

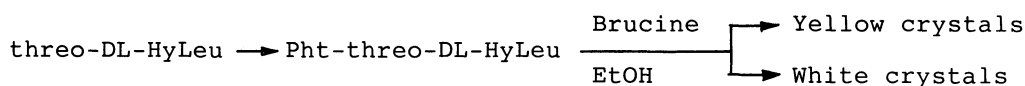
Color Difference between Diastereomers of the Brucine Salt of
Phthaloyl-threo- β -hydroxyleucine¹⁾

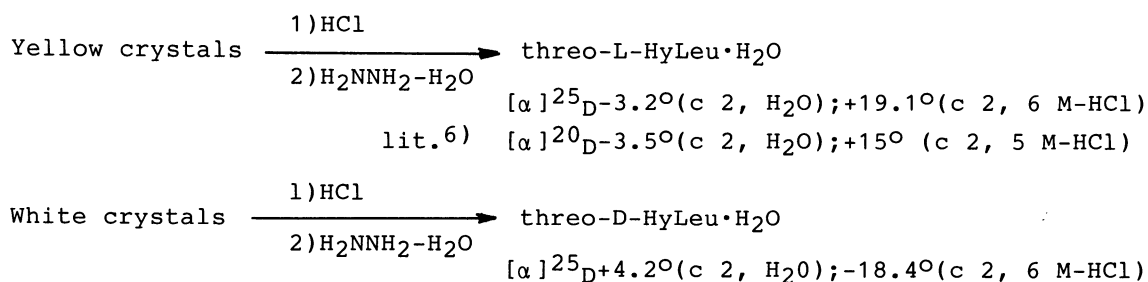
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When phthaloyl-threo-DL- β -hydroxyleucine was resolved using brucine as a resolving agent, yellow and white crystals were obtained. threo-L-Form was obtained from yellow crystals and threo-D-form from white ones. The appearance of yellow color is considered to be due to the stacking of benzene ring of phthaloyl group and of brucine molecule.

During the synthetic study of leucinostatin D,²⁾ threo-L- β -hydroxyleucine (threo-L-HyLeu) has to be synthesized as a component. This amino acid has been already synthesized by several ways, and recently Hayashi et al.³⁾ reported its elegant asymmetric synthesis. To obtain both L- and D-form, isobutyraldehyde was condensed with glycine according to Wieland.⁴⁾ After removal of inorganic ions using ion-exchange resin and repeated recrystallization from water, pure threo-DL-HyLeu could be isolated. Purity was determined by HPLC analysis after derivatization to Z-HyLeu-Sar-L-Phe-OMe.⁵⁾ This racemic compound was phthaloylated and resolved as brucine salt according to Dalby et al.⁶⁾ When brucine salt was crystallized from ethanol, yellow crystals were separated first and then colony of white crystals grew up. After each crystals were separated roughly by mechanical way and recrystallized from ethanol, yellow crystals were obtained as anhydrous form (rod or plate, mp 206-207 °C, $[\alpha]^{25}_D$ -4.3°(c 3, CH₃OCH₂CH₂OH). Found: C, 65.83; H, 6.26; N, 6.23%. Calcd for C₁₄H₁₅NO₅·C₂₃H₂₆N₂O₄: C, 66.16; H, 6.15; N, 6.26%. Lit.⁵⁾ monohydrate; mp 203-204 °C, $[\alpha]^{20}_D$ -1.3°(c 3, CH₃OCH₂CH₂OH)) and white crystals as monohydrate (needle, mp 138-140 °C, $[\alpha]^{25}_D$ -25.8°(c 3, CH₃OCH₂CH₂OH). Found: C, 64.85; H, 6.62; N, 5.88%. Calcd for C₁₄H₁₅NO₅·C₂₃H₂₆N₂O₄·H₂O: C, 64.43; H, 6.28; N, 6.09%). After removal of brucine and phthaloyl group, both amino acids showed following optical rotations.

Results of the Resolution of threo-DL-HyLeu





As a similar compound, threo-DL- β -hydroxynorvaline⁷⁾ was phthaloylated and

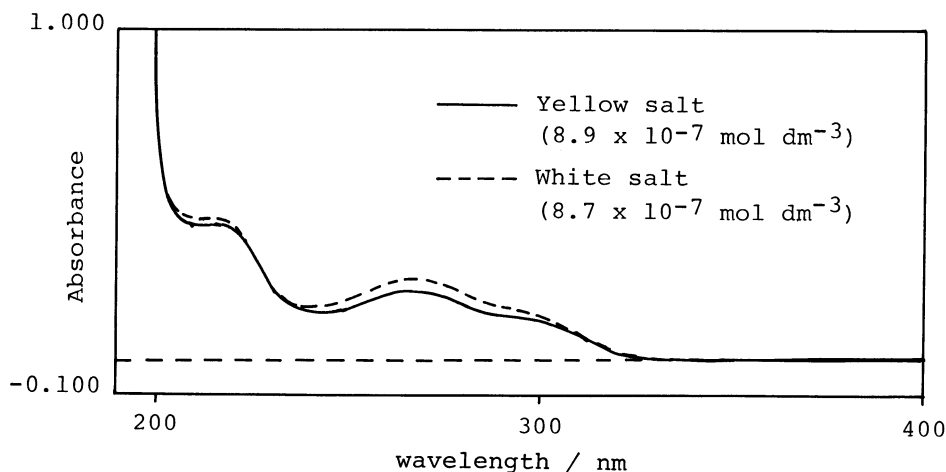


Fig. 1. Absorption spectra of yellow and white brucine salt of phthaloyl threo- β -hydroxyleucine in ethanol at room temperature.

brucine salt was tried to form. In this case too, yellow crystals separated first and almost colorless crystals were obtained from the mother liquor.

The absorption spectra of the ethanol solution of both yellow and white brucine salt of phthaloyl threo- β -hydroxyleucine are very similar as shown in Fig. 1.

The reason why only the crystal of brucine salt of phthaloyl-L-form has yellow color is considered to be interpreted by preferential stacking of aromatic ring of phthaloyl group and of brucine molecule.

Concerning to this phenomena, further studies are now in progress.

References

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