IUCrJ

Volume 5 (2018)

Supporting information for article:

Structural studies of crystalline forms of triamterene with carboxylic acid, GRAS and API molecules

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S1. Triamterene and coformers used in this study

**Figure S1** Triamterene (1) and coformers (a–g) considered in the present study.
S2. Summary of the adduct prediction data and results obtained by experiment

S2.1. Method

Predictions of the adduct formation reactions considered in this study involving 1 and coformers (a–g) in DMSO are expressed as $P_{\text{obs}}$ which is the probability of observing $AB$ (cocrystal) and $A^{-}B^{+}$ (salt) in % terms according to the Cruz-Cabeza (2012) formula.

\[
P_{\text{obs}}(AB, \%) = -17 \Delta pK_a + 72 \text{ for } -1 \leq \Delta pK_a \leq 4
\]

\[
P_{\text{obs}}(A^{-}B^{+}, \%) = 17 \Delta pK_a + 28 \text{ for } -1 \leq \Delta pK_a \leq 4
\]

Where $P_{\text{obs}}$ is the probability of observing the $A-B$ (cocrystal) and $A^{-}B^{+}$ (salt) in % terms.

Using this method the % probability ($P_{\text{obs}}$) values for the proposed reactions were calculated and compared with the experimental results and summarized in Table S1.

S2.2. Results

Table S1  Results of the adduct formation reactions considered in this study.

| Acid | Base | $P_{\text{obs}}$ ($AB$, %) | $P_{\text{obs}}$ ($A^{-}B^{+}$, %) | $\Delta pK_a$ | Predicted result | Experimental result | Product |
|------|------|---------------------------|---------------------------------|--------------|-----------------|---------------------|---------|
| a    | 1    | 52.1                      | 47.9                            | 1.17         | cocrystal       | salt                | 1a·DMSO |
| b    | 1    | 42.4                      | 57.6                            | 1.74         | salt            | salt                | 1b·DMSO |
| c    | 1    | 46.3                      | 53.7                            | 1.51         | salt            | salt                | 1c·DMSO |
| d    | 1    | 47.3                      | 52.7                            | 1.45         | salt            | salt                | 1d·DMSO |
| e    | 1    | 48.5                      | 51.5                            | 1.38         | salt            | salt                | 1e·DMSO |
| f    | 1    | 45.0                      | 55.0                            | 1.59         | salt            | salt                | 1f·DMSO |
| g    | 1    | 54.7                      | 43.3                            | 1.02         | cocrystal       | salt                | 1g·DMSO |

Notes:

- $\Delta pK_a$ is the difference in the $pK_a$ of the most basic atom on 1 and the most acidic atom on the complementary acid. $pK_a$ values of 1 are calculated using the SPARC online calculator, [http://sparc.chem.uga.edu/sparc](http://sparc.chem.uga.edu/sparc) while $pK_a$ values of the coformers (a–f) are obtained from data compiled by R. Williams, [http://research.chem.psu.edu/brpgroup/pKa_compilation.pdf](http://research.chem.psu.edu/brpgroup/pKa_compilation.pdf).
- For ibuprofen (g) the $pK_a$ data is obtained from Sangster J; LOGKOW Databank, Sangster Res. Lab., Montreal, Quebec, Canada (1994).
- Predicted and experimental results of the adduct formation reactions refer to the form predicted according to the Cruz-Cabeza formula and the actual form obtained by crystallization.
### S3. Summary of crystallization data

**Table S2** Synthesis, crystallization experiment and subsequent product designation used throughout this study

| Triamterene/Coformer | Triamterene (mg/mmol) | Coformer (mg/mmol) | Triamterene:Coformer Ratio | Crystallization Solvent (ml) | Time to crystallization (days) | Product designation |
|----------------------|-----------------------|--------------------|-----------------------------|----------------------------|-------------------------------|---------------------|
| Triamterene          | 10/0.039              | N/A                | N/A                         | MeOH (30)                  | 7                             | 1                   |
| Triamterene, acetic acid and DMSO | 40.42/0.159 | 9.58/0.159         | 1 : 1                       | DMSO (2)                   | 4                             | 1a·DMSO             |
| Triamterene, succinic acid and DMSO | 34.1/0.135 | 15.9/0.135         | 1 : 1                       | DMSO (2)                   | 3                             | 1b·DMSO             |
| Triamterene, adipic acid and DMSO | 38.80/0.077 | 11.20/0.077       | 2 : 1                       | DMSO (2)                   | 4                             | 1c·DMSO             |
| Triamterene, pimelic acid and DMSO | 37.99/0.075 | 12.01/0.075       | 2 : 1                       | DMSO (2)                   | 5                             | 1d·DMSO             |
| Triamterene, azelaic acid and DMSO | 36.45/0.072 | 13.55/0.072       | 2 : 1                       | DMSO (2)                   | 5                             | 1e·DMSO             |
| Triamterene, nicotinic acid and DMSO | 40.22/0.079 | 9.78/0.079       | 2 : 1                       | DMSO (2)                   | 4                             | 1f·DMSO             |
| Triamterene, ibuprofen and DMSO | 35.53/0.070 | 14.47/0.070       | 2 : 1                       | DMSO (2)                   | 6                             | 1g·DMSO             |
## S4. Single crystal data

### Table S3  Crystallographic parameters for I and the salt solvates (1a–g DMSO).

|   | 1 | 1a•DMSO | 1b•DMSO | 1c•DMSO | 1d•DMSO | 1e•DMSO | 1f•DMSO | 1g•DMSO |
|---|---|---------|---------|---------|---------|---------|---------|---------|
| **Formula** | C₅H₇N₇ | [C₆H₇N₇]⁺ | [C₆H₇N₇]⁺ | [C₆H₇N₇]⁺ | [C₆H₇N₇]⁺ | [C₆H₇N₇]⁺ | [C₆H₇N₇]⁺ | [C₆H₇N₇]⁺ |
| **Space group** | P1 | P2₁/c | P2₁/c | P1 | P1 | P2₁/n | P2₁/n | P1 |
| **Mr** | 233.28 | 391.46 | 449.49 | 808.95 | 822.98 | 851.03 | 785.92 | 790.96 |
| **Crystal colour** | yellow | colourless | colourless | colourless | colourless | colourless | colourless | colourless |
| **Formula** | C₆H₈O₂⁻ | [C₆H₈O₂⁻]⁻ | [C₆H₈O₂⁻]⁻ | [C₆H₈O₂⁻]⁻ | [C₆H₈O₂⁻]⁻ | [C₆H₈O₂⁻]⁻ | [C₆H₈O₂⁻]⁻ | [C₆H₈O₂⁻]⁻ |
| **Mr** | 391.34 | 421.39 | 421.39 | 421.39 | 421.39 | 421.39 | 421.39 | 421.39 |
| **Crystal system** | triclinic | triclinic | monoclinic | triclinic | triclinic | monoclinic | monoclinic | triclinic |
| **极限Indices** | 0 ≤ h ≤ 19 | 0 ≤ h ≤ 19 | 0 ≤ h ≤ 19 | 0 ≤ h ≤ 19 | 0 ≤ h ≤ 19 | 0 ≤ h ≤ 19 | 0 ≤ h ≤ 19 | 0 ≤ h ≤ 19 |
| **Reference** | (Hughes et al., 2017) | This work | This work | This work | This work | This work | This work | This work |
S5. ORTEP diagrams and hydrogen bond tables

All asymmetric units are drawn using ORTEP-3 for Windows (Farruga, 2012) and employ a labelling scheme consistent with IUPAC and IUCr recommendations for small molecules (see Table S4).

**Table S4**  Crystallographic labelling of molecules of 1 and 1a–g and DMSO.

|       | Triamterene (1) | Coformer (a–g) | Solvent (DMSO) |
|-------|-----------------|----------------|----------------|
| 1     | A, B            | None           | None           |
| 1a·DMSO | A, B       | E, F           | C, D           |
| 1b·DMSO | A       | B              | C              |
| 1c·DMSO | A, B       | [0.5]C, [0.5]D | E, F           |
| 1d·DMSO | A, B, C, D  | E, F           | G, H, I, J    |
| 1e·DMSO | A, B       | C              | D, E           |
| 1f·DMSO | A, B       | C              | D, E           |
| 1g·DMSO | A, B       | C              | D              |

The hydrogen bond tables that follow (Tables S5 – S12) were produced using PLATON (Spek, 2009) and contain details of D-H…A bonds and angles generated for hydrogen bonds satisfying the default criteria of distance (D…A) being < R(D) + R(A) + 0.50Å whilst that of (H…A) is < R(H) + R(A) - 0.12 Å and angle (D-H…A) is > 100.00°; where D is a potential donor, A is a potential acceptor and R is the radius of the designated atom type. In cases where it is obvious that the directed hydrogen bond contributes to the formation of the hydrogen bonded sheet (but is slightly longer than expected) the default criteria have been relaxed and the resulting contacts are highlighted in red (see Tables S6, S7 and S11).

**S5.1. Triamterene (1)**

Crystallographic data for 1 is taken from Hughes *et al.* (2017) and renumbered for the systematic purposes of this study.

![ORTEP diagram](image)
Table S5  Hydrogen bond table for 1.

| No. | Type | Res | Donor--H…A          | [ARU]  | D--H   | H…A   | D…A   | D--H…A   |
|-----|------|-----|---------------------|--------|--------|--------|--------|-----------|
| 1   |      | N2A | H2A…N3B            | [1655.02] | 0.887(15) | 2.167(15) | 3.0430(17) | 169.4(16) |
| 2   |      | N2B | H2B…N3A            | [1555.01] | 0.920(16) | 2.161(15) | 3.0682(17) | 168.6(15) |
| 3   |      | N2A | H3A…N1B            | [1555.02] | 0.922(15) | 2.141(15) | 3.0583(16) | 173.1(14) |
| 4   |      | N2B | H3B…N1A            | [1455.01] | 0.911(15) | 2.138(15) | 3.0436(16) | 172.7(14) |
| 5   |      | N4A | H4A…N8A            | [1455.01] | 0.92(2) | 2.43(2) | 3.1159(17) | 131.3(15) |
| 6   |      | N4B | H4B…N8B            | [1455.02] | 0.90(2) | 2.46(2) | 3.1130(17) | 130.4(14) |
| 7   | INTRA | N4A | H5A…N5A           | [1455.01] | 0.921(18) | 2.399(15) | 2.7668(16) | 103.7(11) |
| 8   |      | N4A | H5A…N7A            | [1455.01] | 0.921(18) | 2.597(16) | 3.1791(18) | 121.7(12) |
| 9   | INTRA | N4B | H5B…N5B           | [1455.01] | 0.916(18) | 2.412(15) | 2.7762(17) | 103.7(11) |
| 10  |      | N7A | H6A…N2B           | [2767.02] | 0.909(18) | 2.338(17) | 3.0426(17) | 134.3(14) |
| 11  |      | N7B | H6B…N2A           | [2776.01] | 0.889(18) | 2.323(18) | 3.0323(17) | 136.7(14) |
| 12  |      | N7A | H7A…N8A           | [2867.01] | 0.905(16) | 2.146(16) | 3.0473(17) | 173.5(15) |
| 13  |      | N7B | H7B…N8B           | [2776.02] | 0.913(16) | 2.125(16) | 3.0288(17) | 170.1(15) |
| 14  | INTRA | C14A | H14A…N7A        | [2867.01] | 0.974(15) | 2.597(16) | 3.0149(19) | 106.0(11) |
| 15  | INTRA | C14B | H14B…N7B       | [2867.01] | 0.973(15) | 2.544(15) | 2.9913(19) | 108.1(11) |

Translation of ARU-code to CIF and Equivalent Position Code:

\[
\begin{align*}
1655. & = [1_655] = 1+x, y, z \\
2776. & = [2_776] = 2-x, 2-y, 1-z \\
1455. & = [1_455] = -1+x, y, z \\
2767. & = [2_767] = 2-x, 1-y, 2-z \\
2867. & = [2_867] = 3-x, 1-y, 2-z
\end{align*}
\]

S5.2. Triamterene and acetic acid (1a-DMSO)

![Figure S3 ORTEP diagram drawn at 50% probability for 1a-DMSO.](image-url)
Table S6  Hydrogen bond table for 1a·DMSO.

| No. | Type | Res  | Donor—H···A | [ARU]   | D—H | H···A | D···A | D—H···A |
|-----|------|------|-------------|---------|------|------|------|---------|
| 1   | 1    | N1A  | H1XA···O1E   | [2666.05] | 0.91(2) | 1.82(2) | 2.7257(19) | 175.7(17) |
| 2   | 2    | N1B  | H1XB···O1F   | [1555.06] | 0.89(2) | 1.84(2) | 2.7278(19) | 176.4(17) |
| 3   | 1    | N2A  | H2A···O2E   | [2666.05] | 0.87(2) | 1.87(2) | 2.735(2) | 174(2) |
| 4   | 2    | N2B  | H2B···O2F   | [1555.06] | 0.90(2) | 1.83(2) | 2.715(2) | 169(2) |
| 5   | 1    | N2A  | H3A···O1C   | [2566.03] | 0.84(2) | 2.10(2) | 2.906(2) | 162(2) |
| 6   | 2    | N2B  | H3B···O1D   | [1555.04] | 0.80(3) | 2.28(2) | 3.065(2) | 168(2) |
| 7   | 1    | N4A  | H4A···N3B   | [1455.02] | 0.87(2) | 2.15(2) | 3.017(2) | 172.2(19) |
| 8   | 2    | N4B  | H4B···N3A   | [1655.01] | 0.81(2) | 2.09(2) | 3.009(2) | 177(2) |
| 9   | 1    | N4A  | H5A···N5A   | [2666.03] | 0.85(2) | 2.526(19) | 2.807(2) | 141.9(17) |
| 10  | INTRA | N4A | H5A···N5A   | [2566.05] | 0.86(3) | 2.22(2) | 2.787(2) | 102.9(16) |
| 11  | INTRA | N4B | H5B···N5B   | [1555.04] | 0.86(3) | 2.22(2) | 2.883(2) | 134.4(18) |
| 12  | 2    | N4B  | H5B···O1C   | [2666.03] | 0.86(3) | 2.22(2) | 2.883(2) | 134.4(18) |
| 13  | 1    | N7A  | H6A···O1E   | [1455.05] | 0.83(2) | 2.165(18) | 2.768(2) | 129.3(16) |
| 14  | 2    | N7B  | H6B···O1F   | [2565.06] | 0.82(2) | 2.246(19) | 2.833(2) | 128.7(16) |
| 15  | 1    | N7A  | H7A···N8A   | [2666.01] | 0.91(2) | 2.20(2) | 3.102(2) | 170(2) |
| 16  | 2    | N7B  | H7B···N8B   | [2565.02] | 0.87(2) | 2.23(2) | 3.089(2) | 172(2) |
| 17  | 1    | C10A | H10A···N3A  | [2566.01] | 0.925(19) | 2.579(19) | 3.482(2) | 165.8(15) |
| 18  | 1    | C14A | H14A···O2F  | [1555.06] | 0.94(2) | 2.51(2) | 3.315(2) | 144.4(16) |
| 19  | 2    | C14B | H14B···O2E  | [2666.05] | 0.90(2) | 2.57(2) | 3.372(2) | 150(2) |
| 20  | 1    | C13A | H13A···O2E  | [2656.05] | 0.84(2) | 2.64(2) | 3.347(3) | 142.5(18) |
| 21  | 2    | C13B | H13B···O2F  | [1565.06] | 0.94(2) | 2.61(3) | 3.464(3) | 156.3(19) |

Translation of ARU-code to CIF and Equivalent Position Code:

[2666.] = [2_666] = 1-x, 1-y, 1-z
[2566.] = [2_566] = -x, 1-y, 1-z
[1455.] = [1_455] = -1+x, y, z
[1655.] = [1_655] = 1+x, y, z
[2565.] = [2_565] = -x, 1-y, -z
[2656.] = [2_656] = 1-x, -y, 1-z
[1565.] = [1_565] = x, 1+y, z
S5.3. Triamterene and succinic acid (1b·DMSO)

Figure S4  ORTEP diagram drawn at 50% probability for 1b·DMSO.

Table S7  Hydrogen bond table for 1b·DMSO.

| No. | Type | Res  | Donor--H…A | [ARU]   | D--H   | H…A    | D…A    | D--H…A |
|-----|------|------|-------------|---------|--------|---------|---------|---------|
| 1   |      | N1A  | H1XA…O1B    | [2746.02] | 0.889(15) | 1.866(15) | 2.755(17) | 179.0(17) |
| 2   |      | N2A  | H2A…O2B     | [2746.02] | 0.915(16) | 1.938(16) | 2.843(2)  | 169.4(14)  |
| 3   |      | N2A  | H3A…O1C     | [1656.03] | 0.816(15) | 2.122(15) | 2.924(2)  | 167.7(14)  |
| 4   | INTRA| O3B  | H3B…O2B     | [2746.02] | 1.05(2)  | 1.49(2)  | 2.526(2)  | 169(2)    |
| 5   |      | N4A  | H4A…N8A     | [2756.01] | 0.902(19) | 2.192(19) | 3.088(2)  | 172.1(17)  |
| 6   |      | N4A  | H5A…O1B     | [1555.02] | 0.873(17) | 2.192(15) | 2.810(2)  | 127.5(12)  |
| 7   | INTRA| N4A  | H5A…N5A     | [1555.02] | 0.873(17) | 2.492(14) | 2.807(2)  | 102.1(10)  |
| 8   |      | N7A  | H6A…O1C     | [2645.03] | 0.885(15) | 2.076(14) | 2.777(2)  | 135.5(12)  |
| 9   |      | N7A  | H7A…N3A     | [2746.01] | 0.817(15) | 2.222(15) | 3.031(2)  | 170.5(15)  |
| 10  |      | C1C  | H2C…O4B     | [4555.02] | 0.96(2)  | 2.35(2)  | 3.213(3)  | 150.7(15)  |
| 11  |      | C2C  | H6C…O4B     | [4555.02] | 0.85(2)  | 2.616(19) | 3.385(4)  | 150.5(15)  |

Translation of ARU-code to CIF and Equivalent Position Code:

[2746.] = [2_746] = 2-x, ½+y, 3/2-z
[4555.] = [4_555] = -x, ½-y, ½+z
[1656.] = [1_656] = 1+x, y, 1+z
[2756.] = [2_756] = 2-x, ½+y, 3/2-z
[2645.] = [2_645] = 1-x, -1/2+y, ½-z
S5.4. Triamterene and adipic acid (1c·DMSO)

Figure S5  ORTEP diagram drawn at 50% probability for 1c·DMSO.
Table S8 Hydrogen bond table for 1c·DMSO.

| No. | Type | Res     | Donor--H…A   | [ARU]   | D–H   | H…A  | D…A   | D–H…A|
|-----|------|---------|--------------|---------|-------|------|-------|-------|
| 1   |      | N2A→H2A…O2D | [1555.04]    | 0.88   | 1.90  | 2.772(4) | 173  |
| 2   |      | N2B→H2B…O2C  | [2666.03]    | 0.88   | 1.91  | 2.748(4) | 157  |
| 3   |      | N2A→H3A…O1E  | [1555.05]    | 0.88   | 2.18  | 3.048(5) | 168  |
| 4   |      | N2B→H3B…O1F  | [1555.06]    | 0.88   | 2.18  | 3.040(8) | 167  |
| 5   |      | N4A→H4A…N3B  | [2566.02]    | 0.88   | 2.13  | 2.996(5) | 167  |
| 6   |      | N4B→H4B…N3A  | [2566.01]    | 0.88   | 2.15  | 3.021(5) | 169  |
| 7   | INTRA| N4A→H5A…N5A  | [1555.05]    | 0.88   | 2.46  | 2.788(5) | 102  |
| 8   | INTRA| N4A→H5A…O1F  | [2566.06]    | 0.88   | 2.08  | 2.808(7) | 140° |
| 9   |      | N4B→H5B…N5B  | [1555.03]    | 0.88   | 2.45  | 2.773(5) | 103  |
| 10  |      | N4B→H5B…O1E  | [2566.05]    | 0.88   | 2.21  | 2.889(5) | 133° |
| 11  |      | N7A→H6A…O1D  | [2655.04]    | 0.84(4)| 2.21(4)| 2.832(5) | 131(4)|
| 12  |      | N7B→H6B…O1C  | [1555.03]    | 0.84(4)| 2.33(4)| 2.911(5) | 128(4)|
| 13  |      | N1A→H1XA…O1D | [1555.04]    | 0.83(5)| 1.85(5)| 2.681(5) | 178(4)|
| 14  |      | N7A→H7A…N8A  | [2655.01]    | 0.82(5)| 2.27(5)| 3.073(5) | 169(5)|
| 15  |      | N7B→H7B…N8B  | [2666.02]    | 0.87(6)| 2.24(6)| 3.101(5) | 170(5)|
| 16  |      | N1B→H1XB…O1C | [2666.03]    | 0.93(6)| 1.77(6)| 2.687(5) | 170(5)|
| 17  | 6>   | C1F→H1F…O2C  | [2666.03]    | 0.98   | 2.53  | 3.500(9) | 170  |
| 18  | 6>   | C1F→H2F…O1D  | [1566.04]    | 0.98   | 2.51  | 3.489(8) | 175  |
| 19  |      | C1E→H3E…O1C  | [2666.03]    | 0.98   | 2.56  | 3.319(5) | 135  |
| 20  |      | C10A→H10A…N3A| [2555.01]    | 0.95   | 2.50  | 3.444(5) | 172  |
| 21  |      | C11B→H11B…S1F| [2566.06]    | 0.95   | 2.82  | 3.641(5) | 146  |
| 22  |      | C13A→H13A…O2D| [1545.04]    | 0.95   | 2.55  | 3.293(5) | 135  |

Translation of ARU-code to CIF and Equivalent Position Code:

- [2566.] = [2_566] = -x, 1-y, 1-z
- [2555.] = [2_555] = -x, -y, 1-z
- [2655.] = [2_655] = 1-x, -y, -z
- [1545.] = [1_545] = -x, -1+y, z
- [2666.] = [2_666] = 1-x, 1-y, 1-z
- [1566.] = [1_566] = x, 1+y, 1+z
- [2566.] = [2_566] = -x, 1-y, 1-z
- [2666.] = [2_666] = 1-x, 1-y, 1-z
- [2556.] = [2_556] = -x, -y, 1-z
- [1556.] = [1_556] = x, y, 1+z
S5.5. Triamterene and pimelic acid (1d-DMSO)

Figure S6  *ORTEP* diagram drawn at 50% probability for 1d-DMSO.
### Table S9

Hydrogen bond table for 1d·DMSO.

| No. | Type | Res           | Donor--H...A | [ARU]   | D--H | H...A  | D...A  | D--H...A |
|-----|------|---------------|--------------|---------|------|-------|-------|--------|
| 1   |      | N1A—H1XA...O1E | [1555.05]    | 0.88    | 1.87 | 2.729(7) | 166   |
| 2   |      | N1B—H1XB...O4F | [1565.06]    | 0.88    | 1.84 | 2.707(6) | 170   |
| 3   |      | N2A—H2A...O2E | [1555.05]    | 0.88    | 1.80 | 2.654(7) | 162   |
| 4   |      | N2B—H2B...O3F | [1565.06]    | 0.88    | 1.91 | 2.743(6) | 158   |
| 5   |      | N2C—H2C...O2F | [1555.06]    | 0.88    | 1.79 | 2.657(7) | 167   |
| 6   |      | N2D—H2D...O4E | [1555.05]    | 0.88    | 1.83 | 2.674(6) | 160   |
| 7   |      | N1C—H1XC...O1F | [1555.06]    | 0.88    | 1.90 | 2.770(7) | 168   |
| 8   |      | N2A—H3A...O1G | [1555.07]    | 0.88    | 2.12 | 2.964(6) | 161   |
| 9   |      | N2B—H3B...O1J | [2566.10]    | 0.88    | 2.07 | 2.907(7) | 159   |
| 10  |      | N2C—H3C...O1H | [1566.08]    | 0.88    | 2.11 | 2.966(6) | 163   |
| 11  |      | N2D—H3D...S11 | [1565.09]    | 0.88    | 2.72 | 3.360(6) | 131   |
| 12  |      | N2D—H3D...O1I | [1565.09]    | 0.88    | 2.05 | 2.881(7) | 156   |
| 13  |      | N1D—H1XD...O3E | [1555.05]    | 0.88    | 1.91 | 2.757(7) | 162   |
| 14  |      | N4A—H4A...N8B | [1555.02]    | 0.88    | 2.17 | 3.047(6) | 176   |
| 15  |      | N4B—H4B...N8A | [1545.01]    | 0.88    | 2.21 | 3.075(7) | 170   |
| 16  |      | N4C—H4C...N8D | [1546.04]    | 0.88    | 2.20 | 3.069(6) | 170   |
| 17  |      | N4D—H4D...N8C | [1574.03]    | 0.88    | 2.24 | 3.118(7) | 176   |
| 18  |      | N4A—H5A...O4F | [1565.06]    | 0.88    | 2.10 | 2.704(7) | 125   |
| 19  |      | INTRA-1 | N4A—H5A...N5A | [ ] | 0.88 | 2.45 | 2.778(6) | 103   |
| 20  |      | INTRA-1 | N4B—H5B...O1E | [1545.05] | 0.88 | 2.13 | 2.739(7) | 126   |
| 21  |      | INTRA-1 | N4B—H5B...N5B | [ ] | 0.88 | 2.52 | 2.827(7) | 101   |
| 22  |      | INTRA-1 | N4C—H5C...O3E | [1546.05] | 0.88 | 2.11 | 2.712(7) | 125   |
| 23  |      | INTRA-1 | N4C—H5C...N5C | [ ] | 0.88 | 2.49 | 2.804(6) | 102   |
| 24  |      | INTRA-1 | N4D—H5D...O1F | [1574.06] | 0.88 | 2.15 | 2.748(7) | 125   |
| 25  |      | INTRA-1 | N4D—H5D...N5D | [ ] | 0.88 | 2.50 | 2.817(7) | 102   |
| 26  |      | N7A—H6A...O1J | [2576.10]    | 0.88    | 2.38 | 3.036(7) | 132   |
| 27  |      | N7B—H6B...O1G | [1555.07]    | 0.88    | 2.19 | 2.889(7) | 136   |
| 28  |      | N7C—H6C...O1J | [1546.09]    | 0.88    | 2.31 | 2.990(7) | 134   |
| 29  |      | N7D—H6D...O1H | [1565.08]    | 0.88    | 2.09 | 2.807(7) | 138   |
| 30  |      | N7A—H7A...N3B | [1565.02]    | 0.88    | 2.17 | 3.048(7) | 173   |
| 31  |      | N7B—H7B...N3A | [1555.01]    | 0.88    | 2.10 | 2.977(6) | 175   |
| 32  |      | N7C—H7C...N3D | [1536.04]    | 0.88    | 2.16 | 3.038(7) | 174   |
| 33  |      | N7D—H7D...N3C | [1564.03]    | 0.88    | 2.09 | 2.965(6) | 172   |
| 34  |      | C2H—H1H...O1H | [2455.08]    | 0.98    | 2.45 | 3.414(9) | 167   |
| 35  |      | C11—H11...O2F | [2556.06]    | 0.98    | 2.47 | 3.185(9) | 130   |
| 36  |      | C1J—H3J...O3F | [2556.06]    | 0.98    | 2.46 | 3.185(8) | 130   |
| 37  |      | C2G—H4G...O1G | [2566.07]    | 0.98    | 2.48 | 3.453(9) | 171   |
| 38  |      | C2J—H5J...N5C | [1664.03]    | 0.98    | 2.61 | 3.493(9) | 150   |
| 39  |      | C2I—H6I...O4E | [1454.05]    | 0.98    | 2.26 | 3.227(9) | 168   |
| 40  |      | C2J—H6J...O2E | [1655.05]    | 0.98    | 2.56 | 3.037(9) | 113   |
| 41  |      | C10D—H10D...O4E | [2575.05] | 0.95 | 2.53 | 3.451(8) | 164   |
| 42  |      | C12B—H12B...O11 | [1555.09] | 0.95 | 2.53 | 3.417(9) | 155   |
| 43  |      | C12C—H12C...O4F | [2547.06] | 0.95 | 2.58 | 3.489(9) | 161   |
Translation of ARU-code to CIF and Equivalent Position Code:

\[ [1565.] = [1_565] = x, 1+y, z \]
\[ [2576.] = [2_576] = -x, 2-y, 1-z \]
\[ [2566.] = [2_566] = -x, 1-y, 1-z \]
\[ [1545.] = [1_545] = x, -1+y, z \]
\[ [1556.] = [1_556] = -x, y, 1+z \]
\[ [1546.] = [1_546] = x, -1+y, 1+z \]
\[ [1536.] = [1_536] = x, -2+y, 1+z \]
\[ [2547.] = [2_547] = -x, -1-y, 2-z \]
\[ [1574.] = [1_574] = x, 2+y, -1+z \]
\[ [1564.] = [1_564] = x, 1+y, -1+z \]
\[ [2575.] = [2_575] = -x, 2-y, -z \]
\[ [2455.] = [2_455] = -1-x, -y, -z \]
\[ [2556.] = [2_556] = -x, -y, 1-z \]
\[ [1664.] = [1_664] = 1+x, 1+y, -1+z \]
\[ [1655.] = [1_655] = 1+x, y, z \]

**S5.6. Triamterene and azelaic acid (1e·DMSO)**

![Diagram](image)

**Figure S7**  *ORTEP* diagram drawn at 50% probability for 1e·DMSO.
### Table S10  Hydrogen bond table for 1e·DMSO.

| No. | Type | Res   | Donor--H…A | [ARU]     | D--H  | H…A     | D…A     | D--H…A  |
|-----|------|-------|-------------|-----------|-------|---------|---------|---------|
| 1   | 1    | N1A   | H1XA…O3C    | [4464.03] | 0.90(4)| 1.82(4) | 2.713(3)| 178(4)  |
| 2   | 2    | N1B   | H1XB…O1C    | [1555.03] | 0.82(3)| 1.89(3) | 2.710(3)| 174(4)  |
| 3   | 1    | N2A   | H2A…O4C    | [4464.03] | 0.87(4)| 1.78(4) | 2.650(5)| 175(3)  |
| 4   | 2    | N2B   | H2B…O2C    | [1555.03] | 0.90(4)| 1.80(4) | 2.696(4)| 175(4)  |
| 5   | 1    | N2A   | H3A…O1E    | [4464.05] | 0.79(4)| 2.17(4) | 2.906(4)| 156(4)  |
| 6   | 2    | N2B   | H3B…O1D    | [1555.04] | 0.85(3)| 2.06(3) | 2.879(4)| 161(3)  |
| 7   | 1    | N4A   | H4A…N8B    | [1555.02] | 0.85(3)| 2.29(3) | 3.128(4)| 166(2)  |
| 8   | 2    | N4B   | H4B…N8A    | [1655.01] | 0.97(4)| 2.19(4) | 3.145(4)| 170(3)  |
| 9   | 1    | N4A   | H5A…O1C    | [1555.03] | 0.81(3)| 2.41(3) | 2.893(3)| 119(3)  |
| 10  | INTRA| N4A   | H5A…N5A    | [ ]       | 0.81(3)| 2.44(3) | 2.784(4)| 107(3)  |
| 11  | 2    | N4B   | H5B…O3C    | [4564.03] | 0.87(4)| 2.18(4) | 2.788(3)| 126(4)  |
| 12  | 1    | N7A   | H6A…O1D    | [1455.04] | 0.90(3)| 2.24(3) | 2.953(4)| 136(3)  |
| 13  | 2    | N7B   | H6B…O1E    | [4464.05] | 0.86(4)| 2.12(3) | 2.869(4)| 146(3)  |
| 14  | 1    | N7A   | H7A…N3B    | [1455.02] | 0.79(4)| 2.24(4)| 3.020(4)| 175(3)  |
| 15  | 2    | N7B   | H7B…N3A    | [1555.01] | 0.88(3)| 2.10(3) | 2.973(4)| 172(3)  |
| 16  | INTRA| 3     | C3C—H4C…O2C | [ ]       | 1.02(3)| 2.53(3) | 2.895(5)| 100(4)  |
| 17  | 4    | C2D   | H4D…O2C    | [1555.03] | 1.04(3)| 2.36(3) | 3.360(5)| 163(3)  |
| 18  | 5    | C2E   | H6E…O2C    | [1555.03] | 1.11(6)| 2.38(5) | 3.461(7)| 167(4)  |
| 19  | INTRA| 3     | C6C—H10C…O4C | [ ]       | 1.07(4)| 2.24(4)| 3.031(6)| 129(3)  |
| 20  | 1    | C14A  | H14A…O4C   | [2545.03] | 1.01(3)| 2.52(3)| 3.470(5)| 157(2)  |

Translation of ARU-code to CIF and Equivalent Position Code:

[4464.] = [4_464] = -1/2+x, 3/2-y, -1/2+z
[1455.] = [1_455] = -1+x, y, z
[1655.] = [1_655] = 1+x, y, z
[4564.] = [4_564] = ½+x, 3/2-y, -1/2+z
S5.7. Triamterene and nicotinic acid (1f·DMSO)

Figure S8  ORTEP diagram drawn at 50% probability for 1f·DMSO
Table S11  Hydrogen bond table for 1f·DMSO

| No. | Type | Res   | Donor—H…A | [ARU]    | D—H  | H…A    | D…A    | D—H…A |
|-----|------|-------|------------|----------|------|--------|--------|--------|
| 1   | 1    | N1A—H1XA…O1C | [4564.03] | 0.96(2)  | 1.72(2) | 2.6638(19) | 171.8(19) |
| 2   | 1    | N2A—H2A…O2C | [4564.03] | 0.91(2)  | 1.88(2)  | 2.788(2) | 178(2) |
| 3   | 2    | N2B—H2B…N1C | [3666.03] | 0.92(2)  | 2.17(2)  | 3.079(2) | 169.8(19) |
| 4   | 1    | N2A—H3A…O1E | [4464.05] | 0.834(18) | 2.039(18) | 2.863(2) | 169.7(16) |
| 5   | 2    | N2B—H3B…O1D | [1565.04] | 0.90(2)  | 2.193(19) | 3.071(2) | 164.1(17) |
| 6   | 1    | N4A—H4A…N8B | [4464.02] | 0.91(2)  | 2.05(2)  | 2.954(2) | 171.4(17) |
| 7   | 2    | N4B—H4B…N8A | [4465.01] | 0.92(2)  | 2.20(2)  | 3.106(2) | 168.8(17) |
| 8   | INTRA | N4A—H5A…N5A | [ ]       | 0.83(2)  | 2.447(19) | 2.775(2) | 104.5(15) |
| 9   | 2    | N4B—H5B…O1C | [1555.03] | 0.880(18) | 2.234(18) | 2.831(2) | 124.9(14) |
| 10  | INTRA | N4B—H5B…N5B | [ ]       | 0.880(18) | 2.453(17) | 2.790(2) | 103.3(13)' |
| 11  | 1    | N7A—H6A…O1D | [4554.04] | 0.890(19) | 2.187(18) | 2.885(2) | 134.9(15) |
| 12  | 2    | N7B—H6B…O1E | [1555.05] | 0.796(18) | 2.202(18) | 2.836(2) | 136.9(16) |
| 13  | 1    | N7A—H7A…N3B | [4564.02] | 0.88(2)  | 2.30(2)  | 3.170(2) | 171.7(19) |
| 14  | 2    | N7B—H7B…N3A | [4565.01] | 0.85(2)  | 2.13(2)  | 2.984(2) | 174.2(19) |
| 15  | 5    | C1E—H1E…O1D | [3656.04] | 0.92(2)  | 2.59(2)  | 3.412(3) | 149.0(19) |
| 16  | INTRA | C3C—H3C…O2C | [ ]       | 0.952(17) | 2.490(17) | 2.815(2) | 100.0(12) |
| 17  | 2    | C14B—H14B…O1D | [3656.04] | 0.984(17) | 2.536(2) | 3.353(2) | 140.4(13) |
| 18  | 4    | C2D—H4D…O2C | [4555.03] | 0.95(3)  | 2.60(3)  | 3.421(3) | 145(2) |

Translation of ARU-code to CIF and Equivalent Position Code:

[4564.] = [4_564] = -1/2+x, 3/2-y, -½+z
[4464.] = [4_464] = -1/2+x, 3/2-y, -1/2+z
[4554.] = [4_554] = ½+x, ½-y, -1/2+z
[1565.] = [1_565] = x, 1+y, z
[3666.] = [3_666] = 1-x, 1-y, 1-z
[4465.] = [4_465] = -1/2+x, 3/2-y, ½+z
[4555.] = [4_555] = 1/2+x, 1/2-y, 1/2+z
S5.8. Triamterene and Ibuprofen (1g·DMSO)

Figure S9  
**ORTEP** diagram drawn at 50% probability for 1g-DMSO.
Table S12  Hydrogen bond table for 1g·DMSO.

| No. | Type | Res      | Donor-H…A | [ARU]     | D–H  | H…A  | D…A  | D–H…A |
|-----|------|----------|------------|-----------|------|------|------|--------|
| 1   | 1    | N2A–H2A…N1B | [2666.02]  | 0.85(3)   | 2.02(3) | 2.857(3) | 166(3) |
| 2   | 2    | N2B–H2B…?   | [ ]        | 0.80(4)   |        |      |      |        |
| 3   | 1    | N2A–H3A…O2C | [1555.03]  | 0.90(4)   | 1.89(4) | 2.774(4) | 165(3) |
| 4   | 1    | N4A–H4A…N3A | [2665.01]  | 0.88(4)   | 2.14(4) | 3.06(3)  | 169(3) |
| 5   | 2    | N4B–H4B…N3B | [2766.02]  | 0.87(4)   | 2.14(4) | 3.06(3)  | 173(3) |
| 6   | INTRA | N4A–H5A…N5A | [ ]      | 0.91(4)   | 2.50(4) | 2.797(4) | 100(2) |
| 7   | 1    | N4A–H5A…O2C | [2665.03]  | 0.91(4)   | 2.27(4) | 2.956(4) | 133(3) |
| 8   | INTRA | N4B–H5B…N5B | [ ]      | 0.88(4)   | 2.49(3) | 2.792(4) | 101(2) |
| 9   | 2    | N4B–H5B…O1D | [2766.04]  | 0.88(4)   | 2.22(3) | 2.927(9) | 137(3) |
| 10  | 2    | N7B–H6B…O1C | [1656.03]  | 0.83(3)   | 2.15(3) | 2.817(4) | 136(3) |
| 11  | 1    | N1A–H1XA…N8B | [2666.02]  | 0.86(3)   | 2.10(3) | 2.960(3) | 175(3) |
| 12  | 1    | N7A–H7A…O1C | [2565.03]  | 0.92(4)   | 1.88(4) | 2.793(4) | 171(4) |
| 13  | 2    | N7B–H7B…N8A | [2666.01]  | 0.87(3)   | 2.14(3) | 3.00(3)  | 170(4) |
| 14  | 3    | C6C–H6C…O1D | [2666.04]  | 0.95      | 2.47    | 3.238(7) | 138   |
| 15  | 4>   | C2D–H6D…O2C | [1555.03]  | 0.98      | 2.33    | 3.266(7) | 159   |

Translation of ARU-code to CIF and Equivalent Position Code:

[2666.] = [2_666] = 1-x, 1-y, 1-z
[2665.] = [2_665] = 1-x, 1-y, -z
[2565.] = [2_565] = -x, 1-y, -z
[2766.] = [2_766] = 2-x, 1-y, 1-z
[1656.] = [1_656] = 1+x, y, 1+z
S6. Experimental (LAG) and simulated PXRD patterns for 1a – g·DMSO

![Experimental and simulated PXRD patterns for 1a·DMSO](image)

**Figure S10** Comparison of the PXRD pattern for adduct 1a·DMSO obtained from (a) LAG with (b) simulated from X-ray structure.

![Experimental and simulated PXRD patterns for 1b·DMSO](image)

**Figure S11** Comparison of the PXRD pattern for the adduct 1b·DMSO obtained from (a) LAG with (b) simulated from X-ray structure.
Figure S12 Comparison of the PXRD pattern for the adduct 1c·DMSO obtained from (a) LAG with (b) simulated from X-ray structure.

Figure S13 Comparison of the PXRD pattern for the adduct 1d·DMSO obtained from (a) LAG with (b) simulated from X-ray structure.

Figure S14 Comparison of the PXRD pattern for the adduct 1e·DMSO obtained from (a) LAG with (b) simulated from X-ray structure.
**Figure S15** Comparison of the PXRD pattern for the adduct 1f·DMSO obtained from (a) LAG with (b) simulated from X-ray structure.

**Figure S16** Comparison of the PXRD pattern for the adduct 1g·DMSO obtained from (a) LAG with (b) simulated from X-ray structure.

**Summary**

These results show that the crystals grown for single crystal analysis were representative of the bulk samples 1a–g·DMSO. The differences between the experimental and simulated PXRD pattern for 1d·DMSO are thought to be due to the preferred orientation of the plate-like crystals noted in this sample.
S7. DSC and TGA of the crystalline product for 1 and 1a–g·DMSO

**Figure S17** The DSC trace for triamterene (1) showing the sharp melting peak at 327.84°C (for reference).

**Figure S18** TGA (a) and DSC (b) trace for 1a·DMSO showing an initial weight loss of 33.58% in the TGA corresponding to the concomitant weight loss of a (acetic acid) and DMSO as calculated (35.07%) from a stoichiometry of 1 : 1 : 1 (I : a : DMSO). The melting point peak of 328.27°C in the DSC corresponds to pure 1.
**Figure S19** TGA (a) and DSC (b) trace for the adduct 1b·DMSO. The TGA trace shows an initial weight loss which is likely due to physically absorbed solvent while second weight loss of 16.82%, related to weight of DMSO as calculated (17.38%) from a stoichiometry of 1 : 1 : 1 (1 : b : DMSO). This is associated with the third endothermic event in the DSC with corresponding enthalpy change of 48.23 J g\(^{-1}\) with an onset temperature of 174.83°C. After removal of solvent the product melts at 255.14°C.

**Figure S20** TGA (a) and DSC (b) trace for the adduct 1c·DMSO. The TGA trace shows an initial weight loss of 17.78%, corresponding to calculated weight loss of DMSO (19.31%) from 1 : c : DMSO (2 :1 : 2 stoichiometry). The DSC trace shows the melting point peak of the product (with solvent removed) at 250.12°C.
Figure S21  TGA (a) and DSC (b) trace for the adduct 1d·DMSO. The TGA trace shows an initial weight loss of 18.20 %, corresponding to calculated weight loss of DMSO (18.98 %) from 1 : d : DMSO (2 : 1 : 2 stoichiometry). The DSC trace shows the melting point peak of the desolvated product at 253.44°C.

Figure S22  TGA (a) and DSC (b) trace for the adduct 1e·DMSO. The TGA trace shows an initial weight loss of 16.93 %, corresponding to calculated weight loss of DMSO (18.36 %) from 1 : e : DMSO (2 : 1 : 2) stoichiometry. The DSC trace shows the melting point peak of the desolvated product at 269.54°C.
Figure S23  TGA (a) and DSC (b) trace for the adduct 1f·DMSO. The experimental weight loss for the DMSO is found to be 16%, which is slightly less than expected (19.88%) calculated from a stoichiometry of 1 : f : DMSO (2 : 1 : 2), possibly due to some solvent loss to the atmosphere prior to performing the thermal analysis. This weight loss is associated with an endothermic event in the DSC with an onset temperature of 137.4 °C. After the removal of DMSO, the TGA trace shows a further weight loss of 15 %, in good agreement with the weight of nicotinic acid (15.7 %) present in the adduct 1f·DMSO (2 : 1 : 2). After the removal of DMSO and nicotinic acid only triamterene is left, which has a melting point peak at 307.19°C.

Figure S24  TGA (a) and DSC (b) trace for the adduct 1g·DMSO. The experimental weight loss of 33.75 % in the TGA trace corresponds to the concomitant weight loss of DMSO and ibuprofen (35.95 %) calculated from a stoichiometry of 2 : 1 : 1 for 1g·DMSO. The first endotherm in the DSC scan with an onset temperature of 171.0°C is related with DMSO loss and second broad endothermic event indicates the degradation and/or removal of ibuprofen. After the removal of DMSO and ibuprofen triamterene is left which gives a melting point peak at 326.7°C.
Table S13  Summary of data obtained from DSC/TGA curves

| Triamterene or Adduct | Melting (or boiling where relevant) point of coformer from the literature (°C) | Melting point onset of first endotherm (°C) | Calculated weight loss (%) | Experiment al weight loss (%) | Melting point onset of final product (°C) |
|-----------------------|--------------------------------------------------------------------------------|-------------------------------------------|----------------------------|----------------------------|------------------------------------------|
| 1                     | N/A                                                                             | N/A                                      | N/A                        | N/A                        | 327.31                                   |
| 1a·DMSO               | 16.2 (117–118)                                                                  | 141.85                                   | 35.07                      | 33.58                      | 326.61                                   |
| 1b·DMSO               | 184–186                                                                         | 174.83                                   | 17.38                      | 16.82                      | 251.85                                   |
| 1c·DMSO               | 151–154                                                                         | 154.69                                   | 19.32                      | 17.78                      | 245.76                                   |
| 1d·DMSO               | 103–105                                                                         | 138.03                                   | 18.99                      | 18.20                      | 248.75                                   |
| 1e·DMSO               | 109–111                                                                         | 129.65                                   | 18.36                      | 16.93                      | 266.49                                   |
| 1f·DMSO               | 236–239                                                                         | 140.70                                   | 19.88(1)                   | 15.96(1)                   | 303.19                                   |
| 1g·DMSO               | 77–78                                                                           | 171.00                                   | 35.80                      | 33.75                      | 323.90                                   |
| Triamterene or Adduct | Calculation of stoichiometry using TGA data (Triamterene : Coformer : Solvent) |
|-----------------------|------------------------------------------------------------------------------|
| 1                     | 1 : 0 : 0                                                                      |
| 1a·DMSO               | 1 : 1 : 1                                                                      |
| 1b·DMSO               | 1 : 1 : 1                                                                      |
| 1c·DMSO               | 2 : 1 : 2                                                                      |
| 1d·DMSO               | 2 : 1 : 2                                                                      |
| 1e·DMSO               | 2 : 1 : 2                                                                      |
| 1f·DMSO               | 2 : 1 : 2                                                                      |
| 1g·DMSO               | 2 : 1 : 1                                                                      |
S8. Summary of stoichiometry derived from SCXRD and thermal data

Table S15  Conformation of stoichiometry from SCXRD and thermal methods

| Crystallization experiment | Product designation | Stoichiometry by SCXRD (Triamterene : Coformer : Solvent) | Confirmation of stoichiometry using Thermal data (Triamterene : Coformer : Solvent) |
|---------------------------|---------------------|----------------------------------------------------------|--------------------------------------------------------------------------------|
| Triamterene               | 1                   | 1 : 0 : 0                                                 | 1 : 0 : 0                                                                        |
| Triamterene, acetic acid  | 1a·DMSO             | 1 : 1 : 1                                                 | 1 : 1 : 1                                                                        |
| and DMSO                  |                     |                                                          |                                                                                  |
| Triamterene, succinic     | 1b·DMSO             | 1 : 1 : 1                                                 | 1 : 1 : 1                                                                        |
| acid and DMSO             |                     |                                                          |                                                                                  |
| Triamterene, adipic acid  | 1c·DMSO             | 2 : 1 : 2                                                 | 2 : 1 : 2                                                                        |
| and DMSO                  |                     |                                                          |                                                                                  |
| Triamterene, pimelic acid| 1d·DMSO             | 2 : 1 : 2                                                 | 2 : 1 : 2                                                                        |
| and DMSO                  |                     |                                                          |                                                                                  |
| Triamterene, azelaic acid| 1e·DMSO             | 2 : 1 : 2                                                 | 2 : 1 : 2                                                                        |
| and DMSO                  |                     |                                                          |                                                                                  |
| Triamterene, nicotinic    | 1f·DMSO             | 2 : 1 : 2                                                 | 2 : 1 : 2                                                                        |
| acid and DMSO             |                     |                                                          |                                                                                  |
| Triamterene, ibuprofen    | 1g·DMSO             | 2 : 1 : 1                                                 | 2 : 1 : 1                                                                        |
| and DMSO                  |                     |                                                          |                                                                                  |

S9. References

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