II. Experimental

1. Materials and Methods:

   The following chemicals were used without further purification. 2,5-diketopiperazine, mercury(II) chloride, vanadyl sulphate, uranyl nitrate, thorium nitrate, lanthanum oxide, europium oxide, uranyl acetate, silver nitrate, nickel chloride tetrahydrate, oxalic acid, succinic acid, glucose, copper(II) chloride dihydrate, lead nitrate, cadmium(II) chloride, zinc nitrate hexahydrate, barium chloride, calcium carbonate and lithium carbonate. Benzoylmethylenetriphenyl-phosphorane was prepared by the deprotonation of the corresponding phosphonium salt with sodium carbonate adopting a published procedure\textsuperscript{1}. Copper hydroxide was obtained by the action of aqueous ammonia and sodium hydroxide on copper sulphate as reported\textsuperscript{2}. Vanadyl acetylacetonate was prepared from vanadyl sulphate by reduction with zinc powder in presence of acetylacetone\textsuperscript{3}.

2. Crystallization of pyrans:

1. 3,5-Bis(2-chlorophenyl)-4-formyl-2,6-dimethylcyclohexan-1-one

   The crude product was refluxed with ethanol in a round-bottomed flask for two hours. The whole solution was allowed to cool to room temperature. Diffraction quality crystals were obtained by crystallizing the product in ethanol. m. p. 100-101° C.
2. r-2,c-6-Bis(p-tolyl)-t-3,t-5-dimethyltetrahydropyran-4-one:

The crude product was refluxed with ethanol for six hours. The clear solution obtained was allowed to cool to room temperature. Diffraction quality crystals were obtained by crystallizing the product in ethanol. m. p. 140-141° C.

3. r-2,c-6-Bis(4-chlorophenyl)3,5-dimethyltetrahydropyran-t-4-ol:

The crude product was heated with hexane-dichloromethane mixture to get a clear solution. This was allowed to cool to room temperature. Diffraction quality crystals were obtained by crystallizing the product in ethanol. m. p. 113-114° C.

4. r-2,c-6-Bis(4-chlorophenyl)-t-3,t-5-dimethyltetrahydropyran-4-one:

The crude sample was refluxed with ethanol for five hours. The clear solution obtained was allowed to cool to room temperature. Diffraction quality crystals were obtained by recrystallizing the product in methylene chloride-hexane mixture. m. p. 190-191° C.

3. Synthetic chemistry using 2,5-diketopiperazine

1. Reaction of 2,5-diketopiperazine with uranyl nitrate hexahydrate:

Uranyl nitrate hexahydrate (1.10 g, 2.20 mmol) was dissolved in a mixture of water and methanol. To this an aqueous hot solution of 2,5-diketopiperazine (0.50 g, 4.38 mmol) was added. The mixture was heated on a water bath for
four hours to form a clear solution. The solution was allowed to cool to room temperature. Diffraction quality crystals were obtained by the vapour diffusion of acetone into the above solution. m. p. 193 - 195° C.

2. Reaction of 2,5-diketopiperazine with mercury(II) chloride:

Mercury(II) chloride (2.37 g, 8.76 mmol) was dissolved in hot methanol. To this a hot solution of 2,5-diketopiperazine (1.00 g, 8.76 mmol) was added. The whole mixture was heated on a water bath for four hours to form a clear solution and was allowed to cool to room temperature. This was kept in a refrigerator. Diffraction quality crystals were obtained by the vapour diffusion of acetone into the above solution. m. p. 198° C.

3. Reaction of 2,5-diketopiperazine with vanadyl acetylacetonate:

Vanadyl acetylacetonate (0.30 g, 1.12 mmol) was dissolved in hot aqueous methanol. To this 2,5-diketopiperazine (0.25 g, 2.25 mmol), dissolved in hot water was added. The mixture was heated over a water bath for four hours. This was allowed to cool to room temperature and kept in a refrigerator. A blue amorphous solid was obtained by vapour diffusion of acetone into the above solution. m. p. 260° C.

4. Reaction of 2,5-diketopiperazine with mercury(II) iodide:

Mercury(II) iodide (0.30 g, 0.66 mmol) was dissolved in a hot mixture of methanol and water. To this hot aqueous solution 2,5-diketopiperazine (0.078 g, 0.68 mmol) was added. The mixture was heated over a water bath to form a
clear solution. The solution was allowed to cool and kept in a refrigerator forming a heterogenous mixture of red and colourless solids. Therefore it was concluded that no reaction occurred between mercury(II) iodide and 2,5-diketopiperazine.

5. Reaction of 2,5-diketopiperazine with uranyl acetate:

Uranyl acetate (0.5 g, 1.14 mmol) was dissolved in hot methanol. To this, hot aqueous solution of 2,5-diketopiperazine (0.13 g, 1.14 mmol) was added. The mixture was heated over a water bath to form a clear solution. This clear solution was allowed to cool to room temperature and then kept in a refrigerator. Vapour diffusion of acetone into the above solution yielded an amorphous solid. m. p. >185° C.

6. Reaction of thorium nitrate penta hydrate with 2,5-diketopiperazine:

Thorium nitrate pentahydrate (1.00 g, 1.75 mmol) in hot methanol was mixed with hot aqueous solution of 2,5-diketopiperazine (0.20 g, 1.75 mmol). The mixture was heated over a water bath to form a clear solution. This clear solution was allowed to cool and kept in the refrigerator. The product obtained was a glassy mass. No further characterization of the product was carried out.

7. Reaction of lanthanum trichloride with 2,5-diketopiperazine:

Lanthanum oxide was taken in a china dish and evaporated with concentrated hydrochloric acid. The mass obtained was leached with water
containing few drops of hydrochloric acid. The liquid was decanted and the solid was dried in pump and kept in the desiccator.

Lanthanum chloride (0.45 g, 1.83 mmol) was taken in a beaker and heated with methanol and water to obtain a clear solution. To this, hot aqueous solution of 2,5-diketopiperazine (0.21 g, 1.84 mmol) was added. The whole mixture was heated over a water bath to form a clear solution and was allowed to cool in a refrigerator. Vapour diffusion of acetone into the above solution yielded a white solid. m. p. >190° C.

8. Reaction of europium chloride with 2,5-diketopiperazine:

Europium oxide was heated with con. hydrochloric acid in a china dish to dryness. The resultant powdered mass was leached with water. The precipitate obtained was filtered off and the residue was dried in a vacuum desiccator.

Europium chloride (0.74 g, 2.86 mmol) so obtained was dissolved in hot methanol. To this, hot aqueous solution of 2,5-diketopiperazine (0.32 g, 2.80 mmol) was added. The whole mixture was heated over a water bath for about five hours to form a clear solution. The solution was kept in a refrigerator. A non-crystalline solid was obtained by the vapour diffusion of acetone into the above solution. The product was washed with petroleum ether. m. p. 275° C. The reaction was repeated with europium sulphate obtained by the action of sulphuric acid on europium oxide to yield diffraction quality crystals.
9. Reaction of silver nitrate with 2,5-diketopiperazine:

Silver nitrate (0.59 g, 3.40 mmol) was taken in a beaker and dissolved in water to which an aqueous hot solution of 2,5-diketopiperazine (0.34 g, 3.09 mmol) was added. The whole mixture was heated over a water bath to form a clear solution. The clear solution was allowed to cool for four days. Diffraction quality crystals were obtained after a few days. m. p. 182° C.

10. Reaction of nickel chloride hexahydrate with 2,5-diketopiperazine:

Nickel chloride hexahydrate (1.00 g, 4.20 mmol) was taken in a round-bottomed flask and dissolved in water. To this, hot aqueous solution of 2,5-diketopiperazine (0.48 g, 4.20 mmol) was added. After the addition was over, the mixture was refluxed for eight hours. The clear solution was allowed to cool to room temperature and kept in refrigerator. Diffraction quality crystals were obtained. The crystals were washed with petroleum ether. m. p. 201° C.

11. Reaction of cobalt chloride with 2,5-diketopiperazine:

Cobalt chloride hexahydrate (1.00 g, 4.20 mmol) was dissolved in water and methanol. To this solution, hot aqueous solution of 2,5-diketopiperazine (0.48 g, 4.20 mmol) was added. The whole mixture was refluxed for eight hours. The clear solution was allowed to cool and kept in a refrigerator. Crystals of diffraction quality separated after few days. m. p. 202° C.
12. Reaction of oxalic acid with 2,5-diketopiperazine:

Oxalic acid (0.5 g, 3.96 mmol) was dissolved in a hot methanol-water mixture. To the resulting clear solution a solution of 2,5-diketopiperazine (0.45 g, 3.96 mmol) in hot water was added. The mixture was heated over a water bath for five hours to obtain a clear solution. This solution was allowed to cool to room temperature. Finally the solution was cooled in the refrigerator. Diffraction quality crystals were obtained by vapour diffusion of acetone into the above solution. m. p. 201 °C.

13. Reaction of terephthalic acid with 2,5-diketopiperazine:

Terephthalic acid (0.50 g, 3.0 mmol) was dissolved in hot ethanol taken in a round-bottomed flask. To this, hot aqueous solution of 2,5-diketopiperazine (0.69 g, 6.0 mmol) was added. The mixture was refluxed using a water condenser. The clear solution was cooled to room temperature and kept in a refrigerator. A colourless solid, m. p. >205 °C, separated after few days.

14. Reaction of copper chloride dihydrate with 2,5-diketopiperazine:

Copper chloride dihydrate (1.0 g, 5.90 mmol) was dissolved in water and methanol to which an aqueous hot solution of 2,5-diketopiperazine (0.67 g, 5.90 mmol) was added. The whole mixture was refluxed for seven hours. The clear solution obtained was allowed to cool to room temperature and kept in the refrigerator. Crystals separated out after few days. m. p. 203 °C.
15. Reaction of benzoylmethylenetriphenylphosphorane with 2,5-diketopiperazine:

The ylide, benzoylmethylenetriphenylphosphorane (0.20 g, 0.52 mmol) was dissolved in hot ethanol and water to which hot aqueous solution of 2,5-diketopiperazine (0.12 g, 1.03 mmol) was added. The mixture was taken in a round-bottomed flask and refluxed using a water condenser for six hours. Then the solution was allowed to cool to room temperature. Crystals separated out by keeping the solution as such for four days. m.p. 178° C.

16. Reaction of glucose and 2,5-diketopiperazine:

Glucose (0.50 g, 2.78 mmol) was dissolved in water and methanol mixture to which hot aqueous solution of 2,5-diketopiperazine (0.63 g, 5.52 mmol) was added. The mixture was heated over a water bath for five hours to form a clear solution. The solution was allowed to cool to room temperature. This was kept in a refrigerator. A colourless solid separated. m.p. >205° C.

17. Reaction between cadmium chloride and 2,5-diketopiperazine:

Cadmium chloride (1.00 g, 5.45 mmol) was dissolved in a mixture of water and methanol in a beaker to which an aqueous hot solution of 2,5-diketopiperazine (0.62 g, 5.44 mmol) was added. The mixture was heated over a water bath for four hours. The solution was allowed to cool to room temperature and kept in a refrigerator for four days. A colourless solid separated. m. p. >210° C.
18. Reaction of barium chloride and 2,5-diketopiperazine:

Barium chloride (1.00 g, 4.80 mmol) was dissolved in a mixture of water and methanol in a beaker. To this, an aqueous hot solution of 2,5-diketopiperazine (0.54 g, 4.74 mmol) was added. The mixture was heated over a water bath for four hours to form a clear solution. The solution was allowed to cool to room temperature and kept in a refrigerator for four days. A white solid separated out. m. p. >207°C.

19. Reaction between calcium chloride and 2,5-diketopiperazine:

Calcium carbonate was evaporated to dryness with con. hydrochloric acid in a china dish. Calcium chloride so obtained was dried in a desiccator. Calcium chloride (1.00 g, 9.00 mmol) was dissolved in a mixture of water and methanol in a beaker. To this an aqueous hot solution of 2,5-diketopiperazine (1.03 g, 9.00 mmol) was added. The mixture was heated over a water bath for four hours to form a clear solution. The solution was allowed to cool to room temperature and kept in a refrigerator for four days. A white solid separated out. m. p. >210°C.

20. Reaction between lithium chloride and 2,5-diketopiperazine:

Lithium carbonate was evaporated with con. hydrochloric acid in a china dish. The lithium chloride obtained was dried in a desiccator. Lithium chloride (1.00 g, 23.5 mmol) was dissolved in a mixture of water and methanol. To this an aqueous hot solution of 2,5-diketopiperazine (2.66 g, 23.3 mmol) was added. The mixture was heated on a water bath for four hours to form a clear solution.
The solution was allowed to cool to room temperature and kept in a refrigerator. Crystals were obtained after few days. m. p. >205° C.

21. Reaction between copper hydroxide and 2,5-diketopiperazine:

Cupric hydroxide was prepared from CuSO$_4$.5H$_2$O as follows. CuSO$_4$.5H$_2$O crystals were dissolved in water to form copper sulphate solution (0.25 g, 1.00 mmol). This solution was heated to 70° C with 10% aqueous ammonia until a deep blue colour appeared. The solution was then allowed to react with a solution containing stoichiometric quantity of NaOH (0.08 g, 2.00 mmol) yielding a blue precipitate. This was filtered, washed repeatedly with warm water. A hot solution of 2,5-diketopiperazine (0.23 g, 2.00 mmol) was added to the suspension of Cu(OH)$_2$ in water. The whole mixture was refluxed well for two hours. A black solid was then separated out which was washed with hot water and dried.

22. Reaction of zinc nitrate hexahydrate with 2,5-diketopiperazine:

Zinc nitrate hexahydrate (1.0 g, 3.36 mmol) was dissolved in a water and methanol in a beaker. To this hot aqueous solution of 2,5-diketopiperazine (0.38 g, 3.37 mmol) was added. The mixture was heated over a water bath for four hours to form a clear solution. The solution was allowed to cool to room temperature and kept in a refrigerator for four days. Diffraction quality of crystals were obtained. m. p. >201°C.
References:

