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Figure S1. PXRD patterns of the PTU cocrystals obtained by LAG, compared with their respective components.
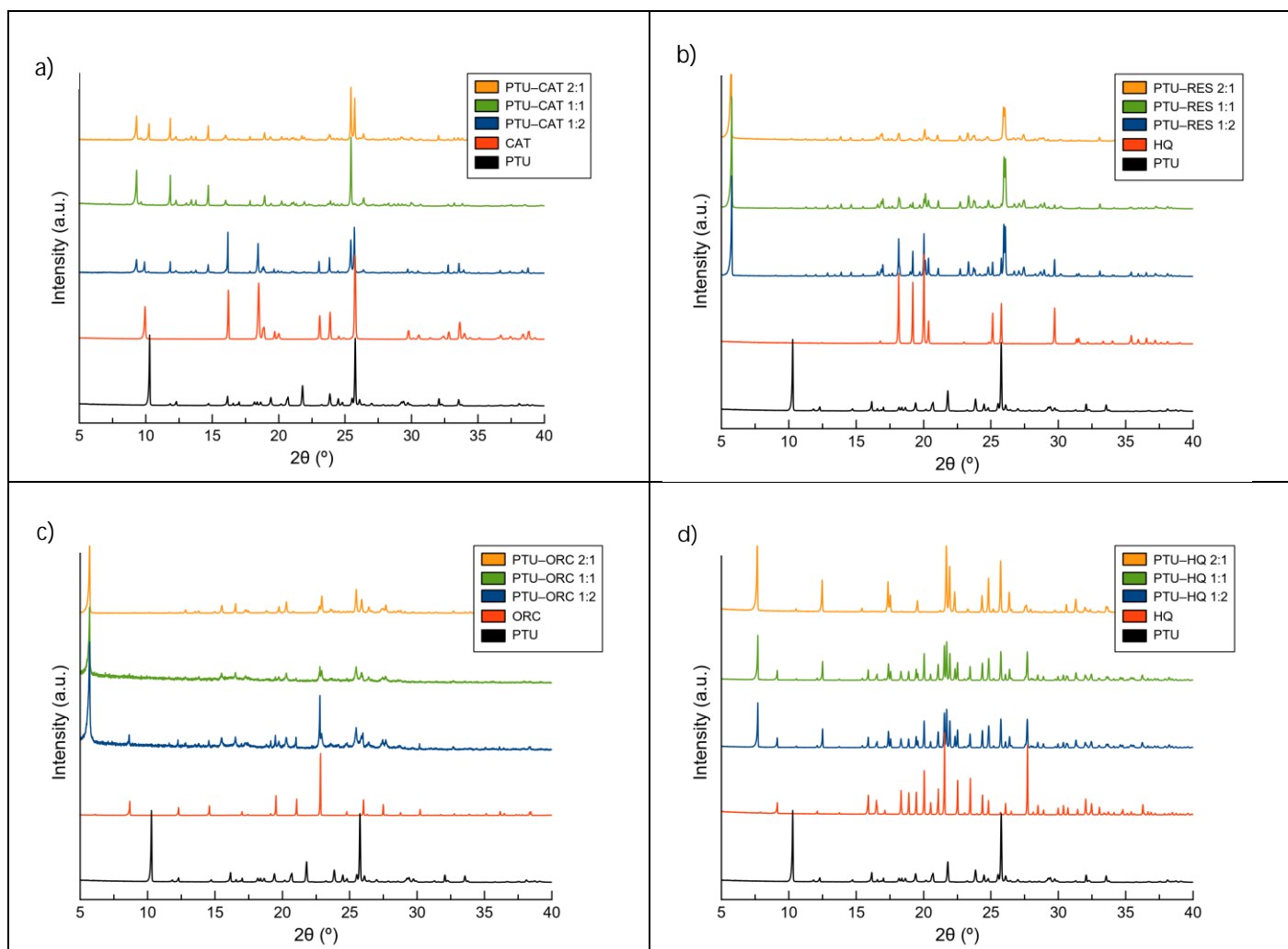
Figure S2. PXRD patterns of PTU cocrystals obtained by grinding the two components at different molar ratios.
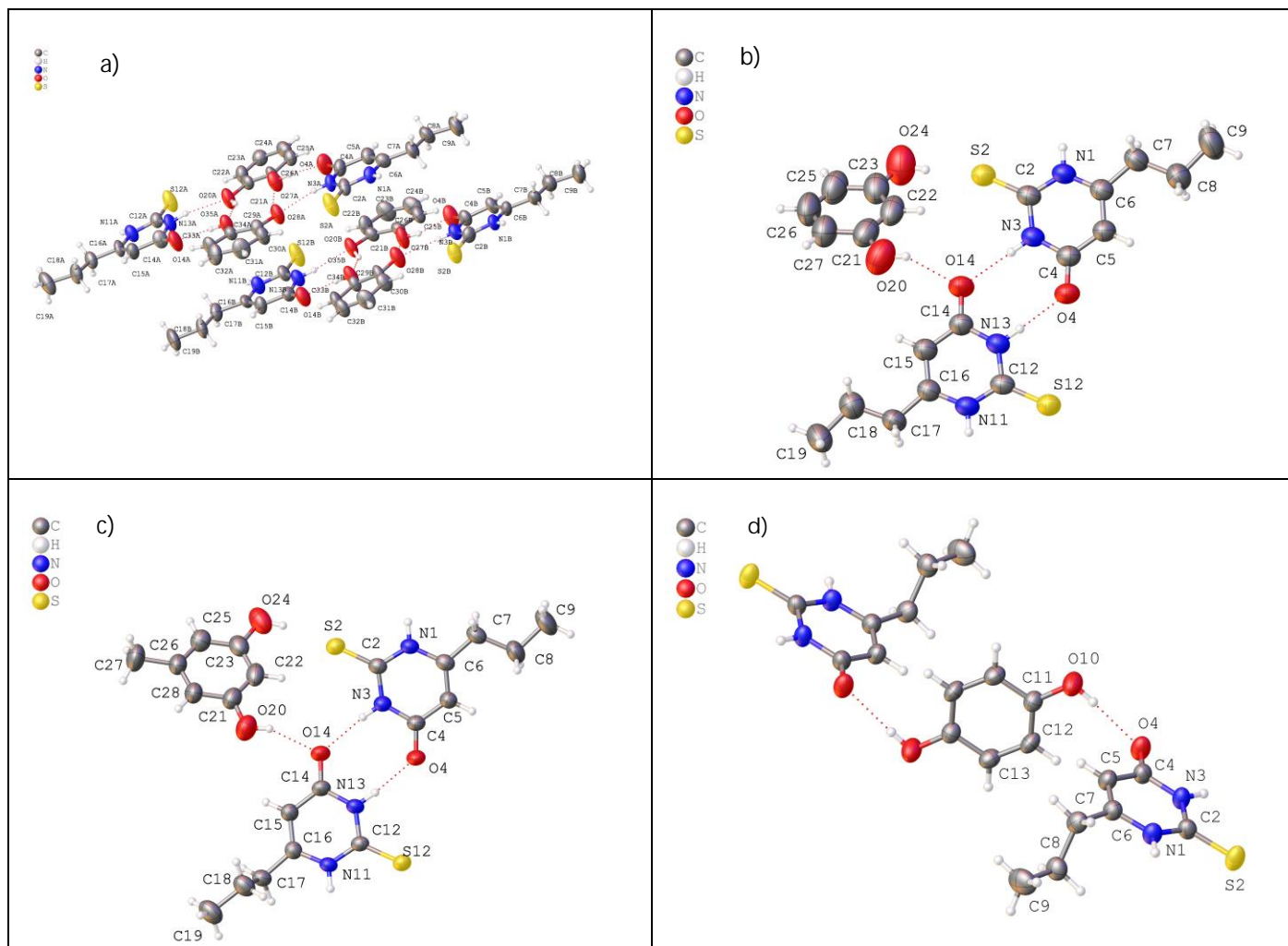
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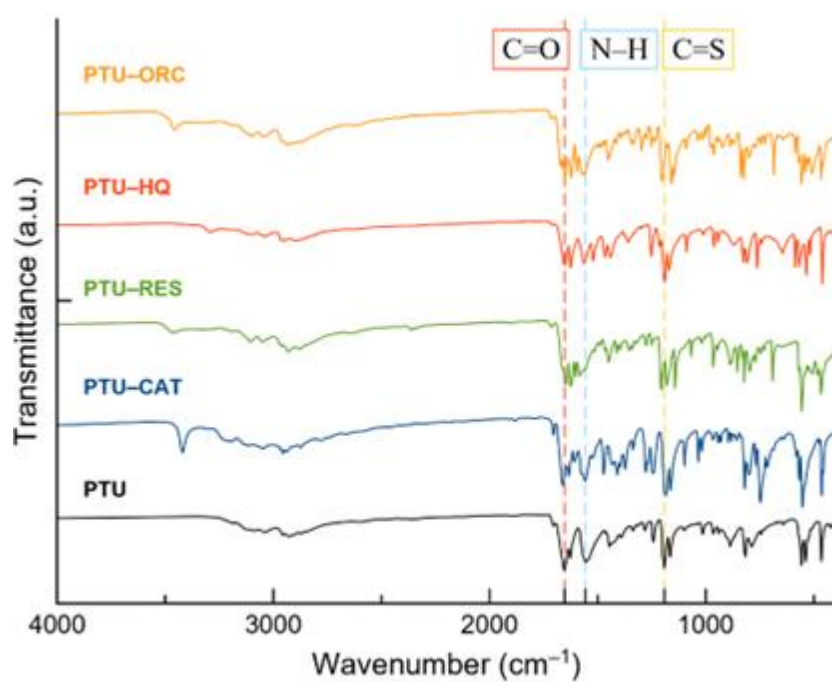
Figure 4. FT-IR spectrum of pure PTU and the cocrystals reported.

c)

d)
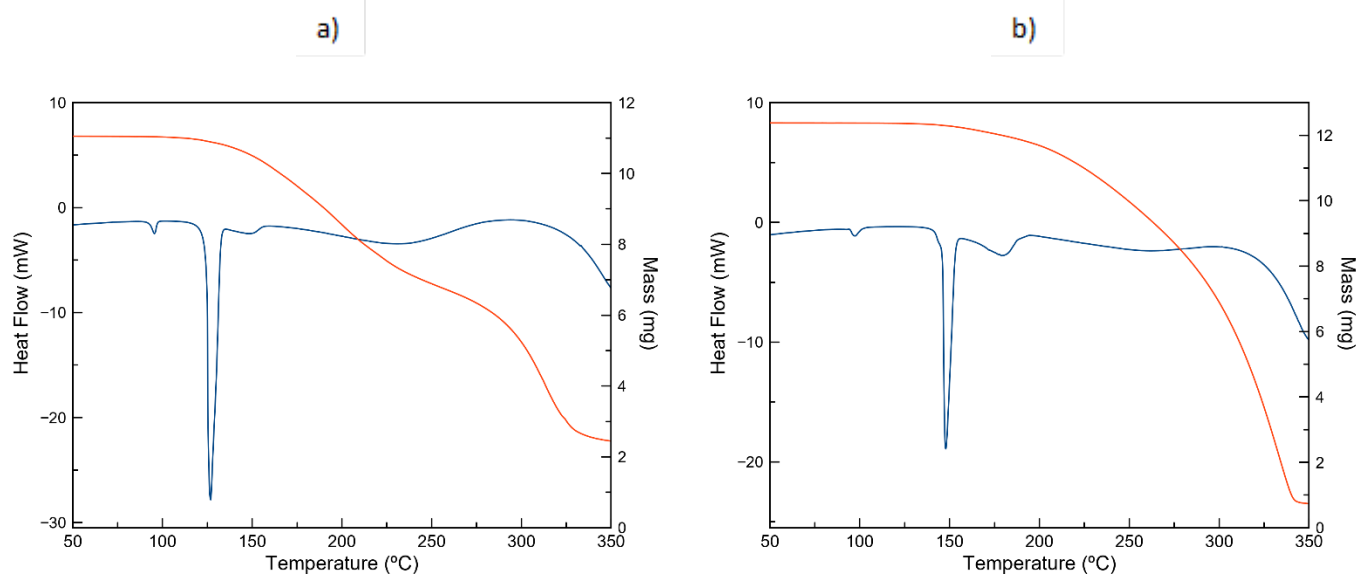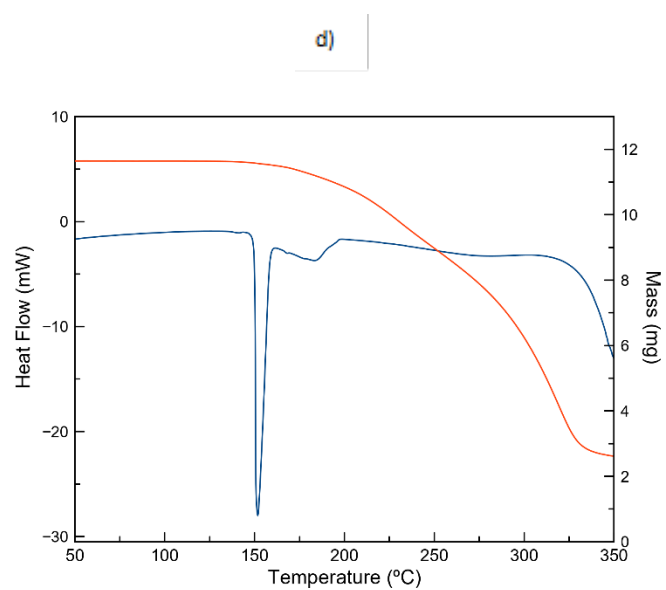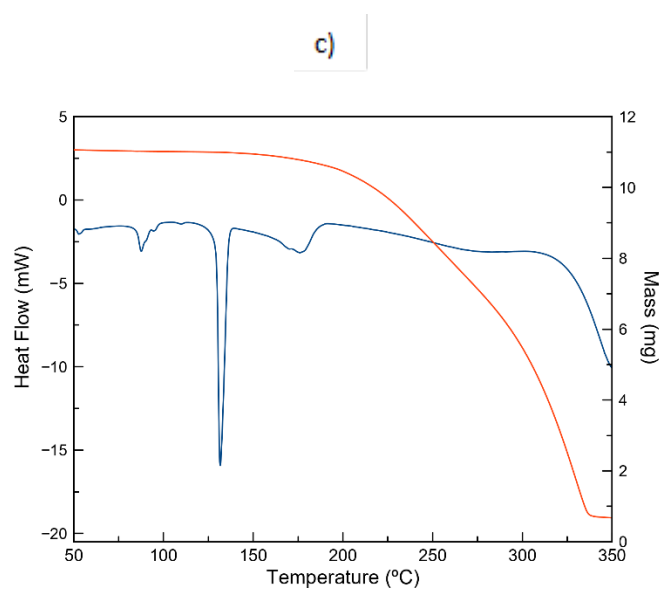
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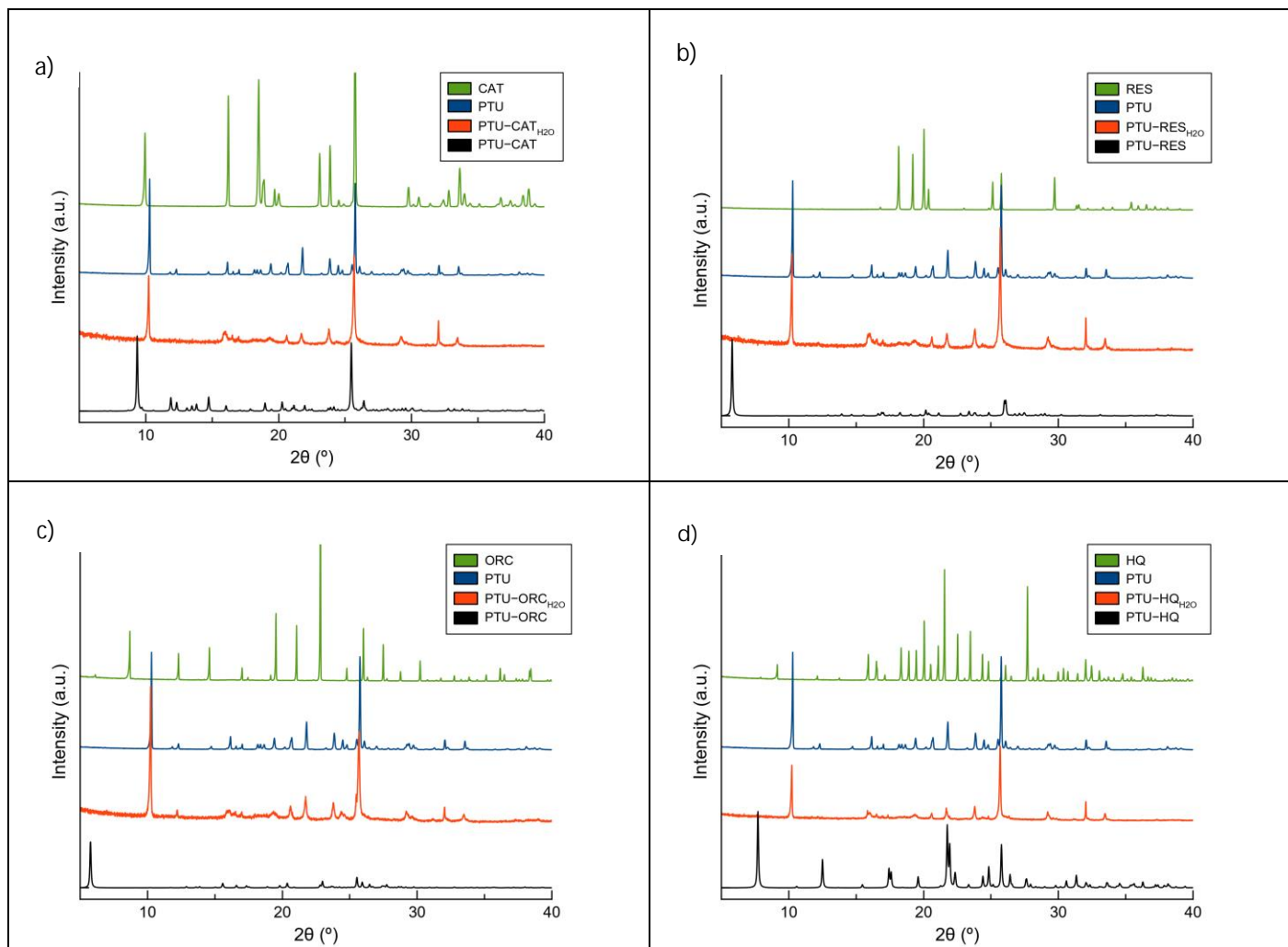
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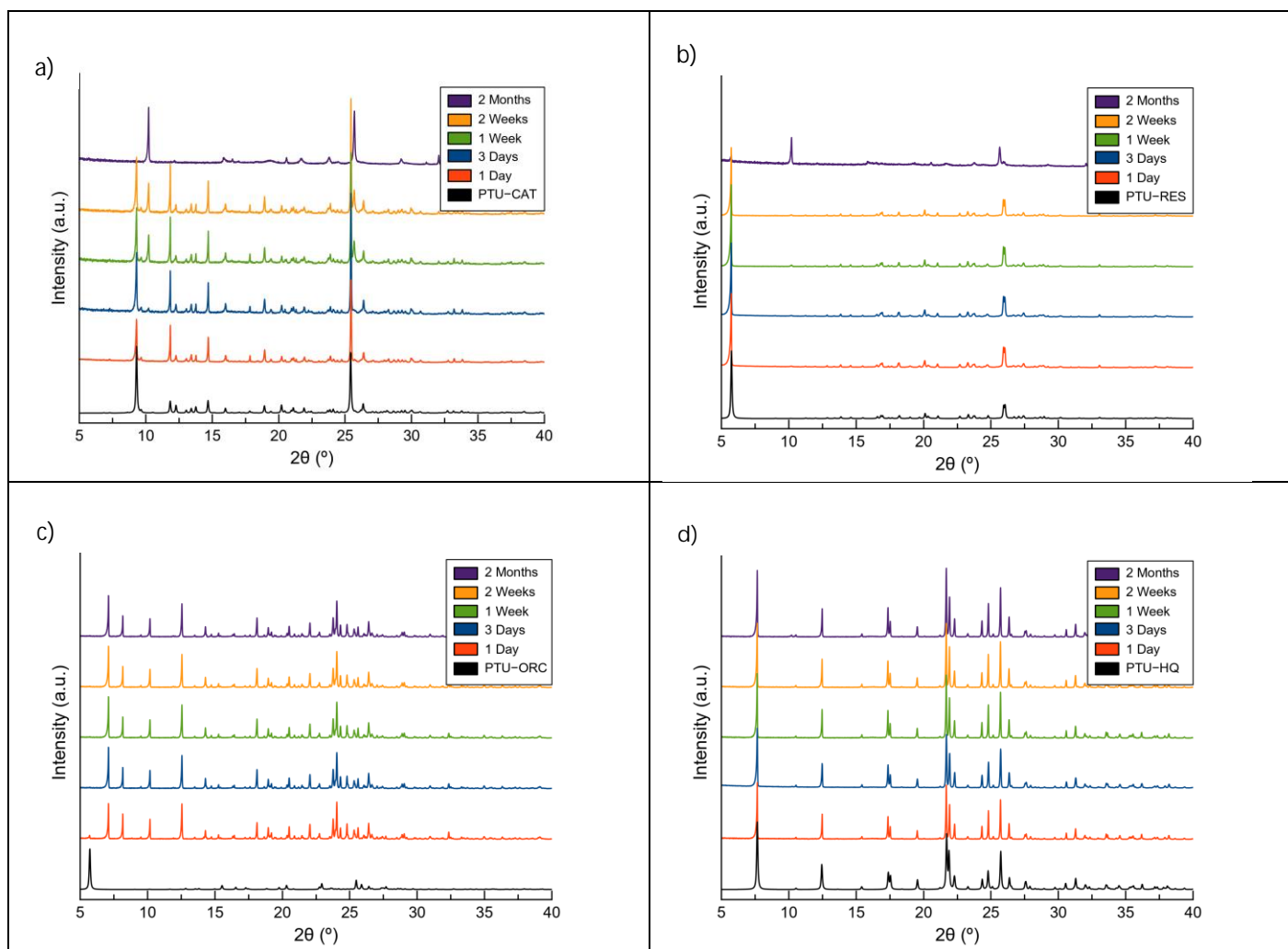
Figure S7. PXRD patterns of reported molecular salts under accelerated ageing conditions for 2 months.
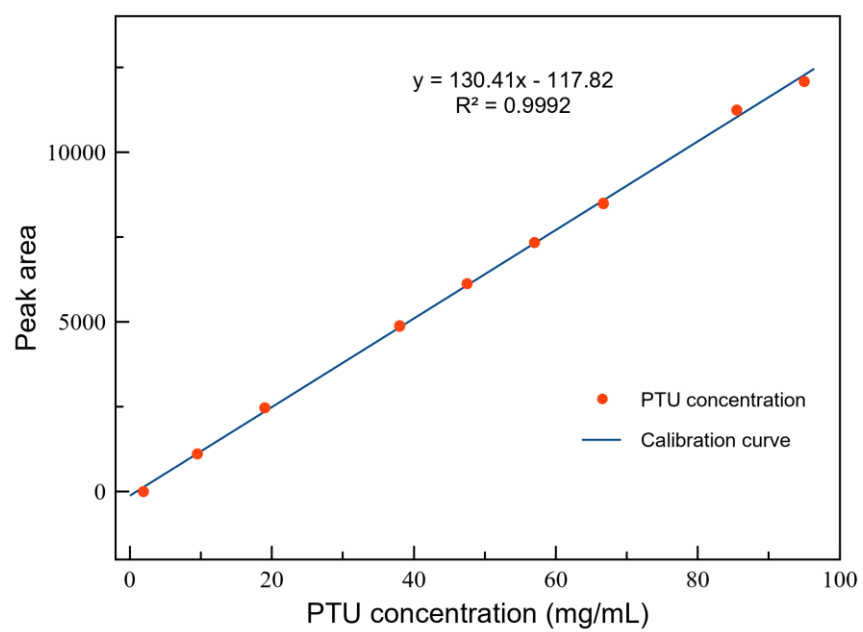
Figure S8. Calibration curve of PTU determined from HPLC data.

Table S1. Crystallographic data and structure refinement details of PTU cocrystals.

Identification code	PTU—CAT	PTU—RES	PTU—HQ	PTU—ORC
Formula	$C_{13}H_{16}N_2O_3S$	$C_{20}H_{26}N_4O_4S_2$	$C_{10}H_{13}N_2O_2S$	$C_{21}H_{28}N_4O_4S_2$
Formula weight	280.34	450.57	450.57	464.59
Crystal system	Monoclinic	Triclinic	Triclinic	Triclinic
Space group	$P2_1$	P-1	P-1	P-1
a/Å	13.701(5)	7.6530(3)	5.777(3)	7.8859(6)
b/Å	14.002(5)	10.2143(4)	8.491(3)	10.1513(7)
c/Å	15.910(6)	15.3443(7)	11.517(5)	15.5615(13)
$\alpha/°$	90	82.998(2)	84.18(2)	81.425(3)
$\beta/°$	110.549(6)	87.179(3)	87.16(2)	81.944(4)
$\gamma/°$	90	73.614(2)	81.02(2)	74.319(3)
V/Å^3	2858.0(17)	1142.03(8)	554.8(4)	1179.42(16)
Z	8	2	1	2
D_c/g cm^{-3}	1.303	1.310	1.348	1.308
F(000)	1184	476	238	492
Reflections collected	38488	13620	6215	19123
Unique reflections	9446	3978	1886	4133
Data / restraints / parameters	9446 / 1 / 693	3978 / 0 / 275	1886 / 0 / 139	4133 / 0 / 285
Goodness-of-fit on F^2	0.974	1.050	1.102	0.999
$R1$ (I > 2σ(I))	0.0682	0.0473	0.0325	0.0506
w$R2$ (I > 2σ(I))	0.1435	0.1264	0.0809	0.1097

Table S2. Hydrogen bonds for PTU cocrystals [Å and deg.].

PTU—CAT	D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
	N(3A)-H(3A)···O(28A)	0.86	2.15	2.989(11)	166.7
	N(3B)-H(3B)···O(28B)	0.86	2.18	3.040(11)	173.0
	N(13A)-H(13A)···O(20A)	0.86	2.20	3.046(11)	168.6
	N(13B)-H(13B)···O(20B)	0.86	2.14	2.994(12)	171.3
	O(20A)-H(20A)···O(35A)	0.82	2.04	2.753(10)	144.9
	O(27A)-H(27A)···O(4A)	0.82	1.83	2.643(12)	168.7
	O(20B)-H(20B)···O(35B)	0.82	2.07	2.768(11)	142.8
	O(27B)-H(27B)···O(4B)	0.82	1.87	2.679(11)	166.5
	O(28A)-H(28A)···O(27A)	0.82	2.10	2.774(10)	139.9
	O(35A)-H(35A)···O(14A)	0.82	1.86	2.677(11)	178.1
	O(28B)-H(28B)···O(27B)	0.82	2.05	2.719(10)	138.8
	O(35B)-H(35B)···O(14B)	0.82	1.84	2.657(11)	173.0
PTU—RES	D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
	N(3)-H(3)···O(14)	0.86	1.98	2.837(3)	176.7
	N(13)-H(13)···O(4)	0.86	1.95	2.796(3)	166.9
	C(22)-H(22)···O(4)#1	0.93	2.59	3.197(4)	123.6
	O(20)-H(20)···O(14)	0.82	2.09	2.820(3)	148.4
	Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+1,-z+1				
PTU—HQ	D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
	N(3)-H(3)···O(4)#1	0.86	1.98	2.839(2)	172.0
	O(10)-H(10)···O(4)	0.82	1.98	2.786(2)	168.2
	Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y,-z+1				
PTU—ORC	D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
	N(3)-H(3)···O(14)	0.86	1.99	2.846(4)	170.3
	N(13)-H(13)···O(4)	0.86	1.91	2.766(4)	174.4
	O(20)-H(20)···O(14)	0.82	2.07	2.809(4)	150.3

Table S3. π-stacking interactions analysis of PTU cocrystals.

PTU-CAT

```
================================================================================================================
  6-Membered Ring ( 1)    N1    -->   C2    -->   N3    -->   C4    -->   C5    -->   C6    -->
  6-Membered Ring ( 2)    N11   -->   C12   -->   N13   -->   C14   -->   C15   -->   C16   -->
  6-Membered Ring ( 3)    C21   -->   C22   -->   C23   -->   C24   -->   C25   -->   C26   -->
  6-Membered Ring ( 4)    C29   -->   C30   -->   C31   -->   C32   -->   C33   -->   C34   -->

================================================================================================================
Analysis of Short Ring-Interactions with Cg-Cg Distances <   6.0 Ang., Alpha <  20.000 Deg. and Beta < 60.0 Deg.
================================================================================================================

Cg(I) Res(I)  Cg(J) [  ARU(J)]    Cg-Cg Transformed J-Plane P, Q, R, S   Alpha Beta Gamma   CgI_Perp    CgJ_Perp  Slippage

Cg1   [ 1] -> Cg1  [ 2565.01] 5.7733(18) -0.9569 0.1140 0.2669  -0.5088  0.00(16) 56.6  56.6 3.1793(14) 3.1794(14) 4.819
Cg1   [ 1] -> Cg3  [ 1455.03]    3.748(2) 0.9289-0.2188-0.2987  -6.7221  6.48(17) 18.6  21.2 3.4932(13) 3.5520(15) 1.195
Cg1   [ 1] -> Cg3  [ 1555.03]    4.541(2) 0.9289-0.2188-0.2987   0.0810  6.48(17) 40.4  43.2 3.3099(13) 3.4564(15) 2.946
Cg2   [ 2] -> Cg4  [ 1455.04]    4.509(2) 0.9582 0.0823-0.2742  -4.9344  5.36(16) 40.8  41.3 3.3867(13) 3.4123(15) 2.947
Cg2   [ 2] -> Cg4  [ 1555.04]    3.904(2) 0.9582 0.0823-0.2742   2.0829  5.36(16) 25.8  21.6 3.6305(13) 3.5142(15) 1.701
Cg3   [ 3] -> Cg1  [ 1555.01]    4.541(2) 0.9569-0.1140-0.2669  -2.6706  6.48(17) 43.2  40.4 3.4564(15) 3.3099(13) 3.109
Cg3   [ 3] -> Cg1  [ 1655.01]    3.748(2) 0.9569-0.1140-0.2669   4.3378  6.48(17) 21.2  18.6 3.5520(15) 3.4932(13) 1.357
Cg4   [ 4] -> Cg2  [ 1555.02]    3.904(2) 0.9458 0.1749-0.2738  -0.3258  5.36(16) 21.6  25.8 3.5142(15) 3.6305(13) 1.436
Cg4   [ 4] -> Cg2  [ 1655.02]    4.509(2) 0.9458 0.1749-0.2738   6.6006  5.36(16) 41.3  40.8 3.4122(15) 3.3868(13) 2.977
                              ----------                        ----------------------------------------------
                              Min or Max  3.748                   0.0  18.6  56.6     -3.631     -3.631

[ 2565] = -X,1-Y,-Z [ 1455] = -1+X,Y,Z [ 1555] = X,Y,Z [ 1455] = -1+X,Y,Z [ 1555] = X,Y,Z [ 1555] = X,Y,Z [ 1655] = 1+X,Y,Z
[ 1555] = X,Y,Z [ 1655] = 1+X,Y,Z


================================================================================================================
Analysis of X-H...Cg(Pi-Ring) Interactions (H..Cg < 3.0 Ang. - Gamma <  40.0 Deg)
================================================================================================================
  X--H(I)    Res(I)  Cg(J) [  ARU(J)]    H..Cg Transformed J-Plane P, Q, R, S H-Perp Gamma    X-H..Cg      X..Cg X-H,Pi

C7   -H7A  [ 1] -> Cg3  [ 1555.03]    2.70  0.9289-0.2188-0.2987   0.0810 -2.70  2.38      143    3.525(3)   53
C17  -H17B [ 2] -> Cg4  [ 1455.04]    2.70  0.9582 0.0823-0.2742  -4.9344  2.69  4.75      140    3.501(4)   54
                              ----------                        ----------------------------------------------
                              Min or Max  2.700                  -2.700  2.4    143.00      3.501 54.00

[ 1555] = X,Y,Z
[ 1455] = -1+X,Y,Z
```

Table S3 (cont.). π-stacking interactions analysis of PTU cocrystals.

PTU-RES

```
  6-Membered Ring ( 1)   N1    -->   C2    -->   N3    -->   C4    -->   C5    -->   C6    -->
  6-Membered Ring ( 2)   N11   -->   C12   -->   N13   -->   C14   -->   C15   -->   C16   -->
  6-Membered Ring ( 3)   C21   -->   C22   -->   C23   -->   C25   -->   C26   -->   C27   -->
=========================================================================================================

Analysis of X-H...Cg(Pi-Ring) Interactions (H..Cg < 3.0 Ang. - Gamma <  40.0 Deg)
=========================================================================================================

   X--H(I)    Res(I)   Cg(J) [   ARU(J)]      H..Cg Transformed J-Plane P, Q, R, S H-Perp Gamma     X-H..Cg        X..Cg X-H,Pi

C19    -H19C  [ 2] -> Cg3   [ 1645.03]      2.85   0.9487-0.3144 0.0344  10.1737 -2.79 11.35          170     3.800(4)   81
                                             ----------                          -------------------------------------------
                                             Min or Max 2.850                    -2.794  11.4      170.00      3.800 81.00
[  1645] = 1+X,-1+Y,Z


=========================================================================================================

Analysis of Y-X...Cg(Pi-Ring) Interactions (X..Cg < 4.0 Ang. - Gamma <  30.0 Deg)
=========================================================================================================

   Y--X(I)    Res(I)   Cg(J) [   ARU(J)]      X..Cg Transformed J-Plane P, Q, R, S X-Perp Gamma     Y-X..Cg        Y..Cg Y-X,Pi

C2     -S2    [ 1] -> Cg1   [ 2566.01] 3.4926(11)  -0.9024-0.4220-0.0873  -3.0087 -3.424 11.35     89.53(8)    3.855(3)  1.01
C12    -S12   [ 2] -> Cg2   [ 2656.02] 3.6052(13)  -0.9225-0.3859 0.0059  -2.4193 -3.503 13.64     85.84(9)    3.861(3)  0.16
C14    -O14   [ 2] -> Cg1   [ 2666.01]  3.422(2)   -0.9024-0.4220-0.0873  -9.9147 3.405  5.70     87.89(18)    3.600(3)  1.72
                                            ----------                          -------------------------------------------
                                            Min or Max 3.422                    -3.503  5.7       89.53      3.600  1.72


[  2566] = -X,1-Y,1-Z
[  2656] = 1-X,-Y,1-Z
[  2666] = 1-X,1-Y,1-Z
```

Table S3 (cont.). π-stacking interactions analysis of PTU cocrystals.
PTU-ORC

```
6-Membered Ring ( 1)  N1     -->  C2     -->  N3     -->  C4     -->  C5     -->  C6     -->

6-Membered Ring ( 2)  N11    -->  C12    -->  N13    -->  C14    -->  C15    -->  C16    -->

6-Membered Ring ( 3)  C21    -->  C22    -->  C23    -->  C25    -->  C26    -->  C28    -->
========================================================================================================
Analysis of X-H...Cg(Pi-Ring) Interactions (H..Cg < 3.0 Ang. - Gamma <  40.0 Deg)
========================================================================================================

   X--H(I)    Res(I)  Cg(J) [   ARU(J)]      H..Cg Transformed J-Plane P, Q, R, S H-Perp Gamma      X-H..Cg       X..Cg X-H,Pi

C19   -H19C  [ 2] -> Cg3  [ 1645.03]     2.90  0.9727-0.1556-0.1723 10.1114  -2.89   4.66      138    3.678(6)    53
                                    ----------                        -------------------------------------------
                                    Min or Max  2.900                 -2.894    4.7     138.00     3.678 53.00

[  1645] = 1+X,-1+Y,Z
                                                          "6ORC     " PLATON-GEOMETRY Page   48
========================================================================================================
Analysis of Y-X...Cg(Pi-Ring) Interactions (X..Cg < 4.0 Ang. - Gamma <  30.0 Deg)
========================================================================================================

   Y--X(I)    Res(I)  Cg(J) [   ARU(J)]      X..Cg Transformed J-Plane P, Q, R, S X-Perp Gamma      Y-X..Cg       Y..Cg Y-X,Pi

C2    -S2    [ 1] -> Cg1  [ 2566.01] 3.4689(19) -0.8291-0.5586-0.0240  -3.7346 -3.425   9.13    89.60(13)   3.835(4)  0.53
C12   -S12   [ 2] -> Cg2  [ 2656.02]   3.619(2) -0.9059-0.4207-0.0485  -3.5236 -3.530  12.77    92.94(14)   4.066(4)  1.21
C14   -O14   [ 2] -> Cg1  [ 2666.01]   3.385(4) -0.8291-0.5586-0.0240 -10.2729  3.192  19.43     78.7(2)    3.368(4)  8.09
                                    ----------                        -------------------------------------------
                                    Min or Max  3.385                 -3.530    9.1      92.94     3.368  8.09

[  2566] = -X,1-Y,1-Z
[  2656] = 1-X,-Y,1-Z
[  2666] = 1-X,1-Y,1-Z
```

Table S3 (cont.). π-stacking interactions analysis of PTU cocrystals.
PTU-HQ

```
  6-Membered Ring ( 1)  N1     -->  C2     -->  N3     -->  C4     -->  C5     -->  C6     -->
  6-Membered Ring ( 2)  C11    -->  C12    -->  C13    -->  C11_a  -->  C12_a  -->  C13_a  -->
------------------------------------------------------------------------------------------------------------

============================================================================================================
Analysis of Short Ring-Interactions with Cg-Cg Distances <   6.0 Ang., Alpha <  20.000 Deg. and Beta < 60.0 Deg.
============================================================================================================

Cg(I) Res(I)  Cg(J) [   ARU(J)]      Cg-Cg Transformed J-Plane P, Q, R, S    Alpha  Beta Gamma   CgI_Perp    CgJ_Perp  Slippage

Cg1    [ 1] -> Cg1   [  1455.01]    5.777(3)  0.6051-0.4845 0.6317   1.9437   0.00(8) 52.8  52.8  3.4959(7)   3.4959(7)   4.599
Cg1    [ 1] -> Cg1   [  1655.01]    5.777(3)  0.6051-0.4845 0.6317   8.9355   0.00(8) 52.8  52.8  3.4959(7)   3.4959(7)   4.599
Cg1    [ 1] -> Cg1   [  2666.01]    4.207(2) -0.6051 0.4845-0.6317  -1.8439   0.00(8) 31.3  31.3  3.5957(7)   3.5957(7)   2.184
Cg1    [ 1] -> Cg2   [  1655.02]    5.355(3)  0.4052 0.9101 0.0873   4.5658  81.92(8) 17.6  84.2  0.5436(7)   5.1057(7)
Cg1    [ 1] -> Cg2   [  2657.02]    5.355(3) -0.4052-0.9101-0.0873  -4.5658  81.92(8) 17.6  84.2  0.5436(7)   5.1057(7)
                                   ----------                               -------------------------------------------
                         Min or Max  4.207                                   0.0  17.6  84.2     -3.596      -3.596

[  1455] = -1+X,Y,Z
[  1655] = 1+X,Y,Z
[  2666] = 1-X,1-Y,1-Z
[  1655] = 1+X,Y,Z
[  2657] = 1-X,-Y,2-Z
```

Table S4. Maximum apparent solubility (S_{max}) of PTU and its cocrystals in pH 6.8 phosphate buffer medium.

	S_{max} (mg·mL^{-1})	Time to reach S_{max} (min)	Solubility enhancement
PTU	1.28	30	
PTU-CAT	1.26	5	0.98X
PTU-RES	1.69	10	1.32X
PTU-ORC	1.66	30	1.29X
PTU-HQ	1.67	5	1.30X