APPENDIX 5

X-Ray Crystallography Reports Relevant to Chapter 4:

Development of a Tandem Conjugate Addition/Prins Cyclization[†]

[†] The work disclosed in this appendix for the x-ray crystallographic analysis of **169** was completed entirely by Larry Henling in the Caltech X-ray crystallography lab.

CRYSTAL STRUCTURE ANALYSIS OF INDOLINE 169

*Figure A5.1. Indoline ent-**169** is shown with 50% probability ellipsoids. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 1024262.*

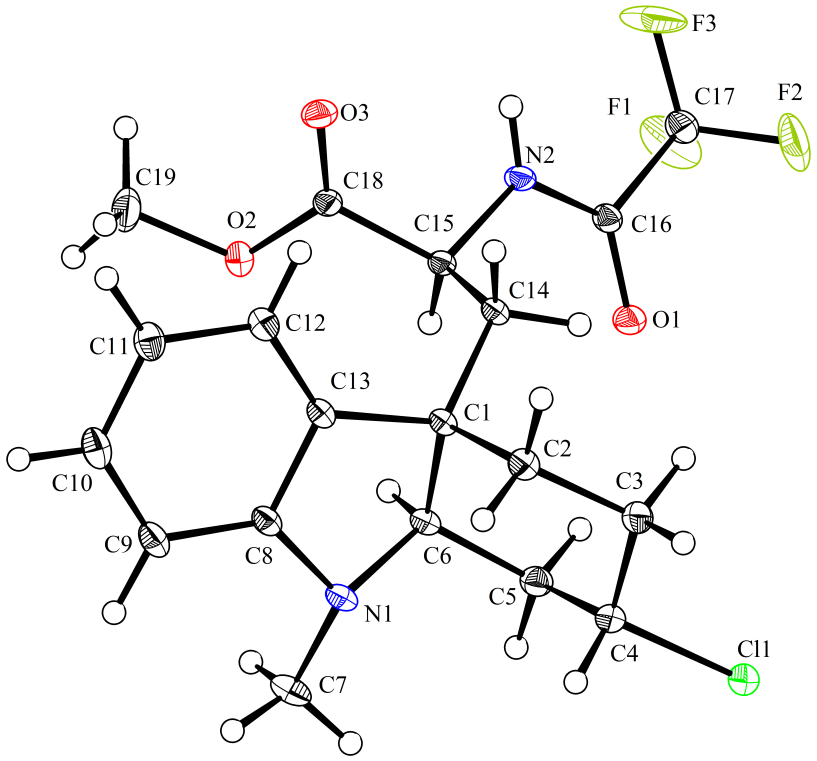

*Table A5.1. Crystal data and structure refinement indoline **169**.*

Empirical formula	$C_{19}H_{22}ClF_3N_2O_3$
Formula weight	418.84
Crystallization solvent	Hexanes/ethanol
Crystal size	0.41 x 0.36 x 0.16 mm^3

Data Collection

Wavelength	0.71073 Å	
Data Collection Temperature	100 K	
Unit cell dimensions	a = 25.1712(14) Å b = 6.5924(4) Å c = 22.8692(13) Å	α= 90° β= 91.144(3)° γ = 90°
Volume	3794.1(4) $Å^3$	
Z	8	
Crystal system	Monoclinic	
Space group	C 1 2/c 1	
Density (calculated)	1.466 Mg/m^3	
F(000)	1744	
θ range for data collection	2.383 to 46.276°	
Completeness to θ = 25.000°	99.9 %	
Index ranges	$-49 \le h \le 51, -13 \le k \le 11, -45 \le l \le 46$	
Reflections collected	124617	
Independent reflections	16624 [R_{int}= 0.0540]	
Absorption coefficient	0.253 mm^{-1}	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.9131	

Table A5.1 (continued)

Structure solution and Refinement

Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	16624 / 10 / 368
Goodness-of-fit on F^2	1.025
Final R indices [I>2σ(I), 4601 reflections]	R1 = 0.0424, *w*R2 = 0.1076
R indices (all data)	R1 = 0.0654, *w*R2 = 0.1204
Extinction coefficient	n/a
Largest diff. peak and hole	0.898 and -0.650 e.$Å^{-3}$

*Table A5.2. Atomic coordinates (x 10^5) and equivalent isotropic displacement parameters ($Å^2$x 10^4) for indoline **169**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.*

	x	y	z	U_{eq}
Cl(1)	81494(2)	86530(3)	41318(2)	191(1)
F(1)	55909(4)	121930(11)	55313(3)	350(2)
F(2)	61581(3)	105543(17)	60353(3)	375(2)
F(3)	53671(4)	93585(14)	59017(4)	492(3)
F(1B)	60520(40)	114280(160)	59070(50)	390(20)
F(2B)	57010(30)	85750(110)	60750(30)	272(14)
F(3B)	53660(40)	113060(150)	56070(40)	353(18)
F(1A)	58200(30)	121770(120)	56890(40)	283(15)
F(2A)	60010(30)	95880(120)	60850(30)	251(14)
F(3A)	52150(30)	102150(120)	56800(30)	251(14)
O(1)	63065(2)	101787(7)	48267(2)	152(1)
O(2)	51942(2)	62921(8)	35600(2)	161(1)
O(3)	51164(2)	43717(8)	43673(2)	171(1)
N(1)	68410(2)	55635(8)	28749(2)	126(1)
N(2)	56778(2)	77005(8)	48939(2)	126(1)
C(1)	66036(2)	48427(8)	38471(2)	103(1)
C(2)	71284(2)	37744(9)	40410(2)	130(1)
C(3)	75492(2)	52373(10)	42907(2)	149(1)
C(4)	76701(2)	68459(10)	38361(2)	144(1)
C(5)	71755(2)	80169(9)	36510(2)	141(1)
C(6)	67331(2)	66243(8)	34310(2)	112(1)
C(7)	68878(3)	68370(11)	23594(3)	189(1)
C(8)	64758(2)	39553(9)	28541(2)	121(1)
C(9)	62818(2)	28861(10)	23700(2)	154(1)
C(10)	59133(3)	13364(10)	24637(3)	170(1)
C(11)	57431(3)	8583(9)	30217(3)	160(1)
C(12)	59472(2)	19294(9)	35063(2)	133(1)
C(13)	63085(2)	34720(8)	34201(2)	112(1)
C(14)	63080(2)	54493(8)	44004(2)	112(1)
C(15)	58192(2)	68288(8)	43281(2)	107(1)
C(16)	59462(2)	93368(8)	50808(2)	122(1)
C(17)	57594(2)	103040(10)	56528(3)	164(1)
C(18)	53377(2)	56824(9)	40940(2)	118(1)
C(19)	47517(3)	52059(13)	32938(3)	226(1)

*Table A5.3. Bond lengths [Å] and angles [°] for indoline **169**.*

Cl(1)-C(4)	1.8164(6)	F(3B)-C(17)	1.194(9)
F(1)-C(17)	1.3428(9)	F(1A)-C(17)	1.247(8)
F(2)-C(17)	1.3284(9)	F(2A)-C(17)	1.243(7)
F(3)-C(17)	1.3077(9)	F(3A)-C(17)	1.376(7)
F(1B)-C(17)	1.188(10)	O(1)-C(16)	1.2204(7)
F(2B)-C(17)	1.502(7)	O(2)-C(18)	1.3288(7)

O(2)-C(19)	1.4481(8)	C(13)-C(1)-C(6)	99.37(4)
O(3)-C(18)	1.2088(7)	C(13)-C(1)-C(14)	116.60(4)
N(1)-C(6)	1.4812(7)	C(14)-C(1)-C(2)	107.84(4)
N(1)-C(7)	1.4540(8)	C(14)-C(1)-C(6)	114.85(4)
N(1)-C(8)	1.4034(8)	C(1)-C(2)-H(2A)	109.7(7)
N(2)-H(2)	0.846(13)	C(1)-C(2)-H(2B)	108.2(8)
N(2)-C(15)	1.4662(7)	H(2A)-C(2)-H(2B)	106.2(10)
N(2)-C(16)	1.3383(7)	C(3)-C(2)-C(1)	113.45(5)
C(1)-C(2)	1.5538(7)	C(3)-C(2)-H(2A)	109.5(7)
C(1)-C(6)	1.5503(7)	C(3)-C(2)-H(2B)	109.5(7)
C(1)-C(13)	1.5142(7)	C(2)-C(3)-H(3A)	110.1(7)
C(1)-C(14)	1.5337(7)	C(2)-C(3)-H(3B)	109.6(8)
C(2)-H(2A)	0.992(12)	H(3A)-C(3)-H(3B)	107.4(10)
C(2)-H(2B)	0.949(12)	C(4)-C(3)-C(2)	109.28(5)
C(2)-C(3)	1.5342(8)	C(4)-C(3)-H(3A)	109.8(7)
C(3)-H(3A)	0.993(11)	C(4)-C(3)-H(3B)	110.7(7)
C(3)-H(3B)	0.965(12)	Cl(1)-C(4)-H(4)	104.0(7)
C(3)-C(4)	1.5201(9)	C(3)-C(4)-Cl(1)	110.09(4)
C(4)-H(4)	0.974(12)	C(3)-C(4)-H(4)	110.7(7)
C(4)-C(5)	1.5180(8)	C(5)-C(4)-Cl(1)	107.77(4)
C(5)-H(5A)	1.001(13)	C(5)-C(4)-C(3)	111.79(5)
C(5)-H(5B)	0.948(12)	C(5)-C(4)-H(4)	112.2(7)
C(5)-C(6)	1.5211(8)	C(4)-C(5)-H(5A)	112.6(7)
C(6)-H(6)	0.987(12)	C(4)-C(5)-H(5B)	108.5(7)
C(7)-H(7A)	0.973(13)	C(4)-C(5)-C(6)	112.10(5)
C(7)-H(7B)	0.961(14)	H(5A)-C(5)-H(5B)	105.6(10)
C(7)-H(7C)	0.970(14)	C(6)-C(5)-H(5A)	108.9(7)
C(8)-C(9)	1.3927(8)	C(6)-C(5)-H(5B)	108.8(7)
C(8)-C(13)	1.4059(7)	N(1)-C(6)-C(1)	102.34(4)
C(9)-H(9)	0.974(12)	N(1)-C(6)-C(5)	115.05(4)
C(9)-C(10)	1.3993(10)	N(1)-C(6)-H(6)	108.5(7)
C(10)-H(10)	0.950(13)	C(1)-C(6)-H(6)	109.3(7)
C(10)-C(11)	1.3904(9)	C(5)-C(6)-C(1)	114.56(4)
C(11)-H(11)	0.976(13)	C(5)-C(6)-H(6)	106.8(7)
C(11)-C(12)	1.4029(8)	N(1)-C(7)-H(7A)	109.9(8)
C(12)-H(12)	0.937(13)	N(1)-C(7)-H(7B)	109.6(9)
C(12)-C(13)	1.3809(8)	N(1)-C(7)-H(7C)	112.7(8)
C(14)-H(14A)	1.004(12)	H(7A)-C(7)-H(7B)	110.3(11)
C(14)-H(14B)	0.967(12)	H(7A)-C(7)-H(7C)	105.6(12)
C(14)-C(15)	1.5364(7)	H(7B)-C(7)-H(7C)	108.6(12)
C(15)-H(15)	0.951(11)	N(1)-C(8)-C(13)	110.37(5)
C(15)-C(18)	1.5169(7)	C(9)-C(8)-N(1)	128.93(5)
C(16)-C(17)	1.5373(8)	C(9)-C(8)-C(13)	120.70(5)
C(19)-H(19A)	0.986(14)	C(8)-C(9)-H(9)	121.6(7)
C(19)-H(19B)	0.966(13)	C(8)-C(9)-C(10)	118.08(5)
C(19)-H(19C)	0.986(16)	C(10)-C(9)-H(9)	120.2(7)
		C(9)-C(10)-H(10)	118.8(8)
C(18)-O(2)-C(19)	115.43(5)	C(11)-C(10)-C(9)	121.56(5)
C(7)-N(1)-C(6)	116.28(5)	C(11)-C(10)-H(10)	119.6(8)
C(8)-N(1)-C(6)	104.75(4)	C(10)-C(11)-H(11)	119.9(8)
C(8)-N(1)-C(7)	118.19(5)	C(10)-C(11)-C(12)	119.76(6)
C(15)-N(2)-H(2)	119.5(9)	C(12)-C(11)-H(11)	120.3(8)
C(16)-N(2)-H(2)	122.5(9)	C(11)-C(12)-H(12)	119.8(8)
C(16)-N(2)-C(15)	117.90(4)	C(13)-C(12)-C(11)	119.32(5)
C(6)-C(1)-C(2)	109.31(4)	C(13)-C(12)-H(12)	120.9(8)
C(13)-C(1)-C(2)	108.48(4)	C(8)-C(13)-C(1)	107.83(5)

C(12)-C(13)-C(1)	131.56(5)	F(1B)-C(17)-F(2B)	103.1(6)
C(12)-C(13)-C(8)	120.57(5)	F(1B)-C(17)-F(3B)	101.8(7)
C(1)-C(14)-H(14A)	109.5(7)	F(1B)-C(17)-C(16)	118.5(5)
C(1)-C(14)-H(14B)	108.7(7)	F(2B)-C(17)-C(16)	105.5(3)
C(1)-C(14)-C(15)	117.79(4)	F(3B)-C(17)-F(2B)	112.6(6)
H(14A)-C(14)-H(14B)	106.0(10)	F(3B)-C(17)-C(16)	114.9(4)
C(15)-C(14)-H(14A)	105.3(7)	F(1A)-C(17)-F(3A)	99.2(5)
C(15)-C(14)-H(14B)	108.9(7)	F(1A)-C(17)-C(16)	115.4(4)
N(2)-C(15)-C(14)	110.18(4)	F(2A)-C(17)-F(1A)	105.4(5)
N(2)-C(15)-H(15)	107.2(7)	F(2A)-C(17)-F(3A)	114.8(5)
N(2)-C(15)-C(18)	107.49(4)	F(2A)-C(17)-C(16)	111.5(3)
C(14)-C(15)-H(15)	111.2(7)	F(3A)-C(17)-C(16)	110.1(3)
C(18)-C(15)-C(14)	112.07(4)	O(2)-C(18)-C(15)	111.98(5)
C(18)-C(15)-H(15)	108.5(7)	O(3)-C(18)-O(2)	124.88(5)
O(1)-C(16)-N(2)	126.14(5)	O(3)-C(18)-C(15)	123.14(5)
O(1)-C(16)-C(17)	117.34(5)	O(2)-C(19)-H(19A)	104.3(8)
N(2)-C(16)-C(17)	116.43(5)	O(2)-C(19)-H(19B)	110.6(8)
F(1)-C(17)-C(16)	108.01(5)	O(2)-C(19)-H(19C)	108.7(9)
F(2)-C(17)-F(1)	104.62(8)	H(19A)-C(19)-H(19B)	114.9(11)
F(2)-C(17)-C(16)	111.85(5)	H(19A)-C(19)-H(19C)	106.3(12)
F(3)-C(17)-F(1)	107.10(8)	H(19B)-C(19)-H(19C)	111.7(12)
F(3)-C(17)-F(2)	109.85(8)		
F(3)-C(17)-C(16)	114.78(5)		

*Table A5.4. Anisotropic displacement parameters ($Å^2 x\ 10^4$) for indoline **169**. 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}
Cl(1)	179(1)	262(1)	132(1)	-11(1)	6(1)	-79(1)
F(1)	537(5)	242(3)	276(3)	-11(2)	110(3)	213(3)
F(2)	280(3)	650(6)	191(2)	-216(3)	-83(2)	147(4)
F(3)	676(6)	429(5)	387(4)	-276(4)	424(4)	-380(5)
O(1)	169(2)	154(2)	135(2)	-3(1)	24(1)	-44(1)
O(2)	162(2)	191(2)	129(2)	-11(1)	-24(1)	-23(1)
O(3)	168(2)	183(2)	164(2)	-10(1)	45(1)	-61(1)
N(1)	144(2)	147(2)	88(1)	7(1)	29(1)	13(1)
N(2)	134(2)	135(2)	110(2)	-32(1)	45(1)	-28(1)
C(1)	118(2)	108(2)	83(2)	0(1)	10(1)	10(1)
C(2)	134(2)	130(2)	127(2)	6(2)	2(1)	23(2)
C(3)	131(2)	187(2)	130(2)	11(2)	-6(1)	4(2)
C(4)	129(2)	187(2)	118(2)	-11(2)	16(1)	-22(2)
C(5)	155(2)	138(2)	130(2)	4(2)	18(2)	-13(2)
C(6)	124(2)	120(2)	93(2)	9(1)	20(1)	14(1)
C(7)	248(3)	207(3)	114(2)	33(2)	54(2)	9(2)
C(8)	137(2)	136(2)	91(2)	-6(1)	11(1)	28(1)
C(9)	183(2)	180(2)	98(2)	-22(2)	-4(2)	36(2)
C(10)	213(2)	161(2)	134(2)	-36(2)	-37(2)	27(2)
C(11)	197(2)	127(2)	153(2)	-15(2)	-25(2)	-1(2)
C(12)	168(2)	111(2)	119(2)	-1(1)	-2(1)	4(2)
C(13)	135(2)	114(2)	89(2)	-4(1)	4(1)	16(1)
C(14)	126(2)	128(2)	82(2)	-4(1)	14(1)	2(1)

C(15)	110(2)	117(2)	93(2)	-14(1)	22(1)	-12(1)
C(16)	139(2)	120(2)	108(2)	-20(1)	17(1)	-7(1)
C(17)	178(2)	175(2)	140(2)	-50(2)	28(2)	-6(2)
C(18)	110(2)	132(2)	113(2)	-26(1)	22(1)	-10(1)
C(19)	190(2)	282(3)	204(3)	-63(2)	-58(2)	-28(2)

*Table A5.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for indoline **169**.*

	x	y	z	U_{eq}
H(2)	5444(5)	7130(20)	5096(6)	24(3)
H(2A)	7051(4)	2713(18)	4335(5)	16(2)
H(2B)	7266(5)	3087(19)	3713(5)	20(3)
H(3A)	7418(5)	5894(18)	4651(5)	16(2)
H(3B)	7866(5)	4491(19)	4398(5)	20(3)
H(4)	7849(5)	6249(18)	3504(5)	21(3)
H(5A)	7248(5)	9060(20)	3344(6)	23(3)
H(5B)	7053(5)	8753(18)	3978(5)	18(3)
H(6)	6413(5)	7476(19)	3374(5)	19(3)
H(7A)	6928(5)	5990(20)	2014(6)	26(3)
H(7B)	7188(5)	7730(20)	2408(6)	34(3)
H(7C)	6573(5)	7650(20)	2283(6)	31(3)
H(9)	6384(5)	3238(19)	1974(5)	21(3)
H(10)	5770(5)	620(20)	2135(6)	24(3)
H(11)	5478(5)	-200(20)	3074(6)	25(3)
H(12)	5834(5)	1603(19)	3883(6)	21(3)
H(14A)	6556(5)	6198(18)	4673(5)	18(3)
H(14B)	6206(4)	4232(18)	4605(5)	16(2)
H(15)	5888(4)	7929(17)	4072(5)	14(2)
H(19A)	4679(5)	5930(20)	2924(6)	29(3)
H(19B)	4457(5)	5150(20)	3557(6)	29(3)
H(19C)	4873(6)	3840(20)	3184(7)	41(4)

*Table A5.6. Torsion angles [°] for indoline **169**.*

Cl(1)-C(4)-C(5)-C(6)	-176.40(4)
O(1)-C(16)-C(17)-F(1)	59.58(8)
O(1)-C(16)-C(17)-F(2)	-55.02(9)
O(1)-C(16)-C(17)-F(3)	178.96(8)
O(1)-C(16)-C(17)-F(1B)	-20.8(6)
O(1)-C(16)-C(17)-F(2B)	-135.5(3)
O(1)-C(16)-C(17)-F(3B)	99.8(5)
O(1)-C(16)-C(17)-F(1A)	28.3(5)
O(1)-C(16)-C(17)-F(2A)	-91.8(4)
O(1)-C(16)-C(17)-F(3A)	139.5(4)
N(1)-C(8)-C(9)-C(10)	-179.58(6)
N(1)-C(8)-C(13)-C(1)	-1.89(6)
N(1)-C(8)-C(13)-C(12)	179.97(5)

N(2)-C(15)-C(18)-O(2)	125.52(5)
N(2)-C(15)-C(18)-O(3)	-54.58(7)
N(2)-C(16)-C(17)-F(1)	-117.14(7)
N(2)-C(16)-C(17)-F(2)	128.26(8)
N(2)-C(16)-C(17)-F(3)	2.24(10)
N(2)-C(16)-C(17)-F(1B)	162.5(6)
N(2)-C(16)-C(17)-F(2B)	47.7(3)
N(2)-C(16)-C(17)-F(3B)	-77.0(5)
N(2)-C(16)-C(17)-F(1A)	-148.4(5)
N(2)-C(16)-C(17)-F(2A)	91.4(4)
N(2)-C(16)-C(17)-F(3A)	-37.2(4)
C(1)-C(2)-C(3)-C(4)	-57.74(6)
C(1)-C(14)-C(15)-N(2)	-164.41(4)
C(1)-C(14)-C(15)-C(18)	75.96(6)
C(2)-C(1)-C(6)-N(1)	76.90(5)
C(2)-C(1)-C(6)-C(5)	-48.30(6)
C(2)-C(1)-C(13)-C(8)	-89.99(5)
C(2)-C(1)-C(13)-C(12)	87.87(7)
C(2)-C(1)-C(14)-C(15)	170.56(4)
C(2)-C(3)-C(4)-Cl(1)	177.86(4)
C(2)-C(3)-C(4)-C(5)	58.11(6)
C(3)-C(4)-C(5)-C(6)	-55.30(6)
C(4)-C(5)-C(6)-N(1)	-67.33(6)
C(4)-C(5)-C(6)-C(1)	50.89(6)
C(6)-N(1)-C(8)-C(9)	157.32(6)
C(6)-N(1)-C(8)-C(13)	-22.82(6)
C(6)-C(1)-C(2)-C(3)	52.13(6)
C(6)-C(1)-C(13)-C(8)	24.13(5)
C(6)-C(1)-C(13)-C(12)	-158.01(6)
C(6)-C(1)-C(14)-C(15)	48.42(6)
C(7)-N(1)-C(6)-C(1)	169.74(5)
C(7)-N(1)-C(6)-C(5)	-65.38(6)
C(7)-N(1)-C(8)-C(9)	25.98(9)
C(7)-N(1)-C(8)-C(13)	-154.15(5)
C(8)-N(1)-C(6)-C(1)	37.30(5)
C(8)-N(1)-C(6)-C(5)	162.18(5)
C(8)-C(9)-C(10)-C(11)	-0.14(9)
C(9)-C(8)-C(13)-C(1)	177.99(5)
C(9)-C(8)-C(13)-C(12)	-0.15(8)
C(9)-C(10)-C(11)-C(12)	-0.71(9)
C(10)-C(11)-C(12)-C(13)	1.12(9)
C(11)-C(12)-C(13)-C(1)	-178.34(5)
C(11)-C(12)-C(13)-C(8)	-0.70(8)
C(13)-C(1)-C(2)-C(3)	159.53(4)
C(13)-C(1)-C(6)-N(1)	-36.57(5)
C(13)-C(1)-C(6)-C(5)	-161.77(4)
C(13)-C(1)-C(14)-C(15)	-67.20(6)
C(13)-C(8)-C(9)-C(10)	0.57(8)
C(14)-C(1)-C(2)-C(3)	-73.35(6)
C(14)-C(1)-C(6)-N(1)	-161.77(4)
C(14)-C(1)-C(6)-C(5)	73.03(6)
C(14)-C(1)-C(13)-C(8)	148.10(5)
C(14)-C(1)-C(13)-C(12)	-34.04(8)
C(14)-C(15)-C(18)-O(2)	-113.28(5)
C(14)-C(15)-C(18)-O(3)	66.62(7)
C(15)-N(2)-C(16)-O(1)	-0.85(9)

C(15)-N(2)-C(16)-C(17)	175.55(5)
C(16)-N(2)-C(15)-C(14)	81.91(6)
C(16)-N(2)-C(15)-C(18)	-155.71(5)
C(19)-O(2)-C(18)-O(3)	-2.63(9)
C(19)-O(2)-C(18)-C(15)	177.28(5)

*Table A5.7. Hydrogen bonds for indoline **169** [Å and °].*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(3)#1	0.846(13)	2.131(13)	2.9754(6)	177.2(13)

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