Solid state reactions, induced by mechanical energy, liquid-assisted grinding (LAG) and ball milling, have become established methods for the preparation of pharmaceutical cocrystals. Examination of the mechanochemical reaction pathways reveal the existence of different intermediate phases of variable crystallinity. Poor physicochemical properties (solubility and permeability) of active pharmaceutical ingredients (API) are a serious concern in clinical development. Cocrystals and salts of APIs often have advantageous physicochemical properties, improved over the parent drugs, without change in therapeutic efficiency. Hydrochlorothiazide (HCT), is a BCS class IV diuretic drug with poor solubility and permeability. Physicochemical properties of HCT have been modified by cocrystallization with piperazine (PPZ), tetramethylpyrazine (TMPZ), picolinamide (PCM), pyrazinamide (PZM), isoniazid (INZ), malonamide (MAM), picolinic acid (PIC) and isonicotinic acid (INIC) using mechanochemical grinding (liquid assisted and neat). The solids obtained were characterized by single crystal X-ray diffraction (SCXRD), powder X-ray diffraction (PXRD), FTIR spectroscopy and DSC and subjected to solubility and membrane permeability studies. SCXRD showed that the N-H...O sulfonamide catemer synthons found in the stable polymorph of pure HCT, have been replaced by drug-coformer heterosynthons in the cocrystals. HCT–PPZ, HCT–PCM and HCT–PIC cocrystals showed improvement in solubility and membrane permeability/diffusion compared to the parent API. The improved solubility and diffusion rates are due to the drug-coformer interactions in the new solid forms. A structure-property relationship is examined to evaluate the solubility and diffusion rates of the new solid forms. The cocrystal with INIC, which could not be prepared previously by conventional methods, was obtained by prolonged grinding for six days.