Supplemental Material

Structure-Property Relationships in Polymorphic and Pseudopolymorphic Modifications of Hydrocortisone

Viktor Suitchmezian, Inke Jeß and Christian Näther

- Details on the structure determination of hydrocortisone chloroform solvate (**4**).
- Details on the structure determination of hydrocortisone N,N'-dimethyl formamide solvate (**5**).
- **Figure S1**: Experimental (top) and calculated (bottom) X-ray powder pattern of hydrocortisone methanol solvate (**2**).
- **Figure S2**: Experimental (top) and calculated (bottom) X-ray powder pattern of hydrocortisone pyridine solvate (**3**).
- **Figure S3**: Experimental (top) and calculated (bottom) X-ray powder pattern of hydrocortisone chloroform solvate (**4**).
- **Figure S4**: Experimental (top) and calculated (bottom) X-ray powder pattern of hydrocortisone N,N'-ddimethyl formamide solvate (**5**).
- **Figure S5**: DSC thermograms of all solvates (**2**)-(**5**) of hydrocortisone.
- **Figure S6**: Experimental X-ray powder pattern of the residues obtained after the first TG step in the thermal decomposition reaction of the chloroform solvate.
- **Figure S7**: Experimental X-ray powder pattern of the residues obtained after removal of the solvent at room temperature under reduced pressure from the N,N'-dimethylformamide solvate.

Table 1. Crystal data and structure refinement for hydrocortisone chloroformsolvate.

Identification code	hycl	
Empirical formula	$C_{21}H_{31}O_5 \cdot HCCl_3$	
Formula weight	482.83	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclicnic	
Space group	$P2_1$	
Unit cell dimensions	a = 12.5947(8) Å	α= 90°.
	b = 12.4413(5) Å	β= 90.571(9)°.
	c = 14.9884(11) Å	γ = 90°.
Volume	2348.5(2) $Å^3$	
Z	4	
Density (calculated)	1.366 Mg/m^3	
Absorption coefficient	0.421 mm^{-1}	
F(000)	1020	
Theta range for data collection	2.10 to 24.94°.	
Index ranges	-14<=h<=14, -14<=k<=14, -15<=l<=17	
Reflections collected	12025	
Independent reflections	7701 [R(int) = 0.0338]	
Completeness to theta = 24.94°	96.0 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7701 / 1 / 542	
Goodness-of-fit on F^2	1.027	
Final R indices [I>2sigma(I)]	R1 = 0.0449, wR2 = 0.1099	
R indices (all data)	R1 = 0.0553, wR2 = 0.1152	
Absolute structure parameter	-0.03(6)	
Extinction coefficient	0.0208(18)	
Largest diff. peak and hole	0.295 and -0.454 $e.Å^{-3}$	

Table 2. Atomic coordinates (·104) and equivalent isotropic displacement parameters (Å2·103). U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
O(1)	2927(2)	102(2)	7000(2)	43(1)
O(2)	4345(2)	4612(2)	9403(1)	28(1)
O(3)	3138(1)	7905(2)	7488(1)	27(1)
O(4)	5132(2)	9208(2)	8679(2)	33(1)
O(5)	3605(2)	9575(2)	9885(1)	30(1)
C(1)	3238(2)	1000(3)	7257(2)	32(1)
C(2)	3098(3)	1359(3)	8212(2)	35(1)
C(3)	3143(2)	2571(3)	8313(2)	29(1)
C(4)	4148(2)	3082(3)	7889(2)	24(1)
C(5)	3973(2)	4316(3)	7805(2)	23(1)
C(6)	3626(2)	4878(3)	8679(2)	23(1)
C(7)	3482(2)	6099(3)	8596(2)	23(1)
C(8)	4411(2)	6662(3)	8133(2)	22(1)
C(9)	4214(2)	7846(3)	7817(2)	23(1)
C(10)	5021(2)	8000(3)	7058(2)	27(1)
C(11)	5309(2)	6863(3)	6706(2)	27(1)
C(12)	4564(2)	6101(3)	7221(2)	25(1)
C(13)	4856(2)	4913(3)	7289(2)	24(1)
C(14)	4942(3)	4417(3)	6354(2)	30(1)
C(15)	5083(3)	3202(3)	6368(2)	31(1)
C(16)	4301(2)	2630(3)	6948(2)	29(1)
C(17)	3813(2)	1711(3)	6670(2)	34(1)
C(18)	5155(2)	2744(3)	8434(2)	28(1)
C(19)	5439(2)	6650(3)	8715(2)	25(1)
C(20)	4332(2)	8671(3)	8578(2)	24(1)
C(21)	3427(2)	8785(3)	9225(2)	31(1)
O(11)	9472(2)	14015(3)	1103(2)	49(1)
O(12)	12492(2)	9463(2)	1508(2)	41(1)
O(13)	9896(2)	6234(2)	1082(2)	38(1)
O(14)	11967(2)	4976(2)	2257(2)	43(1)
O(15)	12783(2)	4671(3)	676(2)	52(1)
C(31)	9859(3)	13141(4)	1316(2)	42(1)
C(32)	10920(3)	12761(4)	966(3)	44(1)
C(33)	11014(3)	11556(3)	950(2)	38(1)
C(34)	10762(2)	11019(3)	1855(2)	34(1)
C(35)	10578(2)	9793(3)	1691(2)	34(1)
C(36)	11452(2)	9232(3)	1142(2)	36(1)
C(37)	11289(2)	8021(3)	1044(2)	35(1)
C(38)	11028(2)	7440(3)	1924(2)	35(1)
C(39)	10611(2)	6276(3)	1843(2)	38(1)
C(40)	10000(3)	6098(4)	2721(2)	40(1)
C(41)	9691(3)	7230(4)	3060(2)	40(1)
C(42)	10044(2)	8006(3)	2312(2)	35(1)
C(43)	10214(2)	9182(3)	2542(2)	34(1)
C(44)	9182(3)	9698(4)	2863(2)	41(1)
C(45)	9267(2)	10916(4)	3006(2)	41(1)
C(46)	9763(2)	11497(3)	2234(2)	36(1)
C(47)	9328(3)	12438(4)	1947(2)	42(1)
C(48)	11674(2)	11276(4)	2541(2)	41(1)
C(49)	11981(2)	7476(4)	2575(2)	39(1)
C(50)	11501(2)	5478(4)	1671(2)	36(1)
C(51)	11866(3)	5322(4)	715(2)	42(1)
C(61)	7344(3)	9862(3)	5756(2)	41(1)
Cl(1)	6091(1)	10409(1)	6004(1)	54(1)
Cl(2)	7217(1)	8535(1)	5354(1)	63(1)
Cl(3)	7995(1)	10676(1)	4986(1)	72(1)
C(62)	8556(4)	14329(4)	4484(3)	61(1)
Cl(4)	8748(1)	15628(1)	4911(1)	80(1)
Cl(5)	9761(1)	13617(2)	4500(1)	99(1)
Cl(6)	7582(1)	13640(2)	5074(1)	107(1)

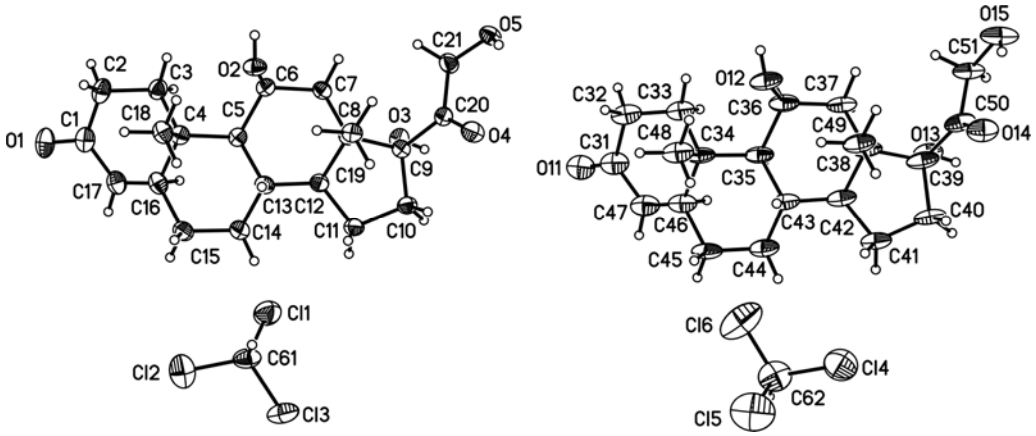

Table 3. Bond lengths [Å] and angles [°].

C(1)-C(2)-C(3)	112.6(3)	C(32)-C(33)-C(34)	113.5(3)
C(2)-C(3)-C(4)	113.2(3)	C(46)-C(34)-C(33)	109.8(3)
C(16)-C(4)-C(5)	107.9(3)	C(46)-C(34)-C(35)	108.8(3)
C(16)-C(4)-C(3)	109.6(3)	C(33)-C(34)-C(35)	108.3(3)
C(5)-C(4)-C(3)	108.7(2)	C(46)-C(34)-C(48)	106.4(3)
C(16)-C(4)-C(18)	105.9(2)	C(33)-C(34)-C(48)	109.4(3)
C(5)-C(4)-C(18)	115.0(3)	C(35)-C(34)-C(48)	114.2(3)
C(3)-C(4)-C(18)	109.7(3)	C(36)-C(35)-C(43)	115.6(3)
C(13)-C(5)-C(6)	114.5(3)	C(36)-C(35)-C(34)	114.8(3)
C(13)-C(5)-C(4)	114.3(2)	C(43)-C(35)-C(34)	113.1(3)
C(6)-C(5)-C(4)	114.6(2)	O(12)-C(36)-C(37)	110.6(3)
O(2)-C(6)-C(7)	111.1(2)	O(12)-C(36)-C(35)	110.8(3)
O(2)-C(6)-C(5)	110.6(2)	C(37)-C(36)-C(35)	113.6(3)
C(7)-C(6)-C(5)	114.3(3)	C(36)-C(37)-C(38)	114.2(3)
C(6)-C(7)-C(8)	113.4(2)	C(49)-C(38)-C(37)	110.9(3)
C(7)-C(8)-C(12)	107.2(2)	C(49)-C(38)-C(42)	111.8(3)
C(7)-C(8)-C(19)	112.0(2)	C(37)-C(38)-C(42)	106.7(3)
C(12)-C(8)-C(19)	112.4(2)	C(49)-C(38)-C(39)	109.9(3)
C(7)-C(8)-C(9)	116.5(2)	C(37)-C(38)-C(39)	116.6(3)
C(12)-C(8)-C(9)	100.3(2)	C(42)-C(38)-C(39)	100.5(3)
C(19)-C(8)-C(9)	107.9(2)	O(13)-C(39)-C(50)	107.3(3)
O(3)-C(9)-C(20)	107.7(2)	O(13)-C(39)-C(38)	107.7(3)
O(3)-C(9)-C(10)	111.4(2)	C(50)-C(39)-C(38)	111.9(3)
C(20)-C(9)-C(10)	113.8(2)	O(13)-C(39)-C(40)	110.8(2)
O(3)-C(9)-C(8)	107.3(2)	C(50)-C(39)-C(40)	115.1(3)
C(20)-C(9)-C(8)	113.0(2)	C(38)-C(39)-C(40)	103.8(3)
C(10)-C(9)-C(8)	103.6(2)	C(39)-C(40)-C(41)	106.1(3)
C(9)-C(10)-C(11)	107.1(3)	C(42)-C(41)-C(40)	104.7(3)
C(12)-C(11)-C(10)	104.1(2)	C(43)-C(42)-C(38)	114.4(3)
C(13)-C(12)-C(11)	118.8(3)	C(43)-C(42)-C(41)	118.5(3)
C(13)-C(12)-C(8)	114.1(3)	C(38)-C(42)-C(41)	103.1(3)
C(11)-C(12)-C(8)	104.2(3)	C(42)-C(43)-C(44)	111.0(3)
C(12)-C(13)-C(14)	110.3(3)	C(42)-C(43)-C(35)	109.1(3)
C(12)-C(13)-C(5)	109.0(2)	C(44)-C(43)-C(35)	108.1(3)
C(14)-C(13)-C(5)	108.6(3)	C(43)-C(44)-C(45)	113.6(3)
C(15)-C(14)-C(13)	113.3(3)	C(46)-C(45)-C(44)	113.3(3)
C(16)-C(15)-C(14)	113.7(3)	C(47)-C(46)-C(45)	119.1(3)
C(17)-C(16)-C(15)	121.2(3)	C(47)-C(46)-C(34)	123.8(3)
C(17)-C(16)-C(4)	122.0(3)	C(45)-C(46)-C(34)	117.0(3)
C(15)-C(16)-C(4)	116.7(3)	C(46)-C(47)-C(31)	122.4(3)
C(16)-C(17)-C(1)	123.6(3)	O(14)-C(50)-C(39)	124.1(3)
O(4)-C(20)-C(21)	119.8(3)	O(14)-C(50)-C(51)	117.7(3)
O(4)-C(20)-C(9)	122.2(3)	C(39)-C(50)-C(51)	118.2(3)
C(21)-C(20)-C(9)	118.0(2)	O(15)-C(51)-C(50)	111.5(3)
O(5)-C(21)-C(20)	113.6(3)	Cl(3)-C(61)-Cl(1)	110.0(2)
O(11)-C(31)-C(47)	121.0(3)	Cl(3)-C(61)-Cl(2)	111.0(2)
O(11)-C(31)-C(32)	122.2(4)	Cl(1)-C(61)-Cl(2)	110.8(2)
C(47)-C(31)-C(32)	116.8(4)	Cl(6)-C(62)-Cl(4)	111.3(3)
C(33)-C(32)-C(31)	112.7(3)	Cl(6)-C(62)-Cl(5)	110.9(3)

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

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O(1)	43(1)	27(2)	60(2)	0(1)	-16(1)	-5(1)
O(2)	24(1)	38(1)	20(1)	4(1)	1(1)	6(1)
O(3)	19(1)	29(1)	33(1)	2(1)	-6(1)	1(1)
O(4)	25(1)	41(2)	33(1)	-9(1)	1(1)	-7(1)
O(5)	24(1)	35(1)	29(1)	-7(1)	3(1)	1(1)
C(1)	24(2)	29(2)	44(2)	1(2)	-9(1)	0(1)
C(2)	31(2)	26(2)	49(2)	6(2)	-2(2)	-5(1)
C(3)	26(2)	26(2)	34(2)	2(1)	2(1)	-2(1)
C(4)	19(1)	26(2)	28(2)	1(1)	-1(1)	2(1)
C(5)	21(1)	25(2)	25(2)	2(1)	-2(1)	1(1)
C(6)	17(1)	25(2)	25(2)	3(1)	0(1)	1(1)
C(7)	20(1)	26(2)	24(2)	-2(1)	0(1)	1(1)
C(8)	17(1)	26(2)	22(2)	1(1)	-1(1)	3(1)
C(9)	19(1)	25(2)	24(2)	-1(1)	-2(1)	1(1)
C(10)	25(1)	30(2)	25(2)	0(1)	4(1)	-2(1)
C(11)	27(2)	30(2)	25(2)	-1(1)	5(1)	-1(1)
C(12)	23(1)	26(2)	24(2)	-1(1)	1(1)	0(1)
C(13)	20(1)	28(2)	24(2)	0(1)	0(1)	3(1)
C(14)	35(2)	30(2)	27(2)	-2(1)	3(1)	1(1)
C(15)	32(2)	31(2)	30(2)	-4(1)	4(1)	1(1)
C(16)	26(1)	28(2)	31(2)	-3(1)	-6(1)	7(1)
C(17)	34(2)	29(2)	38(2)	-5(2)	-5(1)	1(1)
C(18)	24(2)	29(2)	32(2)	-1(1)	-5(1)	6(1)
C(19)	22(1)	29(2)	24(2)	0(1)	-1(1)	2(1)
C(20)	20(1)	23(2)	27(2)	1(1)	0(1)	1(1)
C(21)	27(2)	29(2)	36(2)	-8(1)	7(1)	-4(1)
O(11)	38(1)	66(2)	41(2)	-3(1)	-6(1)	0(1)
O(12)	19(1)	75(2)	30(1)	5(1)	2(1)	-7(1)
O(13)	23(1)	68(2)	23(1)	6(1)	-6(1)	-5(1)
O(14)	39(1)	66(2)	25(1)	9(1)	-2(1)	4(1)
O(15)	27(1)	100(2)	30(1)	13(1)	7(1)	13(1)
C(31)	28(2)	66(3)	31(2)	-2(2)	-8(1)	-3(2)
C(32)	31(2)	69(3)	32(2)	9(2)	3(1)	-2(2)
C(33)	27(2)	60(3)	27(2)	3(2)	1(1)	-3(2)
C(34)	20(2)	66(3)	15(2)	-2(2)	1(1)	-7(2)
C(35)	17(1)	63(3)	21(2)	-1(2)	0(1)	-4(1)
C(36)	19(1)	67(3)	22(2)	2(2)	0(1)	-1(2)
C(37)	21(1)	64(3)	20(2)	7(2)	4(1)	1(2)
C(38)	18(1)	70(3)	16(2)	6(2)	1(1)	-3(2)
C(39)	21(2)	76(3)	18(2)	10(2)	-1(1)	-6(2)
C(40)	24(2)	73(3)	23(2)	10(2)	7(1)	-6(2)
C(41)	24(2)	69(3)	27(2)	3(2)	6(1)	-6(2)
C(42)	20(1)	64(3)	22(2)	6(2)	1(1)	-5(2)
C(43)	20(2)	65(3)	19(2)	3(2)	2(1)	-6(2)
C(44)	24(2)	68(3)	30(2)	0(2)	5(1)	-8(2)
C(45)	20(2)	76(3)	26(2)	-4(2)	6(1)	-6(2)
C(46)	19(2)	68(3)	21(2)	-8(2)	-4(1)	-10(2)
C(47)	25(2)	70(3)	32(2)	-2(2)	-3(1)	-3(2)
C(48)	24(2)	73(3)	26(2)	-1(2)	-4(1)	-7(2)
C(49)	22(2)	71(3)	25(2)	7(2)	0(1)	-6(2)
C(50)	25(2)	65(3)	19(2)	12(2)	-2(1)	-7(2)
C(51)	25(2)	73(3)	28(2)	10(2)	9(1)	5(2)
C(61)	39(2)	60(3)	23(2)	0(2)	2(1)	-8(2)
Cl(1)	44(1)	56(1)	62(1)	4(1)	12(1)	-2(1)
Cl(2)	58(1)	50(1)	79(1)	-7(1)	-11(1)	4(1)
Cl(3)	82(1)	77(1)	57(1)	1(1)	38(1)	-19(1)
C(62)	63(3)	83(4)	37(2)	10(2)	-20(2)	-1(2)
Cl(4)	104(1)	94(1)	43(1)	-4(1)	-5(1)	-14(1)
Cl(5)	83(1)	128(2)	85(1)	20(1)	-16(1)	30(1)
Cl(6)	84(1)	119(2)	119(1)	56(1)	2(1)	-17(1)

Table 5. Hydrogen coordinates ($\cdot 10^4$) and isotropic displacement parameters ($Å^2 \cdot 10^3$).

	x	y	z	U(eq)
H(2O)	3987	4588	9856	41
H(3O)	3071	8498	7256	41
H(5O)	4237	9671	9995	44
H(2A)	3662	1031	8588	42
H(2B)	2405	1096	8430	42
H(3A)	3130	2754	8955	35
H(3B)	2502	2889	8029	35
H(5)	3336	4380	7405	28
H(6)	2918	4574	8837	27
H(7A)	3401	6408	9201	28
H(7B)	2821	6247	8256	28
H(10A)	5665	8370	7285	32
H(10B)	4705	8439	6573	32
H(11A)	5179	6812	6055	33
H(11B)	6063	6692	6833	33
H(12)	3861	6132	6907	29
H(13)	5548	4834	7615	29
H(14A)	4292	4594	6007	37
H(14B)	5552	4745	6044	37
H(15A)	5011	2925	5751	37
H(15B)	5810	3033	6581	37
H(16)	3704	3078	6709	34
H(17)	3852	1527	6056	40
H(18A)	5098	3011	9046	43
H(18B)	5788	3051	8156	43
H(18C)	5212	1959	8441	43
H(19A)	6011	7015	8396	38
H(19B)	5646	5905	8838	38
H(19C)	5307	7022	9280	38
H(21A)	2773	8969	8887	37
H(21B)	3309	8084	9521	37
H(12O)	12841	9598	1063	62
H(13O)	9616	5639	1074	57
H(15O)	12933	4606	1207	78
H(32A)	11015	13041	354	53
H(32B)	11496	13060	1346	53
H(33A)	11746	11360	777	46
H(33B)	10523	11267	489	46
H(35)	9940	9772	1289	40
H(36)	11424	9547	528	43
H(37A)	11942	7702	794	42
H(37B)	10704	7892	612	42
H(40A)	10456	5726	3166	48
H(40B)	9357	5658	2611	48
H(41A)	8916	7280	3155	48
H(41B)	10063	7397	3629	48
H(42)	9479	7981	1839	42
H(43)	10772	9246	3018	41
H(44A)	8974	9356	3431	49
H(44B)	8613	9553	2419	49
H(45A)	8548	11211	3105	49
H(45B)	9696	11054	3552	49
H(46)	9317	11081	1800	43
H(47)	8652	12643	2166	51
H(48A)	12344	10977	2324	62
H(48B)	11505	10954	3119	62
H(48C)	11743	12056	2608	62
H(49A)	12590	7115	2305	59
H(49B)	11795	7109	3131	59
H(49C)	12165	8226	2704	59
H(51A)	11288	4983	362	50
H(51B)	12019	6032	446	50
H(61)	7778	9844	6318	49
H(62)	8312	14395	3850	73

Table 1. Crystal data and structure refinement for hydrocortisone dimethyl formamide solvate.

Identification code	hy_dmftt
Empirical formula	$C_{21}H_{30}O_6 \cdot C_3H_7NO$
Formula weight	435.55
Temperature	170(2) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 13.4186(10) Å α= 90°.
	b = 6.0878(3) Å β= 104.711(9)°.
	c = 14.6595(11) Å γ = 90°.
Volume	1158.27(14) $Å^3$
Z	2
Density (calculated)	1.249 Mg/m^3
Absorption coefficient	0.089 mm^{-1}
F(000)	472
Theta range for data collection	2.38 to 28.02°.
Index ranges	-17<=h<=17, -7<=k<=7, -19<=l<=18
Reflections collected	8423
Independent reflections	3004 [R(int) = 0.0319]
Completeness to theta = 28.02°	98.4 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3004 / 1 / 281
Goodness-of-fit on F^2	1.031
Final R indices [I>2sigma(I)]	R1 = 0.0432, wR2 = 0.1140
R indices (all data)	R1 = 0.0538, wR2 = 0.1201
Absolute structure parameter	-0.8(12)
Extinction coefficient	0.083(9)
Largest diff. peak and hole	0.295 and -0.371 $e.Å^{-3}$

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

	x	y	z	U(eq)
O(1)	6582(2)	1775(6)	9466(2)	58(1)
O(2)	1796(1)	4739(3)	6813(1)	21(1)
O(3)	1954(1)	3344(3)	3356(1)	20(1)
O(4)	-5(1)	7401(3)	3005(1)	27(1)
O(5)	-1244(1)	3944(4)	2711(1)	30(1)
C(1)	5847(2)	2670(6)	8915(2)	34(1)
C(2)	4750(2)	2236(5)	8965(2)	32(1)
C(3)	4003(2)	2474(4)	7994(2)	23(1)
C(4)	4068(2)	4716(4)	7533(2)	17(1)
C(5)	3499(2)	4551(4)	6464(2)	14(1)
C(6)	2390(2)	3589(4)	6269(2)	15(1)
C(7)	1823(2)	3539(4)	5216(2)	16(1)
C(8)	1908(2)	5664(4)	4679(2)	14(1)
C(9)	1596(2)	5441(4)	3571(2)	16(1)
C(10)	2194(2)	7348(5)	3246(2)	21(1)
C(11)	3105(2)	7940(4)	4096(2)	20(1)
C(12)	3067(2)	6194(4)	4843(2)	15(1)
C(13)	3604(2)	6629(4)	5884(2)	15(1)
C(14)	4752(2)	7119(5)	5989(2)	21(1)
C(15)	5388(2)	7206(5)	7020(2)	23(1)
C(16)	5196(2)	5298(4)	7608(2)	21(1)
C(17)	5988(2)	4256(5)	8215(2)	29(1)
C(18)	3641(2)	6536(4)	8079(2)	20(1)
C(19)	1299(2)	7557(4)	4977(2)	18(1)
C(20)	426(2)	5614(4)	3155(2)	17(1)
C(21)	-173(2)	3499(5)	2964(2)	21(1)
O(6)	8591(2)	7448(6)	8503(2)	61(1)
N(1)	8455(2)	6646(7)	9958(2)	50(1)
C(30)	8250(2)	7851(6)	9182(2)	37(1)
C(31)	9093(4)	4716(11)	10083(4)	89(2)
C(32)	7959(5)	7014(16)	10696(3)	124(3)

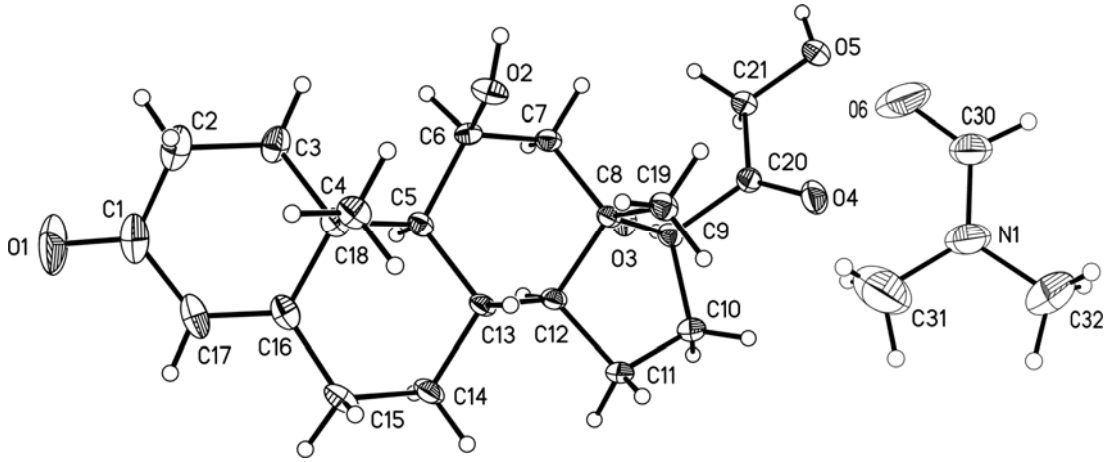

Table 3. Bond lengths [Å] and angles [°].

O(1)-C(1)	1.232(3)	C(3)-C(4)-C(5)	108.42(19)
O(2)-C(6)	1.444(3)	C(13)-C(5)-C(6)	115.01(17)
O(3)-C(9)	1.427(3)	C(13)-C(5)-C(4)	114.05(18)
O(4)-C(20)	1.225(3)	C(6)-C(5)-C(4)	114.14(17)
O(5)-C(21)	1.416(3)	O(2)-C(6)-C(7)	111.24(17)
C(1)-C(17)	1.456(4)	O(2)-C(6)-C(5)	110.63(18)
C(1)-C(2)	1.515(4)	C(7)-C(6)-C(5)	113.41(16)
C(2)-C(3)	1.526(3)	C(8)-C(7)-C(6)	114.58(19)
C(3)-C(4)	1.536(4)	C(7)-C(8)-C(19)	111.85(17)
C(4)-C(16)	1.530(3)	C(7)-C(8)-C(12)	107.42(17)
C(4)-C(18)	1.558(3)	C(19)-C(8)-C(12)	112.68(18)
C(4)-C(5)	1.564(3)	C(7)-C(8)-C(9)	114.91(19)
C(5)-C(13)	1.550(3)	C(19)-C(8)-C(9)	109.63(18)
C(5)-C(6)	1.556(3)	C(12)-C(8)-C(9)	99.81(16)
C(6)-C(7)	1.539(3)	O(3)-C(9)-C(20)	109.89(19)
C(7)-C(8)	1.534(3)	O(3)-C(9)-C(10)	111.83(17)
C(8)-C(19)	1.539(3)	C(20)-C(9)-C(10)	112.4(2)
C(8)-C(12)	1.547(3)	O(3)-C(9)-C(8)	106.80(18)
C(8)-C(9)	1.577(3)	C(20)-C(9)-C(8)	112.33(17)
C(9)-C(20)	1.538(3)	C(10)-C(9)-C(8)	103.27(18)
C(9)-C(10)	1.554(3)	C(11)-C(10)-C(9)	106.87(19)
C(10)-C(11)	1.550(3)	C(12)-C(11)-C(10)	104.46(19)
C(11)-C(12)	1.536(3)	C(11)-C(12)-C(13)	119.79(19)
C(12)-C(13)	1.537(3)	C(11)-C(12)-C(8)	104.37(17)
C(13)-C(14)	1.538(3)	C(13)-C(12)-C(8)	112.88(16)
C(14)-C(15)	1.537(3)	C(12)-C(13)-C(14)	109.70(16)
C(15)-C(16)	1.506(4)	C(12)-C(13)-C(5)	108.60(18)
C(16)-C(17)	1.359(4)	C(14)-C(13)-C(5)	109.39(18)
C(20)-C(21)	1.506(4)	C(15)-C(14)-C(13)	113.37(18)
O(6)-C(30)	1.222(4)	C(16)-C(15)-C(14)	113.8(2)
N(1)-C(30)	1.323(4)	C(17)-C(16)-C(15)	121.1(2)
N(1)-C(32)	1.424(5)	C(17)-C(16)-C(4)	122.2(2)
N(1)-C(31)	1.438(6)	C(15)-C(16)-C(4)	116.6(2)
O(1)-C(1)-C(17)	122.0(3)	C(16)-C(17)-C(1)	123.5(2)
O(1)-C(1)-C(2)	121.1(3)	O(4)-C(20)-C(21)	121.42(19)
C(17)-C(1)-C(2)	116.8(2)	O(4)-C(20)-C(9)	121.3(2)
C(1)-C(2)-C(3)	110.8(2)	C(21)-C(20)-C(9)	117.2(2)
C(2)-C(3)-C(4)	113.4(2)	O(5)-C(21)-C(20)	110.0(2)
C(16)-C(4)-C(3)	109.9(2)	C(30)-N(1)-C(32)	122.1(4)
C(16)-C(4)-C(18)	106.57(19)	C(30)-N(1)-C(31)	123.3(3)
C(3)-C(4)-C(18)	109.68(18)	C(32)-N(1)-C(31)	114.2(4)
C(18)-C(4)-C(5)	114.23(19)	O(6)-C(30)-N(1)	123.5(3)

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

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O(1)	47(1)	73(2)	44(1)	18(1)	-9(1)	27(1)
O(2)	18(1)	24(1)	24(1)	-6(1)	10(1)	-6(1)
O(3)	22(1)	22(1)	18(1)	-4(1)	5(1)	6(1)
O(4)	18(1)	23(1)	37(1)	3(1)	3(1)	5(1)
O(5)	15(1)	36(1)	37(1)	12(1)	1(1)	-6(1)
C(1)	37(1)	33(2)	26(1)	-2(1)	-5(1)	13(1)
C(2)	43(2)	24(2)	22(1)	2(1)	-2(1)	4(1)
C(3)	31(1)	13(1)	22(1)	0(1)	1(1)	2(1)
C(4)	17(1)	14(1)	20(1)	-3(1)	4(1)	0(1)
C(5)	12(1)	12(1)	19(1)	-2(1)	4(1)	0(1)
C(6)	16(1)	13(1)	17(1)	-1(1)	6(1)	-3(1)
C(7)	14(1)	14(1)	19(1)	0(1)	5(1)	-3(1)
C(8)	11(1)	12(1)	19(1)	0(1)	5(1)	0(1)
C(9)	13(1)	16(1)	20(1)	-1(1)	6(1)	2(1)
C(10)	19(1)	23(1)	24(1)	6(1)	8(1)	-2(1)
C(11)	15(1)	21(1)	26(1)	6(1)	8(1)	-3(1)
C(12)	12(1)	15(1)	21(1)	1(1)	7(1)	-1(1)
C(13)	9(1)	12(1)	24(1)	0(1)	5(1)	0(1)
C(14)	11(1)	25(1)	27(1)	0(1)	5(1)	-3(1)
C(15)	12(1)	27(1)	30(1)	-6(1)	4(1)	-5(1)
C(16)	17(1)	22(1)	21(1)	-7(1)	2(1)	2(1)
C(17)	19(1)	37(2)	27(1)	-7(1)	-3(1)	9(1)
C(18)	20(1)	17(1)	23(1)	-5(1)	5(1)	-1(1)
C(19)	16(1)	15(1)	24(1)	-2(1)	7(1)	2(1)
C(20)	16(1)	18(1)	18(1)	1(1)	6(1)	1(1)
C(21)	16(1)	23(1)	23(1)	4(1)	3(1)	-3(1)
O(6)	70(2)	92(2)	24(1)	14(1)	17(1)	9(2)
N(1)	42(1)	82(3)	29(1)	24(2)	13(1)	21(2)
C(30)	30(1)	54(2)	25(1)	11(1)	5(1)	5(1)
C(31)	85(3)	99(5)	91(4)	52(4)	36(3)	49(3)
C(32)	149(5)	194(9)	47(2)	48(4)	58(3)	106(6)

Table 5. Hydrogen coordinates ($\cdot 10^4$) and isotropic displacement parameters ($Å^2 \cdot 10^3$).

	x	y	z	U(eq)
H(1O2)	1287	4063	6871	31
H(1O3)	1777	3346	2778	30
H(1O5)	-1480	2704	2719	45
H(2A)	4561	3286	9409	38
H(2B)	4700	732	9207	38
H(3A)	3292	2253	8055	28
H(3B)	4149	1306	7576	28
H(5)	3894	3402	6215	17
H(6)	2458	2032	6495	18
H(7A)	2101	2313	4912	19
H(7B)	1085	3230	5158	19
H(10A)	2454	6881	2701	26
H(10B)	1738	8635	3055	26
H(11A)	3768	7876	3917	24
H(11B)	3018	9432	4333	24
H(12)	3395	4845	4660	18
H(13)	3272	7908	6118	18
H(14A)	5042	5971	5652	25
H(14B)	4815	8545	5684	25
H(15A)	6129	7239	7032	28
H(15B)	5226	8587	7309	28
H(17)	6671	4579	8181	35
H(18A)	3686	7965	7784	30
H(18B)	4047	6569	8736	30
H(18C)	2919	6217	8058	30
H(19A)	1377	8886	4624	27
H(19B)	1564	7833	5654	27
H(19C)	568	7158	4842	27
H(21A)	18	2694	2446	25
H(21B)	0	2561	3534	25
H(31)	7816	9096	9151	44
H(32A)	9128	4069	10702	134
H(32B)	9787	5118	10043	134
H(32C)	8798	3647	9588	134
H(33A)	8202	5931	11197	186
H(33B)	7212	6868	10446	186
H(33C)	8121	8496	10951	186

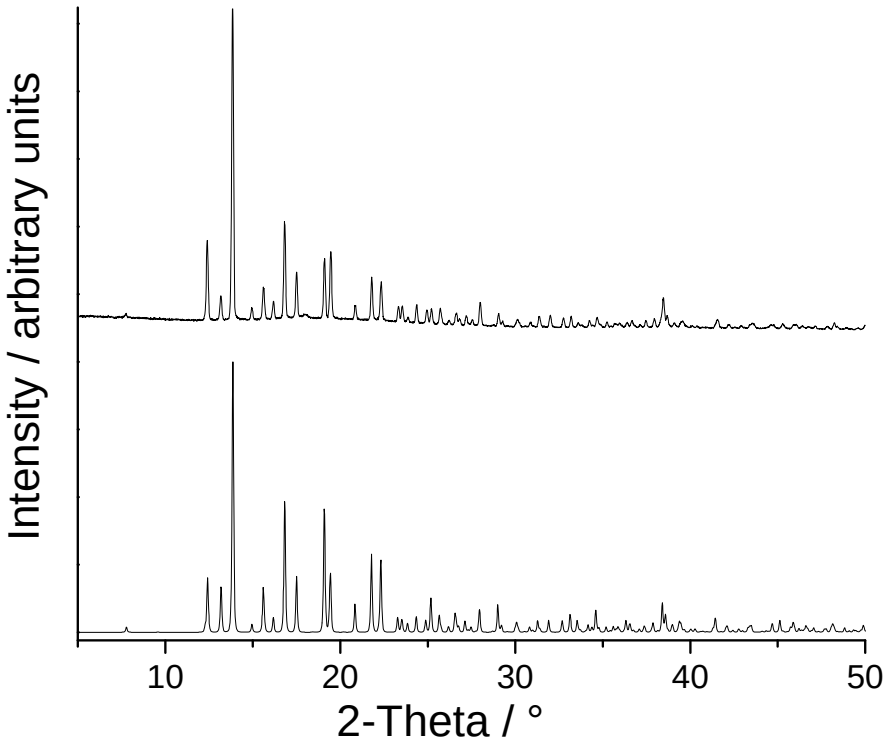

Figure S1: Experimental (top) and calculated (bottom) X-ray powder pattern of hydrocortisone methanol solvate (**2**).

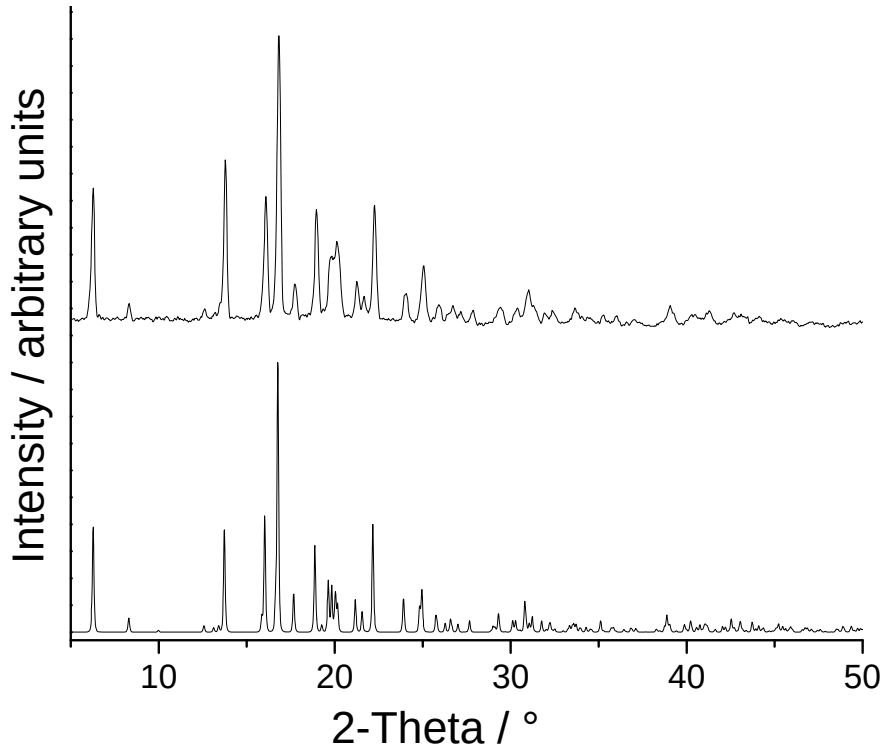

Figure S2: Experimental (top) and calculated (bottom) X-ray powder pattern of hydrocortisone pyridine solvate (**3**).

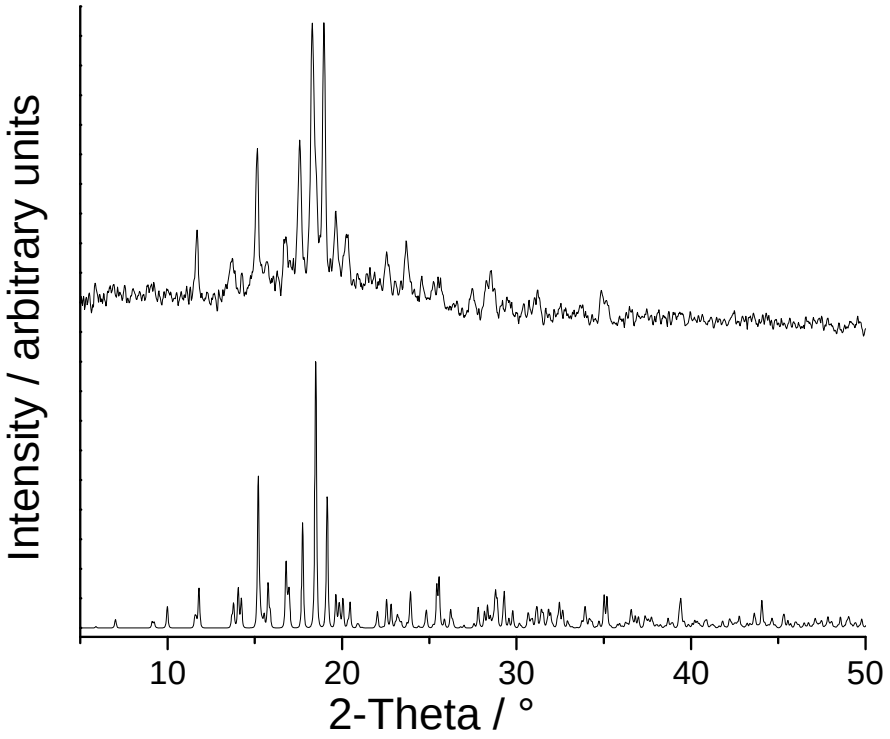

Figure S3: Experimental (top) and calculated (bottom) X-ray powder pattern of hydrocortisone chloroform solvate (**4**).

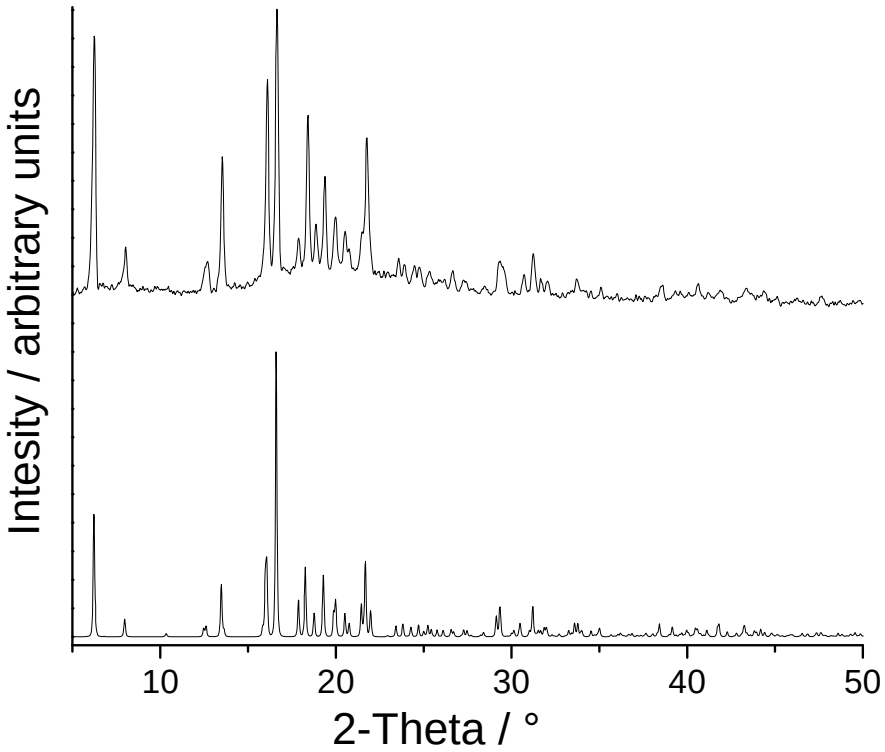

Figure S4: Experimental (top) and calculated (bottom) X-ray powder pattern of hydrocortisone N,N-dimethylformamide solvate (**5**).

Differential scanning calorimetry

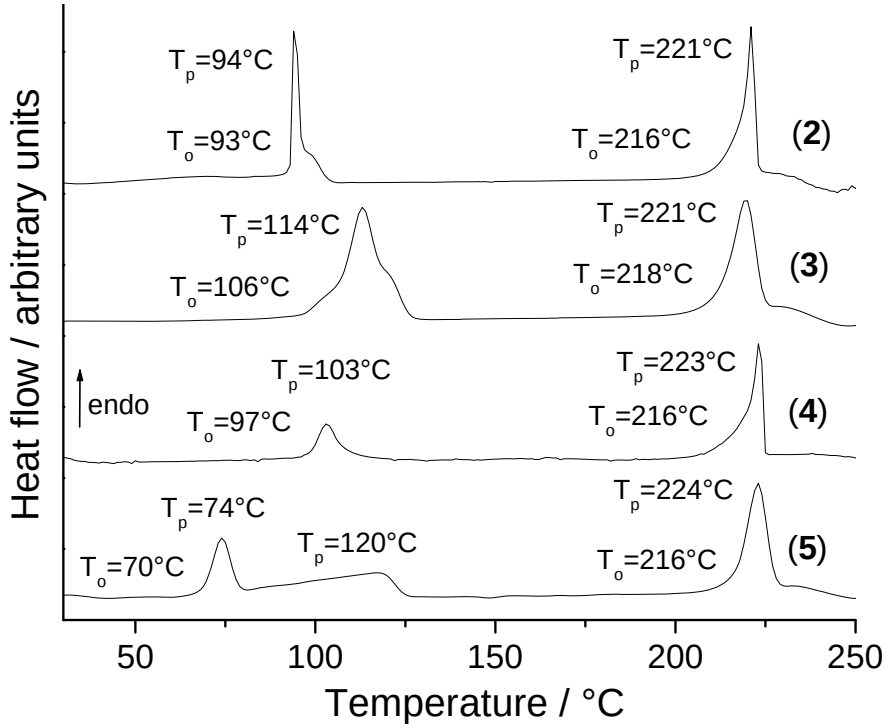

Figure S5: DSC curves for the methanol (**2**), pyridin (**3**), chloroform (**4**) and N,N'-dimethylformamide (**5**) solvates of hydrocortisone.

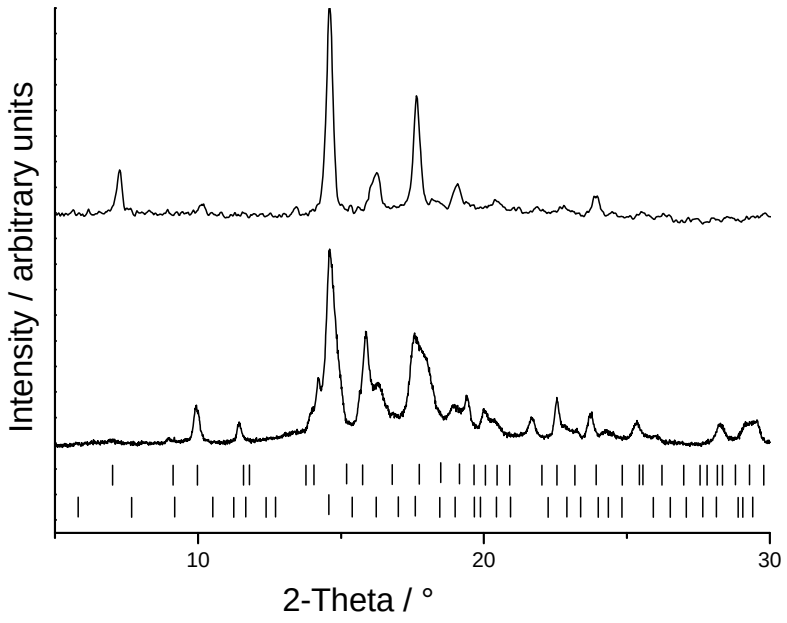

Figure S6: Experimental X-ray powder pattern of the residues obtained after the first TG step in the thermal decomposition reaction of the chloroform solvate (**4**, top) and for the residue (**4**) obtained after stirring an excess of hydrocortisone for two weeks in chloroform (bottom). Ticks: chloroform solvate (top) and form I (bottom).

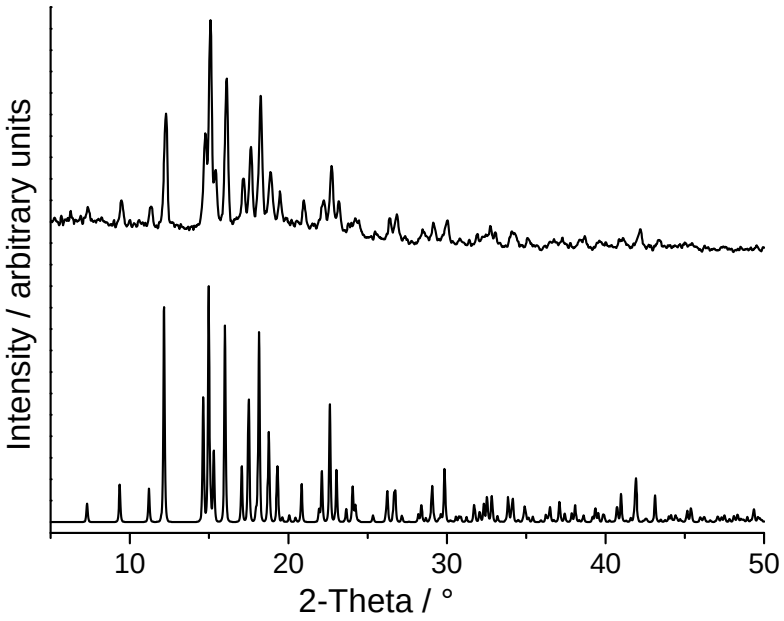

Figure S7: Experimental X-ray powder pattern of the residues obtained after removal of the solvent at room temperature under reduced pressure from the N,N'-dimethylformamide solvate (**5**, top) and the calculated X-ray powder diffraction pattern for form **III** (bottom).