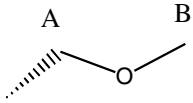
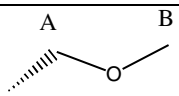
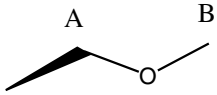
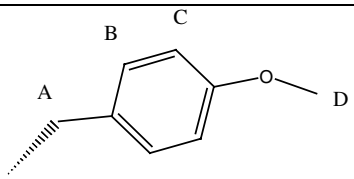
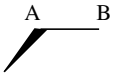
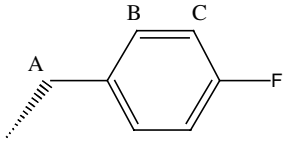
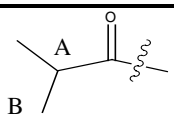
Aue, W. P., Bartholdi, E. & Ernst, R. R. *J. Chem. Phys*. **1976**, 64, 2229.

Bax, A. & Davis, D. G. *J. Magn. Reson*. **1985**, 65, 355.

Jeener, J., Meier, B. H., Bachmann, P. & Ernst, R. R. *J. Phys. Chem*. **1979**, 71, 4546.

Bothner-by, A. A., Stephens, R. L., Lee, J. M., Warren, C. D. & Jeanloz, R. W. *J. Am. Chem. Soc*. **1984**, 106, 811.

Table 8: Ressonance assignment of molecule **5** in CD_2Cl_2

Residue	Fragment	Alpha	Beta	Gamma	Side chain
Ring1	ring	3.098	3.787 3.674	2.370 2.967	
Trans*	Iso-amyl				A 1.666, 2.079 B 1.139 C 1.509 D 0.890
Cis*	Methoxy methyl				A 3.540, 3.859 B 3.302
Ring2	ring	3.035	3.912 3.753	2.284 1.858	
Trans*	methyl				1.379
Cis*	Methoxy methyl				A 3.893, 3.575 B 3.339
Ring3	ring	3.178	3.572 3.247	2.225 2.077	A 2.654 B 1.071
Trans*	Methoxy methyl				A 3.418, 4.095 B 3.298
Cis*	p-Methoxy benzyl				A 3.410, 2.863 B 7.070 C 6.837 D 3.790
Ring4	ring	2.999	3.677 3.134	2.262 2.052	
Trans*	ethyl				A 1.705, 2.228 B 0.832
Cis*	p-flouro benzyl				A 3.328, 2.845 B 7.059 C 6.906
	Isobutyric Amide				A 2.654 B 1.071
		Methyl ester			3.639

* Carbon 2 substituents were named with respect to the carbonyl carbon

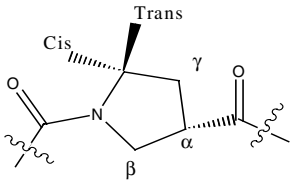


TABLE 9: NOE derived restraints used in structure calculations.

Resonance 1	Resonance 2	Intensity
Ring1 Gamma	Ring2 Beta	Medium
Terminal Methyl ester	Ring2 Gamma	Weak
Ring3 H Cis B	Ring2 Beta	Weak
Ring4 H Cis B	Ring3 Beta	Weak
Ring3 H Cis B	Ring4 H Trans B	Weak
Ring3 H Cis B	Ring1 H Trans D	Weak
Ring3 H Cis C	Ring1 H Trans B	Weak
Ring3 H Cis C	Ring1 H Trans D	Weak
Ring2 H Alpha	Ring4 H Cis C	Medium
Ring4 H Cis B	Ring2 H Trans A	Weak
Ring4 H Cis C	Ring2 H Trans A	Weak
Ring2 H Alpha	Ring3 Beta	Strong

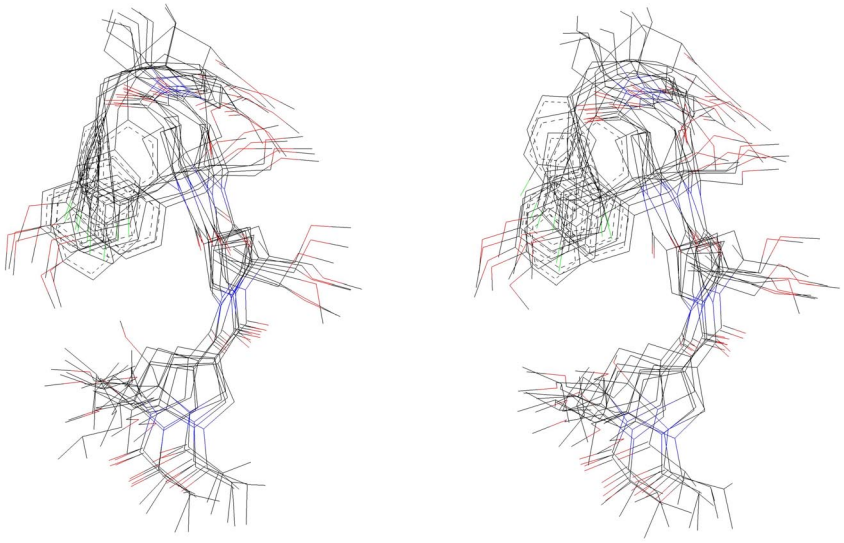
STRUCTURE CALCULATIONS:

The above listed NOE derived restraints were used to determine a solution structure for **5** in CD_2Cl_2. Initially the program DYANA (Guntert et al 1997) was used to generate structures. The DYANA program performs simulated annealing via molecular dynamics in torsion angle space. The program uses a simplified molecular force field consisting of only hard sphere repulsions and NMR derived restraints. Library entries for the various β-amino acid residues in **5** were created as described in the DYANA manual. Starting coordinates for the residues were obtained from minimized structures generated using the MMFF as implemented in PC model software. Residues were constructed with both pseudo axial and pseudo equatorial geometry for the alpha carboxyl group (different envelope ring geometries). Multiple simulations were performed using models of **5** constructed from both types of monomers (pseudo axial or equatorial) and with either E or Z amide bonds. Typically 500 random structures were generated and annealed with standard parameters in DYANA. The twenty lowest energy structures were analyzed. Only the model consisting of pseudo equatorial resiudes with Z-amides satisfied the NMR restraints. The twenty best structures from the pseudo equatorial, Z-amide model were further analyzed by simulated annealing in SYBYL using a with a more realistic molecular force field.

Simulated annealing (SA) in Sybyl was performed as stated in the footnote 18. The final structures from a 10 cycle SA run were subjected to 1000 cycles of conjugate gradient minimization without restraints. The SA structures changed only slightly after minimization. The changes were the result of residual energy in the molecules from the SA where the final temperature was 200 K. Thus, the SA

structures represent local minima. Figure 3 shows an overlay of the minimized and unminimized structures. Table 10 lists RMSD comparisons of various ensembles of minimized and unminimized structures.

Guntert, P.; Mumenthaler, C.; Wuthrich, K. *J. Mol. Biol.* **1997** 273, 283-298.



A B

Figure 3. A) overlay of 9 minimized structures from SA. B) overlay of same 9 structures before minimization

Table 10: Pairwise RMSD comparisons of minimized and unminimized structures

Structures compared (averages of pair wise RMSDs)	Heavy atom RMSD	Backbone RMSD
9 best SA structures unminimized (36 pair wise comparisons)	1.25 ±0.24	0.51±0.17
9 best SA structures minimized (36 pair wise comparisons)	1.05±0.32	0.40±0.18
Each minimized structure against all 9 unminimized structures (81 comparisons)	1.09±0.32	0.43±0.17
Each minimized structures w/ best fit of unminimized structures (9 comparisons)	0.55±0.22	0.22±0.10
All 9 minimized and all 9 unminimized structures (153 pair wise comparisons)	1.12±0.31	0.44±0.18