Isostructural Polymorphs of the Local Anaesthetic Drugs Falicaine and Dyclonine

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The hydrochloride salts of the local anaesthetic drugs falicaine (propipocaine) (1-(4-Propoxyphenyl)-3-(1-piperidinyl)-1-propanone hydrochloride, PPCHC) and dyclonine (1-(4-Butoxyphenyl)-3-(1-piperidinyl)-1-propanone hydrochloride, DCNHC), which differ only in the length of the -O-alkyl chain, were characterised by thermal analytic (hot stage microscopy, differential scanning calorimetry, thermogravimetry) and vibrational spectroscopic methods (FTIR-, FT-Raman-spectroscopy), powder X-ray diffractometry, magic-angle spinning NMR and water vapour sorption analysis.

Two polymorphic modifications could be found and characterized respectively. Mod. II° is the thermodynamically stable form at room temperature, is present in both commercial products and crystallizes from all tested solvents. The X-ray powder patterns of the mod. II° of the two substances are very similar indicating isostructural crystals. The DSC-curves of the stable forms show an endothermal transformation to the high temperature form (mod. I) at about 10 K below the melting points (PPCHC: 166.5°C, DCNHC: 175.0°C). Mod. I also crystallizes from the supercooled melt. According to the heat of transition rule[1] the two forms are enantiotropically related. The moisture sorption isotherms at 25°C show a distinctly higher affinity to water for the less stable mod. I of both substances, which also indicates a lower thermodynamic stability.

Carbon-13 CPMAS spectra have been obtained and assigned. They also strongly suggest that the two forms IIº are isostructural. Moreover, they show that the phenylene groups in the two forms I are undergoing 180º ring flips at rates comparable to the NMR timescale, whereas the two forms IIº are relatively immobile. Finally, the NMR suggests the two forms I may be isostructural as well.

References

1 Burger A., Ramberger R.: On the Polymorphism of Pharmaceuticals and other Molecular Crystals. I. Mikrochim. Acta II (1979) 259-271