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# Systematic synthesis of a 6-component organic-salt alloy of naftopidil, and pentanary, quaternary and ternary multicomponent crystals

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# Systematic Synthesis of Six Component Organic Salt Alloy of Naftopidil and Pentanary, Quaternary and Ternary Multicomponent Crystals

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Rambabu Dandela and Srinu Tothadi equally contributed to the work

**Table S1** Cocrystallization of naftopidil with five aromatic acids.

| Solid form | Naftopidil (mmol) | Coformer (mg, mmol) | Method, Solvent | Solvent of crystallization |
|---|---|---|---|---|
| Hexacomponent (123456) alloy | 1.0 mmol | Each coformer 0.2 mmol | Mortar-pestle grinding, $CH_3OH$ (2-3 drops) | $CH_3OH$ (30-40 mg of crystalline material was taken in 5 mL) |
| Pentanary (13456) alloy<br>Pentanary (12456) alloy<br>Pentanary (12356) alloy<br>Pentanary (12346) alloy Pentanary (12345) alloy | 1.0 mmol | Each coformer 0.25 mmol | Mortar-pestle grinding, $CH_3OH$ (2-3 drops) | $CH_3OH$ (30-40 mg of crystalline material was taken in 5 mL) |
| Quaternary (1234) alloy<br>Quaternary (1235) alloy<br>Quaternary (1236) alloy<br>Quaternary (1245) alloy<br>Quaternary (1246) alloy<br>Quaternary (1256) alloy<br>Quaternary (1345) alloy<br>Quaternary (1346) alloy<br>Quaternary (1356) alloy<br>Quaternary (1456) alloy | 1.0 mmol | Each coformer 0.333 mmol | Mortar-pestle grinding, $CH_3OH$ (2-3 drops) | $CH_3OH$ (30-40 mg of crystalline material was taken in 5 mL) |
| Ternary (123) alloy<br>Ternary (124) alloy<br>Ternary (125) alloy<br>Ternary (126) alloy<br>Ternary(134) alloy<br>Ternary (135) alloy<br>Ternary (136) alloy<br>Ternary (145) alloy<br>Ternary (146) alloy | 1.0 mmol | Each coformer 0.5 mmol | Mortar-pestle grinding, $CH_3OH$ (2-3 drops) | (30-40 mg of crystalline material was taken in 5 mL) |

| | | | | |
|---|---|---|---|---|
| Ternary (156) alloy | | | | |
| Binary salts (12)<br>Binary salts (13)<br>Binary salts (14)<br>Binary salts (15)<br>Binary salts (16) | 1.0 mmol | Each coformer 1.0 mmol | Mortar-pestle grinding, $CH_3OH$ (2-3 drops) | (30-40 mg of crystalline material was taken in 5 mL) |
| Naftopidil-2,4,6-trihydroxybenzoic acid salt | 1.0 mmol | 1.0 mmol | Mortar-pestle grinding, $CH_3OH$ (2-3 drops) | (30-40 mg of crystalline material was taken in 5 mL) |

**Table S2** Crystallographic data of salts and salt alloys of Naftopidil (1).

| | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|
| Empirical Formula | $C_{24}H_{29}N_2O_3 \cdot C_7H_5O_2$ | $C_{24}H_{29}N_2O_3 \cdot C_7H_5O_3$ | $C_{24}H_{29}N_2O_3 \cdot C_7H_5O_4$ | $C_{24}H_{29}N_2O_3 \cdot C_7H_5O_4$ | $C_{24}H_{29}N_2O_3 \cdot C_{24}H_{28}N_2O_3 \cdot 2(C_7H_5O_4)$ |
| Formula weight | 514.60 | 530.60 | 546.60 | 546.60 | 1092.19 |
| Crystal System | Monoclinic | Monoclinic | Monoclinic | Monoclinic | Monoclinic |
| Space Group | $P2_1/c$ | $P2_1/c$ | $P2_1/c$ | $P2_1/c$ | $P2_1$ |
| T (K) | 293(2) | 293(2) | 293(2) | 100(2) | 293(2) |
| $a$ (Å) | 11.0695 (2) | 11.2350 (5) | 11.3258 (4) | 10.843 (4) | 11.4733 (3) |
| $b$ (Å) | 17.7360 (3) | 17.6516 (6) | 17.8349 (7) | 17.862 (6) | 17.6286 (5) |
| $c$ (Å) | 13.5179 (3) | 13.4798 (6) | 13.4077 (7) | 13.913 (6) | 13.6530 (4) |
| $\alpha$ (°) | 90 | 90 | 90 | 90 | 90 |
| $\beta$ (°) | 97.3794 (19) | 96.269 (4) | 95.800 (4) | 91.715 (12) | 93.290 (2) |
| $\gamma$ (°) | 90 | 90 | 90 | 90 | 90 |
| $V$ (Å$^3$) | 2632.00 (9) | 2657.27 (18) | 2694.4 (2) | 2693.4 (17) | 2756.89 (13) |
| $D_{calc}$ (g cm$^{-3}$) | 1.299 | 1.326 | 1.347 | 1.348 | 1.316 |
| Z | 4 | 4 | 4 | 4 | 2 |
| $F$(000) | 1096 | 1128 | 1160 | 1160 | 1158 |
| Residual electron density | 0.44, -0.29 | 0.32, -0.17 | 0.41, -0.29 | 0.81, -0.35 | 0.21, -0.19 |

| $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | | | | | |
|---|---|---|---|---|---|
| h range | -13→ 13 | -13 → 13 | -13 → 13 | -14→ 14 | -13→ 11 |
| k range | -21 → 21 | -20 → 13 | -15 → 21 | -24 → 24 | -19 → 20 |
| l range | -16 → 16 | -14 → 16 | -14 → 15 | -18 → 18 | -14 → 16 |
| measured reflections, | 24778 | 11084 | 11635 | 66674 | 11695 |
| independent reflections, | 4626 | 4667 | 4734 | 6923 | 8293 |
| Reflections with $I > 2\sigma(I)$ | 3831 | 3368 | 3717 | 5449 | 6342 |
| $R_{int}$ | 0.042 | 0.040 | 0.041 | 0.068 | 0.049 |
| $R_1$ [$I > 2\sigma(I)$] | 0.057 | 0.064 | 0.088 | 0.054 | 0.061 |
| $wR_2$ (all) | 0.153 | 0.170 | 0.256 | 0.142 | 0.170 |
| Goodness of fit | 1.13 | 1.10 | 1.15 | 1.07 | 1.05 |
| X-ray diffractometer | Rigaku OD | Rigaku OD | Rigaku OD | BRUKER APEX | Rigaku OD |
| CCDC No. | 1817128 | 1817160 | 1817125 | 1817161 | 1817170 |

Naftopidil ternary alloys: 125 and 156 were characterized by PXRD/NMR and are not listed here.

| | 123 | 124 | 126 | 134 | 135 |
|---|---|---|---|---|---|
| Empirical Formula | $C_7H_5O_{2.9}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_{5.42}O_{3.42}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_{4.84}O_{2.4}\cdot C_7H_5O_{3.32}\cdot 2(C_{24}H_{29}N_2O_3)$ | $C_7H_5O_{3.51}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_{5.55}O_{3.14}\cdot C_{24}H_{29}N_2O_3$ |
| Formula weight | 529.00 | 537.74 | 1056.56 | 538.76 | 533.39 |
| Crystal System | Monoclinic | Monoclinic | Monoclinic | Monoclinic | Monoclinic |
| Space | $P2_1/c$ | $P2_1/c$ | $P2_1$ | $P2_1/c$ | $P2_1/c$ |

| Group | | | | | |
|---|---|---|---|---|---|
| T (K) | 100(2) | 100(2) | 100(2) | 100(2) | 100(2) |
| *a* (Å) | 11.197 (2) | 11.282 (4) | 11.346 (2) | 11.253 (4) | 11.176 (4) |
| *b* (Å) | 17.627 (4) | 17.856 (7) | 17.508 (4) | 17.660 (6) | 17.608 (5) |
| *c* (Å) | 13.199 (3) | 13.460 (5) | 13.400 (3) | 13.247 (4) | 13.305 (4) |
| $\alpha$ (°) | 90 | 90 | 90 | 90 | 90 |
| $\beta$ (°) | 96.347 (6) | 96.060 (12) | 98.15 (3) | 95.787 (11) | 95.426 (10) |
| $\gamma$ (°) | 90 | 90 | 90 | 90 | 90 |
| $V$ (Å$^3$) | 2589.0 (9) | 2696.3 (17) | 2635.0 (10) | 2619.1 (15) | 2606.6 (14) |
| $D_{calc}$(g cm$^{-3}$) | 1.357 | 1.325 | 1.332 | 1.366 | 1.359 |
| Z | 4 | 4 | 2 | 4 | 4 |
| $F$(000) | 1125 | 1143 | 1123 | 1144 | 1135 |
| Residual electron density $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.44, -0.36 | 0.32, -0.33 | 0.29, -0.25 | 0.73, -0.36 | 0.35, -0.65 |
| h range | -15→ 15 | -15 → 15 | -16 → 16 | -17→ 16 | -15→ 14 |
| k range | -24 → 24 | -23 → 23 | -24 → 24 | -27 → 27 | -24 → 25 |
| l range | -18 → 18 | -17 → 17 | -19 → 19 | -18 → 20 | -17 → 18 |
| measured reflections, | 53638 | 88550 | 65036 | 57701 | 39100 |
| independent reflections, | 7114 | 6635 | 15959 | 9884 | 7888 |
| Reflections with $I > 2\sigma(I)$ | 6706 | 5411 | 10798 | 8381 | 6366 |
| $R_{int}$ | 0.025 | 0.056 | 0.071 | 0.039 | 0.047 |
| $R_1$ [$I > 2\sigma(I)$ | 0.041 | 0.070 | 0.083 | 0.052 | 0.062 |

| ] | | | | | |
|---|---|---|---|---|---|
| $wR_2$ (all) | 0.122 | 0.231 | 0.164 | 0.154 | 0.140 |
| Goodness of fit | 1.10 | 1.64 | 1.06 | 1.10 | 1.12 |
| X-ray diffractometer | BRUKER APEX | Rigaku OD | BRUKER APEX | BRUKER APEX | BRUKER APEX |
| CCDC No. | 1817165 | 1817164 | 1817158 | 1817169 | 1817149 |

Naftopidil ternary alloys

| | 136 | 145 | 146 |
|---|---|---|---|
| Empirical Formula | $C_7H_5O_{3.47}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_5O_4\cdot C_{24}H_{29}N_2O_3$ | $C_7H_4O_4\cdot C_{24}H_{29}N_2O_3$ |
| Formula weight | 538.12 | 546.60 | 545.59 |
| Crystal System | Monoclinic | Monoclinic | Monoclinic |
| Space Group | $P2_1/c$ | $P2_1/c$ | $P2_1/c$ |
| T (K) | 100(2) | 100(2) | 100(2) |
| *a* (Å) | 11.487 (7) | 11.195 (15) | 11.475 (6) |
| *b* (Å) | 17.514 (10) | 17.69 (3) | 17.669 (9) |
| *c* (Å) | 13.310 (9) | 13.449 (18) | 13.248 (7) |
| $\alpha$ (°) | 90 | 90 | 90 |
| $\beta$ (°) | 95.95 (3) | 94.40 (5) | 94.87 (2) |
| $\gamma$ (°) | 90 | 90 | 90 |
| *V* (Å$^3$) | 2663 (3) | 2655 (7) | 2676 (2) |
| $D_{calc}$(g cm$^{-3}$) | 1.342 | 1.367 | 1.354 |
| Z | 4 | 4 | 4 |
| *F*(000) | 1143 | 1160 | 1156 |
| Residual electron | 0.25, -0.34 | 0.51, -0.38 | 0.58, -0.49 |

| | | | |
|---|---|---|---|
| density $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$) | | | |
| h range | -15→ 15 | -15 → 15 | -16 → 16 |
| k range | -23 → 23 | -25 → 25 | -25 → 25 |
| l range | -17 → 17 | -19 → 19 | -18 →18 |
| measured reflections, | 76404 | 63575 | 88884 |
| independent reflections, | 6567 | 8027 | 8099 |
| Reflections with $I > 2\sigma(I)$ | 4598 | 6474 | 6717 |
| $R_{int}$ | 0.166 | 0.060 | 0.073 |
| $R_1$ [$I > 2\sigma(I)$] | 0.104 | 0.099 | 0.111 |
| $wR_2$ (all) | 0.222 | 0.219 | 0.251 |
| Goodness of fit | 1.12 | 1.18 | 1.21 |
| X-ray diffractometer | BRUKER APEX | BRUKER APEX | BRUKER APEX |
| CCDC No. | 1817150 | 1817129 | 1817146 |

Naftopidil quaternary alloy: 1256 and 1345 were characterized by PXRD/NMR and are not listed here.

| | 1234 | 1235 | 1236 | 1245 |
|---|---|---|---|---|
| Empirical Formula | $C_7H_{5.12}O_{3.33}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_5O_{3.17}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_5O_{3.27}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_5O_{3.46}\cdot C_{24}H_{29}N_2O_3$ |
| Formula weight | 536.03 | 533.35 | 534.95 | 537.99 |
| Crystal System | Monoclinic | Monoclinic | Monoclinic | Monoclinic |
| Space Group | $P2_1/c$ | $P2_1/c$ | $P2_1/c$ | $P2_1/c$ |
| T (K) | 297(2) | 293(2) | 293(2) | 100(2) |

| | | | | |
|---|---|---|---|---|
| *a* (Å) | 11.296 (2) | 11.20 (2) | 11.369 (4) | 11.102 (5) |
| *b* (Å) | 17.807 (4) | 17.71 (3) | 17.660 (6) | 17.701 (9) |
| *c* (Å) | 13.459 (3) | 13.40 (3) | 13.539 (5) | 13.437 (6) |
| $\alpha$ (°) | 90 | 90 | 90 | 90 |
| $\beta$ (°) | 96.00 (3) | 94.85 (7) | 95.632 (17) | 94.667 (18) |
| $\gamma$ (°) | 90 | 90 | 90 | 90 |
| *V* (Å$^3$) | 2692.6 (10) | 2648 (9) | 2705.1 (16) | 2632 (2) |
| $D_{calc}$(g cm$^{-3}$) | 1.322 | 1.338 | 1.313 | 1.358 |
| Z | 4 | 4 | 4 | 4 |
| *F*(000) | 1139 | 1134 | 1137 | 1143 |
| Residual electron density $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.25, -0.30 | 0.68, -0.72 | 0.30, -0.25 | 0.56, -0.61 |
| h range | -14→ 14 | -15 → 15 | -16 → 16 | -14→ 14 |
| k range | -22→ 22 | -24 → 25 | -25→ 24 | -23 → 23 |
| l range | -16 → 16 | -19 → 19 | -19 → 19 | -17 → 17 |
| measured reflections, | 62700 | 67030 | 90604 | 61552 |
| independent reflections, | 5404 | 7947 | 8175 | 6497 |
| Reflections with $\underline{I > 2\sigma(I)}$ | 4670 | 5620 | 5373 | 5857 |
| $R_{int}$ | 0.039 | 0.142 | 0.050 | 0.048 |
| $R_1$ [$I > 2\sigma(I)$] | 0.045 | 0.106 | 0.089 | 0.099 |
| $wR_2$ (all) | 0.139 | 0.208 | 0.192 | 0.256 |
| Goodness of fit | 1.08 | 1.08 | 1.07 | 1.00 |
| X-ray diffractometer | BRUKER APEX | BRUKER APEX | BRUKER APEX | BRUKER APEX |

| CCDC No. | 1817159 | 1817130 | 1817147 | 1817148 |
|---|---|---|---|---|

Naftopidil quaternary alloy:

| | 1246 | 1346 | 1356 | 1456 |
|---|---|---|---|---|
| Empirical Formula | $C_7H_5O_{3.4}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_5O_{3.81}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_{4.91}O_{3.51}\cdot C_7H_6O_{3.52}\cdot 2(C_{24}H_{29}N_2O_3)$ | $C_7H_5O_4\cdot C_{24}H_{29}N_2O_3$ |
| Formula weight | 537.03 | 543.56 | 1078.60 | 546.60 |
| Crystal System | Monoclinic | Monoclinic | Monoclinic | Monoclinic |
| Space Group | $P2_1/c$ | $P2_1/c$ | $P2_1$ | $P2_1/c$ |
| T (K) | 293(2) | 293(2) | 100(2) | 100(2) |
| *a* (Å) | 11.410 (4) | 11.405 | 11.246 (10) | 11.319 (2) |
| *b* (Å) | 17.772 (6) | 17.746 | 17.607 (16) | 17.672 (4) |
| *c* (Å) | 13.550 (5) | 13.511 | 13.523 (13) | 13.391 (3) |
| $\alpha$ (°) | 90 | 90 | 90 | 90 |
| $\beta$ (°) | 95.891 (19) | 95.49 | 94.19 (4) | 93.90 (3) |
| $\gamma$ (°) | 90 | 90 | 90 | 90 |
| *V* (Å$^3$) | 2733.1 (17) | 2722.0 | 2670 (4) | 2672.4 (10) |
| $D_{calc}$(g cm$^{-3}$) | 1.305 | 1.326 | 1.341 | 1.359 |
| Z | 4 | 4 | 2 | 4 |
| *F*(000) | 1141 | 1154 | 1123 | 1160 |
| Residual electron density $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.26, -0.21 | 0.28, -0.32 | 0.54, -0.29 | 0.28, -0.33 |
| h range | -14→ 14 | -16 → 16 | -16 → 16 | -13→ 14 |
| k range | -21 → 22 | -25 → 25 | -25 → 25 | -22 → 22 |
| l range | -16 → 16 | -19 → 19 | -18 → 19 | -16 → 16 |
| measured | 46089 | 69144 | 63374 | 48278 |

| reflections, | | | | |
|---|---|---|---|---|
| independent reflections, | 5487 | 8182 | 16100 | 5387 |
| Reflections with $I > 2\sigma(I)$ | 4300 | 5170 | 8744 | 4822 |
| $R_{int}$ | 0.056 | 0.057 | 0.112 | 0.040 |
| $R_1$ [$I > 2\sigma(I)$] | 0.075 | 0.081 | 0.097 | 0.072 |
| $wR_2$ (all) | 0.165 | 0.225 | 0.198 | 0.154 |
| Goodness of fit | 1.07 | 1.10 | 1.04 | 1.19 |
| X-ray diffractometer | BRUKER APEX | BRUKER APEX | BRUKER APEX | BRUKER APEX |
| CCDC No. | 1817151 | 1817162 | 1817168 | 1817167 |

Naftopidil pentanary alloy: 13456 and 12456 were characterized by PXRD/NMR and are not listed here.

| | 12345 | 12346 | 12356 |
|---|---|---|---|
| Empirical Formula | $C_{7.1}H_{5.33}O_{3.35}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_5O_{3.69}\cdot C_{24}H_{29}N_2O_3$ | $C_7H_{4.8}O_{3.31}\cdot C_7H_5O_{3.32}\cdot 2(C_{24}H_{29}N_2O_3)$ |
| Formula weight | 537.73 | 541.66 | 1071.08 |
| Crystal System | Monoclinic | Monoclinic | Monoclinic |
| Space Group | $P2_1/c$ | $P2_1/c$ | $P2_1$ |
| T (K) | 100(2) | 100(2) | 100(2) |
| $a$ (Å) | 11.153 (4) | 11.405 (5) | 11.237 (5) |
| $b$ (Å) | 17.701 (5) | 17.591 (8) | 17.571 (6) |
| $c$ (Å) | 13.336 (4) | 13.269 (6) | 13.374 (6) |
| $\alpha$ (°) | 90 | 90 | 90 |
| $\beta$ (°) | 95.232 (17) | 95.526 (15) | 94.584 (16) |

| | | | |
|---|---|---|---|
| $\gamma$ (°) | 90 | 90 | 90 |
| $V$ (Å$^3$) | 2621.8 (13) | 2650 (2) | 2632.4 (18) |
| $D_{calc}$(g cm$^{-3}$) | 1.362 | 1.358 | 1.351 |
| Z | 4 | 4 | 2 |
| $F$(000) | 1143 | 1150 | 1138 |
| Residual electron density $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.42, -0.50 | 0.47, -0.49 | 0.52, -0.48 |
| h range | -15→ 15 | -16 → 16 | -15 → 15 |
| k range | -25→ 25 | -25 → 25 | -24→ 24 |
| l range | -18 → 18 | -16 → 18 | -18 → 18 |
| measured reflections, | 63397 | 86570 | 80672 |
| independent reflections, | 7929 | 8037 | 14648 |
| Reflections with $I$> 2σ($I$) | 6429 | 6291 | 11616 |
| $R_{int}$ | 0.055 | 0.064 | 0.046 |
| $R_1$ [$I$ >2σ($I$)] | 0.064 | 0.084 | 0.053 |
| $wR_2$ (all) | 0.173 | 0.178 | 0.153 |
| Goodness of fit | 1.17 | 1.07 | 1.07 |
| X-ray diffractometer | BRUKER APEX | BRUKER APEX | BRUKER APEX |
| CCDC No. | 1817166 | 1817126 | 1817127 |

Naftopidil hexanary alloy:

| | 123456 |
|---|---|

| | |
|---|---|
| Empirical Formula | $C_7H_5O_{3.49}\cdot C_{24}H_{29}N_2O_3$ |
| Formula weight | 538.44 |
| Crystal System | Monoclinic |
| Space Group | $P2_1/c$ |
| T (K) | 100(2) |
| *a* (Å) | 11.279 (5) |
| *b* (Å) | 17.633 (7) |
| *c* (Å) | 13.377 (6) |
| $\alpha$ (°) | 90 |
| $\beta$ (°) | 94.51 (2) |
| $\gamma$ (°) | 90 |
| *V* (Å$^3$) | 2652.2 (18) |
| $D_{calc}$(g cm$^{-3}$) | 1.348 |
| Z | 4 |
| *F*(000) | 1144 |
| Residual electron density $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.28, -0.24 |
| h range | -14→ 14 |
| k range | -21→ 21 |
| l range | -16 → 16 |
| measured reflections, | 31190 |
| independent reflections, | 5299 |
| Reflections with $\underline{I> 2\sigma(I)}$ | 4387 |
| $R_{int}$ | 0.054 |
| $R_1$ [$I >2\sigma(I)$] | 0.072 |
| $wR_2$ (all) | 0.162 |

| | |
|---|---|
| Goodness of fit | 1.19 |
| X-ray diffractometer | BRUKER APEX |
| CCDC No. | 1817163 |

Naftopidil-2,4,6-trihydroxybenzoic acid salt:

| | Naftopidil-2,4,6-trihydroxybenzoic acid salt |
|---|---|
| Empirical Formula | $C_7H_5O_5 \cdot C_{24}H_{29}N_2O_3$ |
| Formula weight | 562.60 |
| Crystal System | Monoclinic |
| Space Group | $P2_1/c$ |
| T (K) | 100(2) |
| *a* (Å) | 11.074 (2) |
| *b* (Å) | 17.895 (3) |
| *c* (Å) | 14.000 (2) |
| $\alpha$ (°) | 90 |
| $\beta$ (°) | 92.85 (8) |
| $\gamma$ (°) | 90 |
| *V* (Å$^3$) | 2770.9 (8) |
| $D_{calc}$(g cm$^{-3}$) | 1.349 |
| Z | 4 |
| *F*(000) | 1192 |
| Residual electron density $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å$^{-3}$) | 0.41, -0.48 |
| h range | -15→ 15 |
| k range | -25→ 25 |

| | |
|---|---|
| l range | -19 → 19 |
| measured reflections, | 14029 |
| independent reflections, | 8405 |
| Reflections with $I > 2\sigma(I)$ | 6782 |
| $R_{int}$ | 0.066 |
| $R_1$ [$I > 2\sigma(I)$] | 0.046 |
| $wR_2$ (all) | 0.142 |
| Goodness of fit | 1.11 |
| X-ray diffractometer | BRUKER APEX |
| CCDC No. | 1840048 |

**Table S3** s.o.f. derived from X-ray crystal structure refinement.

| | | **1** | **2** | **3** | **4** | **5** | **6** |
|---|---|---|---|---|---|---|---|
| 1 | Hexacomponent (123456) alloy | 1.00 | 0.12 | 0.27 | 0.27 | 0.14 | 0.20 |
| 2 | Pentanary (12346) alloy | 1.00 | 0.8 | 0.15 | 0.39 | | 0.38 |
| 3 | Pentanary (12345) alloy | 1.00 | 0.23 | 0.19 | 0.35 | 0.23 | |
| 4 | Pentanary (12356) alloy | 1.00 | 0.095 | 0.495 | | 0.20 | 0.21 |
| 5 | Quaternary (1234) alloy | 1.00 | 0.12 | 0.43 | 0.45 | | |
| 6 | Quaternary (1236) alloy | 1.00 | 0.10 | 0.53 | | | 0.37 |
| 7 | Quaternary (1246) alloy | 1.00 | 0.16 | | 0.42 | | 0.42 |
| 8 | Quaternary (1346) alloy | 1.00 | | 0.19 | 0.43 | | 0.38 |
| 9 | Quaternary (1456) alloy | 1.00 | | | 0.46 | 0.20 | 0.34 |
| 10 | Quaternary (1235) alloy | 1.00 | 0.13 | 0.57 | | 0.30 | |
| 11 | Quaternary (1245) alloy | 1.00 | 0.27 | | 0.37 | 0.36 | |
| 12 | Quaternary 1356 alloy | 1.00 | | 0.485 | | 0.26 | 0.255 |
| 13 | Ternary (123) alloy | 1.00 | 0.10 | 0.90 | | | |
| 14 | Ternary (124) alloy | 1.00 | 0.29 | | 0.71 | | |
| 15 | Ternary (126) alloy | 1.00 | 0.57 | | | | 0.43 |
| 16 | Ternary (134) alloy | 1.00 | | 0.49 | 0.51 | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 17 | Ternary (135) alloy | 1.00 | | 0.86 | | 0.14 | |
| 18 | Ternary (136) alloy | 1.00 | | 0.53 | | | 0.47 |
| 19 | Ternary (145) alloy | 1.00 | | 0.65 | 0.35 | | |
| 20 | Ternary (146) alloy | 1.00 | | | 0.53 | | 0.47 |

**Table S4** Refcodes of $R_2^2$ (9) motif.

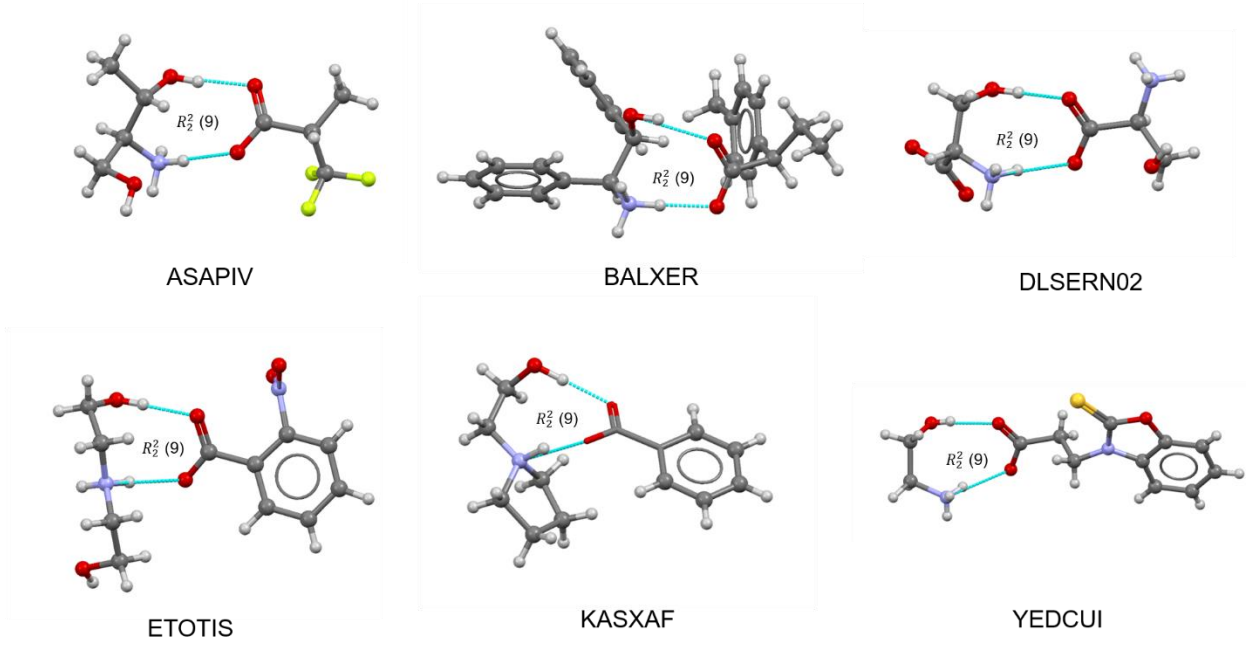
CSD Refocodes containing the O–H···O + N–H···O synthon

| **Refcodes** | **Refcodes** | **Refcodes** | **Refcodes** |
|---|---|---|---|
| LEBSIX | HMGLUT | OJUQER | VABSAU |
| TEGJOH | HUZQIE | ORUWUU | VIMNOL10 |
| YEDCUI | ICIMOX | ORUXAB | WANKIF |
| ASAPIV | IHUFOG | PCACAP | WANKOL |
| AXOVIU | INEDOV | PEPFIA | WAXZAY |
| AYEPIF | IPUMUC | PETQAH | WAXZEC |
| AZABEI | IVULOB | PUKRET | WELYUH |
| BALXER | JAPWIJ | QAKQIE | WIRREU |
| BURXIX | JUHLUT10 | QAWSUC | WIRRIY |
| CABPOK | JUHLUT12 | QORROE | WIRROE |
| CAGXEN | KAPZOQ | RONSAQ | WOHRUH |
| CAZGOA | KAQBAF | RUVNEC | XUHZAD |
| CIJMEO | KASWEI | SARBUI | XUZBUQ01 |
| CUDCAG | KASXAF | SEMWAI | YAWLIU |
| CUGPIF | KASXIN | SEQGAX01 | YENGOP |
| CUYBIJ | KEMXIJ | SERGLY | YENGOP01 |
| DETHIU | KEZFIG | SEZLOZ | YIKLUB |
| DHPROL10 | KEZFOM | SOQQUK | YIVCIQ |
| DINYEE10 | KIXBID | SUWBER | YUCSOE |
| DLSERN02 | KIYHOP | TEYSIB | YUFMAN |
| DOTRAF | KULMOU | TEYSOH | ZASKIQ |
| DUMJUS | KUZVOR | TEYSUN | ZAVMER |
| ETOTIS | LEFHIN | TYRXEA10 | ZIXTEF |
| FOVMUZ | LEKRIC | UBUCIG | ZUTRIR |
| GADXUH | LEWQOV | UDUWEX | ZUYJOU |
| GADYUI | LEZMIM | UGEYUA | |
| GEPNEW | LIGZUX | ULICAV01 | |
| GICHIK | LIHBAG | UMIYUM | |
| GICHOQ | LIHBIO | UPUVOR | |
| GIDVEU | LIHGAL | UPUVUX | |
| GISKAW | LSERMH10 | UPUWAE | |
| HEVJAT | MAKXED | UPUWEI | |
| HEZXAM | MICLAM | URAWER | |

| | | | |
|---|---|---|---|
| HISMAZ<br>HIVYER | NAJFIO<br>NIDSOK | UREWAQ<br>USOCIP | |

CSD version 5.38 updates (Nov 2016). Filters: 3D coordinates determined Only Organics
Number of Hits: 130 Hits shows $R_2^2$ (9) motif in CSD. Duplicate occurrences of the same motif in the same crystal structures (Refcodes) were removed manually and best unique structure is reported.

Following crystal structure of salts show $R_2^2$ (9) motif and their CSD refcodes



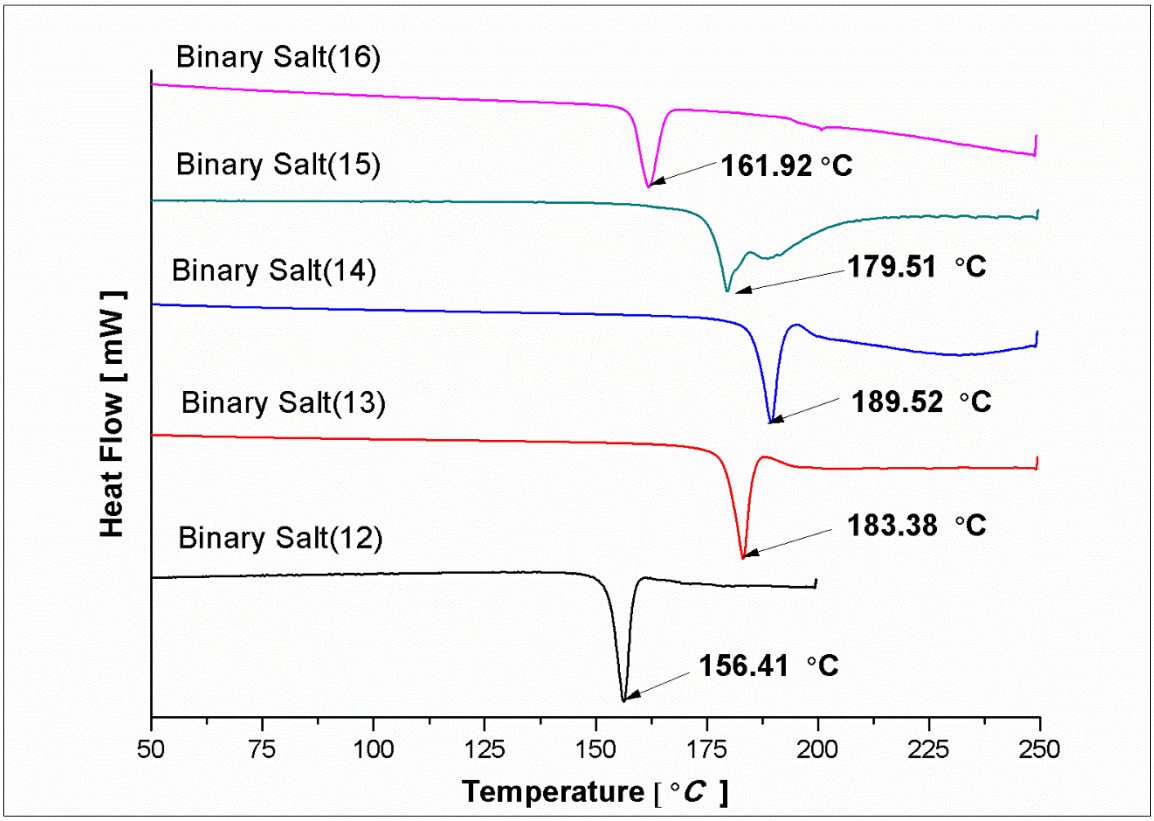



**Figure S1** DSC thermogram of binary salts.

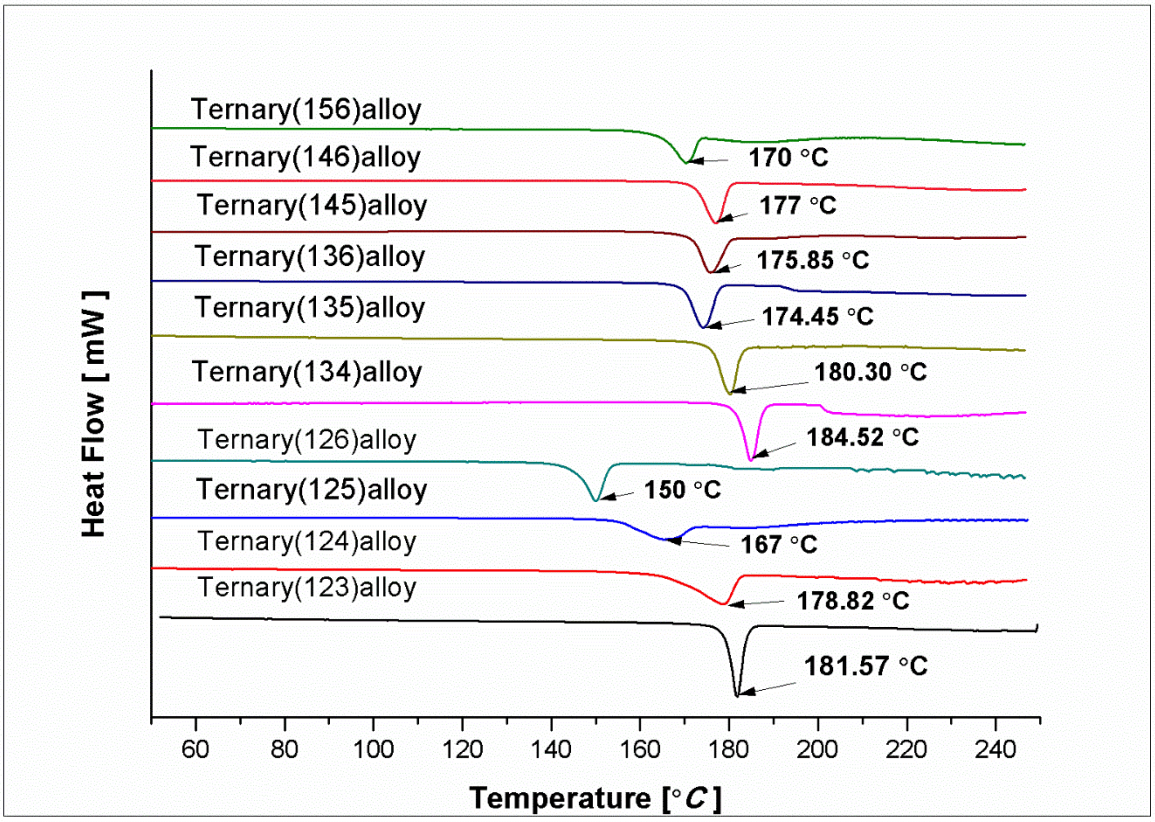



**Figure S2** DSC thermogram of ternary alloy.

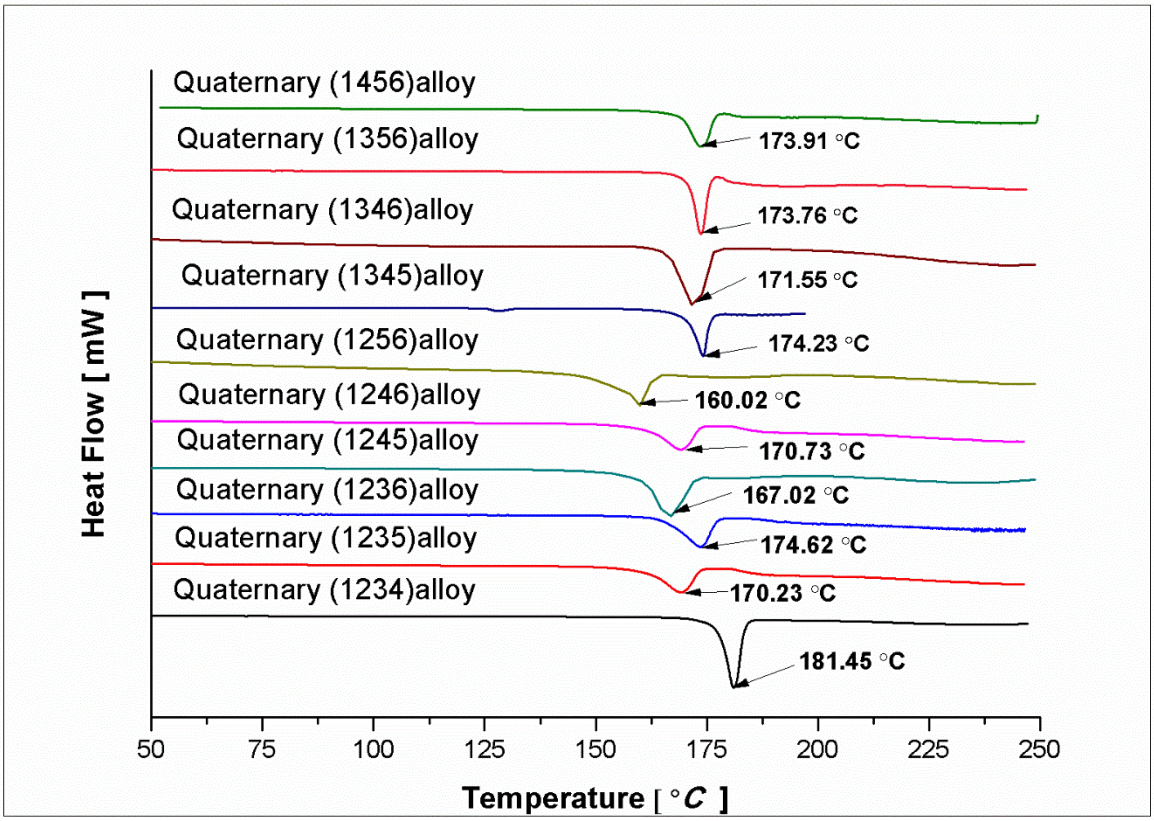



**Figure S3** DSC thermogram of quaternary alloy.

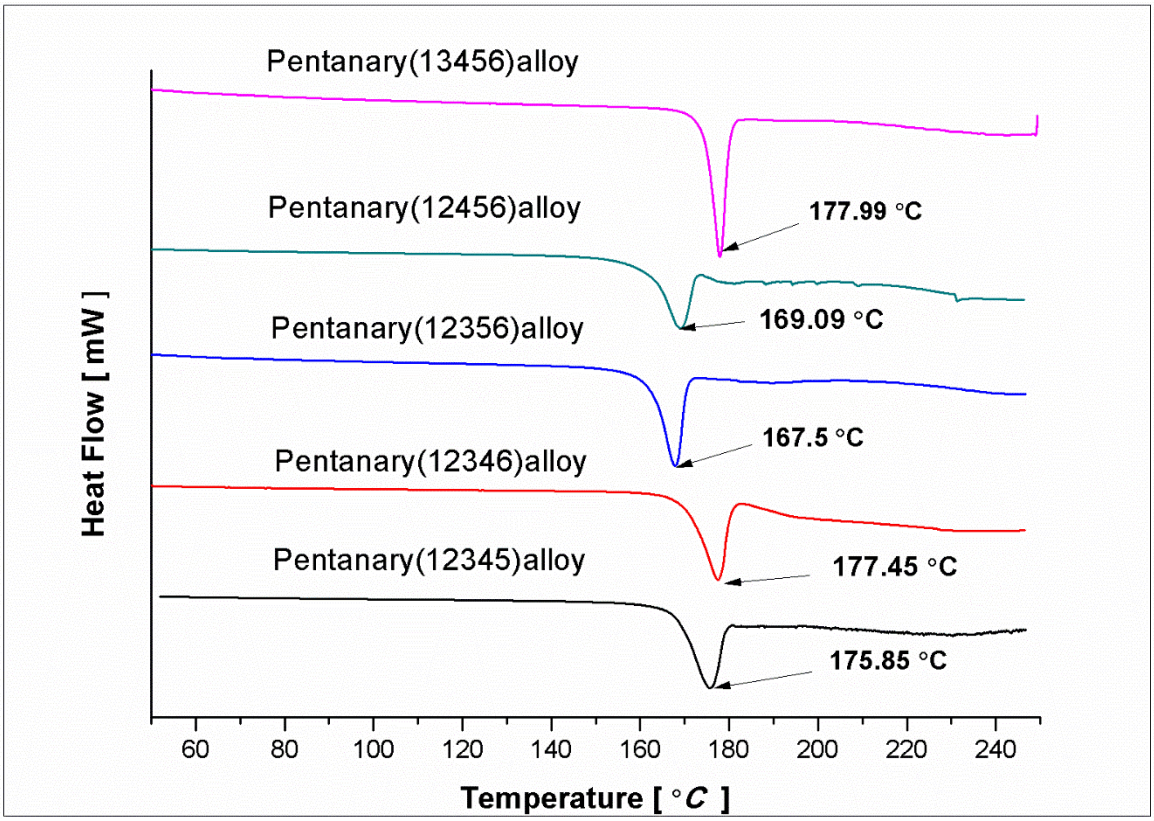



**Figure S4** DSC thermogram of Pentanary alloy.

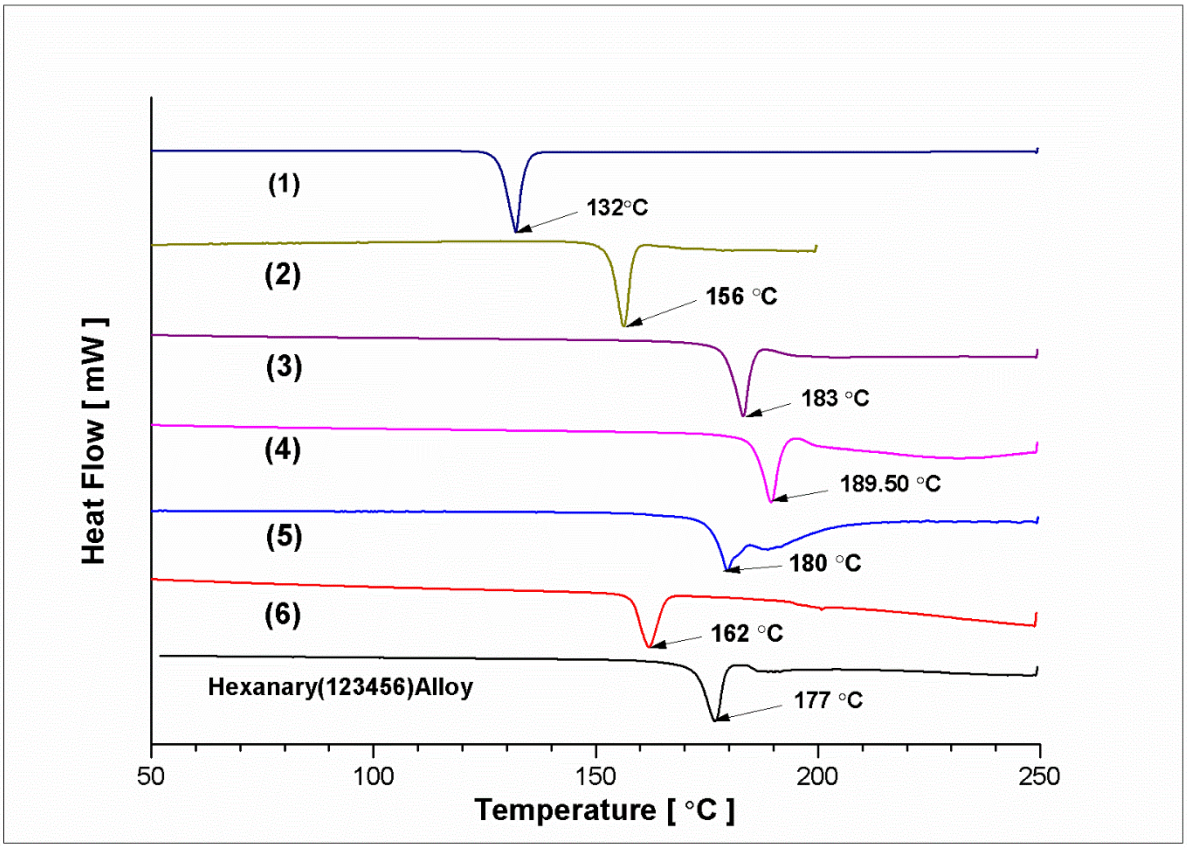



**Figure S5a** DSC thermogram of hexanary alloy is compared with coformers (aromatic acids).

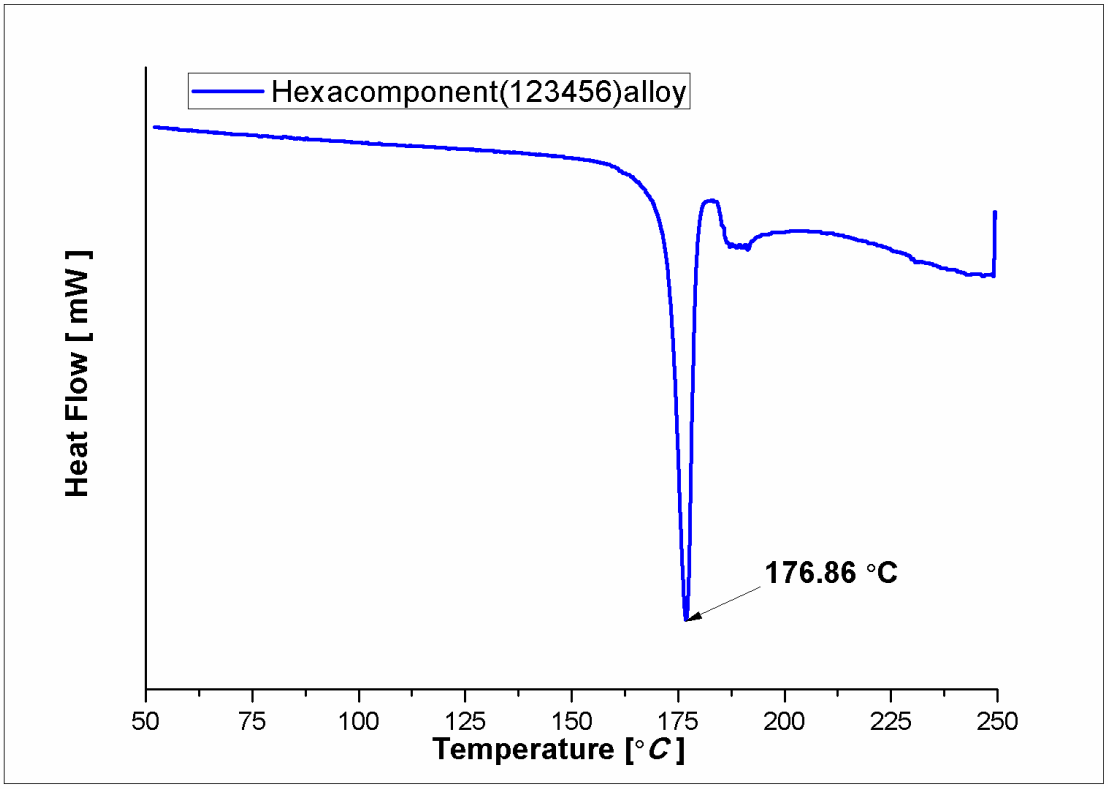
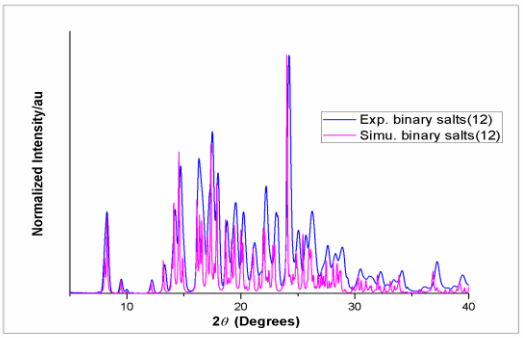
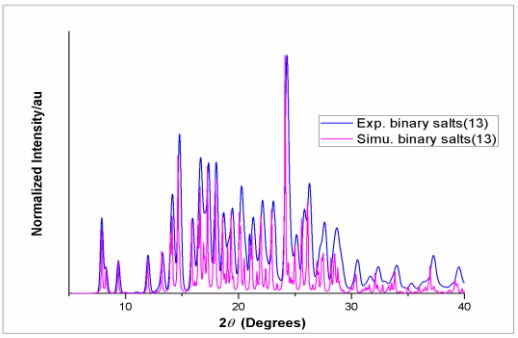



**Figure S5b** DSC thermogram of Hexacomponent alloy.



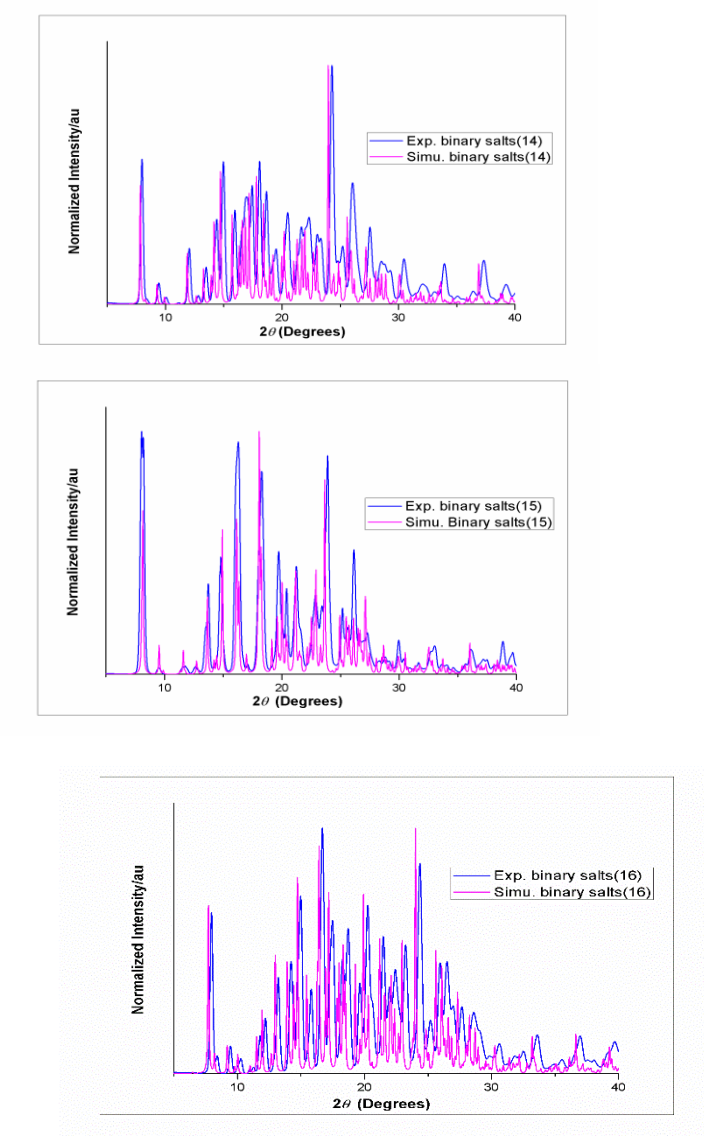



**Figure S6a** PXRD patterns of Binary salts: Blue indicates experimental PXRD pattern and pink indicates the calculated pattern based on the single crystal X-ray diffraction data.

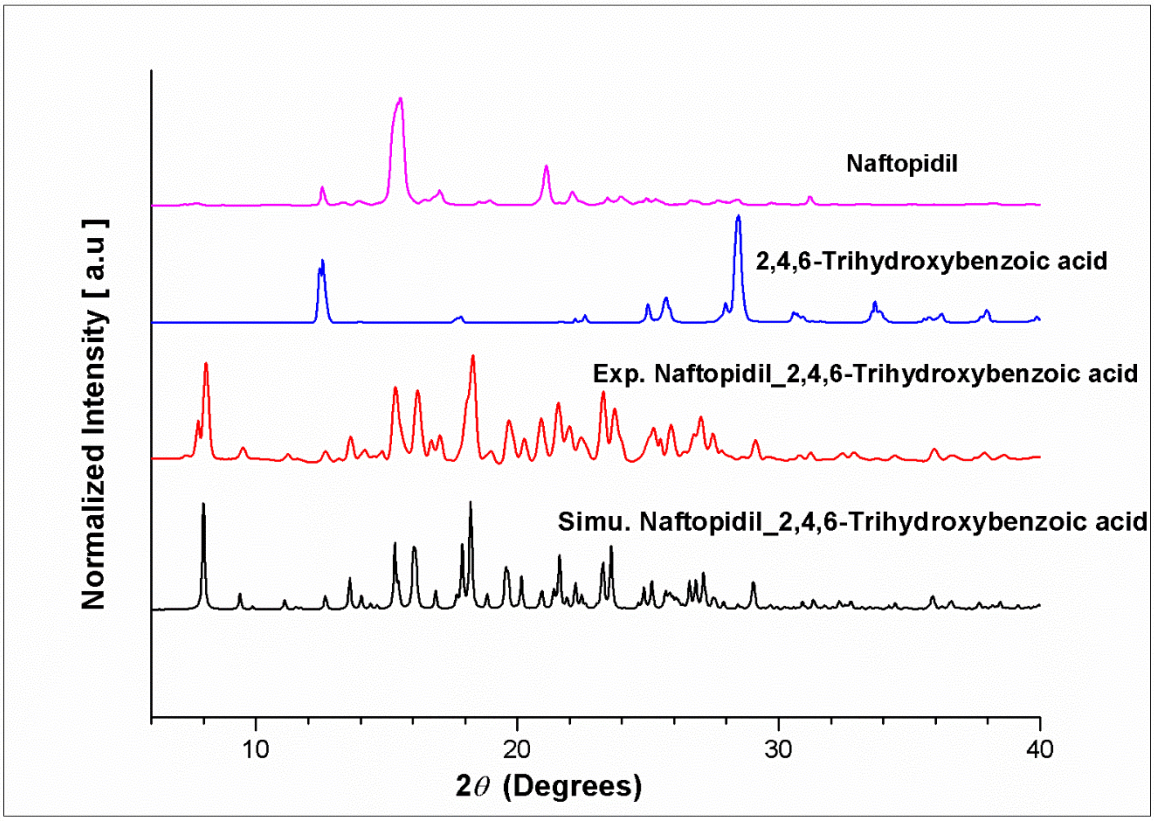
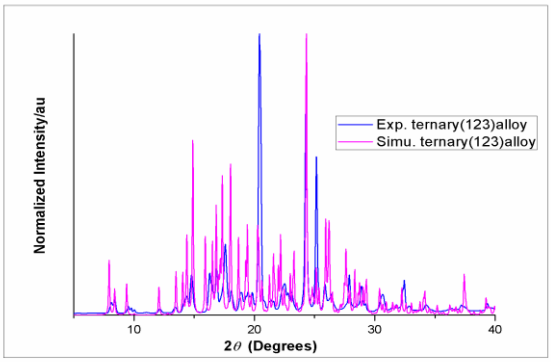
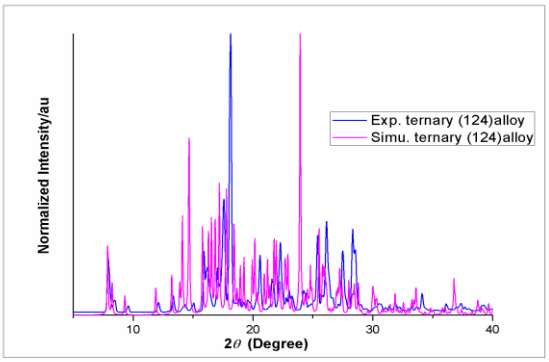
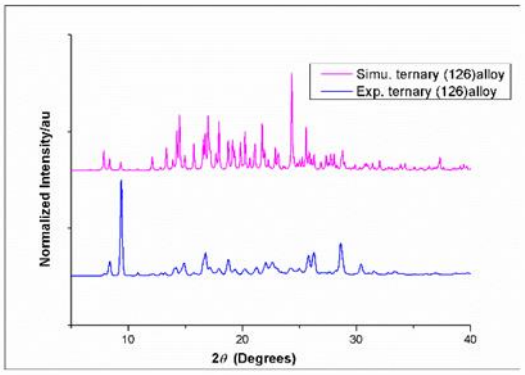
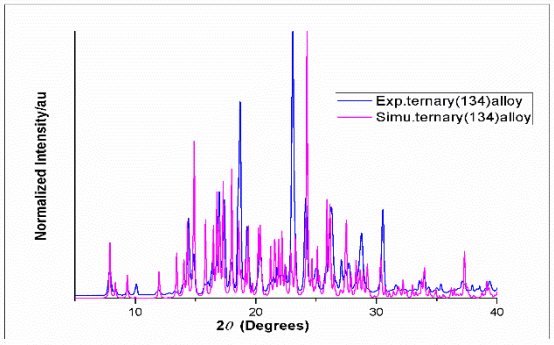


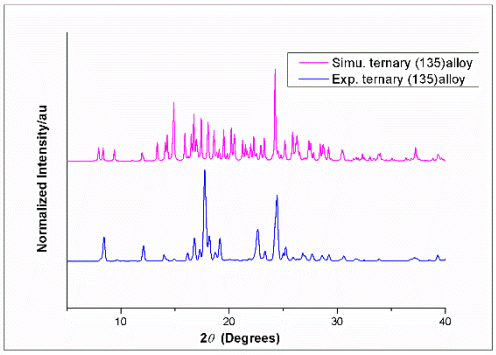

**Figure S6b** PXRD patterns of Binary salt of Naftopidil and 2,4,6-trihydroxybenzoic acid.

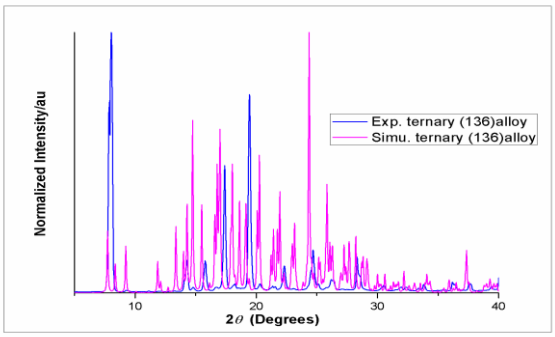

Normalized Intensity/au
Exp. ternary(123)alloy
Simu. ternary(123)alloy
10
20
30
40
2θ (Degrees)

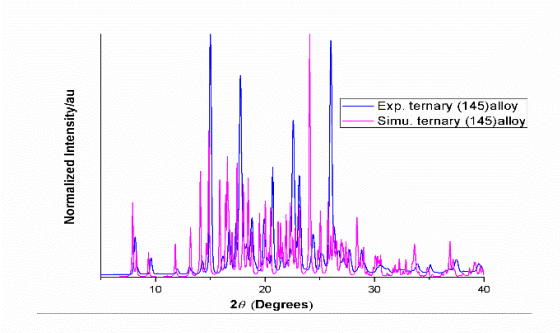

Normalized Intensity/au
Exp. ternary (124)alloy
Simu. ternary (124)alloy
10
20
30
40
2θ (Degree)


Normalized Intensity/au
Simu. ternary (126)alloy
Exp. ternary (126)alloy
10
20
30
40
2θ (Degrees)


Normalized Intensity/au
Exp.ternary(134)alloy
Simu.ternary(134)alloy
10
20
30
40
2θ (Degrees)


Normalized Intensity/au
Simu. ternary (135)alloy
Exp. ternary (135)alloy
10
20
30
40
2θ (Degrees)


Normalized Intensity/au
Exp. ternary (136)alloy
Simu. ternary (136)alloy
10
20
30
40
2θ (Degrees)


Normalized Intensity/au
Exp. ternary (145)alloy
Simu. ternary (145)alloy
10
20
30
40
2θ (Degrees)

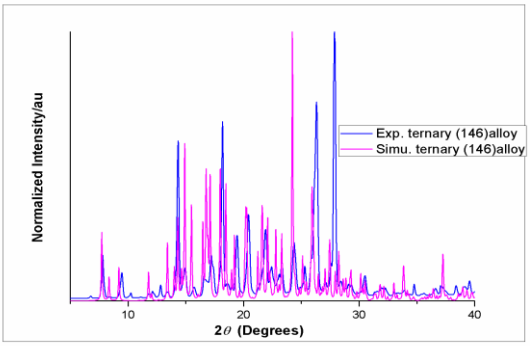
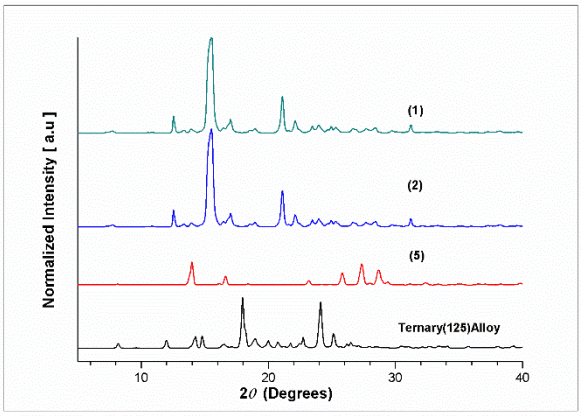

Normalized Intensity/au
Exp. ternary (146)alloy
Simu. ternary (146)alloy
10
20
30
40
2θ (Degrees)

**Figure S7a** PXRD patterns of ternary organic salt alloys: Blue indicates experimental PXRD pattern and pink indicates the simulated pattern based on the single crystal X-ray diffraction data.



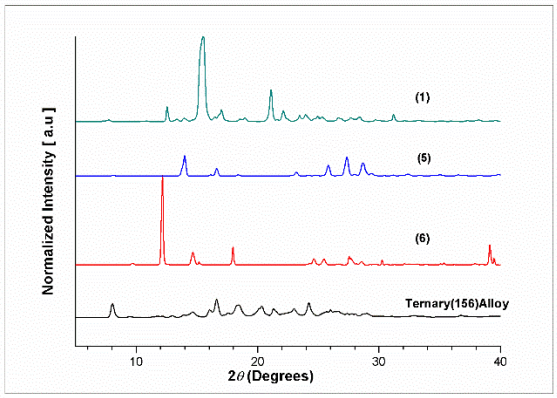
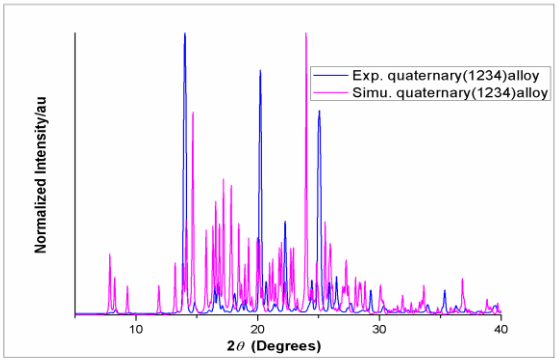
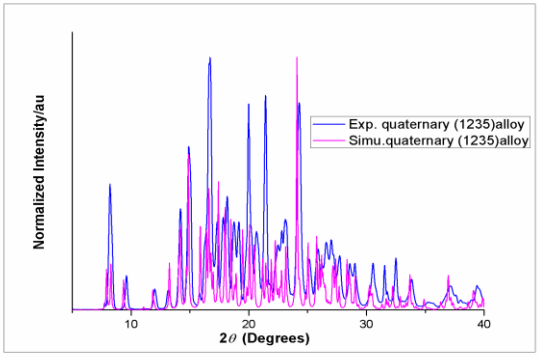
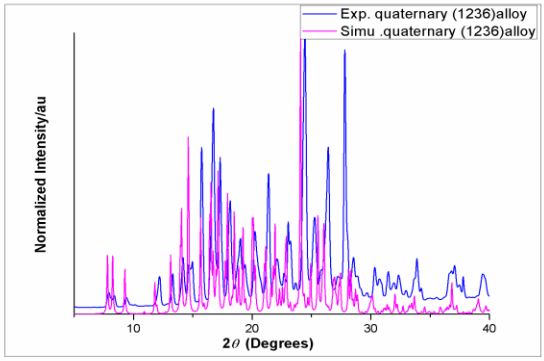
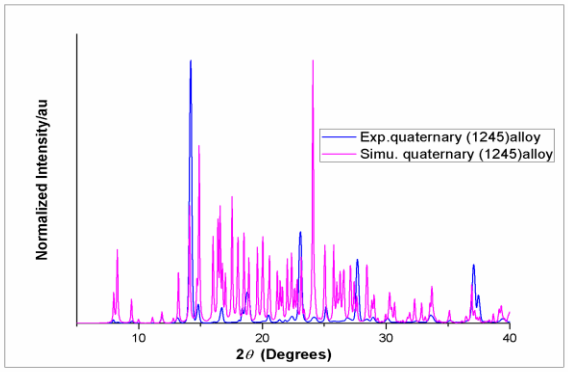




**Figure S7b** PXRD patterns of 125 and 156 ternary organic salt alloys: Naftopidil (1) and aromatic acids PXRD pattern are compared with corresponding ternary slat alloys.



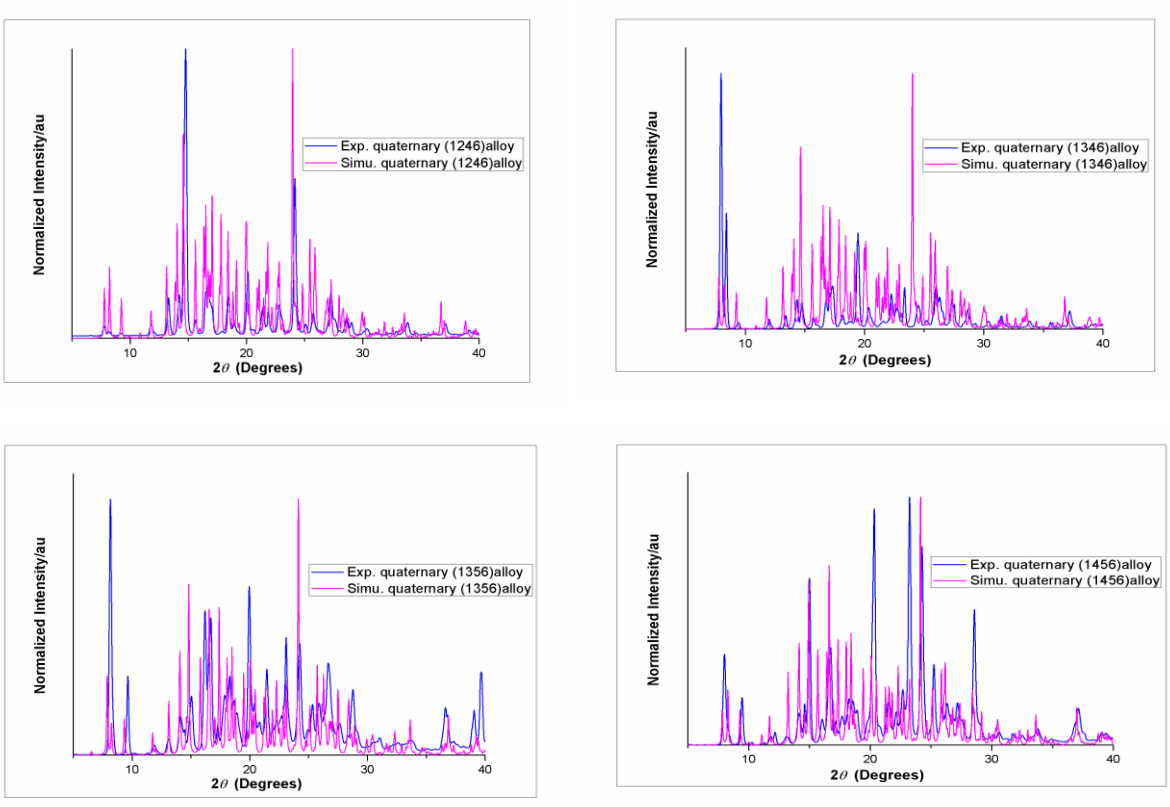



**Figure S8a** PXRD patterns of quaternary organic salt alloys: Blue indicates experimental PXRD pattern and pink indicates the simulated pattern based on the single crystal X-ray diffraction data.

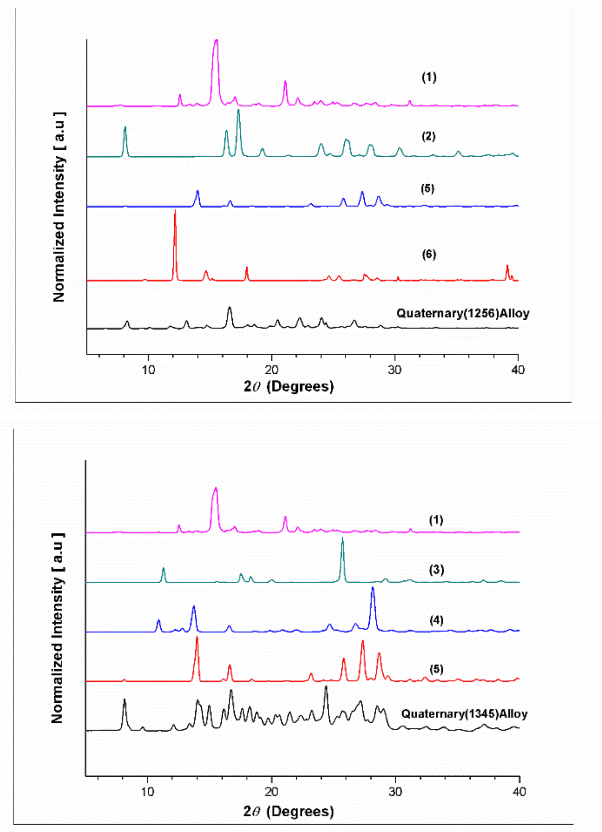


**Figure S8b** PXRD patterns of 1256 and 1345 quaternary organic salt alloys. Naftopidil (1) and acids PXRD pattern are compared with corresponding quaternary slat alloys.

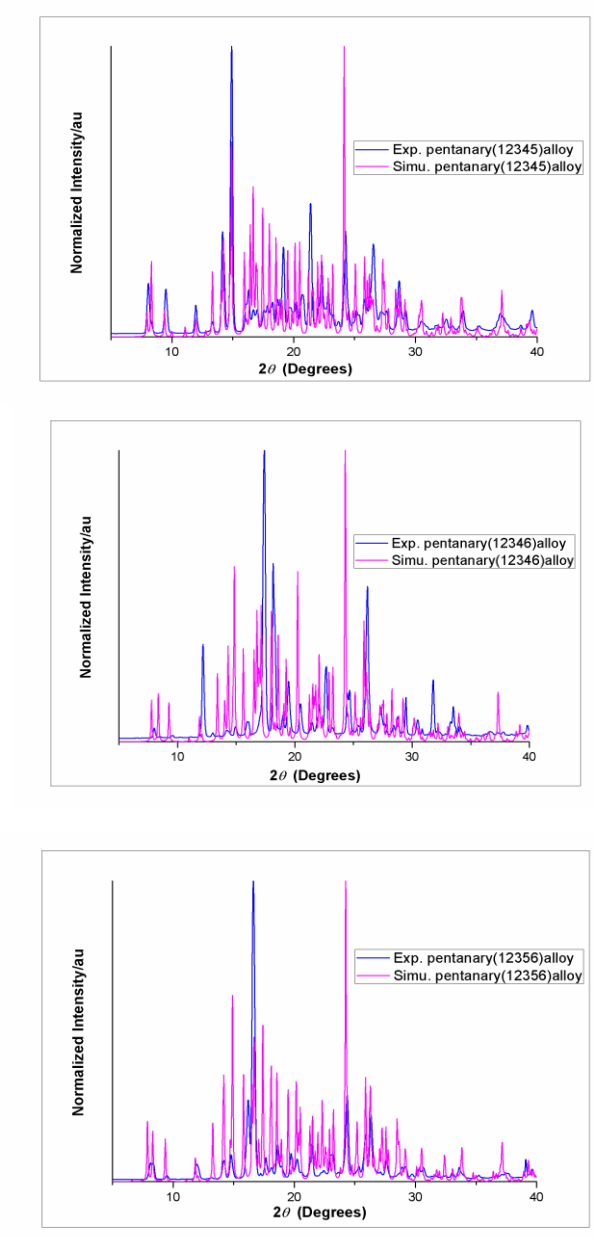



**Figure S9a** PXRD patterns of pentanary organic salt alloys: Blue indicates experimental PXRD pattern and pink indicates the simulated based on the single crystal X-ray diffraction data.

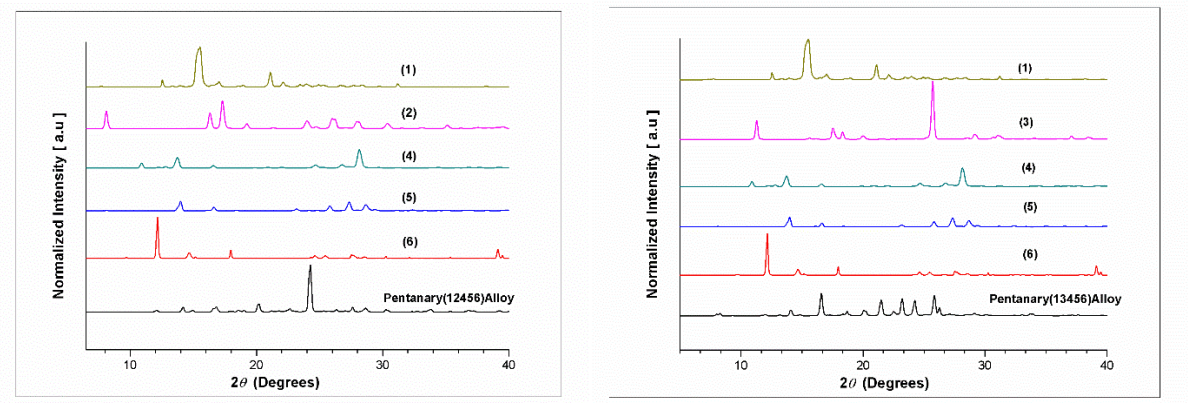



**Figure S9b** PXRD patterns of 12456 and 13456 pentanary organic salt alloys. Naftopidil (1) and acids PXRD pattern are compared with corresponding pentanary slat alloys.

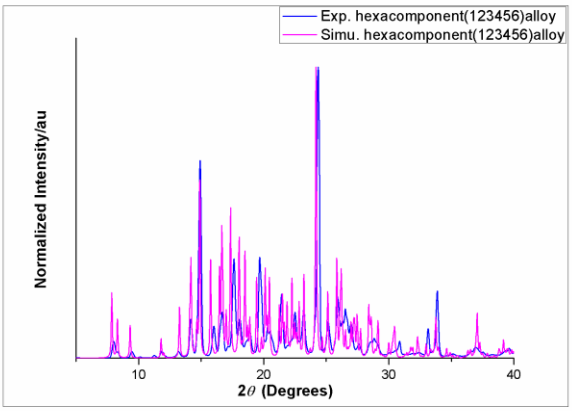



**Figure S10** PXRD patterns of hexanary organic salt alloys: Blue indicates experimental PXRD pattern and pink indicates the simulated based on the single crystal X-ray diffraction data.

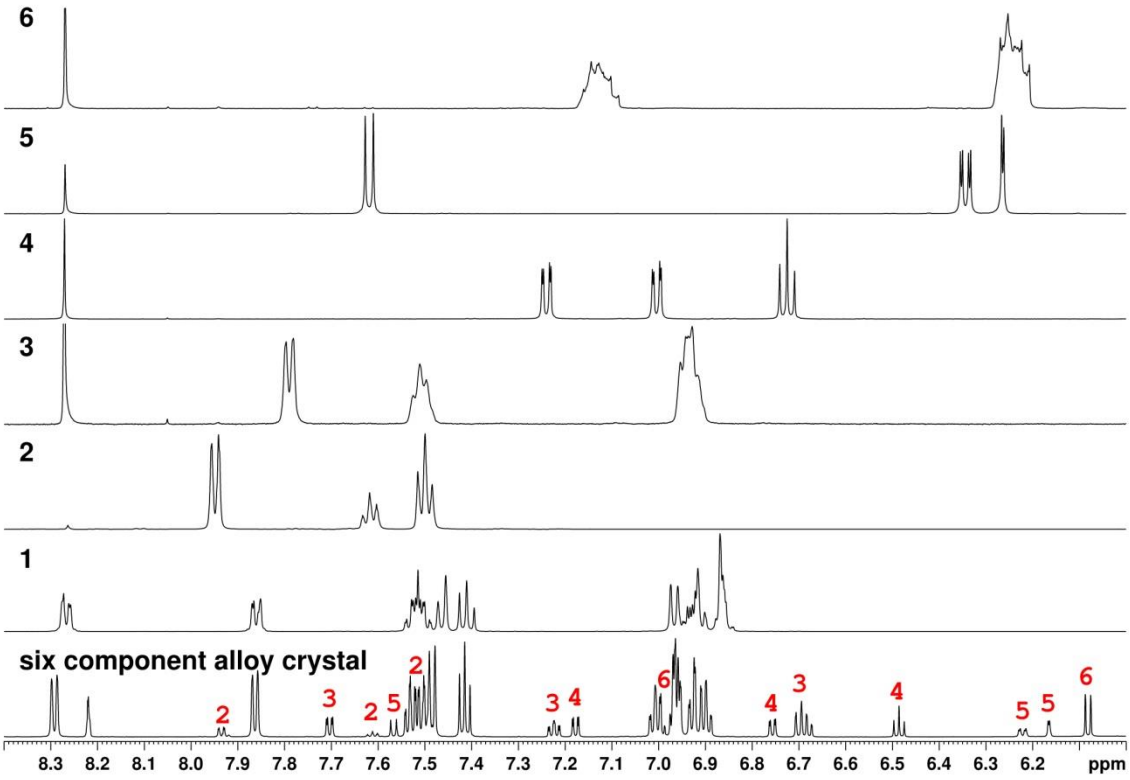



**Figure S11** Stacked $^{1}$H NMR plot of hexacomponent (123456) salt alloy crystal along with the five carboxylic acid units (2-6, indicated in black font) and the drug (1). For the sake of clarity, only the expanded region between 6-8.4 ppm is shown, in which almost all of the resonances from the carboxylic acid components are populated. The resonances corresponding to the individual carboxylic acid components in the spectrum of the hexanaray crystal are indicated in red font.

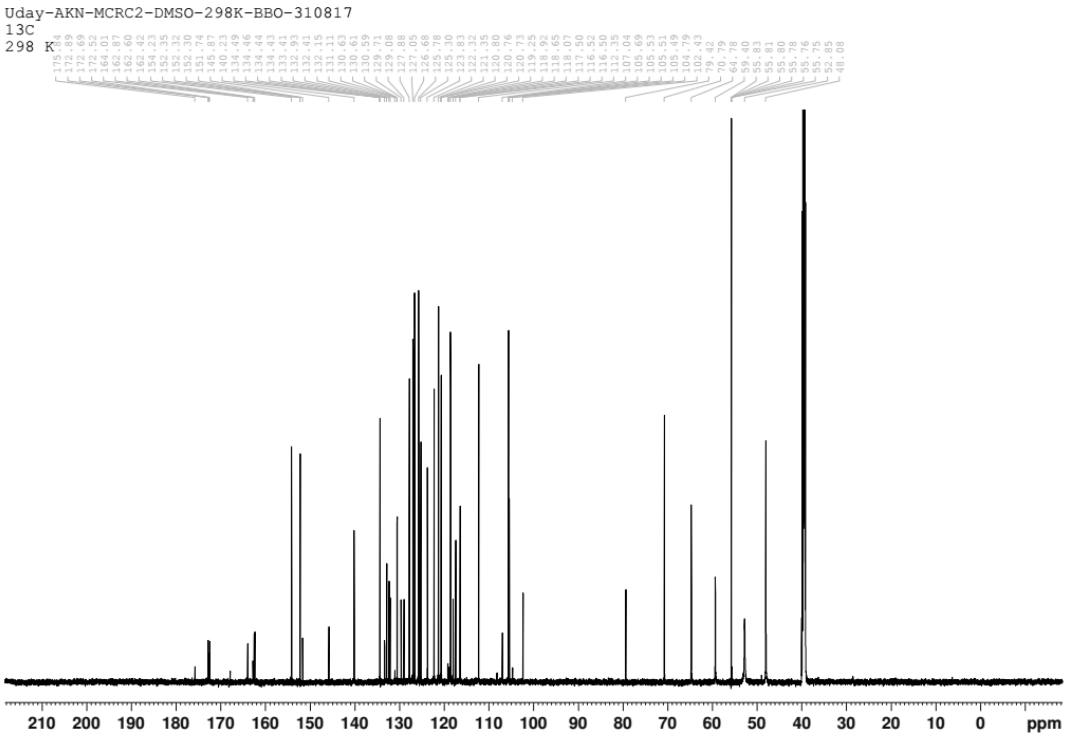



**Figure S12** $^{13}$C NMR plot of the hexacomponent (123456) alloy crystal.

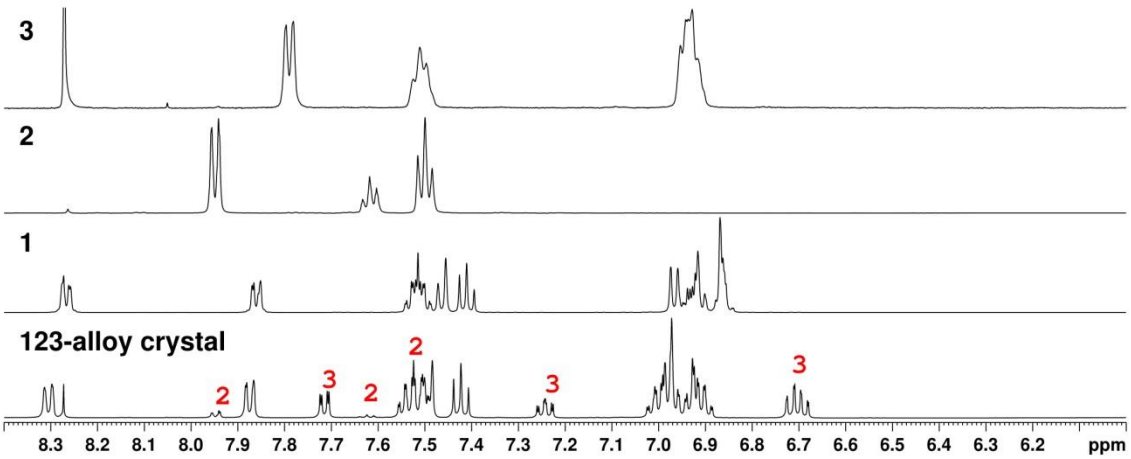


**Figure S13** Stacked $^{1}$H NMR plot of ternary (123) alloy crystal along with the two carboxylic acid units (2-3, indicated in black font) and the drug (1). The resonances corresponding to the individual carboxylic acid components in the spectrum of the alloy crystal are indicated in red font.

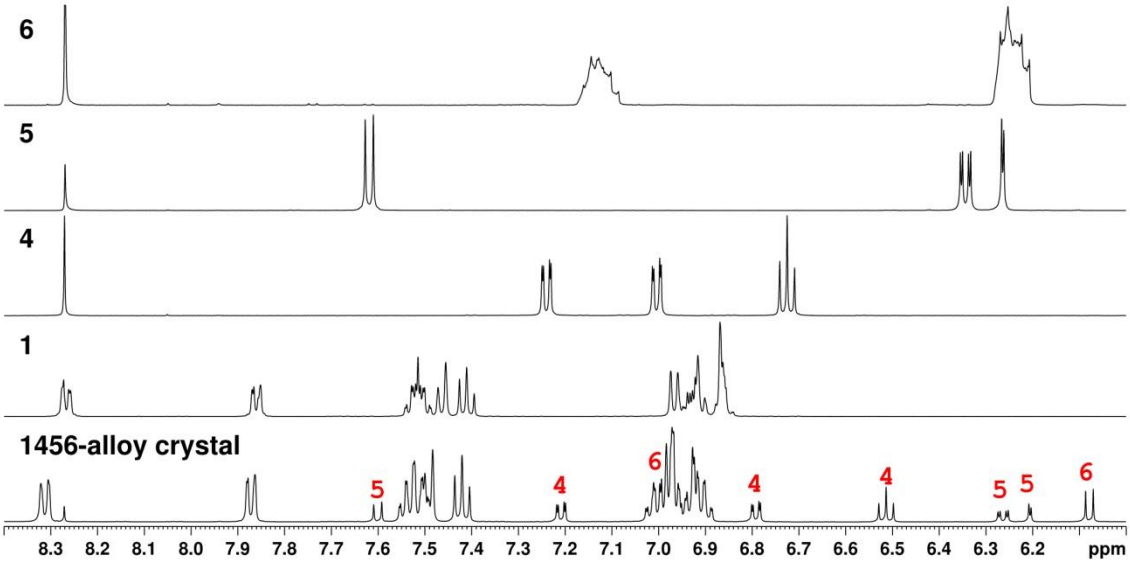



**Figure S14** Stacked $^{1}$H NMR plot of quaternary (1456) alloy crystal along with the three carboxylic acid units (4-6, indicated in black font) and the drug (1). The resonances corresponding to the individual carboxylic acid components in the spectrum of the alloy crystal are indicated in red font.

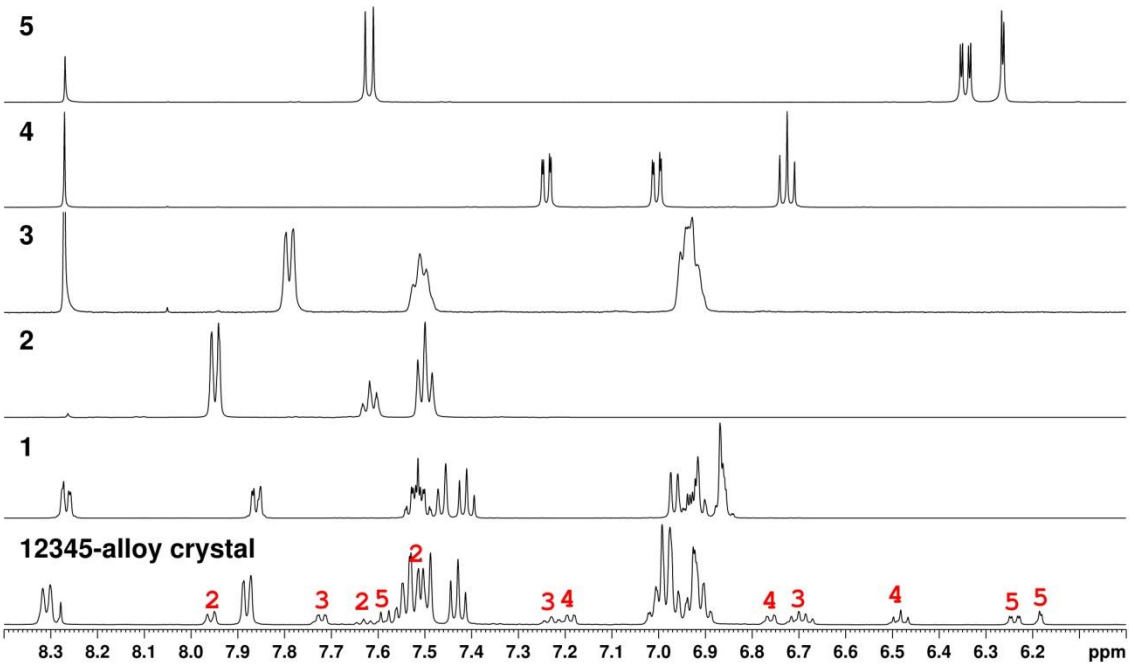



**Figure S15** Stacked $^{1}$H NMR plot of pentenary (12345) alloy crystal along with the four carboxylic acid units (2-5, indicated in black font) and the drug (1). The resonances corresponding to the individual carboxylic acid components in the spectrum of the alloy crystal are indicated in red font.

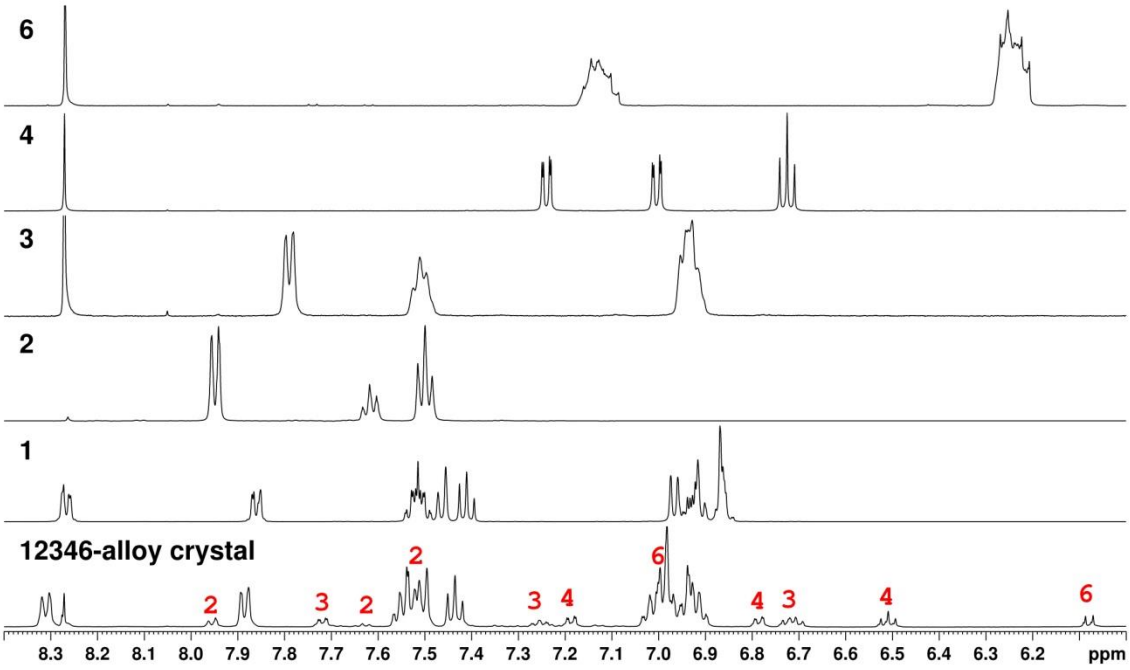



**Figure S16** Stacked $^{1}$H NMR plot of pentenary (12346) alloy crystal along with the four carboxylic acid units (2-4, 6, indicated in black font) and the drug (1). The resonances corresponding to the individual carboxylic acid components in the spectrum of the alloy crystal are indicated in red font.

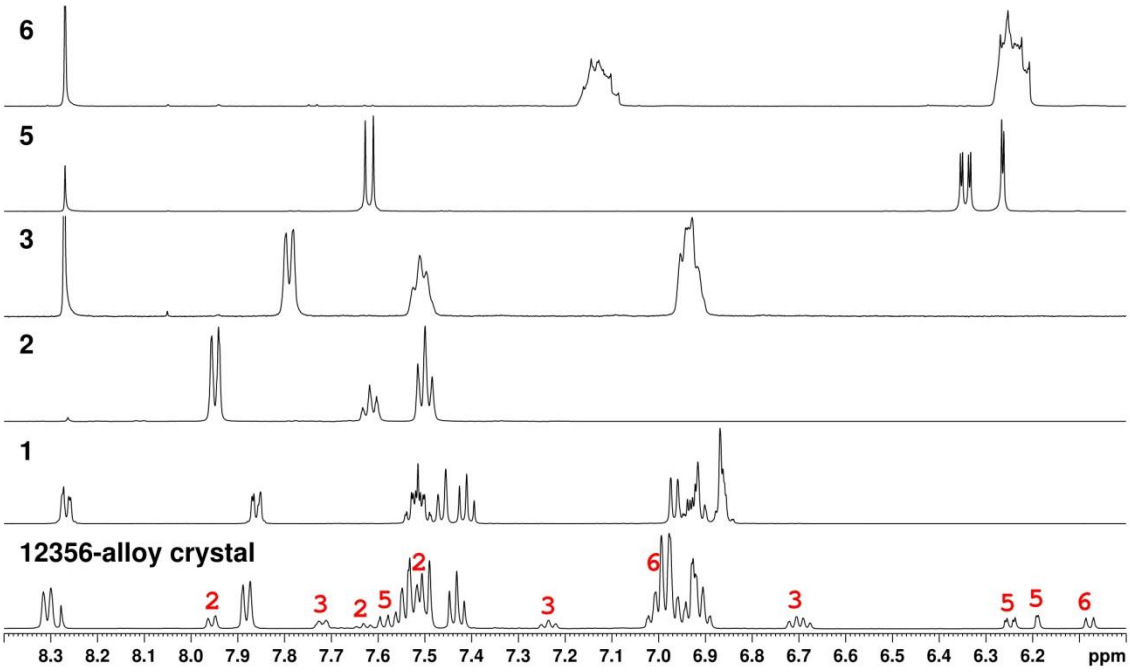



**Figure S17** Stacked $^{1}$H NMR plot of pentenary (12356) alloy crystal along with the four carboxylic acid units (2-3, 5-6 indicated in black font) and the drug (1). The resonances corresponding to the individual carboxylic acid components in the spectrum of the alloy crystal are indicated in red font.

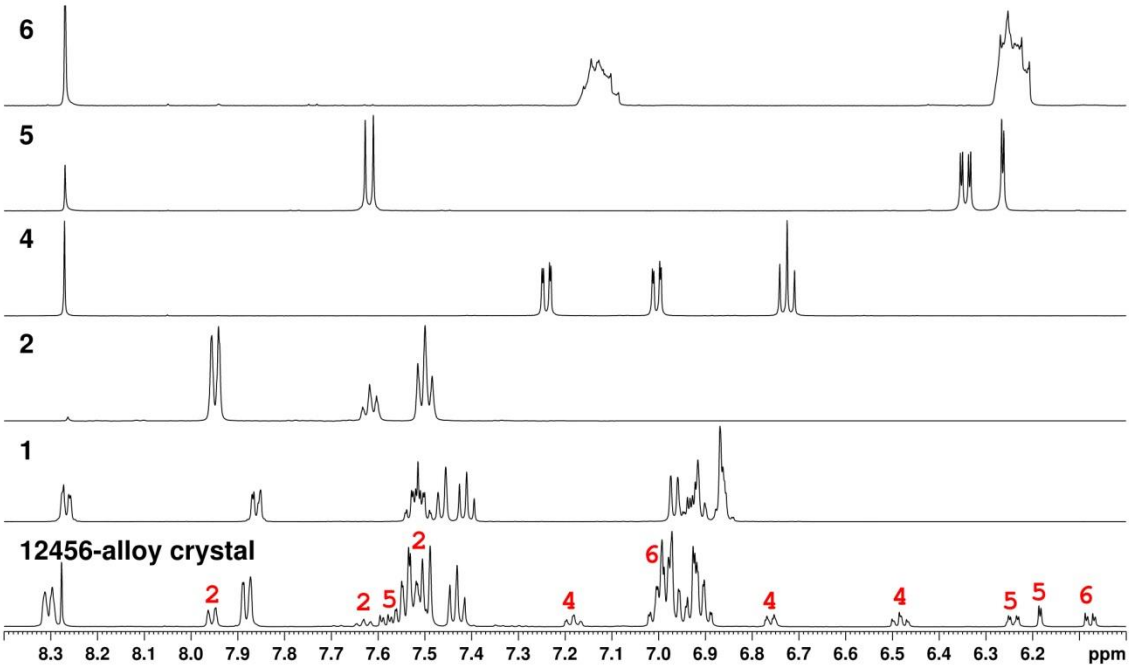



**Figure S18** Stacked $^{1}$H NMR plot of pentenary (12456) alloy crystal along with the four carboxylic acid units (2, 4-6, indicated in black font) and the drug (1). The resonances corresponding to the individual carboxylic acid components in the spectrum of the alloy crystal are indicated in red font.

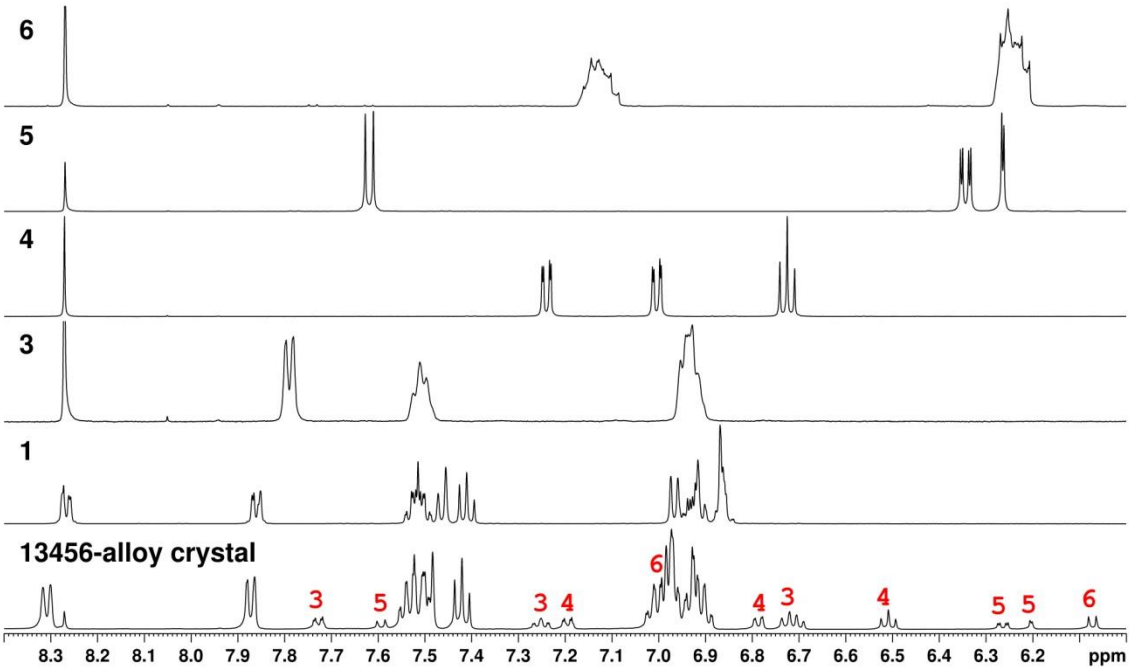



**Figure S19** Stacked $^{1}$H NMR plot of pentenary (13456) alloy crystal along with the four carboxylic acid units (3-6, indicated in black font) and the drug (1). The resonances corresponding to the individual carboxylic acid components in the spectrum of the alloy crystal are indicated in red font.

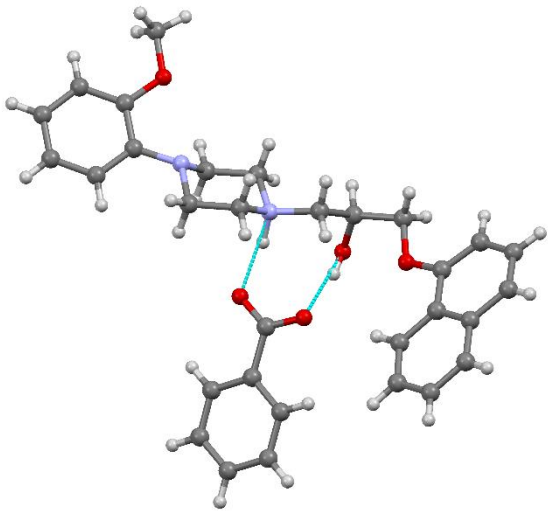


**Figure S20** Binary salt (12).

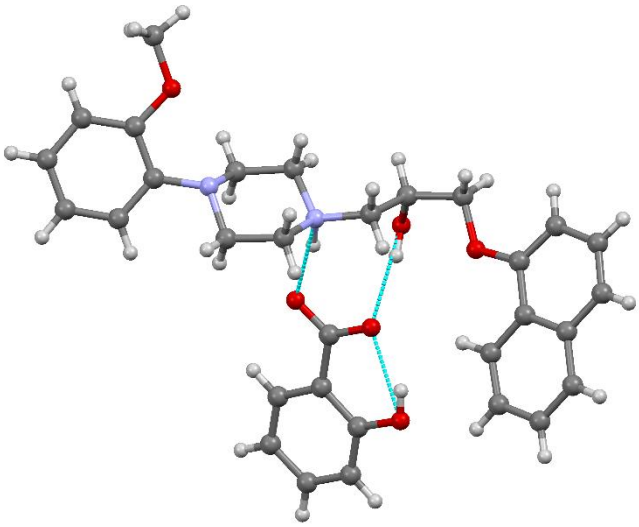


**Figure S21** Binary salt (13).

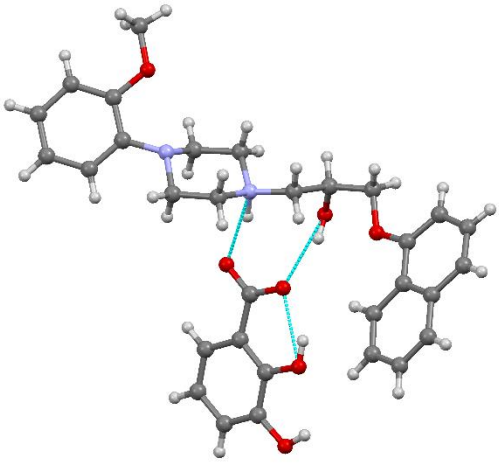


**Figure S22** Binary salt (14).

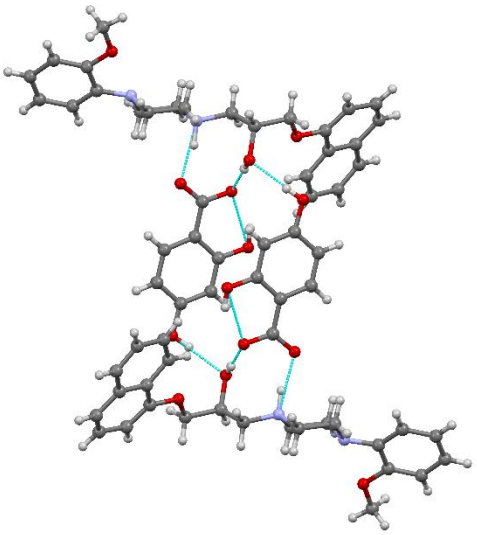


**Figure S23** Binary salt (15).

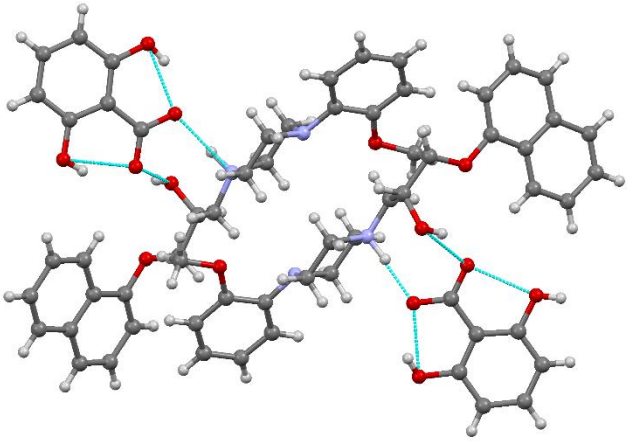


**Figure S24** Binary salt (16).

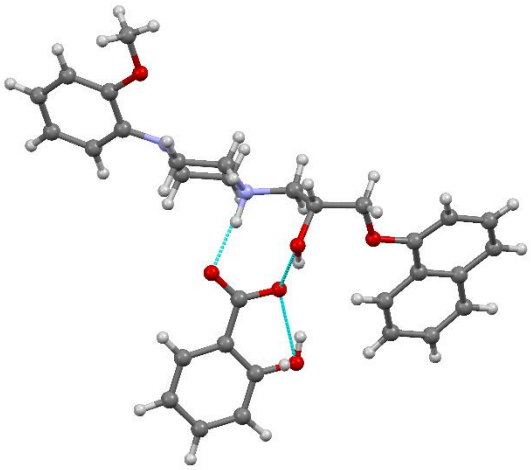


**Figure S25** Organic alloy (123).

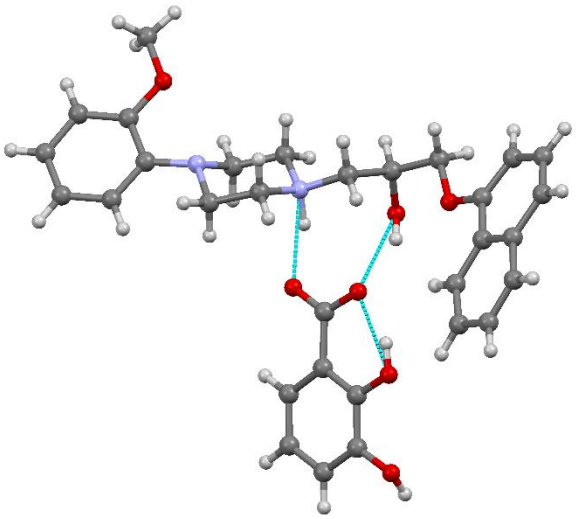


**Figure S26** Organic alloy (124).

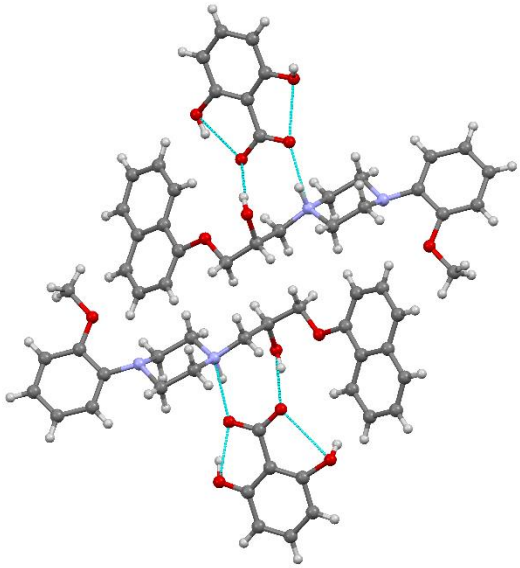


**Figure S27** Organic alloy (126).

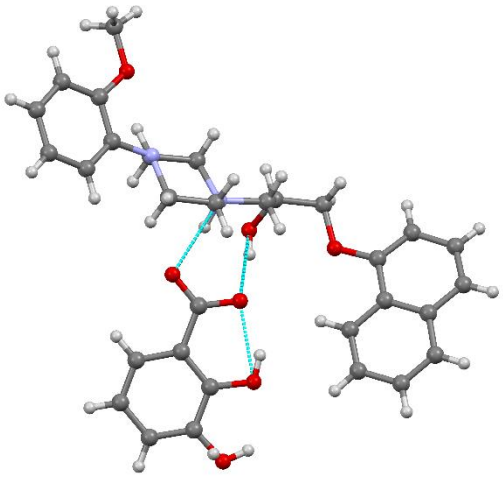


**Figure S28** Organic alloy (134).

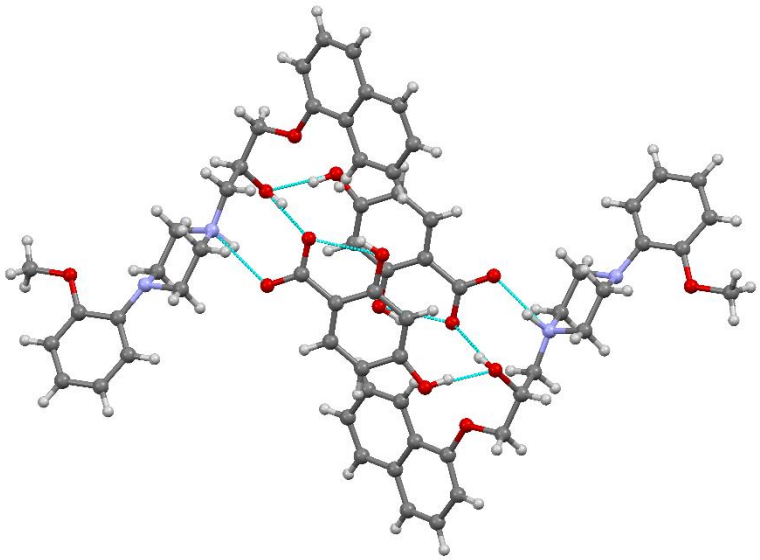


**Figure S29** Organic alloy (135).

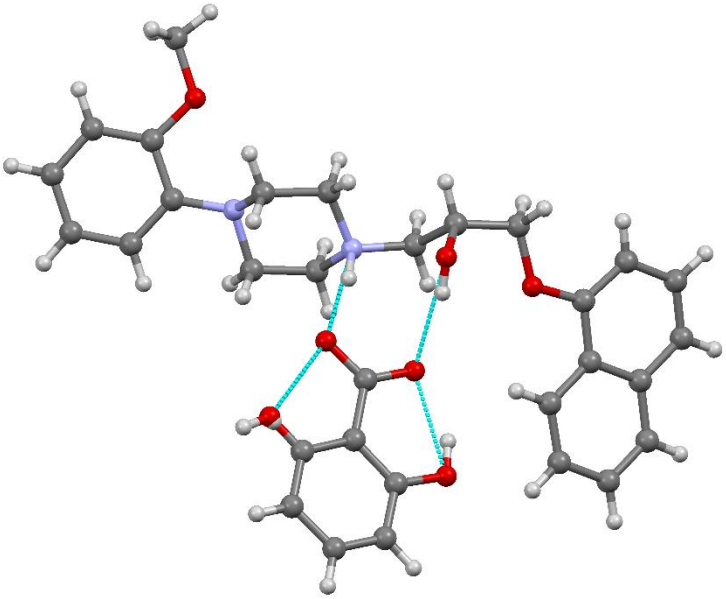


**Figure S30** Organic alloy (136).

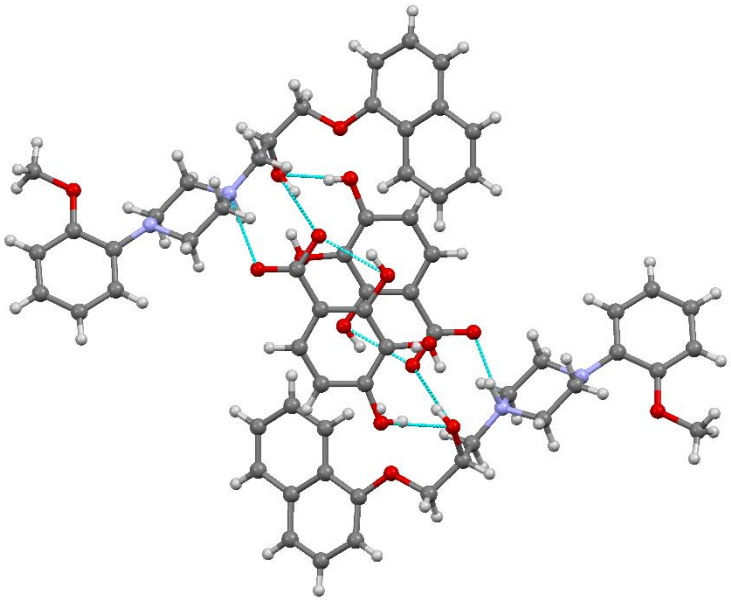


**Figure S31** Organic alloy (145).

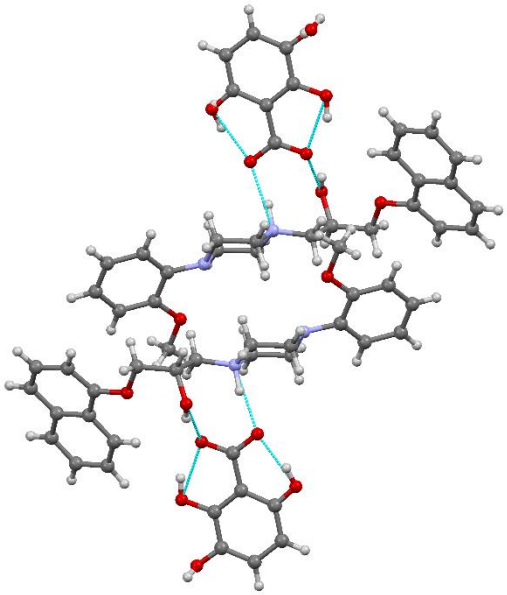


**Figure S32** Organic alloy (146).

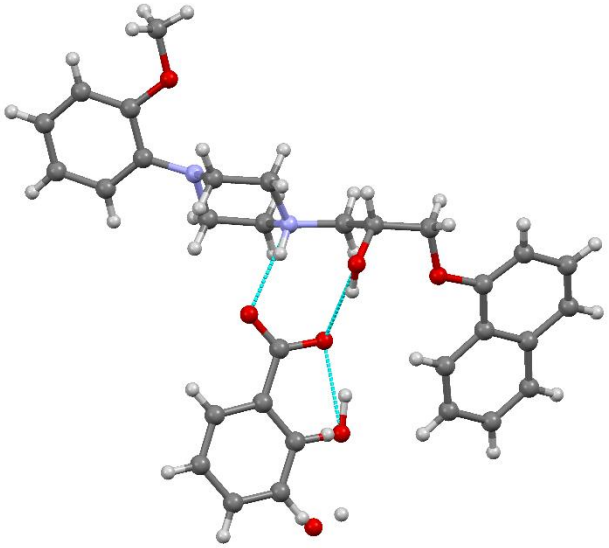


**Figure S33** Organic alloy (1234).

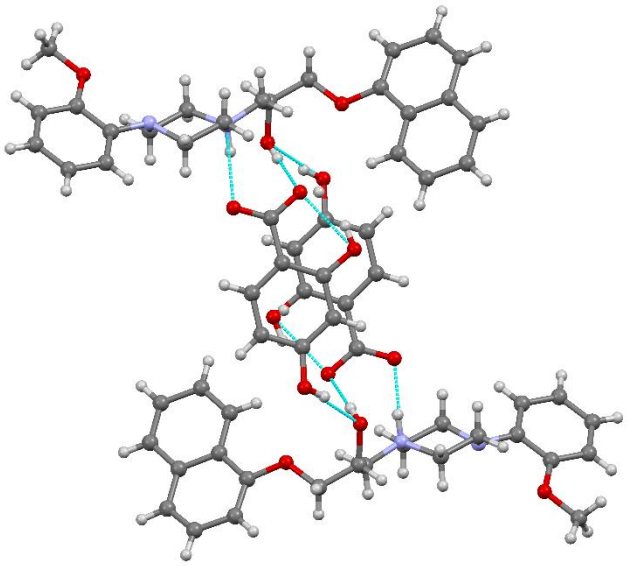


**Figure S34** Organic alloy (1235).

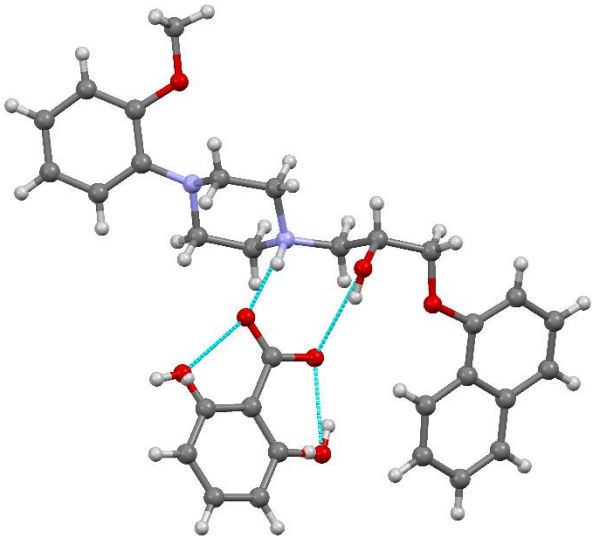


**Figure S35** Organic alloy (1236).

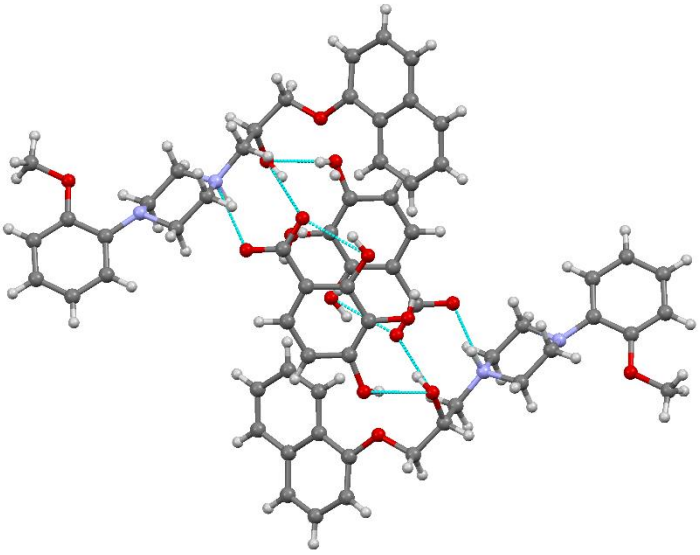


**Figure S36** Organic alloy (1245).

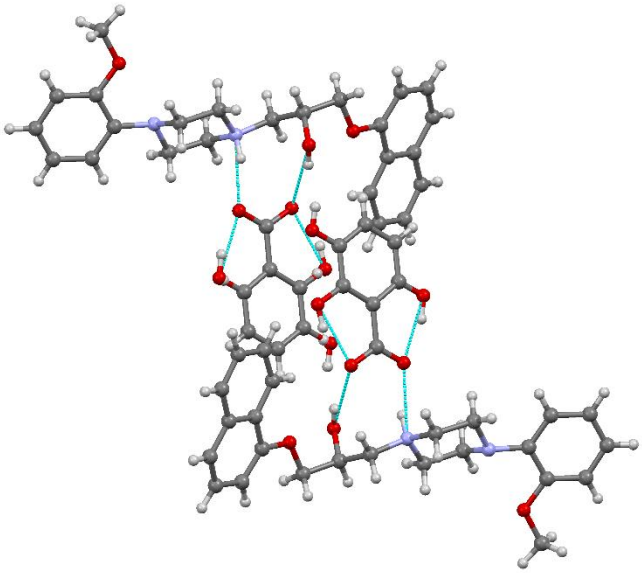


**Figure S37** Organic alloy (1246).

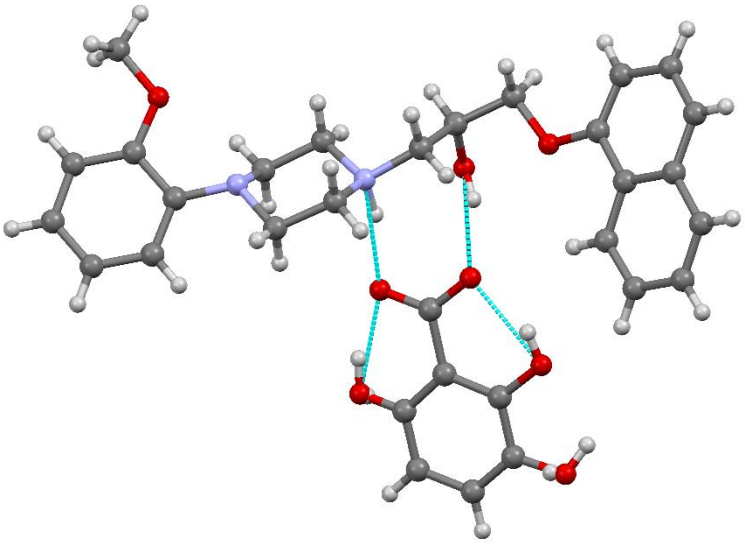


**Figure S38** Organic alloy (1346).

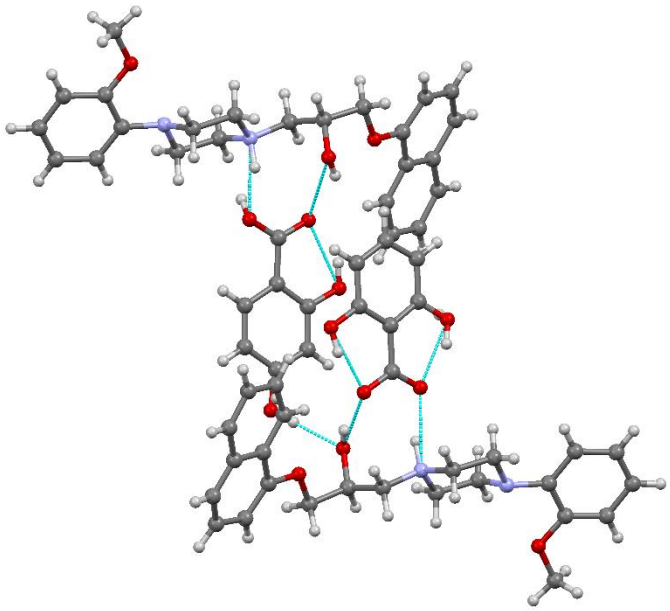


**Figure S39** Organic alloy (1356).

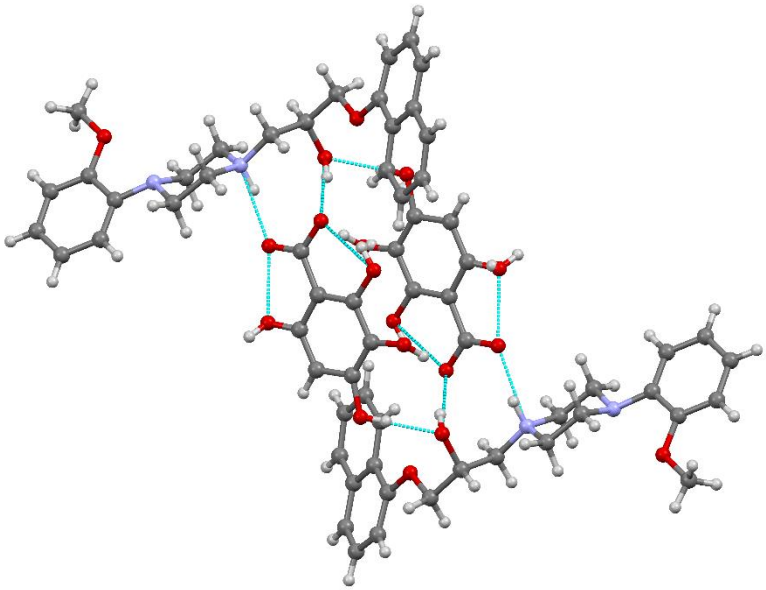


**Figure S40** Organic alloy (1456).

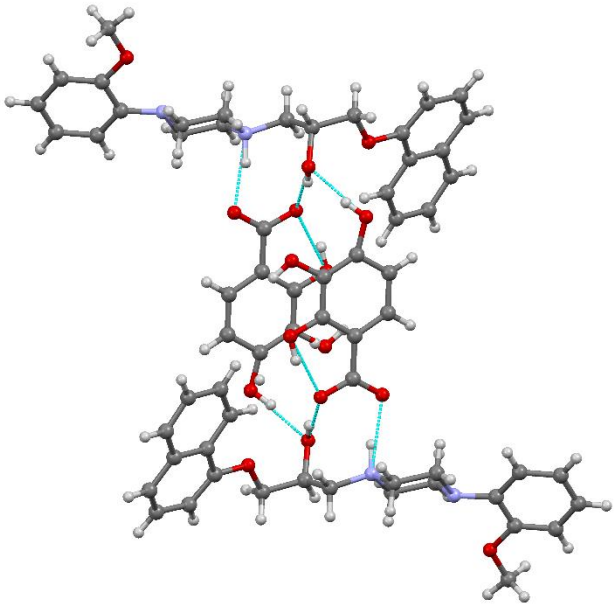


**Figure S41** Organic alloy (12345).

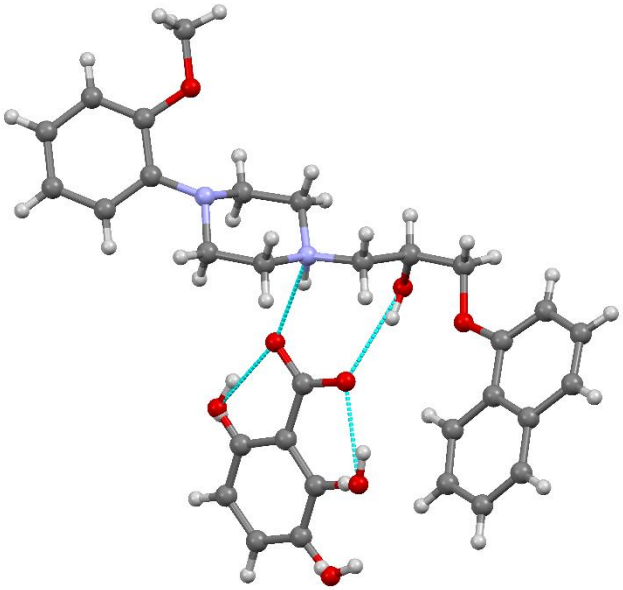


**Figure S42** Organic alloy (12346).

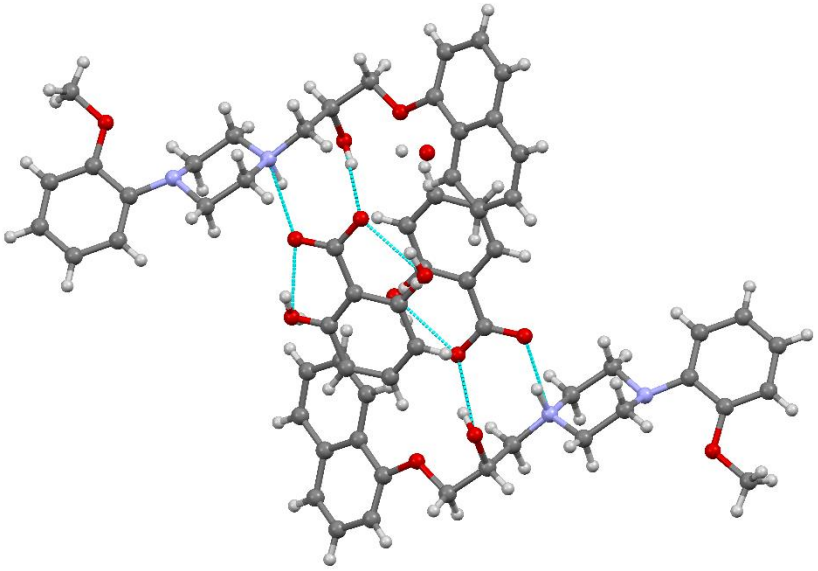


**Figure S43** Organic alloy (12356).

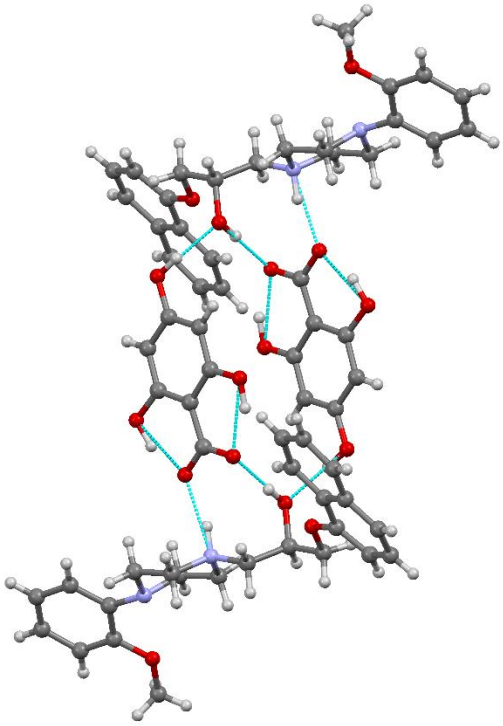


**Figure S44** Binary slat of Naftopidil-2,4,6-trihydroxy benzoic acid.