Microbatch under-oil salt screening of organic cations: single-crystal growth of active pharmaceutical ingredients

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S1. General methods

a) 100 µL of silicone oil

5 µL of 90% saturated analyte solution and 5 µL of counter-ion solution
(used volumes can be varied)

b) slow evaporation of water through the silicone oil

$ t_1 = 0 \text{ hour} $, $ t_1 > 0 \text{ hour} $

c) crystallization occurs in the drop

$ t_2 > t_1 $, $ t_2 > t_1 $

Figure S1 Principle of the microbatch under oil crystallization technique
Figure S2 Example of the mixture of NaCl (in the middle) and amorphous residuum (around NaCl)

Table S1 List of originally used anion sources and their respective salt concentrations (147 conditions)

| Salts                          | Molarity | Salts                          | Molarity |
|--------------------------------|----------|--------------------------------|----------|
| Sodium bromide                 | 4.082    | Sodium D-mandelate              | 0.251    |
| Sodium bromide                 | 2.000    | Sodium D-mandelate              | 0.100    |
| Sodium iodide                  | 5.337    | Sodium L-mandelate              | 0.251    |
| Sodium iodide                  | 3.000    | Disodium succinate              | 0.391    |
| Sodium tetrafluoroborate       | 4.076    | Disodium succinate              | 0.200    |
| Sodium tetrafluoroborate       | 2.000    | Sodium DL-aspartate             | 0.250    |
| Sodium methanesulfonate        | 3.651    | Sodium DL-aspartate             | 0.100    |
| Sodium methanesulfonate        | 1.700    | Sodium L-aspartate              | 0.244    |
| Sodium triflate                | 0.819    | Sodium L-aspartate              | 0.100    |
| Sodium triflate                | 0.400    | Disodium DL-tartrate            | 0.282    |
| Potassium hexafluorophosphate  | 0.244    | Disodium DL-tartrate            | 0.150    |
| Potassium hexafluorophosphate  | 0.100    | Disodium (+)-O,O'-dibenzoyl-D-tartrate | 0.022 |
| Sodium 3-nitrobenzensulfonate  | 0.423    | Sodium N-acetylglycinate        | 0.178    |
| Sodium 3-nitrobenzensulfonate  | 0.200    | Sodium N-acetylglycinate        | 0.100    |
| Potassium thiocyanate          | 7.341    | Disodium maleate                | 0.126    |
| Compound                              | Quantity | Compound                              | Quantity |
|---------------------------------------|----------|---------------------------------------|----------|
| Potassium thiocyanate                 | 3.500    | Sodium pyrrolidone carboxylate         | 0.531    |
| Sodium nitrate                        | 4.605    | Sodium pyrrolidone carboxylate         | 0.250    |
| Sodium nitrate                        | 2.000    | Disodium N-acetylglutamate             | 0.572    |
| Sodium benzoate                       | 1.817    | Disodium N-acetylglutamate             | 0.250    |
| Sodium benzoate                       | 0.800    | Disodium DL-malate                     | 1.051    |
| Potassium phthalate monobasic         | 0.271    | Disodium DL-malate                     | 0.500    |
| Potassium phthalate monobasic         | 0.150    | Sodium p-toluenesulfonate              | 0.153    |
| Sodium formate                        | 6.002    | Sodium camphorsulfonate                | 0.291    |
| Sodium formate                        | 3.000    | Sodium camphorsulfonate                | 0.150    |
| Sodium acetate                        | 2.577    | Trisodium citrate                      | 0.050    |
| Sodium acetate                        | 1.200    | Trisodium citrate                      | 0.025    |
| Sodium trifluoroacetate               | 2.401    | Disodium pamoate                       | 0.124    |
| Sodium trifluoroacetate               | 1.000    | Disodium pamoate                       | 0.050    |
| Sodium iodoacetate                    | 0.244    | Disodium fumarate                      | 0.688    |
| Sodium hippurate                      | 0.244    | Disodium fumarate                      | 0.350    |
| Sodium potassium L-tartrate           | 1.050    | Sodium propionate                      | 3.984    |
| Sodium potassium L-tartrate           | 0.500    | Sodium propionate                      | 2.000    |
| Potassium antimony tartrate           | 0.041    | Potassium D-saccharate                 | 0.045    |
| Sodium diethyldithiocarbamate          | 0.011    | Potassium D-saccharate                 | 0.020    |
| Disodium malonate                     | 0.488    | Sodium valerate                        | 0.097    |
| Disodium malonate                     | 0.250    | Sodium valerate                        | 0.050    |
| Sodium pyruvate                       | 2.980    | Disodium hydrogen phosphate            | 0.428    |
| Sodium pyruvate                       | 1.500    | Disodium hydrogen phosphate            | 0.200    |
| Sodium salicylate                     | 2.227    | Sodium dihydrogen phosphate            | 3.399    |
| Sodium salicylate                     | 1.000    | Sodium dihydrogen phosphate            | 1.700    |
| Sodium 2-ethylhexanoate               | 2.111    | Sodium chloride                        | 2.942    |
| Sodium 2-ethylhexanoate               | 1.000    | Sodium chloride                        | 1.500    |
| Sodium L-glutamate                    | 1.986    | Sodium isethionate                     | 1.908    |
| Sodium L-glutamate                    | 0.900    | Sodium isethionate                     | 1.000    |
Sodium sulphate & 0.955 & Disodium oxalate & 0.138 \\
Sodium sulphate & 0.500 & Disodium oxalate & 0.075 \\
Sodium tetrphenylborate & 0.409 & Sodium hydrogen carbonate & 0.564 \\
Sodium tetrphenylborate & 0.200 & Sodium hydrogen carbonate & 0.300 \\
Sodium dodecylsulfate & 0.007 & Sodium benzenesulfonate & 0.130 \\
Sodium diclofenac & 0.002 & Sodium benzenesulfonate & 0.075 \\
Potassium gluconate & 1.095 & Sodium hexanoate & 1.955 \\
Potassium gluconate & 0.500 & Sodium hexanoate & 1.000 \\
Sodium saccharine & 0.238 & Disodium carbonate & 1.014 \\
Sodium 1-naphthalenacetate & 0.428 & Disodium carbonate & 0.500 \\
Sodium 1-naphthalenacetate & 0.200 & Sodium 4-aminosalicylate & 1.488 \\
Sodium 1-naphthalensulfonate & 0.346 & Sodium 4-aminosalicylate & 0.750 \\
Sodium 1-naphthalensulfonate & 0.150 & Sodium propionate & 1.000 \\
Sodium 2-naphthalensulfonate & 0.127 & Sodium propionate & 0.500 \\
Disodium 2, 6-naphthalenedisulfonate & 0.084 & Sodium dihydrogen phosphate & 0.850 \\
Sodium DL-lactate & 1.450 & Sodium chloride & 0.750 \\
Sodium DL-lactate & 0.600 & Sodium isethionate & 0.500 \\
Sodium L-lactate & 1.450 & Sodium hexanoate & 0.500 \\
Sodium L-lactate & 0.600 & Disodium carbonate & 0.250 \\
Sodium diphenylacetate & 0.329 & Sodium 4-aminosalicylate & 0.375 \\
Sodium diphenylacetate & 0.100 & Sodium adipate & 0.630 \\
Disodium isophthalate & 0.061 & Sodium L-malate & 1.710 \\
Disodium terephthalate & 0.060 & Sodium dicyanamide & 0.700 \\
Sodium meta-hydroxybenzoate & 1.315 & Sodium nicotinate & 2.288 \\
Sodium meta-hydroxybenzoate & 0.600 & Sodium nicotinate & 1.125 \\
Sodium DL-mandelate & 0.251 & Sodium octanoate & 0.900 \\
Sodium DL-mandelate & 0.100 & Disodium 1,5-Naphthalenedisulfonate & 0.180 \\
Potassium sorbate & 2.079 & Sodium cinnamate & 0.180 \\
Sodium cholate & 0.933 & Disodium glutarate & 0.965
Table S2  List of selected anion sources and their respective salt concentrations (97 conditions)

| Salts                        | Molarity | Salts                        | Molarity |
|------------------------------|----------|------------------------------|----------|
| Sodium fluoride              | 0.50     | Sodium DL-lactate            | 3.42     |
| Sodium chloride              | 3.00     | Sodium L-lactate             | 3.42     |
| Sodium chloride              | 1.50     | Sodium diphenylacetate       | 0.33     |
| Sodium bromide               | 4.00     | Disodium isophthalate        | 1.40     |
| Sodium bromide               | 2.00     | Disodium terephthalate       | 0.060    |
| Sodium iodide                | 5.30     | Sodium meta-hydroxybenzoate  | 2.90     |
| Sodium iodide                | 2.50     | Sodium DL-mandelate          | 0.25     |
| Sodium iodide                | 1.25     | Sodium D-mandelate           | 0.25     |
| Sodium tetrafluoroborate     | 4.00     | Sodium L-mandelate           | 0.25     |
| Sodium tetrafluoroborate     | 2.00     | Sodium 2-phenylpropionate    | 1.70     |
| Sodium methanesulfonate      | 3.60     | Disodium succinate           | 1.13     |
| Sodium methanesulfonate      | 1.80     | Potassium DL-aspartate       | 0.25     |
| Sodium triflate              | 0.80     | Sodium L-aspartate           | 0.25     |
| Potassium hexafluorophosphate| 0.24     | Disodium DL-tartrate         | 0.55     |
| Sodium 3-nitrobenzensulfonate| 0.42     | Disodium L-tartrate          | 1.00     |
| Potassium thiocyanate        | 7.30     | Disodium (+)-O,O'-dibenzoyl-D-tartrate | 0.26 |
| Potassium thiocyanate        | 3.50     | Sodium N-acetylglycinate     | 2.28     |
| Potassium thiocyanate        | 1.75     | Disodium maleate             | 0.66     |
| Sodium nitrate               | 4.60     | Sodium pyrrolidone carboxylate| 4.96   |
| Sodium nitrate               | 2.30     | Disodium N-acetylglutamate   | 1.63     |
| Sodium benzoate              | 1.80     | Disodium DL-malate           | 2.27     |
| Potassium phthalate monobasic| 0.27     | Sodium p-toluenesulfonate    | 0.70     |
| Sodium formate               | 6.00     | Sodium camphorsulfonate      | 2.28     |
| Sodium formate               | 3.00     | Trisodium citrate            | 1.20     |
| Sodium acetate      | 2.60 | Disodium citrate | 0.96 |
|---------------------|------|------------------|------|
| Sodium trifluoroacetate | 2.40 | Disodium pamoate  | 0.14 |
| Sodium hippurate    | 1.46 | Disodium fumarate | 0.725|
| Sodium potassium L-tartrate | 1.40 | Sodium propionate | 5.20 |
| Potassium antimony tartrate | 0.054 | Sodium propionate | 2.60 |
| Sodium diethyldithiocarbamate | 0.011 | Potassium D-saccharate | 0.05 |
| Disodium malonate   | 2.97 | Sodium valerate   | 3.19 |
| Sodium pyruvate     | 3.00 | Trisodium phosphate | 0.36 |
| Sodium pyruvate     | 1.50 | Disodium hydrogen phosphate | 0.43 |
| Sodium salicylate   | 2.20 | Sodium dihydrogen phosphate | 4.00 |
| Sodium salicylate   | 1.10 | Sodium dihydrogen phosphate | 2.00 |
| Sodium 2-ethylhexanoate | 4.20 | Sodium isethionate | 2.20 |
| Sodium 2-ethylhexanoate | 2.10 | Sodium isethionate | 1.10 |
| Sodium L-glutamate  | 2.00 | Disodium oxalate  | 0.14 |
| Sodium L-glutamate  | 1.00 | Sodium hydrogen carbonate | 0.60 |
| Sodium sulfate      | 1.00 | Sodium benzenesulfonate | 1.10 |
| Sodium tetraphenylborate | 0.40 | Sodium hexanoate  | 2.70 |
| Sodium tetraphenylborate | 0.20 | Disodium carbonate | 1.00 |
| Potassium gluconate | 1.10 | Sodium adipate    | 1.19 |
| Sodium saccharine   | 1.57 | Sodium L-malate   | 2.92 |
| Sodium 1-naphthalenacetate | 0.43 | Sodium dicyanamide | 0.700|
| Sodium 1-naphthalensulfonate | 0.35 | Sodium nicotinate | 2.96 |
| Sodium 2-naphthalensulfonate | 0.13 | Sodium nicotinate | 1.48 |
| Disodium 2, 6-naphthalenedisulfonate | 0.085 | Sodium octanoate | 1.56 |
| Salt free           |      |                  |      |
Table S3  Crystallization results of ephedrinium chloride and alkaline iodide as a function of the ratio of iodide to ephedrinium, the cation of the iodide salt and the used silicone oil.

Silicone oil with 50 cSt viscosity

| Molar ratio of iodide to ephedrinium | 1   | 2.5 | 5   | 10  | 15  | 25  | 50  | 100 | 200 |
|-------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| LiI                                 |     |     | D3: |     |     |     |     |     |     |
|                                     |     |     | needles<sup>a</sup> |     |     |     |     |     |     |
| NaI                                 |     |     | D3: |     |     |     |     |     |     |
|                                     |     |     | needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D3: big needle |     |     |     |     |     |     |
| KI                                  |     |     | D3: big needle |     |     |     |     |     |     |
|                                     |     |     | D3: needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D3: needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D5: needle<sup>a</sup> |     |     |     |     |     |     |

Silicone oil with 5 cSt viscosity

| Molar ratio of iodide to ephedrinium | 1   | 2.5 | 5   | 10  | 15  | 25  | 50  | 100 | 200 |
|-------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| LiI                                 |     |     | D3: |     |     |     |     |     |     |
|                                     |     |     | needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D3: needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D3: big needle |     |     |     |     |     |     |
| NaI                                 |     |     | D3: needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D3: plate |     |     |     |     |     |     |
|                                     |     |     | D3: needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D5: needle<sup>a</sup> |     |     |     |     |     |     |
| KI                                  |     |     | D3: needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D3: needles<sup>a</sup> |     |     |     |     |     |     |
|                                     |     |     | D3: needles<sup>a</sup> |     |     |     |     |     |     |

Legend: DX: crystals were observed after X days. 100 μl of the premixed solutions were generated by pipetting appropriate volumes of a 1.15 M ephedrinium chloride and a 4 M alkaline iodide solution. 10 μl premixed solutions were placed at the bottom of 100 μl of the indicated silicone oil. <sup>a</sup>: well was scratched at day 3. All measured crystals belong to the orthorhombic polymorph I with \(a = 7.3\) Å, \(b = 18.9\) Å, \(c = 25.7\) Å and a volume of 3562 Å³ (Nievergelt et al., 2018).
### Table S4  Crystallization results of ephedrinium chloride and sodium oxalate as a function of the ratio of oxalate to ephedrinium and the used silicone oil.

Silicone oil with 50 cSt viscosity

| Molar ratio of oxalate to ephedrinium | 0.01 | 0.033 | 0.1 | 0.33 | 1   | 3.33 | 10   | 33.3 | 100 |
|---------------------------------------|------|-------|-----|------|-----|------|------|------|-----|
| Na₂Oxalate                            |      |       | D1  | D1   | D1  | D1   | D1   | D1   | D16 |
|                                       |      |       | D16:| EphHCl|D16:| EphHCl|D16:| EphHCl|

Silicone oil with 5 cSt viscosity

| Molar ratio of oxalate to ephedrinium | 0.01 | 0.033 | 0.1 | 0.33 | 1   | 3.33 | 10   | 33.3 | 100 |
|---------------------------------------|------|-------|-----|------|-----|------|------|------|-----|
| Na₂Oxalate                            |      |       | D1  | D1   | D1  | D1   | D1   | D1   | D16 |
|                                       |      |       | D16:| EphHCl|D16:| EphHCl|D16:| EphHCl|

Legend: DX: crystals were observed after X days. All observed crystals were bis ephedrinium oxalate (Nievergelt et al., 2018), unless otherwise noted. 100 μl of the premixed solutions were generated by pipetting appropriate volumes of a 1.15 M ephedrinium chloride and a 0.14 M sodium oxalate. 10 μl of the premixed solutions were placed at the bottom of 100 μl of the indicated silicone oil. Additionally for the ratios of 0.1 and 1, solutions were directly mixed within the silicone oil to give a drop of 10 μl. The results were identical as for the corresponding premixed solutions.
S2. Crystallography

S2.1. [(R-carnitinenitrile)(S-carnitinenitrile)$_2$][chloride]$_3$

R,S-carnitinenitrile chloride surprisingly crystallized with three units of carnitinenitrile chloride (S-carnitinenitrile : R-carnitinenitrile ratio 2:1) in the asymmetric unit of the space group $P2_1$. Each hydroxy group hydrogen bonds to just one chloride ion, thereby forming ion pairs.

Figure S3  Top: displacement ellipsoid representation of [(R-Car)(S-Car)$_2$]3Cl, ellipsoids are drawn at 50% probability. Below: packing diagram of [(R-Car)(S-Car)$_2$]3Cl.
S2.2. [R,S-carnitinenitrile][iodide]

R,S-carnitinenitrile iodide crystallized with two formula units in the asymmetric unit of the space group *Pbca*. One of the carnitinenitrile cations has a disordered hydroxy group, as a result of both enantiomers randomly occupying the same crystallographic site. These hydroxy groups point to different iodide anions. There are weak hydrogen bonds between of the carnitinenitrile cation hydroxy groups and iodide anions.

**Figure S4** Top: displacement ellipsoid representation of [(+/-)-Car]I, ellipsoids are drawn at 50% probability. The disorder of the hydroxy group is omitted for clarity. Bottom: packing diagram of [(+/-)-Car]I.
S2.3. [R-carnitinenitrile][chloride]

R-carnitinenitrile chloride crystallized with one formula unit in the asymmetric unit of the chiral space group $P2_1$. Ion pairs result from a hydrogen bond between the chloride anion and the hydroxy group (O5) of the carnitinenitrile cation.

![Figure S5](https://example.com/f5.png)

**Figure S5** Left: displacement ellipsoid representation of [(-)-Car]Cl, ellipsoids are drawn at 50% probability. Right: packing diagram of [(-)-Car]Cl.

S2.4. [R-carnitinenitrile][bromide]

R-carnitinenitrile bromide crystallized with one formula unit in the asymmetric unit in the chiral space group $P2_1$. The structure is essentially isostructural with the chloride salt. One hydrogen bond between the bromide anion and the hydroxy group (O5) of the R-carnitinenitrile cation links the components into ion pairs.

![Figure S6](https://example.com/f6.png)

**Figure S6** Left: displacement ellipsoid representation of [(-)-Car]Br, ellipsoids are drawn at 50% probability. Right: packing diagram of [(-)-Car]Br.
S2.5. [R-carnitinenitrile][iodide]

R-carnitinenitrile iodide crystallized with one formula unit in the asymmetric unit of the chiral space group $P2_12_12_1$. One hydrogen bond between the iodide anion and the hydroxyl group (O5) of the $R$-carnitinenitrile cation links the components into ion pairs.

**Figure S7** Left: displacement ellipsoid representation of $[(-)-\text{Car}]I$, ellipsoids are drawn at 50% probability. Right: packing diagram of $[(-)-\text{Car}]I$. 
S2.6. [R-carnitinenitrile]$_2$[tetrafluoroborate][chloride]

Bis(R-carnitinenitrile)-tetrafluoroborate-chloride crystallized from a mixture of 5 µl of a 6.54 M R-carnitinenitrile chloride solution and 5 µl of a 4 M sodium tetrafluoroborate solution. The asymmetric unit of the space group $P2_12_12_1$ contains two $R$-carnitinenitrile cations, one chloride anion and one tetrafluoroborate anion. The tetrafluoroborate anions are disordered and they have no hydrogen bonding interaction. The displacement ellipsoids of the fluorine atoms were restrained to be similar during refinement. The structure is stabilized by two hydrogen bonds to the chloride anion from the hydroxy groups of two different $R$-carnitinenitrile cations. The chloride and tetrafluoroborate anions are stacked in an alternating fashion in the direction of the $c$ axis. The dataset used for the structure determination had a relatively low completeness of 98.2 % to a $\Theta$ angle of 74.33°. This is caused by a small crystal and the use of symmetric kappa constraints to 1° and 60° for the strategy calculation in CrysAlisPro 1.171.39.12b. Unfortunately, all experiments to grow better single crystals have failed. On the other hand, the completeness of 98.2 % to the theta angle of 74.33° with the combination of low $R$ indicators (0.0343; 0.0873 for all data) shows the accuracy of the result.

Figure S8  Left: displacement ellipsoid representation of [(-)-Car]$_2$[BF$_4$]Cl, ellipsoids are drawn at 50% probability. Right: packing diagram of [(-)-Car]$_2$[BF$_4$]Cl.
S2.7. [Diltiazem][bromide]

Diltiazem bromide crystallized with one formula unit in the asymmetric unit of the chiral space group $P2_12_12_1$. The structure is essentially isostructural with the published chloride salt (Kojic-Prodic et al., 1984). During the refinement, it was necessary to use a different weighting scheme than normal. Instead of the modified Sheldrick weighting scheme, here a polynomial Chebychev weighting scheme was used (Prince, 1982, Watkin, 1994) since it gave lower $R$-values and lower shifts. One weak hydrogen bond between the bromide ion and the protonated tertiary amino group of diltiazem (N11) links the components into ion pairs. The distance between N11 and Br30 is 3.172(5) Å. However, there is another close intramolecular interaction between the keto group of the acetate fragment and the second keto group of diltiazem (O19···O15). The distance between these oxygen atoms is 2.943(7) Å.

**Figure S9** Top: displacement ellipsoid representation of [DilH]Br, ellipsoids are drawn at 50% probability. Below: packing diagram of [DilH]Br.
S2.8. [Diltiazem][iodide]

Diltiazem iodide crystallized with one formula unit in the asymmetric unit of the chiral space group $P_{2_1}2_12_1$. The structure is essentially isostructural with that of the published chloride salt (Kojic-Prodic et al., 1984) and the aforementioned bromide salt. The crystal structure is stabilized by one weak hydrogen bond between iodide and the protonated tertiary amino group of diltiazem (N11). The distance between N11 and I30 is 3.3966(18) Å. However, there is another close intramolecular interaction between the keto group of the acetate fragment and the second keto group of diltiazem (O19⋯O15). The distance between the oxygen atoms is 2.978(3) Å.

![Figure S10](image)

**Figure S10**  Top: displacement ellipsoid representation of [DilH]I, ellipsoids are drawn at 50% probability. Below: packing diagram of [DilH]I.
S2.9. [Diltiazem][nitrate]

Diltiazem nitrate crystallized with one formula unit in the asymmetric unit of the chiral space group $P2_12_12_1$. Interestingly, the crystal is essentially isomorphous with the published chloride salt (Kojic-Prodic et al., 1984), as well as the aforementioned bromide and iodide salts. Ion pairs are formed by two hydrogen bonds between two oxygen atoms (O31; O32) of the nitrate anion and the protonated tertiary amino group of diltiazem (N11). Moreover, there is a close intramolecular interaction between the keto group of the acetate fragment and the second keto group of diltiazem (O19⋅⋅⋅O15). The distance between the oxygen atoms is 3.032(2) Å.

**Figure S11**  Top: displacement ellipsoid representation of [DilH][NO$_3$], ellipsoids are drawn at 50% probability. Below: packing diagram of [DilH][NO$_3$].
S2.10. [Diltiazem][dihydrogenphosphate]-1.5(H₂O)

Diltiazem dihydrogenphosphate crystallized with four units of diltiazem dihydrogenphosphate in the asymmetric unit of the chiral space group P1. The asymmetric unit also contains 6 molecules of water. There is a close intramolecular interaction between the keto group of the acetate moiety and the second keto group of all molecules of diltiazem (O19⋅⋅⋅O15) (3.021(4) Å 3.038(3) Å 3.035(3) Å 3.020(4) Å). CheckCIF reports a 90% match for the structure to one with a halved b-axis. Certainly, there is partial translation symmetry along b. However, it is obvious, that phosphate anions do not follow pseudo-translation. Even the side chains in (b/2)-related molecules of diltiazem differ significantly (see the bottom of Figure S12). Structure refinement in the halved-b unit cell does not reflect the real symmetry, and results in disorders. Hence, we preferred structure refinement in the supercell. It was possible to index about 70% of the reflections in a monoclinic cell with the dimensions: a: 8.79182(5) Å, b: 6.33050(4) Å, c: 46.6314(3) Å, β: 92.1049(5)°. The reflections could be nicely integrated by applying the space group I2 (Rint 6.5%) and the structure could be solved within that space group. However, that refinement did not yield a satisfying result as the position and geometry of the anion did not make any sense.
Figure S12  Top: displacement ellipsoid representation of [DilH][H$_2$PO$_4$][H$_2$O]$_{1.5}$, ellipsoids are drawn at 50% probability. Middle: packing diagram of [DilH][H$_2$PO$_4$][H$_2$O]$_{1.5}$. Bottom: Molecular packing of diltiazem dihydrogenphosphate, view along the $b$ axis.
S2.11. [(1S,2R)-(+)‐ephedrinium]₂[L‐malate]·(H₂O)

Two cations of (1S,2R)‐(+‐)‐ephedrinium crystallized together with one L‐malate anion and one water molecule in the asymmetric unit of the chiral space group \( P1 \).

**Figure S13**  Left: displacement ellipsoid representation of [(1S,2R)‐EphH]₂[L‐malate](H₂O), ellipsoids are drawn at 50% probability. Right: packing diagram of [(1S,2R)‐EphH]₂[L‐malate](H₂O).

S2.12. [(1S,2R)-(+)‐ephedrinium]₂[L‐tartrate]·(H₂O)

Two cations of (1S,2R)‐(+‐)‐ephedrinium crystallized together with one L‐tartrate anion and one water molecule in the asymmetric unit of the chiral space group \( P2_1 \).

**Figure S14** Top: displacement ellipsoid representation of [(1S,2R)‐EphH]₂[L‐tartrate](H₂O), ellipsoids are drawn at 50% probability. Below: packing diagram of [(1S,2R)‐EphH]₂[L‐tartrate](H₂O).
S2.13. [(1S,2R)-(+) -ephedrinium][nitrate], polymorph II

(1S,2R)-(+) -ephedrinium nitrate crystallized as thin plates with two formula units in the asymmetric unit of the chiral space group $P2_1$. The unit cell dimensions were $a = 6.0401$ (3) Å, $b = 29.3553$ (8) Å, $c = 7.3828$ (3) Å, $\beta = 112.806$ (5)$^\circ$ and $V = 1206.70$ (9) Å$^3$. This is a new polymorphic form of ephedrinium nitrate. Later, three-dimensional crystals (Figure S15) crystallized, which were identified to be the known nitrate salt, polymorph I, (Collier et al., 2006) with unit cell dimensions of $a = 5.536$ (5) Å, $6.839$ (9) Å, $15.669$ (12) Å, $\beta = 97.28$ (7)$^\circ$ and $V = 588(1)$ Å$^3$. As polymorph I was already known, only the initial unit cell constants were determined.

Figure S15  Microscope picture of (1S,2R)-(+) -ephedrinium nitrate crystals in Infinium oil: Polymorph I (three-dimensional crystals top and bottom) and polymorph II (thin plate -like crystals in the middle).

Figure S16  Top: displacement ellipsoid representation of (1S,2R)-(+) -ephedrinium nitrate, (polymorph II) ellipsoids are drawn at 50% probability. Below: packing diagram of (1S,2R)-(+) -ephedrinium nitrate (polymorph II).
S2.14. [(1S,2R)-(−)-ephedrinium][pyrrolidone carboxylate]⋅(H₂O)

(1S,2R)-(−)-ephedrinium pyrrolidone carboxylate crystallized in a 1:1 ratio together with one water molecule in the asymmetric unit of the chiral space group \( P2_1 \).

![Figure S17](image1)

**Figure S17** Left: displacement ellipsoid representation of \([(1S,2R)-\text{EphH}]\)[pyrrolidone carboxylate]⋅[H₂O], ellipsoids are drawn at 50% probability. Right: packing diagram of \([(1S,2R)-\text{EphH}]\)[pyrrolidone carboxylate]⋅[H₂O].

S2.15. [Trazodone][nitrate]

Trazodone nitrate crystallized with one formula unit in the asymmetric unit of the monoclinic space group \( P2_1/c \).

![Figure S18](image2)

**Figure S18** Left: displacement ellipsoid representation of [TrazH][NO₃], ellipsoids are drawn at 50% probability. Right: packing diagram of [TrazH][NO₃].
S2.16. [Trazodone][tetrafluoroborate]

Trazodone tetrafluoroborate crystallized with one formula unit in the asymmetric unit of the monoclinic space group $P2_1/c$. Three out of four fluorine atoms of the tetrafluoroborate anion are disordered in a 91:9 ratio.

Figure S19  Left: displacement ellipsoid representation of [TrazH][BF$_4$], ellipsoids are drawn at 50% probability. The minor part of the disordered tetrafluoroborate was omitted for clarity. Right: packing diagram of [TrazH][BF$_4$].
S2.17. [Trazodone][thiocyanate]

Trazodone thiocyanate crystallized with two formula units in the asymmetric unit of the triclinic space group $P\overline{1}$. One thiocyanate is disordered in a 1:1 ratio, one trazodonium cation and the corresponding thiocyanate are disordered in a 51:49 ratio. Suitable restraints for distances and displacement ellipsoids (SADI, DFIX and RIGU) had to be applied.

Figure S20  Left: displacement ellipsoid representation of [TrazH][SCN], ellipsoids are drawn at 50% probability. Only one moiety of both disordered thiocyanate anions and one disordered trazodonium cation is shown for clarity. Right: packing diagram of [TrazH][SCN], again not showing any disorder.
**Table S5**  Crystallographic information tables.

[Diltiazem][bromide]

Crystal data
Chemical formula  C\textsubscript{22}H\textsubscript{27}N\textsubscript{2}O\textsubscript{4}S·Br
\(M_r\)  495.44
Crystal system, space group  Orthorhombic, \(P2_12_12_1\)
Temperature (K)  160
\(a, b, c\) (\(\text{Å}\))  6.1060 (3), 9.0317 (6), 42.330 (4)
\(V\) (\(\text{Å}^3\))  2334.4 (3)
\(Z\)  4
Radiation type  Cu \(K\alpha\)
\(\mu\) (\(\text{mm}^{-1}\))  3.48
Crystal shape  Plate
Crystal size (mm)  0.07 \times 0.04 \times 0.01

Data collection
Diffractometer  XtaLAB Synergy, Dualflex, Pilatus 200K
Absorption correction  Multi-scan
\(\text{CrysAlis PRO}, \text{(Rigaku Oxford Diffraction, 2015)}\)
\(\text{T}_{\text{min}}, \text{T}_{\text{max}}\)  0.69, 0.95
No. of measured, independent and observed \([I > 2.0\sigma(I)]\) reflections  24363, 4772, 4199
\(R_{\text{int}}\)  0.102
\(\theta\) values (°)  \(\theta_{\text{max}} = 74.5, \theta_{\text{min}} = 4.2\)
\((\text{sin} \theta/\lambda)_{\text{max}}\) (\(\text{Å}^{-1}\))  0.625

Refinement
\(R[F^2 > 2\sigma(F^2)], wR(F^2), S\)  0.067, 0.092, 1.09
No. of reflections  4772
No. of parameters  272
H-atom treatment  H-atom parameters constrained
\(\Delta \rho_{\text{max}}, \Delta \rho_{\text{min}}\) (e \(\text{Å}^{-3}\))  0.93, −0.72
Absolute structure  Flack (1983), 1977 Friedel-pairs
Absolute structure parameter  −0.04 (3)

Computer programs: \textit{CrysAlis PRO}, \text{(Rigaku Oxford Diffraction, 2015)}, Superflip (Palatinus \& Chapuis, 2007), \textit{CRYSTALS} (Betteridge \textit{et al.}, 2003), \textit{CAMERON} (Watkin \textit{et al.}, 1996).
[Diltiazem][iodide]

Crystal data
Chemical formula \( \text{C}_{22}\text{H}_{27}\text{N}_{2}\text{O}_{4}\text{S} \cdot \text{I} \)
\( M_r \) 542.44
Crystal system, space group Orthorhombic, \( P2_12_12_1 \)
Temperature (K) 160
\( a, b, c (\text{Å}) \) 6.2219 (1), 9.0228 (1), 43.0569 (5)
\( V (\text{Å}^3) \) 2417.17 (5)
\( Z \) 4
Radiation type Cu \( K\alpha \)
\( \mu (\text{mm}^{-1}) \) 11.46
Crystal shape Prism
Crystal size (mm) 0.39 \times 0.05 \times 0.03

Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K
Absorption correction Multi-scan
\( T_{\text{min}}, T_{\text{max}} \) 0.47, 0.70
No. of measured, independent and observed \([I > 2.0\sigma(I)]\) reflections 15587, 4935, 4860
\( R_{\text{int}} \) 0.030
\( \theta \) values (°) \( \theta_{\text{max}} = 74.5, \theta_{\text{min}} = 4.1 \)
\( (\sin \theta/\lambda)_{\text{max}} (\text{Å}^{-1}) \) 0.625

Refinement
\( R[F^2 > 2\sigma(F^2)], wR(F^2), S \) 0.021, 0.053, 0.99
No. of reflections 4935
No. of parameters 272
H-atom treatment H-atom parameters constrained
\( \Delta \rho_{\text{max}}, \Delta \rho_{\text{min}} (\text{e Å}^{-3}) \) 0.36, −0.37
Absolute structure Flack (1983), 2050 Friedel-pairs
Absolute structure parameter −0.013 (3)

Computer programs: CrysAlis PRO, (Rigaku Oxford Diffraction, 2015), SIR92 (Altomare et al., 1994), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).
[Diltiazem][nitrate]

Crystal data
Chemical formula \(C_{22}H_{27}N_2O_4S\cdot\text{NO}_3\)

\(M_r\) 477.54

Crystal system, space group Orthorhombic, \(P_2_12_12_1\)

Temperature (K) 160

\(a, b, c\) (Å) 6.3765 (1), 8.8174 (1), 42.9420 (7)

\(V\) (Å\(^3\)) 2414.38 (6)

\(Z\) 4

Radiation type Cu \(K\alpha\)

\(\mu\) (mm\(^-1\)) 1.59

Crystal shape Prism

Crystal size (mm) 0.62 × 0.05 × 0.03

Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K

Absorption correction Multi-scan

\(T_{\text{min}}, T_{\text{max}}\) 0.58, 0.96

No. of measured, independent and observed \([I > 2.0\sigma(I)]\) reflections 25295, 4925, 4641

\(R_{\text{int}}\) 0.051

\(\theta\) values (°) \(\theta_{\text{max}} = 74.5\), \(\theta_{\text{min}} = 4.1\)

\((\sin \theta/\lambda)_{\text{max}}\) (Å\(^{-1}\)) 0.625

Refinement
\(R[F^2 > 2\sigma(F^2)], wR(F^2), S\) 0.039, 0.093, 0.99

No. of reflections 4925

No. of parameters 299

H-atom treatment H-atom parameters constrained

\(\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}\) (e Å\(^{-3}\)) 0.35, −0.26

Absolute structure Flack (1983), 2051 Friedel-pairs

Absolute structure parameter 0.030 (18)

Computer programs: CrysAlis PRO, (Rigaku Oxford Diffraction, 2015), Superflip (Palatinus & Chapuis, 2007), CRYSTALS (Betteridge \textit{et al.}, 2003), CAMERON (Watkin \textit{et al.}, 1996).
[Diltiazem][dihydrogenphosphate](H$_2$O)$_{1.5}$

Crystal data
Chemical formula (C$_{22}$H$_{27}$N$_2$O$_4$S)(H$_2$O$_4$P)(H$_2$O)$_{1.5}$
$M_r$ 539.53
Crystal system, space group Triclinic, $P1$
Temperature (K) 160
$a$, $b$, $c$ (Å) 8.7929 (1), 12.6645 (1), 23.7867 (2)
$\alpha$, $\beta$, $\gamma$ (°) 82.3345 (7), 81.4117 (7), 89.9824 (7)
$V$ (Å$^3$) 2595.21 (4)
$Z$ 4
Radiation type Cu $K\alpha$
$\mu$ (mm$^{-1}$) 2.17
Crystal shape Lath
Crystal size (mm) 0.17 × 0.07 × 0.02
Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K
Absorption correction Multi-scan
$T_{\text{min}}$, $T_{\text{max}}$ 0.62, 0.96
No. of measured, independent and observed [$I > 2.0\sigma(I)$] reflections 264132, 19821, 18568
$R_{\text{int}}$ 0.066
$\theta$ values (°) $\theta_{\text{max}} = 72.1$, $\theta_{\text{min}} = 3.5$
$(\sin \theta/\lambda)_{\text{max}}$ (Å$^{-1}$) 0.617
Refinement
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, $S$ 0.049, 0.128, 1.00
No. of reflections 19783
No. of parameters 1376
No. of restraints 66
H-atom treatment H atoms treated by a mixture of independent and constrained refinement
$\Delta \rho_{\text{max}}$, $\Delta \rho_{\text{min}}$ (e Å$^{-3}$) 1.49, −0.46
Absolute structure Flack (1983), 9652 Friedel-pairs
Absolute structure parameter 0.020 (11)

Computer programs: CrysAlis PRO, (Rigaku Oxford Diffraction, 2015), Superflip (Palatinus & Chapuis, 2007), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).
[R-Carnitinenitrile][chloride]

Crystal data
Chemical formula \( \text{C}_7\text{H}_{15}\text{N}_2\text{O} \cdot \text{Cl} \)
\( M_r \) 178.66
Crystal system, space group Monoclinic, \( P2_1 \)
Temperature (K) 160
\( a, b, c \) (Å) 7.2902 (2), 8.9099 (3), 7.8789 (3)
\( \beta \) (°) 107.024 (3)
\( V \) (Å\(^3\)) 489.35 (3)
\( Z \) 2
Radiation type Mo K\( \alpha \)
\( \mu \) (mm\(^{-1}\)) 0.34
Crystal shape Plate
Crystal size (mm) 0.30 × 0.20 × 0.07
Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K
Absorption correction Multi-scan
\( T_{\text{min}}, T_{\text{max}} \) 0.59, 0.98
No. of measured, independent and observed \([I > 2.0\sigma(I)]\) reflections 15361, 3726, 3428
\( R_{\text{int}} \) 0.039
\( \theta \) values (°) \( \theta_{\text{max}} = 33.1, \theta_{\text{min}} = 2.7 \)
\( (\sin \theta/\lambda)_{\text{max}} \) (Å\(^{-1}\)) 0.769
Refinement
\( R[F^2 > 2\sigma(F^2)], wR(F^2), S \) 0.032, 0.081, 0.95
No. of reflections 3726
No. of parameters 101
No. of restraints 1
H-atom treatment H-atom parameters not refined
\( \Delta \rho_{\text{max}}, \Delta \rho_{\text{min}} \) (e Å\(^{-3}\)) 0.39, −0.29
Absolute structure Flack (1983), 1757 Friedel-pairs
Absolute structure parameter −0.01 (4)

Computer programs: CrysAlis PRO, (Rigaku Oxford Diffraction, 2015), SIR92 (Altomare et al., 1994), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).
[R-Carnitinenitrile][bromide]

Crystal data
Chemical formula C₇H₁₅N₂O·Br
\(M_r\) 223.11
Crystal system, space group Monoclinic, \(P2_1\)
Temperature (K) 160
\(a, b, c\) (Å) 7.5269 (2), 9.1017 (3), 7.9300 (3)
\(\beta\) (°) 107.161 (4)
\(V\) (Å³) 519.08 (3)
\(Z\) 2
Radiation type Mo \(K\alpha\)
\(\mu\) (mm⁻¹) 3.92
Crystal shape Plate
Crystal size (mm) 0.12 × 0.10 × 0.03
Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K
Absorption correction Multi-scan
\(T_{\text{min}}, T_{\text{max}}\) 0.64, 0.90
No. of measured, independent and observed \([I > 2.0\sigma(I)]\) reflections 16508, 3402, 3118
\(R_{\text{int}}\) 0.034
\(\theta\) values (°) \(\theta_{\text{max}} = 31.5, \theta_{\text{min}} = 2.7\)
\((\sin \theta/\lambda)_{\text{max}}\) (Å⁻¹) 0.735

Refinement
\(R[F^2 > 2\sigma(F^2)], wR(F^2), S\) 0.029, 0.072, 0.97
No. of reflections 3402
No. of parameters 101
No. of restraints 1
H-atom treatment H-atom parameters constrained
\(\Delta \rho_{\text{max}}, \Delta \rho_{\text{min}}\) (e Å⁻³) 0.47, −0.53
Absolute structure Flack (1983), 1581 Friedel-pairs
Absolute structure parameter 0.043 (10)

Computer programs: CrysAlis PRO, (Rigaku Oxford Diffraction, 2015), SIR92 (Altomare et al., 1994), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).
**[R-Carnitinenitrile][iodide]**

Crystal data
- Chemical formula: \( \text{CC}_7\text{H}_{15}\text{N}_2\text{O}\cdot\text{I} \)
- \( M_r \): 270.11
- Crystal system, space group: Orthorhombic, \( P2_12_12_1 \)
- Temperature (K): 160
- \( a, b, c (\text{Å}) \): 7.5850 (1), 10.8242 (2), 13.0468 (3)
- \( V (\text{Å}^3) \): 1071.16 (3)
- \( Z \): 4
- Radiation type: Mo Kα
- \( \mu (\text{mm}^{-1}) \): 2.95
- Crystal shape: Prism
- Crystal size (mm): 0.25 × 0.12 × 0.10

Data collection
- Diffractometer: XtaLAB Synergy, Dualflex, Pilatus 200K
- Absorption correction: Multi-scan
- \( T_{\text{min}}, T_{\text{max}} \): 0.47, 0.75
- No. of measured, independent and observed \([I > 2.0\sigma(I)]\) reflections: 17375, 3606, 3544
- \( R_{\text{int}} \): 0.021
- \( \theta \) values (°): \( \theta_{\text{max}} = 32.9, \theta_{\text{min}} = 2.4 \)
- \( (\sin \theta/\lambda)_{\text{max}} (\text{Å}^{-1}) \): 0.764

Refinement
- \( R[F^2 > 2\sigma(F^2)], wR(F^2), S \): 0.013, 0.030, 0.99
- No. of reflections: 3606
- No. of parameters: 101
- H-atom treatment: H-atom parameters constrained
- \( \Delta\rho_{\text{max}}, \Delta\rho_{\text{min}} (\text{e Å}^{-3}) \): 0.39, −0.41
- Absolute structure: Flack (1983), 1481 Friedel-pairs
- Absolute structure parameter: −0.018 (12)

Computer programs: CrysAlis PRO, (Rigaku Oxford Diffraction, 2015), Superflip (Palatinus & Chapuis, 2007), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).
[R-Carnitinenitrile]$_2$[tetrafluoroborate][chloride]

Crystal data
Chemical formula 2(C$_7$H$_{15}$N$_2$O)$\cdot$BF$_4$$\cdot$Cl
$M_r$ 408.67
Crystal system, space group Orthorhombic, $P2_12_12_1$
Temperature (K) 160
$a$, $b$, $c$ (Å) 9.4006 (1), 13.2619 (2), 16.6581 (2)
$V$ (Å$^3$) 2076.76 (5)
$Z$ 4
Radiation type Cu $K\alpha$
$\mu$ (mm$^{-1}$) 2.09
Crystal shape Block
Crystal size (mm) 0.13 $\times$ 0.07 $\times$ 0.05

Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K
Absorption correction Multi-scan
$T_{min}$, $T_{max}$ 0.75, 0.90
No. of measured, independent and observed $|I| > 2.0\sigma(I)$ reflections 22105, 4175, 3958
$R_{int}$ 0.037
$\theta$ values (°) $\theta_{max} = 74.5$, $\theta_{min} = 4.3$
(sin $\theta$/λ)$_{max}$ (Å$^{-1}$) 0.625

Refinement
$R(F^2 > 2\sigma(F^2))$, $wR(F^2)$, $S$ 0.033, 0.090, 1.00
No. of reflections 4175
No. of parameters 264
No. of restraints 19
H-atom treatment H-atom parameters constrained
$\Delta \rho_{max}$, $\Delta \rho_{min}$ (e Å$^{-3}$) 0.34, −0.19
Absolute structure Flack (1983), 1797 Friedel-pairs
Absolute structure parameter 0.015 (13)

Computer programs: CrysAlis PRO, (Rigaku Oxford Diffraction, 2015), Superflip (Palatinus & Chapuis, 2007), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).
[R,S-Carnitinenitrile][chloride]

Crystal data
Chemical formula \( \text{C}_7\text{H}_{15}\text{N}_2\text{O} \cdot \text{Cl} \)

\( M_r \)

178.66

Crystal system, space group Monoclinic, \( P2_1 \)

Temperature (K)

183

\( a, b, c (\text{Å}) \)

7.2588 (3), 8.9399 (4), 22.7927 (9)

\( \beta (°) \)

95.818 (4)

\( V (\text{Å}^3) \)

1471.47 (11)

\( Z \)

6

Radiation type Mo Kα

\( \mu (\text{mm}^{-1}) \)

0.34

Crystal shape Block

Crystal size (mm)

0.13 × 0.08 × 0.06

Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K

Absorption correction Multi-scan

\( T_{\text{min}}, T_{\text{max}} \)

0.77, 0.98

No. of measured, independent and observed \([I > 2.0\sigma(I)]\) reflections

23769, 10401, 7769

\( R_{\text{int}} \)

0.032

\( \theta \) values (°)

\( \theta_{\text{max}} = 32.6, \theta_{\text{min}} = 2.5 \)

\( (\sin \theta/\lambda)_{\text{max}} (\text{Å}^{-1}) \)

0.758

Refinement
\( R[F^2 > 2\sigma(F^2)], wR(F^2), S \)

0.052, 0.128, 1.00

No. of reflections

10401

No. of parameters

299

No. of restraints

1

H-atom treatment H-atom parameters constrained

\( \Delta \rho_{\text{max}}, \Delta \rho_{\text{min}} (\text{e Å}^{-3}) \)

0.75, −0.43

Absolute structure Flack (1983), 4756 Friedel-pairs

Absolute structure parameter −0.03 (4)

Computer programs: CrysAlis PRO, (Rigaku Oxford Diffraction, 2015), Superflip (Palatinus & Chapuis, 2007), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).
**[R,S-Carnitinenitrile][iodide]**

Crystal data

Chemical formula: C$_7$H$_{15}$N$_2$O·I

$M_r$: 270.11

Crystal system, space group: Orthorhombic, $Pbca$

Temperature (K): 160

$a$, $b$, $c$ (Å): 13.4725 (2), 9.8551 (1), 32.7259 (4)

$V$ (Å$^3$): 4345.11 (9)

$Z$: 16

Radiation type: Cu $K\alpha$

$\mu$ (mm$^{-1}$): 22.83

Crystal shape: Plate

Crystal size (mm): 0.12 $\times$ 0.10 $\times$ 0.05

Data collection

Diffractometer: XtaLAB Synergy, Dualflex, Pilatus 200K

Absorption correction: Multi-scan

$T_{\text{min}}$, $T_{\text{max}}$: 0.12, 0.34

No. of measured, independent and observed [$I > 2.0\sigma(I)$] reflections: 17435, 4437, 4082

$R_{\text{int}}$: 0.032

$\theta$ values (°): $\theta_{\text{max}} = 74.5$, $\theta_{\text{min}} = 4.3$

$(\sin \theta/\lambda)_{\text{max}}$ (Å$^{-1}$): 0.625

Refinement

$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, $S$: 0.049, 0.113, 1.01

No. of reflections: 4437

No. of parameters: 209

No. of restraints: 2

H-atom treatment: H-atom parameters constrained

Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.03P)^2 + 31.74P]$, where $P = (\max(F_{o}^2,0) + 2F_{c}^2)/3$

$\Delta\rho_{\text{max}}$, $\Delta\rho_{\text{min}}$ (e Å$^{-3}$): 1.97, -1.61

Computer programs: CrysAlis PRO (Rigaku Oxford Diffraction, 2017), Superflip (Palatinus & Chapuis, 2007), CRYSTALS (Betteridge et al., 2003), CAMERON (Watkin et al., 1996).
[(1S,2R)-(+)-ephradinium]$_2$[L-malate]·(H$_2$O)

Crystal data

Chemical formula $\quad 2$C$_{10}$H$_{16}$NO·C$_4$H$_4$O$_5$·H$_2$O

$M_r=482.56$

Crystal system, space group

Triclinic, $P1$

Temperature (K) $\quad 160$

$a, b, c$ (Å) $\quad 5.82130$ (7), 7.27088 (8), 15.90214 (13)

$\alpha, \beta, \gamma$ (°) $\quad 94.7215$ (8), 96.6693 (8), 109.5246 (11)

$V$ (Å$^3$) $\quad 624.78$ (1)

$Z=1$

Radiation type $\quad$ Cu $K\alpha$

$\mu$ (mm$^{-1}$) $\quad 0.79$

Crystal size (mm) $\quad 0.3 \times 0.21 \times 0.01$

Data collection

Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K

Absorption correction Gaussian

$\text{CrysAlis PRO 1.171.40.16c}$ (Rigaku Oxford Diffraction, 2018)

Numerical absorption followed by empirical absorption correction.

$T_{\text{min}}, T_{\text{max}}$ $\quad 0.463, 1.000$

No. of measured, independent and observed $[I > 2\sigma(I)]$ reflections $\quad 19924, 4803, 4709$

Refinement

$R[F^2 > 2\sigma(F^2)], wR(F^2), S$ $\quad 0.027, 0.074, 1.06$

No. of reflections $\quad 4803$

No. of parameters $\quad 322$

No. of restraints $\quad 3$

H-atom treatment $\quad$ mixed

$\Delta \rho_{\text{max}}, \Delta \rho_{\text{min}}$ (e Å$^{-3}$) $\quad 0.16, -0.18$

Absolute structure $\quad$ Flack $x$ determined using 2188 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$

(Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).

Abs. struct. parameter $\quad 0.00$ (6)

Computer programs: $\text{CrysAlis PRO 1.171.40.16c}$ (Rigaku OD, 2018), $\text{SHELXL}$ (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009).
[(1S,2R)-(+-)-ephedrinium][nitrate],-polymorph II

Crystal data
Chemical formula $\text{C}_{10}\text{H}_{16}\text{NO}\cdot\text{NO}_3$
$M_r$ 228.25
Crystal system, space group Monoclinic, $P2_1$
Temperature (K) 160
$a$, $b$, $c$ (Å) 6.0401 (3), 29.3553 (8), 7.3828 (3)
$\beta$ (°) 112.806 (5)
$V$ (Å$^3$) 1206.70 (9)
$Z$ 4
Radiation type Cu $K\alpha$
$\mu$ (mm$^{-1}$) 0.82
Crystal size (mm) $0.40 \times 0.07 \times 0.01$

Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K
Absorption correction CrysAlis PRO 1.171.39.46 (Rigaku Oxford Diffraction, 2018)
Numerical absorption followed by empirical absorption correction.

$T_{\text{min}}, T_{\text{max}}$ 0.811, 1.000
No. of measured, independent and observed $[I > 2\sigma(I)]$ reflections 12312, 4637, 3727

Refinement
$R(F^2 > 2\sigma(F^2))$, $wR(F^2)$, 0.068, 0.190, 1.09
$S$ 1.09
No. of reflections 4637
No. of parameters 295
No. of restraints 1
H-atom treatment H-atom parameters constrained
$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$ (e Å$^{-3}$) 0.63, −0.30
Absolute structure Flack $x$ determined using 1465 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$
(Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Abs. struct. parameter 0.1 (2)

Computer programs: CrysAlis PRO 1.171.39.46 (Rigaku OD, 2018), SHELXL (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009).
[(1S,2R)-(+) -ephedrinium][pyrrolidone carboxylate]⋅(H₂O)

Crystal data
Chemical formula C₁₀H₁₆NO•C₅H₆NO₃•H₂O
Mr 312.36
Crystal system, space group Monoclinic, P2₁
Temperature (K) 160
a, b, c (Å) 11.47377 (11), 6.14747 (5), 11.71348 (12)
β (°) 111.9780 (11)
V (Å³) 766.16 (1)
Z 2
Radiation type Cu Kα
µ (mm⁻¹) 0.84
Crystal size (mm) 0.38 × 0.04 × 0.03

Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K
Absorption correction Gaussian
CrysAlis PRO 1.171.39.46 (Rigaku Oxford Diffraction, 2018) Numerical absorption correction based on gaussian integration over a multifaceted crystal model Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

Tmin, Tmax 0.708, 1.000
No. of measured, independent and observed [I > 2σ(I)] reflections 13893, 3268, 3223
Rint 0.024
(sin θ/λ)max (Å⁻¹) 0.636

Refinement
R[F² > 2σ(F²)], wR(F²), S 0.025, 0.066, 1.04
No. of reflections 3268
No. of parameters 205
No. of restraints 1
H-atom treatment H-atom parameters constrained
Δρmax, Δρmin (e Å⁻³) 0.20, −0.14
Absolute structure Flack x determined using 1425 quotients [[(I+)-(I-)]/[(I+)+(I-)]] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).

Absolute structure parameter 0.03 (5)

Computer programs: CrysAlis PRO 1.171.39.46 (Rigaku OD, 2018), SHELXL (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009).
[(1S,2R)-(+-)ephedrinium]2[L-tartrate](H2O)

Crystal data

Chemical formula 2(C10H16NO)·C4H4O6·H2O

Mr 498.56

Crystal system, space group Monoclinic, P21

Temperature (K) 160

a, b, c (Å) 6.07189 (12), 32.9414 (4), 7.1383 (1)

β (°) 114.168 (2)

V (Å³) 1302.63 (4)

Z 2

Radiation type Cu Kα

μ (mm⁻¹) 0.81

Crystal size (mm) 0.48 × 0.35 × 0.01

Data collection

Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K

Absorption correction CrysAlis PRO 1.171.39.46 (Rigaku Oxford Diffraction, 2018)

Numerical absorption followed by empirical absorption correction.

 Tmin, Tmax 0.370, 1.000

No. of measured, independent and observed [I > 2σ(I)] reflections 31569, 5216, 5091

R int 0.047

(sin θ/λ)max (Å⁻¹) 0.636

Refinement

R[F² > 2σ(F²)], wR(F²), S 0.042, 0.111, 1.10

No. of reflections 5216

No. of parameters 329

No. of restraints 2

H-atom treatment H atoms treated by a mixture of independent and constrained refinement

Δρ max, Δρ min (e Å⁻³) 0.34, −0.29

Absolute structure Flack x determined using 2347 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).

Abs. struct. parameter 0.00 (7)

Computer programs: CrysAlis PRO 1.171.39.46 (Rigaku OD, 2018), SHELXL (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009).
[Trazodonium][nitrate]

Crystal data

Chemical formula \( [\text{C}_{19}\text{H}_{23}\text{ClN}_{5}\text{O}]\text{NO}_{3} ] \)

\( M_r \) 434.88

Crystal system, space group

Monoclinic, \( P2_1/c \)

Temperature (K) 160

\( a, b, c \) (Å) 12.6065 (3), 13.0726 (3), 12.6694 (3)

\( \beta \) (°) 106.397 (3)

\( V \) (Å\(^3\)) 2003.00 (8)

\( Z \) 4

Radiation type Mo Kα

\( \mu \) (mm\(^{-1}\)) 0.23

Crystal size (mm) 0.53 × 0.20 × 0.17

Data collection

Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K

Absorption correction Gaussian

CrysAlis PRO 1.171.39.46 (Rigaku Oxford Diffraction, 2018) Numerical absorption correction based on gaussian integration over a multifaceted crystal model. Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

\( T_{\text{min}}, T_{\text{max}} \) 0.560, 1.000

No. of measured, independent and observed \([I > 2\sigma(I)]\) reflections 21495, 6532, 5530

\( R_{\text{int}} \) 0.020

\( \sin(\theta/\lambda)_{\text{max}} \) (Å\(^{-1}\)) 0.771

Refinement

\( R[F^2 > 2\sigma(F^2)] \), \( wR(F^2), S \) 0.036, 0.106, 1.05

No. of reflections 6532

No. of parameters 274

H-atom treatment H atoms treated by a mixture of independent and constrained refinement

\( \Delta \rho_{\text{max}}, \Delta \rho_{\text{min}} \) (e Å\(^{-3}\)) 0.40, −0.29

Computer programs: CrysAlis PRO 1.171.39.46 (Rigaku OD, 2018), SHELXT (Sheldrick, 2015), SHELXL (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009).
[Trazodonium][tetrafluoroborate]

Crystal data
Chemical formula \([\text{C}_{19}\text{H}_{23}\text{ClN}_{5}\text{O}]\text{[BF}_4\text{]}\)

\[M_r\] 459.68

Crystal system, space group
Monoclinic, \(P2_1/c\)

Temperature (K) 160

\(a, b, c\) (Å) 12.46473 (13), 12.98315 (16), 13.42014 (13)

\(\beta\) (°) 106.7648 (11)

\(V\) (Å\(^3\)) 2079.49 (4)

\(Z\) 4

Radiation type Cu K\(\alpha\)

\(\mu\) (mm\(^-1\)) 2.15

Crystal size (mm) 0.19 \(\times\) 0.17 \(\times\) 0.02

Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K

Absorption correction Gaussian

CrysAlis PRO 1.171.39.46 (Rigaku Oxford Diffraction, 2018) Numerical absorption correction based on gaussian integration over a multifaceted crystal model. Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

\(T_{\text{min}}, T_{\text{max}}\) 0.531, 1.000

No. of measured, independent and observed \([I > 2\sigma(I)]\) reflections 48534, 4315, 4165

\(R_{\text{int}}\) 0.029

\((\sin \theta/\lambda)_{\text{max}}\) (Å\(^-1\)) 0.636

Refinement

\(R[F^2 > 2\sigma(F^2)], wR(F^2), S\) 0.042, 0.104, 1.16

No. of reflections 4315

No. of parameters 293

H-atom treatment H-atom parameters constrained

\(\Delta \rho_{\text{max}}, \Delta \rho_{\text{min}}\) (e Å\(^{-3}\)) 0.33, −0.31

Computer programs: CrysAlis PRO 1.171.39.46 (Rigaku OD, 2018), SHELXT (Sheldrick, 2015), SHELXL (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009).
[Trazodonium][thiocyanate]

Crystal data
Chemical formula \([C_{19}H_{23}ClN_5O][CNS]\)

\(M_t\) 430.95

Crystal system, space group Triclinic, \(P1\)

Temperature (K) 160

\(a, b, c\) (Å) 12.1482 (2), 13.1848 (2), 13.82510 (17)

\(\alpha, \beta, \gamma\) (°) 90.2630 (12), 90.2180 (12), 108.0045 (15)

\(V\) (Å³) 2105.89 (6)

\(Z\) 4

Radiation type \(Cu K\alpha\)

\(\mu\) (mm\(^{-1}\)) 2.73

Crystal size (mm) 0.23 × 0.19 × 0.07

Data collection
Diffractometer XtaLAB Synergy, Dualflex, Pilatus 200K

Absorption correction Gaussian

\(T_{\text{min}}, T_{\text{max}}\) 0.532, 1.000

No. of measured, independent and observed \([I > 2\sigma(I)]\) reflections 52525, 8412, 7824

\(R_{\text{int}}\) 0.032

\((\sin \theta/\lambda)_{\text{max}}\) (Å\(^{-1}\)) 0.636

Refinement

\(R(F^2 > 2\sigma(F^2)), wR(F^2), S\) 0.057, 0.136, 1.05

No. of reflections 8412

No. of parameters 723

No. of restraints 45

H-atom treatment H-atom parameters constrained

\(\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}\) (e Å\(^{-3}\)) 0.51, −0.55

Computer programs: CrysAlis PRO 1.171.39.46 (Rigaku OD, 2018), SHELXT (Sheldrick, 2015), SHELXL (Sheldrick, 2015), Olex2 (Dolomanov et al., 2009).
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